# Key Documents of the Biomedical Aspects of Deep-Sea Diving

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Volume II

# DIVING GASES (OTHER THAN HYDROGEN)

Articles selected by R. W. Hamilton, Jr., Ph.D
Hamilton Research, Ltd.
Tarrytown, New York 10591

# 5

# DIVING GASES (Other Than Hydrogen)

R. W. HAMILTON, JR.

The fundamental diving gas is air, and since its history is essentially that of diving itself, it is not necessary to develop it separately.

The leading alternative diving gas is helium. The basic paper espousing this gas is by Sayers, Yant, and Hildebrand (1925), although they refer to earlier mention of its potential. The initial reasoning was the (predicted) benefit in decompression due to helium's lower solubility and higher diffusivity. It was soon discovered, however, that nitrogen was the cause of narcosis experienced with deep air diving (Behnke, Thomson, and Motley, 1935), and that helium was easier to breathe and did not cause narcosis (Behnke and Yarbrough, 1938), a fact quantified by Shilling and Willgrube (1937). Helium's usefulness in diving was forecast by Nohl's 420 ft dive in 1938 (End, 1938) and strinkigly confirmed in the salvage of the *Squalus* (Behnke and Willmon, 1939). The development of decompression tables for helium by the EDU was reported by Momsen in 1942 (in a revision of his original 1939 report (Momsen and Wheland, 1939).

With helium's benefits came problems with speech, cold, and HPNS. A representative approach to helium speech was presented by Gerstman et al. (1966).

The thermal section mentions heat loss due to helium in thermally comfortable environments. The striking thermal drain of breathing cold helium (actually, any gas will do it) was demonstrated by Goodman et al. (1971). HPNS and the use of trimix to counteract it is covered in the sections on Inert Gas Narcosis and Diving Medicine: the High Pressure Neurologic Syndrome.

Other "helium group" gases considered for diving are neon and argon. Neon had been considered as a diving gas for years. There has been a few experiments, but the group led by Hamilton (Schreiner et al., 1972) had access to enough unrefined mixture of neon and helium (75/25) to fully demonstrate its effectiveness in lab and sea; its high cost has limited its use since then. Argon is too narcotic, dense, and soluble to be seriously considered for a primary diving gas, but its use in welding has caused its properties to be of interest. Its narcotic properties were first described by (guess who!) Behnke and Yarbrough (1939).

Another application of these and other gases is in gas-sequencing to improve decompression (Keller and Buhlmann, 1965), and possible by a multigas "cocktail" (Webster, 1955). Methane, $CF_4$, and other gases have been tried experimentally but are not used in diving as yet; hydrogen is, and it is covered in another section.

Use of different gases may lead to counterdiffusion problems; the steady state aspect of this phenomenon was first noted at the EDU by Blenkarn et al. (1971) and was explained by Graves and coworkers (1973). Counterdiffusion sickness due to gas switching was demonstrated in humans by Harvey and colleagues (D'Aoust et al., 1977).

One other "gas" worth mentioning is the non-air mixture of nitrogen and oxygen. The use of mixtures richer in oxygen than air was developed by the U.S. Navy, but I have not been able to find an appropriate seminal paper on this subject; the idea most likely originiated with Behnke. The "NOAA OPS" concept involving air excursions from a nitrogen-oxygen habitat atmosphere is covered in the section on saturation diving.

# DIVING GASES
## (Other Than Hydrogen)

R. W. HAMILTON, JR.

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

Behnke A. R., Willmon T. L.: USS Squalus. Medical aspects of the rescue and salvage operations, and the use of oxygen in deep-sea diving. *US Nav Med Bull* 1939; 37:629–640.

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Goodman M. W., Smith N. E., Colston J. W., Rich E. L.: *Hyperbaric respiratory heat loss study*. Final report to the Office of Naval Research under Contract N00014-71-C-0099. Annapolis, MD, Westinghouse Ocean Res Eng Center, 1971.

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The following articles are referenced in this section but appear in the section indicated in parentheses:

Behnke A. R., Thomson R. M., Motley, E. P.: The psychologic effects from breathing air at 4 atmospheres pressure. *Am J Physiol* 1935; 112:554–558. (Inert Gas Narcosis)

Behnke A. R., Yarbrough O. D.: Physiologic studies of helium. *US Nav Med Bull* 1938; 36:542–558 (Inhert Gas Narcosis)

Behnke A. R., Yarbrough O. D.: Respiratory resistance, oil-water solubility, and mental effects of argon, compared with helium and nitrogen. *Am J Physiol* 1939; 126:409–415. (Inert Gas Narcosis)

End E: The use of new equipment and helium gas in a world record dive. *J Ind Hyg Toxicol* 1938; 20:511–520. (Inert Gas Narcosis)

Keller H., Bühlmann A. A.: Deep diving and short decompression by breathing mixed gases. *J Appl Physiol* 1965; 20:1267–1270. (Decompression Theory)

Shilling C. W., Willgrube W. W.: Quantitative study of mental and neuromuscular reactions as influenced by increased air pressure. *US Nav Med Bull* 1937; 35:373–380. (Inert Gas Narcosis)

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## U. S. S. SQUALUS

### MEDICAL ASPECTS OF THE RESCUE AND SALVAGE OPERATIONS AND THE USE OF OXYGEN IN DEEP-SEA DIVING

By Lieutenant A. R. Behnke, Medical Corps, United States Navy, and Lieutenant T. L. Willmon, Medical Corps, United States Navy

### PART I—RESCUE OF THE SQUALUS SURVIVORS

On the morning of May 23, 1939, preliminary preparations were already under way at the experimental diving unit, Navy Yard, Washington, D. C., to conduct diving tests in the vicinity of Portsmouth, N. H., beginning about June 7.

For a period of 20 months the personnel of the diving unit under the supervision of Lieutenant Commander Momsen had been conducting laboratory experiments and tests in the pressure tank to ascertain the value of helium-oxygen mixtures in deep-sea diving.

At about 11:30 a. m., a critical experiment in a series designed to determine the level of maximum nitrogen elimination from the body during oxygen breathing was interrupted by the announcement "The *Squalus* is down off Portsmouth; stand by to leave within 2 hours."

Shortly after 2 p. m. the personnel of the unit, supplied with diving apparatus and tanks of helium left by airplane from Anacostia field for Portsmouth. Arriving at Portsmouth in the early evening, preparations were made during a cold, drizzly rain to rescue survivors of the disaster.

By means of temporary telephone communication, and then by tapping signals it was learned that the *Squalus*, flooded aft of the control room, was lying on a fairly even keel at a depth of 240 feet, 16 miles east of Portsmouth. In the control room and forward, 33 men were alive. The pressure in this part of the boat had built up to 13 pounds per square inch. Aft of the control room in the flooded portion of the ship, the fate of 26 men was unknown.

Diving operations were now contingent upon the arrival of the U. S. S. *Falcon* from New London. In the meantime, a submersible decompression chamber was sent to the scene of the disaster aboard a Coast Guard cutter to provide recompression for possible survivors escaping from the after end of the boat by means of the Momsen "lung."

Aboard the sister submarine *Sculpin*, which first sighted smoke bombs released from the sunken *Squalus*, Rear Admiral Cole and staff officers were making plans for the rescue of survivors.

Early the next morning, May 24, the *Falcon*, carrying the rescue chamber, arrived, and by 9:30 a. m. was moored over the sunken submarine.

Then occurred a series of remarkable operations, characterized by calm and faultless execution. All hands, conscious of the momentous task of rescue, worked in perfect unison.

Sibitzky, the first diver down, landed forward on the submarine, about 8 feet from the torpedo room hatch, where the downhaul cable of the diving bell was to be attached. His dive successful, the rescue chamber was started on its way to the submarine.

In the early afternoon, the first group of survivors was brought to the surface. These men appeared calm and relaxed. There was no evidence of hysteria. All were cold and some were in a condition of mild shock. About one-third of the survivors suffered from headache, undoubtedly the result of increased carbon-dioxide concentration.

The development of bends, although the survivors had been subjected to an excess pressure of 13 pounds for over 30 hours, was extremely remote. The recompression chamber, however, was utilized to supply warmth, and, if necessary, for oxygen therapy. Medical treatment was directed toward maintaining absolute rest, and supplying heat and fluids, consisting of coffee and malted milk, to which liberal amounts of sugar were added.

Particularly effective were the hot towels placed over the upper abdominal and hepatic areas. Within a few hours, the survivors had recovered sufficiently so that they could be safely transported to Portsmouth Naval Hospital.

Shortly after midnight, or about 15 hours after the start of operations, the fourth and last group of survivors was brought to the surface. This last ascent of the diving bell was marred by the jamming of the downhaul cable and for more than 4 hours the survivors were trapped at a depth of 240 feet, unable to surface.

In the meantime, strands of cable leading from the rescue chamber to the *Falcon* began to part. Two divers failed to attach a new cable, and the task now resolved itself into severing the downhaul cable leading from the chamber to the submarine.

In successfully cutting the downhaul cable, Squire, the diver, had to descend to a depth of 220 feet in cold water (39° F.), enveloped by complete darkness. Moreover, breathing air at this depth induces in divers a condition of intoxication so that coordinated activity requires intense effort.

By the time that the downhaul cable was severed, the rescue chamber was suspended by a weakened safety cable. For fear of breaking this controlling wire by hauling with power machinery, officers and men under the direction of Commander McCann and Lieutenant Commander Momsen actually pulled the rescue chamber to the surface.

Rescue operations ended on the morning of May 25, when Badders and Mihalowski, descending in the rescue chamber to the after hatch of the submarine under a pressure of 108 pounds per square inch, reported that the torpedo room was flooded.

Meanwhile all of the survivors had been sent to the hospital and with the exception of three, were in good condition. Hospitalization served not only to prevent complications, particularly the development of pneumonia, but also to keep the survivors in a single group under naval surveillance.

Of conditions in the submarine prior to rescue, Lieutenant Naquin, the commanding officer of the *Squalus*, made the following comments:

> Every effort was made to conserve the energy of the men who spent a great deal of time sleeping. The men were instructed to remain calm as excitement would increase oxygen consumption and carbon dioxide output. The oxygen

supply and available carbon dioxide absorbent were adequate for about 72 hours.[1]

The carbon dioxide concentration probably reached about 3 percent. One tank of oxygen was used in the control room (containing about one-half of the survivors) and another tank in the torpedo room. The intermediate battery compartment was not inhabited since it was feared that chlorine gas might be generated as a result of entrance of sea water into the storage batteries. After a number of hours the odor of chlorine was detected in this compartment, and the men wore "lung" appliances converted into chlorine protectors enroute from the control room to the torpedo room, where escape into the diving bell was effected.

Carbon dioxide absorption was facilitated by spreading absorbent throughout the compartments. A noticeable improvement in respirability followed each fresh addition.

Except for the men engaged in communicating with surface vessels by tapping signals, there was no activity on the part of any of the survivors, who remained in the same positions throughout the period prior to rescue (28 to 40 hours).

With respect to food, the emergency ration of beans was eaten by only a few and in small quantity. The men particularly relished and ate almost exclusively canned pineapple, tomatoes, and peaches, which were available in the commissary storeroom. Fluids were derived entirely from the canned goods, as the fresh water supply in the control and torpedo rooms, although potable, had an unpleasant taste.

The atmosphere in the submarine was dark, cold, and moist. The men suffered acutely from cold, which was only partially relieved by eating.

It is apparent that the survivors while awaiting rescue consumed a minimum amount of oxygen. The remarkable discipline present under trying conditions certainly prevented the early occurrence of oxygen lack and high carbon-dioxide increase.

The atmospheric conditions in the submarine were, however, not conducive to effort. The men existed in a dark atmosphere, saturated with moisture at a temperature between 45° and 55° F. Moreover, they were under a pressure of 13 pounds per square inch. It was impossible to keep warm even with blankets as the body heat was rapidly lost through conduction in the moist atmosphere.

The communicators especially were taxed severely in their efforts to send and to receive messages. In fact, any exertion caused great discomfort.

The maintenance of an adequate oxygen concentration and the limitation of carbon-dioxide content were so well directed by the commanding officer that life in the compartments could have been maintained for at least 72 hours.

## PART II—SALVAGE OPERATIONS

The *Squalus* disaster provided a crucial test for the preparation embodied in a long period of experimentation and training incident to

[1] An allowance roughly of 0.5 cubic foot per hour is made for the carbon-dioxide output and about 0.6 cubic foot per hour for oxygen consumption by men at rest. In this type of submarine the available air space is approximately 450 cubic feet per man. According to the manual of the Bureau of Construction and Repair, the limiting concentration of carbon dioxide is set at 3 percent, and of oxygen at 17 percent. Without adding oxygen or absorbent for carbon dioxide, such limiting concentrations would be reached in from 12 to 15 hours if the men were moderately active or in 24 to 30 hours if the men remained at rest.

submarine rescue and salvage operations. These developments have been engineering and medical in scope.

The engineering accomplishments include the raising of the submarines *S–51* and *S–4*, and the development of the rescue chamber and the submarine escape appliance (the "lung").

Coincident with these advances have been physiologic studies and experiments providing quantitative data as to the effects of pressure and of gases under pressure on personnel. These studies participated in by naval medical officers at the Harvard school of public health and at the experimental diving unit have centered in the introduction of a simple and effective method of utilizing oxygen in the decompression of divers, in the application of oxygen therapy for the treatment of compressed-air illness, and in the employment of helium-oxygen mixtures for work at depths in excess of 150 feet.

It remained, however, to test newly acquired knowledge and recently developed methods of procedure by actual deep-sea diving. A sunken submarine at a depth of 240 feet unfortunately provided the test.

Although 6 weeks of engineering and diving effort was nullified when the bow of the *Squalus* emerged from the water on July 13, nevertheless the diving operations were satisfactory. For without effective diving the involved engineering feat of placing pontoons, and of reeving chains under a submarine could not have been accomplished.

The diving record is further unique in that from May 24 to August 1, 372 dives were made without the occurrence of a single case of bends. Several accidents in which divers losing consciousness on the bottom and blown to the surface, were treated effectively by compression and oxygen therapy.

In contrast with previous diving methods, the distinguishing features of the diving technic were the successful employment of helium-oxygen mixtures for deep diving in cold water, made necessary by the failure of the standard method using air, and the effective use of oxygen permitting the decompression of divers without injury.

Of the engineering innovations relative to diving, several were especially important, namely, the fabrication of fireproof, electrically heated garments for cold-water diving, improved recirculation of gas through the diver's helmet, and the perfection of telephone communication.

DIVING ON AIR.—Since helium diving was still in the experimental stage at the beginning of salvage work, it was deemed advisable to follow the accepted method of air diving.

In previous salvage operations on the *S–51* at a depth of 132 feet and on the *S–4* at a depth of 104 feet, air diving was effective although the incidence of bends was high.

Diving in semidarkness, however, to a depth of 240 feet for the purpose of tunneling under the submarine and attaching hoses proved to be too dangerous when the divers breathed air. Two factors, the accumulation of carbon dioxide, and nitrogen narcosis impaired neuromuscular coordination to the extent that simple tasks could be carried out only with great difficulty.

The responses of the divers were marred by lapses in memory and loss of consciousness. On one occasion, the diver losing control of his air supply was blown to the surface. It was not only dangerous but futile for divers with impaired faculties to work at a depth of 240 feet in a maze of hoses and cables. The confusion of the divers is apparent from the following statements made by them:

I found the after torpedo room hatch, then went to the starboard rail and forward about 15 feet. At this time thinking became difficult. I started to tie the descending line to the rail and suddenly realized that I was just waving my arms and not accomplishing anything. Managed to steady down and tied what I believed to be two half hitches. I had a moment of blankness; when I observed the knots again, was surprised to see that I had made several turns with the line and had tied clove hitches and then half hitches. Heard order to come up. Went up on descending line outside of rail and waited to be pulled up. Was told I was fouled and to get back on submarine. Got back and faintly remember starting up again and being pulled up.

(Diver lost cable due to incoordination and asked that it be sent down to him again.) I waited for the cable to be sent down again; this time I cut it loose and made sure it was clear of the descending line, walked aft along the rail to the hatch, and put the shackle down against the pin. After feeling for the pin for some time, lying pretty close to the deck (because of poor visibility) with my air cut a little low, I saw slight moisture on my face plate (early carbon dioxide indication) and hadn't discovered the location of the pin.

I got on my feet, opened the exhaust another turn, opened my air, cleared the face plate. I looked over the shackle and saw the pin in the shackle, where I had been told it would be.

After discovering the pin, I laughed out with joy, and mumbled a few words intended for myself, but loud enough for the topside to hear. I could tell the way the topside was asking, "Was I all right," that they were worried about me. Told topside that I was O. K. and now knew what I was doing."

I made a normal descent, but as I started to get aboard the submarine I had a turn around my leg with the descending line. Had to struggle a bit to get it clear. Got on the submarine, called topside and reported. Did not hear any answer. I am not sure but I think that I asked them if they heard me, to give me the telephone signal on my life line. I must have lost consciousness for the next thing I remember is that I was jerked up off the submarine. I must have had control of myself on the way up, for when I regained consciousness I had the control valve in my hand.

As to the nature of nitrogen narcosis it may be stated that beginning at about 4 atmospheres' pressure (100 feet) and increasing progressively, nitrogen acts as a depressant to produce symptoms comparable

to those manifested in alcoholic intoxication or to those associated with the excitement stage of anesthesia.[2 3 4 5]

While we were aware of the symptoms of nitrogen narcosis at a depth of 240 feet, we were surprised at their intensity. For the application of pressure in a chamber equivalent to a depth of 240 feet elicits reactions of considerably lessened severity.

Additional diving tests indicated that the difference in reactions between chamber and deep-sea diving could be attributed to the increase in carbon dioxide concentration in the diver's helmet.

The symptoms, however, were not typical of high carbon dioxide tension in the lungs but rather of air at a depth of 300 feet or more. Increased depth of respiration, for example, did not precede loss of consciousness.

Apparently the increase in carbon dioxide augmented the narcotic action of nitrogen.

As a possible explanation of this phenomenon we refer to the dilatation of cerebral vessels when the carbon dioxide tension is increased in the lungs.[6] Presumably as a result of increased vascularity more nitrogen will diffuse into brain tissue per unit of time.

It is likewise true that the toxic effects of oxygen at high pressures are intensified by raising the carbon dioxide tension in the lungs.[7] Conversely, lowering the carbon dioxide tension by hyperventilation decreases the untoward symptoms.

HELIUM-OXYGEN DIVING.—The substitution of helium for nitrogen in the air minimizes the narcotic symptoms associated with air breathing under pressure.[3 4 5] To divers accustomed to breathing air under pressure, the use of helium afforded considerable relief. The following statement from a diver was typical:

> This dive (on helium) was the best dive I have ever experienced. I did not feel deeper than 50 feet at any time; my head was clear and my mental faculties were working well at all times.

It may be of interest to record that the helium supplied to the *Falcon* was shipped from Lakehurst in cylinders containing about 1.5 cubic feet under a pressure of 2,000 pounds. At the Portsmouth Navy Yard, helium and oxygen cylinders were "split" and the gases mixed

[1] Behnke, A. R., Thomson, R. M., and Motley, E. P., Psychologic effects from breathing air at 4 atmospheres' pressure, Am. J. Physiol. **112**: 554–558, July 1935.

[2] Behnke, A. R., and Yarbrough, O. D., Physiologic studies of helium, U. S. Nav. M. Bull. **36**: 542–558, Oct. 1938.

[3] Behnke, A. R. and Yarbrough, O. D., Respiratory resistance, oil-water solubility, and mental effects of argon, compared with helium and nitrogen. Amer. Journ. Physiol. **126**, June 1939.

[4] End, E., Rapid decompression following inhalation of helium-oxygen mixtures under pressure. Am. J. Physiol. **120**: 712–718, Dec. 1937.

[5] Behnke, A. R., Forbes, H. S., and Motley, E. P., Circulatory and visual effects of oxygen at 3 atmospheres' pressure, Am. J. Physiol. **114**: 436–442, Jan. 1936.

[6] Shaw, L. A., Behnke, A. R., and Messer, A. C., Role of carbon dioxide in producing symptoms of oxygen poisoning, Am. J. Physiol. **108**: 652–661, June 1934.

to give cylinders containing about 75 percent helium and 25 percent oxygen. Analysis of the gas composition was performed in a laboratory set up near the dock.

After allowing several days for complete mixing, the cylinders were transported to the *Falcon* and set up in a manifold from which a hose led to the diver's helmet.

In the diving helmet the gas was recirculated through carbon dioxide absorbent by means of an aspirator. The aspirator or circulator is an ingenious mechanism working on the same principle as a water suction pump and consisting of a tiny jet facing into a venturi tube. The flow of a small volume of gas through the jet at an excess pressure of 150 pounds aspirates gas from the helmet into the container filled with carbon dioxide absorbent. The recirculating system has a high efficiency, as only about one-fifth of the gas supply is necessary compared with the open circuit.

Without an efficient method of recirculation the use of helium is not practical. On one occasion before adjustments were made in the helium supply to the helmet, a diver developed asphyxial symptoms at a depth of 240 feet and was blown to the surface. Under such conditions gas emboli rapidly form in the blood stream and accumulate in the pulmonary bed to produce a severe asphyxia known among divers and caisson workers as the chokes. Recovery followed oxygen administration in the pressure chamber. [8]

DECOMPRESSION OF DIVERS.—The problem inherent in bringing divers to the surface is to provide for the elimination of excess gas dissolved in the body tissues without bubble formation.

The history of diving, however, is marred by faulty methods of decompression giving rise to gas embolism and the resulting symptoms of pain, asphyxia, and paralysis.

If we could keep a diver under pressure and at the same time effect the removal of gas from his tissues, and if, in addition, the major part of decompression could be carried out in a pressure chamber on the surface, then our problem would be solved.

These objectives were accomplished in the decompression of divers aboard the *Falcon* by the administration of oxygen in a recompression chamber at the 50-foot level following comparatively rapid ascent to the surface.

Essentially the substitution of oxygen for air or the helium-oxygen mixture in the lungs allows excess nitrogen or helium gas to diffuse from the body at a maximum pressure head; and the maintenance of pressure at two and one-half atmospheres (50-foot level) prevents bubble formation.

[8] Yarbrough, O. D., and Behnke, A. R., Treatment of compressed air illness utilizing oxygen, Journal Hyg. and Toxicology 21: 213–218, June 1939

A diver, for example, following a 20-minute working period at a depth of 240 feet, surfaced in 15 minutes, stopping only at the 80, 60, and 50-foot levels. He was then taken to the recompression chamber and given oxygen to breathe for a period of 45 minutes following which it was safe to effect his return to normal atmospheric pressure.

Bringing a diver rapidly to the surface for subsequent recompression, or surface decompression as the practice is usually designated, was forced upon diving personnel in the salvage of the *S–51* in 1925 because cold water and tides rendered decompression in the open sea impracticable. The procedure 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 the method lies in the formation of extensive gas embolism during the interval between surfacing the diver and his subsequent recompression.

During the 15-minute period in the water, however, the high-pressure head of helium in the blood stream and body fluids is lowered to the point where it is safe to bring the diver to the surface provided recompression is applied within several minutes.

Should bubbles begin to form in the interval period, recompression to the 50-foot level with the diver breathing oxygen brings about a resolution of bubbles and promotes a maximum elimination of gas as previously determined by laboratory measurements.

In sharp contrast to the novel practice of effecting decompression by breathing oxygen at a single, optimum level, is the procedure followed in previous salvage operations (*S–51*, *S–4*) of breathing air in carefully graded stages during the diver's stay in the pressure chamber. The assumption underlying this method is that the body tissues can hold gas in supersaturation for an extended period of time to permit the pressure to be lowered in stages. Diffusion of excess dissolved gas from the body under these conditions is precarious because of the imminent probability of bubble formation as a result of the higher pressure head of gas in the body compared with the lungs.

The problem of administering oxygen economically in the recompression chamber has been solved by adopting the mask developed by Boothby and his coworkers. The divers were able to wear this appliance without discomfort, and the fractional rebreathing of oxygen prevented irritating dryness of the throat frequently complained of when oxygen is breathed in an open circuit.

By administering oxygen only to the diver by means of a mask, the fire hazard is minimized. Were it necessary to fill the chamber with oxygen under pressure, the fire hazard would preclude oxygen therapy from further consideration.

THE ELECTRICALLY HEATED SUIT.—The hazards of decompression are greatly increased by exposure in cold water. Especially subject to

cold are divers breathing and surrounded by a helium atmosphere in which presumably body heat is more rapidly dissipated through conduction than it is in an air atmosphere.

To counteract the harmful effect of cold, predisposing as it does to bends and preventing efficient manipulation of the hands, a manufacturer, carrying out suggestions from the experimental diving unit, fabricated a fireproof, electrically heated garment. The heat supply, controlled from the surface, comes from storage batteries.

Wearing these garments the divers were comfortable not only while working on the bottom but also while standing on the stage during decompression.

VOICE CHANGES.—The peculiar nasal quality imparted to the voice by helium is not improved at deep depths, indicating that the density of the helium-oxygen mixture is not responsible for the sound distortion.

So serious was the impaired audibility of the diver's conversation over the telephone that it became imperative to improve sound equipment. As a result of efforts to improve communication, sound reception from the telephone when the diver was at a depth of 240 feet was rendered as clear as at the surface.

EQUALIZATION OF PRESSURE.—For a period of 6 weeks in which over 200 dives were made, divers did not have any difficulty equalizing pressure on the tympanic membranes. About the middle of July, however, upper respiratory tract infection sealing the auditory tubes prevented as many as six divers from working in a single day. Whether air or helium mixture was breathed apparently made little difference in the ability to equalize pressure.

## PART III.—PHYSIOLOGIC BASIS FOR OXYGEN ADMINISTRATION IN DEEP-SEA DIVING

In view of the increasing scope of oxygen administration, and its proved value in deep-sea diving, it may be well to review briefly some of the physiologic studies of oxygen effects at increased pressures.

In theory oxygen would be an ideal gas for deep-sea diving since bubbles forming in the body after decompression would be quickly absorbed by the tissues.

In practice, however, pure oxygen has been found to be toxic, producing symptoms referable to the lungs and the nervous system. At a pressure of one atmosphere after prolonged exposure pulmonary edema develops in rats, dogs, and rabbits. At a pressure of 4 atmospheres convulsive seizures signalize the most striking phenomenon of oxygen poisoning.[9] [10]

[9] Behnke, A. R., Johnson, F. S., Poppen, J. R., and Motley, E. P., Effect of oxygen on man at pressures from one to four atmospheres, Am. J. Physiol. 110: 565-572, Jan. 1935.

[10] Schilling, C. W., and Adams, B. H., Study of convulsive seizures caused by breathing oxygen at high pressures, U. S. Nav. M. Bull. 31: 112-121, April 1933.

While the exact nature of oxygen poisoning is a matter of conjecture, of great importance is the time elapsing before toxic symptoms appear. On the basis of animal experiments at least 24 hours were required before pulmonary edema developed, and at a pressure of 4 atmospheres about 45 minutes elapsed before convulsions were manifest.

Although the tolerance of various animals to high oxygen pressures had been established, the problem in 1932 called for tolerance tests in man. From these tests conducted by naval medical officers at the Harvard school of public health, it was found that at atmospheric pressure healthy men could breathe oxygen for a period of at least 6 hours without showing symptoms indicative of pulmonary irritation. At higher pressures the effect of oxygen on the nervous system superseded the pulmonary manifestations.

At a pressure of 3 atmospheres, for example, definite and sometimes alarming symptoms occurred during the fourth hour of oxygen inhalation.[6] Preceded by a period of normality and with fairly abrupt onset, a rise in blood pressure, increase in pulse rate, and contraction of visual fields terminating in loss of vision, pointed to the action of oxygen on the nervous system.

Although loss of vision and an epileptic type of seizure pointed to a severe functional disturbance, complete recovery invariably followed these symptoms when air was again breathed.

From these tests developed several facts worthy of emphasis, namely, that the harmful effect of oxygen on the nervous system begins to manifest itself at a pressure of 3 atmospheres, at which level the oxygen in physical solution is sufficient to take care of tissue requirements and hemoglobin is not necessary as an oxygen carrier;[11] that the nervous symptoms, therefore, are concomitant with the building up of the oxygen tension in venous blood; that 1.8 volumes percent of oxygen are dissolved in arterial blood per atmosphere of oxygen; that the acidity of the venous blood is increased by a pH change of 0.03 when pure oxygen is inhaled; and that increasing the carbon dioxide tension in the lungs greatly enhances the toxicity of oxygen.[7]

Successive daily exposures to induce convulsions were then carried out by placing dogs in a chamber and raising the pressure to 5 atmospheres. After 30 exposures residual injury could not be detected.

On the basis of these observations, although the cause of oxygen toxicity was not determined, it appeared justifiable to use high oxygen pressures for the treatment and prevention of compressed-air illness.

Oxygen therapy was then evaluated in compressed-air illness. In a series of tests on dogs rapidly decompressed from a pressure of 65 pounds, multiple emboli formed throughout the vascular system,

[11] Behnke, A. R., and others, Studies on effects of high oxygen pressure; effect on high oxygen pressure on carbon dioxide and oxygen content, acidity, and carbon dioxide combining power of blood, Am. J. Physiol. 107: 13-28, Jan. 1934.

blocking blood flow, and unless treatment supervened, produced death by asphyxiation, due to nitrogen bubbles obstructing blood flow through the pulmonary capillaries.

The administration of oxygen in a chamber at a pressure of 30 pounds compressed the bubbles and relieved the asphyxia.[12]

Later, at the experimental diving unit, recompression utilizing oxygen was employed to treat injured divers. Out of 50 patients suffering from bends, 49 responded to the initial treatment without recourse to additional pressure therapy.[8]

With respect to the decompression of divers, rational oxygen administration depends upon the determination of the pressure level at which maximum diffusion of nitrogen or helium takes place from the body following exposure to increased pressure.

At the present time experiments in which gas measurements were made in a pressure chamber have progressed sufficiently to indicate that the most favorable level ranges between 50 and 60 feet.

At pressures equivalent to these depths oxygen is well tolerated, at least for a period of time sufficient to eliminate excess nitrogen or helium regardless of previous depth or exposure.

Taking these facts into consideration, it has been possible in the decompression of divers to bring them rapidly to the 50-foot level where they remain breathing oxygen until the excess gas pressure in the body has decreased, as shown by experimental graphs, to the point where immediate surfacing is safe. Thus, the complicated and precarious practice of decompression has evolved into a simple and effective procedure.

# Urticaria Following the Sequential Breathing of Various Inert Gases at a Constant Ambient Pressure of 7 ATA: A Possible Manifestation of Gas-induced Osmosis

C. Douglas Blenkarn, Charles Aquadro, Brian A. Hills and Herbert A. Saltzman

*F. G. Hall Environmental Laboratory, Duke University Medical Center, Durham, North Carolina 27706*

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# Urticaria Following the Sequential Breathing of Various Inert Gases at a Constant Ambient Pressure of 7 ATA: A Possible Manifestation of Gas-induced Osmosis

G. Douglas Blenkarn, Charles Aquadro, Brian A. Hills and Herbert A. Saltzman

*F. G. Hall Environmental Laboratory, Duke University Medical Center, Durham, North Carolina 27706*

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**An erythematous maculopapular eruption was observed over the skin of each of three subjects soon after switching their breathing mixture from normoxic helium to normoxic nitrogen at the same simulated depth of 200 feet. The lesions and other symptoms occurred before the subjects had experienced any decompression; although they appeared very similar to the cutaneous reactions frequently termed "skin bends." They were not observed upon skin within the head-tent and hence over those areas exposed to the breathing mixture at all times. The urticaria has therefore been attributed to some cause arising from the concentration gradient maintained between cutaneous blood and chamber atmosphere in the affected areas rather than considered a manifestation of decompression sickness. Gas-induced osmosis is discussed as a possible initiating mechanism and is shown to be quantitatively consistent with the clinical observations.**

IN MARCH, 1970, during a "saturation" dive at a simulated depth of 200 feet in a gaseous environment of helium and oxygen, all three experimental subjects developed urticaria during or shortly after breathing a normoxic nitrogen gas mixture. To experienced observers these cutaneous symptoms and signs were similar to those frequently observed following decompresion, and therefore considered a manifestation of decompression sickness.[9] However, no decompression preceded the above observations, suggesting an association of the urticaria with some inherent difference in the inert gases such as a physical property whose effect upon the tissue is enhanced under hyperbaric conditions. This communication describes the events and discusses hypothetical mechanisms that may explain these observations.

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## PROCEDURE AND RESULTS

The intent of this exercise was to study gas exchange, the EEG, evoked cortical responses and reaction times —after a steady respiratory state had been attained with each of three background inert gases at the surface and at simulated depths of 100 and 200 feet.[12] Studies at the surface (March 19) and at 100 feet (March 23), prior to complete "saturation" with helium, were uneventful.

Following an overnight equilibration at 200 feet with the atmosphere in the chamber ($O_2 = 0.3$ Atm, with balance of helium containing less than 2 per cent nitrogen, March 24), the three experimental subjects breathed sequentially, via a mouthpiece and through a low resistance nonrebreathing circuit, normoxic gas mixtures ($P_{IO_2} = 0.21$ Atm) in which the background gas was nitrogen, helium or neon. Each breathing gas mixture was also circulated through a semi-closed head tent circuit (HT), thereby eliminating any error that might result from breathing other than through the mouthpiece of the nonrebreathing valve (Figure 1). The order in which each gas was breathed by each of the three subjects at 200 feet (7 ATA) and spirometer temperatures recorded are outlined in Table I. The subjects were all recumbent and each study lasted approximately three hours. The details of each nitrogen exposure are given in Table II.

The first subject (F) initially breathed a normoxic gas mixture of 0.21 ATA $O_2$ in nitrogen. Within 5 to 10 minutes he noted the onset of a slowly progressive, pruritic ("prickly") sensation along the upper extremities. This sensation continued over the next two hours during the subsequent episodes of helium and neon breathing, but stopped shortly after the experiment. At this time a mild erythematous, maculopapular eruption was observed on the proximal anterior and posterior aspects of both forearms. This eruption disappeared completely during the next 60 minutes. Subject F also complained of a moderately severe centrally located headache which began midway through the

three-hour study and disappeared shortly after taking 1.2 gm acetylsalicylic acid at the end of the experiment. The subject attributed the headache to a tight nose-clip.

The second subject (T) breathed sequentially normoxic gas mixtures in which the inert gas was first neon, then helium, and finally nitrogen. Approximately 15 minutes after terminating the exposure to the normoxic nitrogen gas mixture, and while breathing the chamber gas (oxygen plus helium), he became aware of pruritus of both lower extremities. Soon thereafter an intensely pruritic erythematous maculopapular eruption involving the skin of the upper extremities, both the anterior and posterior thorax and abdominal wall was observed (Figure 2a). No cutaneous manifestations were observed on the lower extremities. Three areas of purplish-blue discoloration with some surrounding skin blanching or mottling were observed on the right arm and the anterior-superior aspect of the right axilla. Later a few scattered petechiae over the upper torso were also observed. The lesions of Subject T were felt to resemble those of "skin bends" by experienced observers both within and without the chamber. As an interim and conservative form of therapy and prophylaxis pending a more definitive diagnosis, Subject T was required to breathe intermittently through a mask a helium gas mixture containing 1.5 ATA of oxygen. During the time he breathed this gas

TABLE I. ORDER OF INERT GASES BREATHED DURING EXPERIMENT* AT 200 FEET (7 ATA) AND SPIROMETER TEMPERATURES RECORDED (°C)**

| | |
|---|---|
| Subject F | Nitrogen (31.8), Helium (31.0), Neon (34.2) |
| Subject T | Neon (29.1), Helium (32.0), Nitrogen (29.6) |
| Subject W | Nitrogen (27.9), Helium (27.1), Neon (30.5) |

*Each gas mixture includes 0.21 Ata oxygen.

**Spirometer temperature fluctuations probably do not fully reflect chamber temperature fluctuations due to a buffering effect of the spirometer water.

TABLE II. NITROGEN EXPOSURE TIMES AT 200 FEET OF SEA WATER (7 ATA)

| Subject | Introduction of $N_2$ | Cardiorespiratory Measurements | EEG Study | Total Time |
|---|---|---|---|---|
| Gas Mixtures | .21 Ata $O_2$ in $He + N_2$* | .21 Ata $O_2$ in $N_2$** | .25 Ata $O_2$ in $N_2$*** | |
| F | 8:47 - 8:57<br>10 min. | 8:57 - 9:31<br>34 min. | 9:31 - 9:44<br>13 min. | 57 min. |
| T | 14:53 - 15:03<br>10 min. | 15:03 - 15:35<br>32 min. | 15:35 - 15:46<br>11 min. | 53 min. |
| W | 16:21 - 16:30.5<br>9.5 min | 16:30.5 - 17:05<br>34.5 min. | 17:05 - 17:15<br>10 min. | 54 min. |

*approx. 50-50 He-$N_2$ mix via mouthpiece with .21 Ata $O_2/N_2$ in HT (For gradual introduction of Nitrogen-oxygen breathing to minimize narcotic effect).

**via mouthpiece with .21 Ata $O_2/N_2$ in HT.

***via HT, mouthpiece out (.25 Ata $O_2$ with $N_2$ in HT to prevent undesirable reduction in $P_{IO_2}$ due to oxygen consumption from circuit).

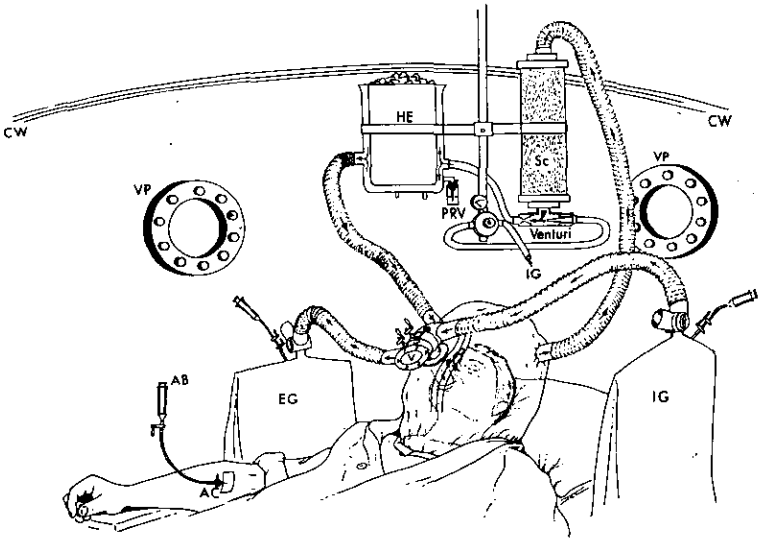


Fig. 1. The resting subject within the chamber walls (C.W.) breathed spontaneously through a directional breathing valve (V) from a Douglas bag containing inspired gas (IG). Exhaled gas was collected in another Douglas bag (EG). At the same time arterial blood (AB) was collected from an indwelling cannula (AC). The same inspired gas (IG) also circulates around the breathing valve and face, within a plastic head tent, affixed to the upper thorax with plastic sealing tape. The flow and physical characteristics of the gas circulating about the face reflect: the addition of small amounts of gas (5-10 L/min) at increased pressure through the Venturi jet, the entrainment of large volumes of gas (40-60 L/min) through a scrubber (SC) containing a chemical absorbent for removing $CO_2$ (necessary when the head tent is the primary source of the breathing gas), into a heat exchanger filled with ice, and finally completing a semiclosed circuit by returning to the head tent. A pressure relief valve (PRV) vents gas from within the hood if the pressure exceeds one cm $H_2O$ above that in the ambient environment. In the event of leaks within this system outgassing will occur and the circulating medium within the head tent conforms reliably to that introduced through the Venturi jet.

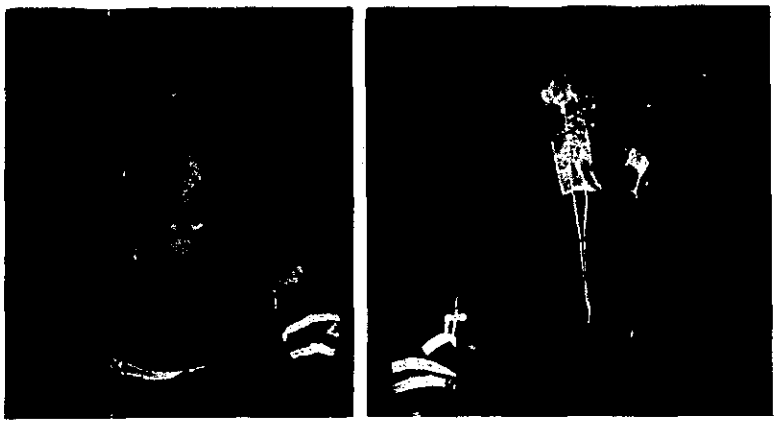

Fig. 2. Urticarial response in Subject T (a) and Subject W (b) following inhalation of 0.2 ATA $O_2$ and 6.79 ATA $N_2$ in a helium environment. The head and neck, which were enclosed in the head tent, were free of cutaneous lesions.

he noticed some decrease in severity of the pruritus, no further progression of the urticarial skin lesions and total disappearance of the blue discolored areas. There was no cutaneous emphysema and dermographism could not be ellicited. During the subsequent three hours at the same depth, the lesion showed no further progression and perhaps very slight regression.

The third subject (W) breathed, in sequence, normoxic gas mixtures in which the inert gas was first nitrogen, then helium, and finally neon. Approximately five minutes after commencing to breathe the first special gas mixture (0.21 ATA of oxygen in nitrogen), Subject W recalled that his vision had become blurred for approximately 5-10 minutes. Within a few minutes normal vision returned spontaneously, but he then noticed pruritus of his back, buttocks, and legs. At this time, and coincident with the discovery of the pronounced skin lesions of Subject T, an erythematous maculopapular, urticarial type eruption was observed on the anterior and posterior aspect of the proximal portion of the right forearm and superior to the site of the indwelling radial artery cannula. The forearm was not pruritic, perhaps due to the presence of small amounts of lidocaine hydrochloride (Xylocaine) in the solution used to flush the arterial cannula.* The pruritus of the other areas was mild and subsided in two hours at which time the experiment was completed. Not until then was it observed that this subject also had an urticarial type eruption located over much of his anterior and posterior torso, but which was less severe than Subject T (Figure 2b). No distinguishable lesions were observed on the skin of the head and neck, i.e. those areas enclosed in the head tent, of any of the three experimental subjects.

Shortly after completing the studies on the third subject (W), all three subjects were treated by mask-breathing a helium-oxygen mixture containing 1.5 ATA of oxygen over a 15-minute period. This served as an interim treatment or prophylaxis for all of the subjects while further diagnosis and disposition was being established. Subsequently a slow and gradual decrease in the size and coloration of the discernible eruptions was observed in Subjects T and W. Although by this time Subject F had no complaints or visible eruptions, he was treated along with Subjects T and W. He felt that his symptoms and objective manifestations had been similar to those observed in the past by him when he had been exposed to rapid decompression in an altitude chamber.

After review of these manifestations in conference with additional biomedical authorities, it was agreed that these unexpected urticarial type eruptions were in all probability a result of the sequential exposure to different gases at the same ambient pressure and that they might be analogous to the phenomenon often called "skin bends." Since the urticaria might have been a manifestation of decompression sickness, the subjects were exposed to a greater simulated depth of 250 feet to evaluate the response. This was undertaken at 22:30 (10:30 p.m., March 24). Lesions continued to show minimal improvement during this maneuver. The operational decision was made to remain overnight at the 250 foot depth on the helium:oxygen mixture only in the a.m. At a simulated depth of 250 feet in the a.m. of March 25 studies were performed uneventfully in all three subjects, while they breathed only a gaseous mixture of oxygen (0.21 Ata) and helium. No further cutaneous eruptions occurred. The rash was still noticeable on subjects T and W when decompression was started on Wednesday, March 25 and continued to regress over the next several days. By this time, Subject T had approximately 15 petechiae scattered over the upper trunk, but his skin was otherwise clear.

It was elected not to expose the subjects further to special gas mixtures under these conditions, because of the unknown risks to health associated with an unanticipated phenomenon whose mechanism was not clearly understood.

*A normal saline solution used to flush and maintain patency of arterial cannulae contained lidocaine hydrochloride (Xylocaine) .008 gms% and Heparin .004 gms%. Less than 40 ml was administered to each subject during each three-hour experimental period. The plastic arterial cannula 17 ga., .0391 I.D., 2¾ in. (Bard-Stille Select-A-Flow Cannula) was inserted in the radial or brachial artery.

## DISCUSSION

The occurrence of pruritus and cutaneous eruptions related to pronounced pressure changes is well known among divers and diving physicians.[9] These manifestations may occur during or immediately following decompression and the early manifestations can be reversed or ameliorated by prompt recompression or oxygen therapy. The cutaneous manifestations of decompression sickness ("skin bends") reported to date can be classified into three categories:

1. Those conditions manifest primarily as multifocal and transient pruritus without observable skin changes. These usually occur during decompression from deep simulated "bounce" dives as opposed to long or shallow exposures or to those followed by gradual decompression.[1]

2. A more serious cutaneous manifestation which may be characterized initially by an intense itching, localized more frequently about the shoulder girdle, arms, thorax, and abdomen, followed by the development of a maculopapular eruption with erythema, cyanosis and mottling. These cutaneous changes may precede or be associated with other simultaneous manifestations of decompression sickness. No crepitus or cutaneous emphysema is observed and the distribution seems to be unrelated to the peripheral nerves. Prompt recompression may often be rapidly effective in reversing these cutaneous manifestations, otherwise regression may extend over two to three days if untreated.[9]

3. Skin lesions which are not urticarial but have consisted of extensive marbling and cutaneous emphysema.[6] These have occurred in cases of severe and often fatal decompression sickness in association with extensive systemic involvement.

One can consider several pathophysiological mechanisms for the appearance of the "skin bends" phenomenon. Rashbass,[11] in studies on the etiology of itching on decompression, could induce pruritus in most subjects upon rapid decompression from simulated dives of 18 minutes at 240 feet. Since pruritus could be prevented in those areas of skin immersed in water at body temperature prior to decompression, he concluded that such immersion had blocked the percutaneous uptake of inert gas. Thus he reasoned that gas "which had diffused inwards from the outside" could augment total skin gas and so facilitate the formation of bubbles in this tissue and produce itching upon decompression. Kidd and Elliott[9] feel that the phenomenon which Rashbass studied is of no prognostic value since it is self-resolving. Skin lesions do not develop subsequently and no treatment or change in decompression is warranted.

It has been postulated that the more severe cutaneous involvement (2nd category) is due to bubble formation with associated capillary hemorrhage and direct stimulation of sensory nerve endings.[10] Hesser[3] has suggested that low temperature during decompression results in reduced cutaneous blood flow and slower inert gas elimination from the skin. This impression was supported by his noting the absence of paresthesia in divers' arms that had been insulated.

It seems reasonable that the subdivision of manifestations into these three groups is somewhat arbitrary and, as in other manifestations of decompression sickness, the severity of its presentation may vary within a wide spectrum.[9]

Pruritus in association with an evanescent erythematous maculopapular eruption, such as urticaria, is common in dermatologic and general practice and may arise from a multitude of causes. The original theory of Sir Thomas Lewis to explain the formation of the urticarial wheal remains popular; i.e. that histamine liberation is the last link in the chain of events which leads to the local leakage of plasma from the minute vessels into the connective tissue of the dermis. Many mediators of histamine release from tissue mast cells have been implicated.[7] In addition to certain drugs and ingestants (allergic urticaria), physical causes have been demonstrated such as cold (essential cold urticaria), sunlight (urticaria solaris), and after minimal trauma (fractitious urticaria).

No report could be found of cutaneous eruptions resulting from breathing the commonly employed inert gas mixtures at any pressure prior to decompression. Factors other than sequential exposure to different inert gases were considered to be unlikely explanations for the urticaria of the subjects in this experiment. A cause of hypersensitivity within the general chamber environment should have afflicted some or all of the six exposed occupants in a random manner but, in fact, involved only the three experimental subjects.

The saline solution used to maintain patency of the arterial cannulae in all three subjects contained very small amounts of local anesthetic and heparin. It seemed unlikely that there was a pharmacologic basis for the cutaneous eruptions on account of continued and uneventful use both before and after the occurrence of the cutaneous eruptions. The possible presence of an allergic factor within the breathing assembly used by the experimental subjects also seemed unlikely since the identical assembly was used by the same subjects one day later at 250 feet (8.5 ATA) without any untoward manifestations while breathing a normoxic helium mixture. Lastly, none of the subjects had histories of any previous urticarial eruptions.

Urticaria occurred following the introduction of nitrogen breathing immediately after breathing helium and while being immersed in a helium environment under "saturation" conditions. This chronology of the eruptions is suggestive of an etiologic factor related to an intrinsic difference between inert gases—as manifest quantitatively by some simple physical parameter.

One of the more obvious differences is the solubility in tissue, nitrogen forming a more concentrated molar solution than helium at the same tension. Thus the total concentration of gas within the cutaneous vascular bed should increase upon switching to nitrogen in the breathing mixture as $N_2$ replaces He. In an aqueous tissue this replacement would be reciprocal such that the total tension of all gases remains constant. However, for a tissue with an appreciable lipid content such

as skin, the blood:tissue partition coefficient is larger for helium than for nitrogen, indicating a fall in He tension more rapid than the simultaneous rise in $N_2$ tension if blood perfusion limits the rate of blood:tissue exchange.[3] On the other hand, if diffusion makes a significant contribution in controlling the gas transfer,[4] the helium diffusion rate exceeds that of nitrogen by a factor greater than the solubility ratio. Thus whatever the relative contributions of each process in limiting blood:tissue gas exchange, the total tension of $N_2$ and He will show a transient fall and therefore cannot exceed the external hydrostatic pressure at any time and so induce cavitation. Hence the skin lesions observed upon switching inert gases cannot be attributed to bubbles.

It would appear particularly significant that distinguishable lesions were not observed over regions of the skin within the head tent and thus exposed to the breathing mixture. Urticaria apparently occurred only where the outer layer of the epidermis was saturated with helium while the cutaneous vascular bed was saturated with nitrogen, i.e., in skin across which a gas concentration differential was being maintained. Recent findings have shown that such steady-state gas concentration differentials can induce osmosis across excised sections of such tissues as bladder and peritoneum.[5] If this also applies to skin, then there would be a flux of water towards the vessels. Any such displacement of cutaneous water is potentially undesirable since it may produce significant cellular distortion and/or rupture which may incite histamine and possibly serotonin release. Thus the focal edema, and microcirculatory alterations observed, may have been created initially by gas-induced osmosis and subsequently augmented by the release of vasoactive substances.

The magnitude of the driving force for water movement can be estimated from the expression for the gas-induced osmotic pressure ($\Delta\Pi$) as:

$$\Delta\Pi = \sigma P(\alpha_n - \alpha_h) \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where $\Delta\Pi$ is expressed in the same units as the partial pressure ($P$) of each of the inert gases, $\alpha_n$ and $\alpha_h$ are the Bunsen coefficients of nitrogen and helium respectively while $\sigma$ is the reflection coefficient* which has been estimated to be of the order of 0.0378 for gases.[5] Taking values for 37°C of $\alpha_n = 0.0141$ and $\alpha_h = 0.0095$ at 200 feet ($P$ = 5150 mm Hg absolute), equation 1 gives:

$$\Delta\Pi = 0.90 \text{ mm Hg}$$

Such a value for the gas-osmotic driving force is appreciable relative to net extravascular pressure gradients.

For nitrogen breathing at 100 feet ($P$ = 2880 mm Hg absolute), equation 1 gives $\Delta\Pi = 0.50$ mm Hg while if the inspired gas were neon ($\alpha_n = 0.0109$) at 200 feet ($P$ = 5150 mm Hg), $\Delta\Pi$ = 0.27 mm Hg. Thus the driving force ($\Delta\Pi$), and hence skin water flux, would have been appreciably smaller for inspiration of the $Ne:O_2$ mixture at 200 feet or the $N_2:O_2$ mixture at 100 feet than for the $N_2:O_2$ mixture at 200 feet which provoked the urticaria.

Thus the data is quantitatively consistent with a mechanism based upon gas-induced osmosis as the force initiating the occurrence of lesions, and is certainly more compatible with this explanation than with any relating the symptoms to decompression sickness.

It should be noted that there was considerable variation of ambient temperatures in the experimental compartment as indicated by spirometer temperature measurement (27.1 - 34.2°C). Subjects and attendants noticed sensations varying from being uncomfortably cool to uncomfortably warm. Nevertheless, there were no significant changes in either oral or rectal temperatures during the experimental exposures. The factors should be considered as another variable which may have affected the degree of cutaneous circulation, the rate of uptake and elimination of inert gases and consequently the rate of change of postulated gas osmotic gradients (Table I).

One important reason for elucidating this phenomenon is the increasing popularity of switching gas mixtures during dives. This practice has been stimulated by the epochal diving experiments of Keller and Buhlmann[2] which indicated that decompression time for excursion diving could be abbreviated by this technique. These investigators have never observed any cutaneous phenomena in many experiments when subjects were changed from helium to nitrogen breathing at various depths while the chamber environment usually remained similar in composition to the inspired gas.

If the cutaneous vascular lesions observed during our experiment are a manifestation of changing inert gas concentrations in tissues, then it is conceivable that cellular disruption and subsequent changes may be occurring in other tissues. However, it is our present opinion that this cutaneous phenomenon was probably not a manifestation of a systemic process but was more likely a reaction caused by local gas concentration differentials within the skin.

The importance of this surprising finding of a cutaneous eruption, at a constant increased ambient pressure and during sequential exposure to different inert breathing gases, is very great if the proposed relationship is confirmed and the pathophysiology more surely defined. Sequential breathing of different inert gases as a means of reducing the risk and duration of decompression may have to be approached more cautiously. There is a definite need for further evaluation and definition of the phenomena observed in this experiment.

*The reflection coefficient is an index of selective permeability. In practice it must be lower for helium than for nitrogen ($\sigma$) on account of its smaller molecular diameter, so that placing both equal to $\sigma$ in equation 1 gives a conservative estimate of $\Delta\Pi$.

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# Venous Gas Bubbles: Production by Transient, Deep Isobaric Counterdiffusion of Helium Against Nitrogen

Abstract. *When awake goats were subjected to isobaric gas switching from saturation (17 hours) on 4.7 atmospheres of nitrogen (0.3 atmosphere of oxygen) to 4.7 atmospheres of helium (0.3 atmosphere of oxygen), bubbles detected by 5-megahertz Doppler ultrasound in the posterior vena cava 20 to 60 minutes after the switch continued for 4 hours. Similar experiments carried out at 6.7 atmospheres of inert gas and 0.3 atmosphere of oxygen produced more bubbles for as long as 12 hours after the gas switch. This is believed to be the first objective demonstration of the phenomenon of deep isobaric supersaturation under transient operational diving conditions at relatively shallow diving depths. Detection of bubbles by Doppler ultrasound confirms the potential importance of the phenomenon to shallow saturation diving and holds promise for better quantification of its effects as well as those of its counterpart, isobaric undersaturation, which can confer a decompression advantage.*

Isobaric supersaturation (*1*, *2*) and the resulting production of cutaneous and deep-tissue bubbles by counterdiffusion at constant pressure of two or more gases with unequal permeation rates has been identified in man (*1*, *2*) and demonstrated in animals (*3–5*) both in vitro and in vivo (*6*); it is generally considered to explain certain abnormalities that can be encountered in relatively deep (greater than 100 m) saturation diving (*6*). Two interrelated forms have been distinguished: (i) "superficial isobaric counterdiffusion" through skin and other tissues in direct contact with the ambient atmosphere, and (ii) "deep isobaric counterdiffusion" between tissue fluids and capillary circulation (*6*). Each is capable of supersaturating tissue, and the superficial form has been shown to produce not only gas lesions in man (*7*), but also continuous gas embolism in animals (*3–5*) under steady-state conditions. However, the probability of risk from the phenomenon in "deep" tissues in shallow-water diving involving transient gas switching rather than steady-state experimental situations is not known (*8*).

*We now report the in vivo production* of bubbles detected with Doppler ultrasound (*9*) in awake goats after a rapid isobaric switch of the inert gas in the chamber from nitrogen to helium at 40.2 m (132 feet) and 60.35 m (198 feet) of seawater (7 atm absolute) (all measures are expressed in terms of meters of seawater). These are the shallowest depths at which this phenomenon has been demonstrated. Further, the fact that it was produced by transient rather than steady-state conditions is of both practical and theoretical importance to the physiology and medicine of diving, particularly in reference to projected submarine rescue procedures requiring successive exposure to different inert gas atmospheres at these pressures.

Use of continuous-wave Doppler ultrasound for detection of vascular bubbles has become an accepted technique in hyperbaric physiology; the system and counter in use in our laboratory are theoretically capable of detecting bubbles 1 $\mu$m in diameter and have been experimentally demonstrated to detect 10-$\mu$m bubbles (*9*).

Eight adult goats weighing between 40 and 70 kg had Doppler ultrasonic transducer cuffs surgically implanted around the posterior vena cava (*9*). Animals were exposed in pairs to one of two *different regimens. The first consisted of* saturation to 40.2 m of seawater in normoxic nitrogen. Compression was at the rate of approximately 4.6 m/min, varied slightly as required to minimize noise-induced anxiety in the animals. The animals were held for 17 hours at 40.2 m at an $O_2$ pressure of 0.3 atm [the remainder was $N_2$ ($CO_2$ less than 0.09 percent)], after which it was assumed that saturation was virtually complete.

Isobaric gas flushing of the $N_2$-$O_2$ environment with He-$O_2$ was accomplished within 5 minutes at a flow rate of approximately 17 m$^3$/min [600 standard cubic feet per minute (SCFM)] for the 40.2-m dives, and 19.8 m$^3$/min (700 SCFM) for the 60.35-m dives. After the gas exchange, the residual chamber $N_2$ percentage varied from 0.3 to 5 percent as a maximum. These kinetics allow mathematical treatment of the gas switch as essentially a step function for all but the fastest tissues.

Ultrasonic Doppler monitoring and recording of bubble signals began 5 minutes before switching gases and continued for the duration of the isobaric phase of the dive and at regular intervals during the subsequent decompression. The earliest bubbles were detected 20 minutes after the first 40.2-m gas switch and continued to be detected in varying numbers for 4 hours. Two more 40.2-m dives were carried out with very few bubbles detected both in the same two animals and in another pair (*10*). The isobaric switch from saturation at 60.35 m produced bubbles in every case, which suggests that a threshold may exist near 40.2 m for isobaric bubble formation. After the switch from the 60.35-m saturation, bubbles were detected as early as 30 minutes, lasted several hours, and were detected for as long as 10 or 11 hours under isobaric conditions. No serious skin lesions were observed in this study; however, it is not possible to exclude such results because of the greater difficulty in perceiving skin discoloration in these animals.

Figure 1 shows a combined plot of Doppler bubble signal counts after an isobaric gas switch at 60.35 m and calculated curves showing the fractional saturation of $N_2$ and He and the total supersaturation ratio ($N_2$ + He) (Fig. 1A) and the total excess inert gas concentration after the isobaric switch for three pairs of $N_2$ + He half-times, corresponding to 13 + 5, 93 + 41, and 139 + 63 minutes, respectively (Fig. 1B) (*11*). The long period over which bubble signals were heard is striking. This immediately identifies bubbles with the so-called "slower" tissues. Although the approximately *unimodal distribution of bubbles with* time (Fig. 1A) may suggest the importance of a particular half-time (*12*), other experiments show either fairly constant rates of bubble production or bimodal

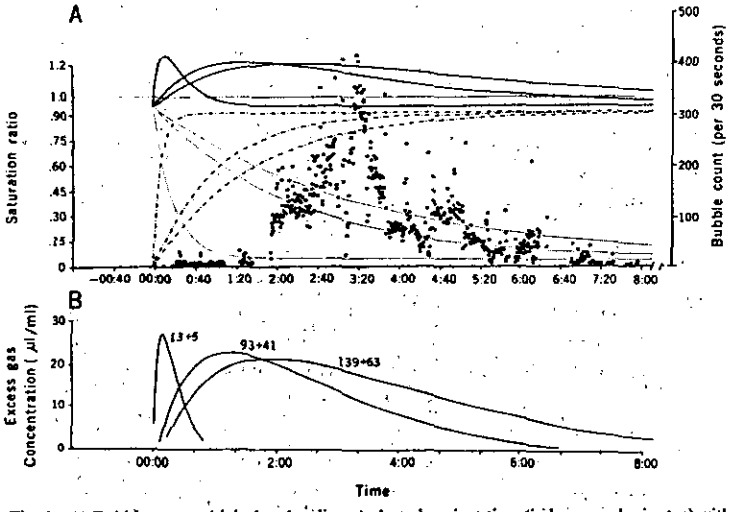


*Fig. 1. (A) Bubble counts (right-hand ordinate) plotted against time (in hours and minutes) with calculated gas saturation and total supersaturation plotted on the same time scale. Only inert gases He and $N_2$ have been included in the computation; thus the initial fractional saturation is less than 1.0 (0.956) at time zero. Values for $N_2$ (·····), He (– · –), and total gas tension (——) are plotted for the 13 + 5, 93 + 41, and 139 + 63 $N_2$ + He pairs of half-times. At every point in time, total gas tension is the sum of the He and $N_2$ fractional saturations. (B) Excess gas concentration [the excess volume of gas (microliters per milliliter at standard temperature and pressure)] dissolved in the tissue as a result of supersaturation. The maximum gas concentration precedes the maximum supersaturation by approximately 30 minutes in the 93 + 41 tissue pair; similar results were seen for the other tissue pairs.*

and trimodal counts with time for approximately the same time period. Speculation as to the precise tissue half-times associated with bubbles, therefore, cannot yet be supported by our results; rather, the time of first appearance and the total duration of bubble signals under isobaric conditions are more reliable criteria with which to establish critical supersaturations and critical tissue half-times. This time ranged between 20 and 60 minutes for the goat, although an identical experiment on a pig showed a much greater latency (*13*).

A second consideration refers to the theoretical curves of supersaturation and gas concentration with time. Because of the different gas fractions composing the supersaturation ratios, the maximum excess gas concentration (calculated from Henry's law and an assumed average tissue composition of 15 percent fat), does not coincide with the time of maximum supersaturation for the slower tissues; the greatest discrepancy of this sort is shown for the tissue pair at 93 + 41 minutes (*12*), for which the calculated maximum excess inert gas concentration occurred 70 minutes after the gas switch, and the highest supersaturation ratio occurred after 90 minutes. Also, the most extreme supersaturation and the greatest excess gas concentration occurs rapidly but briefly in the fastest tissues, whereas the slower tissues exhibit less extreme values for a longer period.

In interpreting Fig. 1, it is essential to understand the arbitrary nature of tissue gas-tension calculations. It is accepted (*14–18*) that He saturates and desaturates the body faster than $N_2$. This result is related to its more rapid aqueous as well as gaseous diffusion (*19*). However, because the multiexponential parallel-compartment model (*16, 20*) has been used in our calculations, we have arbitrarily paired He and $N_2$ half-times that we must then assume refer to the same actual tissue elements. This assumption itself contradicts part of the rationale supporting use of a multiple parallel-compartment model, since the latter overcomes the lack of physiological reality by having a spectrum of half-times known to span a realistic physiological range of rates (*16, 20*). With two gases, however, there is no way to decide which He half-time is best applied to which $N_2$ half-time. On the other hand, the use of a constant ratio of permeation rates for $N_2$ and He for every half-time is obviously an oversimplification because He diffuses faster, is less soluble, and has a lower fat-water partition coefficient than $N_2$ (*18*). We have used the pairing shown in Fig. 1 only because it is consistent, has been used in our operational decompression model (*11, 12*), and demonstrates the kinds of relationships that must be examined in these situations. Green (*7*) and Harvey and Lambertsen (*21*) have presented theoretical treatments concerning expected maximum supersaturation as a function of the $N_2$ + He diffusion ratios and the potential problem in operational diving.

Calculations made from accepted models for He and $N_2$ predict supersaturation in all perfused or "deep" tissues produced by isobaric counterdiffusion, without decompression (Fig. 1). These predictions are confirmed by the presence of gas bubbles detected by Doppler ultrasound. The demonstration of this phenomenon in large animals suggests its importance to human divers at relatively shallow depths. Reversing the direction of the gas switch (that is, from He and $O_2$ to $N_2$ and $O_2$) should provide undersaturation and therefore a decompression advantage (*11, 18*).

An attractive alternative diffusion-dependent model has been described by Tepper (*23*), which can account for higher supersaturation ratios than the summing approach described above and used by Green (*7*) and Harvey and Lambertsen (*21*). Deciding on the most useful model will be facilitated by the judicious use of gases of diverse physical properties in counter studies in vivo, such as those described above, as well as in vitro. The prediction of the diffusion model of Tepper (*23*) more accurately corresponded to the actual depths at which human symptoms have been encountered.

Two of us (C.A.H. and W.L.H.) performed identical gas-switching studies with human volunteers at 3 and 4 atm absolute; we saw no effects at 3 atm absolute, but at 4 atm absolute we observed and photographed the production of urticaria and blotchy subcutaneous skin lesions similar to those reported by Blenkarn *et al.* (*2*) and Lambertsen *et al.* (*1*). These subjects were monitored by ultrasonic Doppler probes placed over the pulmonary artery, but no bubbles were detected. One probable limb bend was observed and successfully treated by pressurizing with He and $O_2$ at an additional atm of pressure. This additional 25 percent increase in pressure, while relieving the limb bend (a "deep" tissue incident) exacerbated the urticaria and subcutaneous lesions. Procedures therefore should take into account the sum of the inert gas tensions as well as the total excess gas present; as stressed by Buhlman (*18*), decompressions can be either helped by appropriate or hindered by inappropriate inert gas sequencing. More important, we now have an appropriate technique for testing critical con-

cepts such as deep-tissue half-times (*14*), diffusion versus perfusion limitations, gas-induced fluid shifts (*24*), preexisting gas micronuclei (*21*, *22*), and appropriate ascent criteria in a way that is insensitive to the experimental difficulty inherent in decompression.

BRIAN G. D'AOUST, K. H. SMITH
H. T. SWANSON, R. WHITE
*Virginia Mason Research Center, Seattle, Washington 98101*
CLAUDE A. HARVEY*
WILLIAM L. HUNTER
*Naval Submarine Medical Center, Groton, Connecticut 06340*
TOM S. NEUMAN, ROBERT F. GOAD
*Submarine Development Group 1, San Diego, California 92132*

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8. The first reports identifying this phenomenon as a gas bubble lesion associated with cutaneous gas lesions and vestibular derangement in man were those of C. J. Lambertsen's group (*1*, *2*) and were presented at the Fifth Symposium on Underwater Physiology in 1972. They demonstrated that man develops cutaneous gas lesions at 37 atm absolute breathing $N_2$ or Ne at high ambient pressures of He. Experimental confirmation by Idicula *et al.* (*3*) demonstrated copious production of bubbles in anesthetized pigs under a total ambient pressure of 1 atm when $N_2O$ was respired and the animals were surrounded by He. The severity of lesions in the latter experiment was directly proportional to the solubility of the gas respired. This result identifies solubility and therefore total gas concentration as one of the critical parameters in predicting bubble formation and is confirmed by other research [E. Hemmingsen, *Science* **167**, 1493 (1970); B. G. D'Aoust and L. S. Smith, *Comp. Biochem. Physiol.* **49**, 331 (1976); D. L. Beyer, B. G. D'Aoust, E. Casillas, L. S. Smith, paper presented at the Sixth Symposium on Underwater Physiology, San Diego, 6 to 10 July 1975.
9. D. Haugen and E. Belcher, "Final report ONR N00014-69C-0402" (Applied Physics Laboratory, University of Washington, Seattle, 1976); E. O. Belcher, thesis, University of Washington (1976).] Under a surgical plane of anesthesia, a right lateral thoracotomy was made to expose the required major vessels of the heart. The Doppler ultrasonic bubble detection cuff was placed around the posterior vena cava, after which the chest wall was closed; the leads from the Doppler cuff were run subcutaneously to the lateral dorsum of the back approximately 5 cm posterior to the scapula, where they exited through a Dacron-covered storage pack (which allowed healing) with a sterile seal around the connectors. Further details are available in K. H. Smith and B. G. D'Aoust ["Final report ONR N000129-76MB-498" (Virginia Mason Research Center, Seattle, Wash., 1976)].
10. The appearance of bubbles in the first 40.2-m experiment but not in two subsequent ones (either with the same pair of animals or with two more naive subjects) suggests the potential importance of a possible fright reaction to an initially high noise level associated with gas flushing. Such a reaction may have physiologically predisposed the animals to bubble production through vasoconstriction and resulting lower perfusion of slow tissues. Gas flushing in subsequent experiments was carried out in such a way as to slowly increase the onset of noise during the gas flush.
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12. The total tissue tension and fractional saturation values for He and $N_2$ (Fig. 1) have been computed from the equation

$$\pi_2 = fD_1 + fR(T - 1/K) - (\pi_1 - fD_1 - fR/K)e^{-KT}$$

where $T$ is the step time in minutes, $\pi_1$ is the initial gas tension at $T = 0$, $\pi_2$ is the final gas tension at $T$, $D_1$ is the depth at $T = 0$, $R$ is the rate of change of pressure ($dP/dT$) in meters per minute, $f$ is the inert gas decimal fraction, $K$ (the tissue constant) is $0.693/T_{1/2}$, and $T_{1/2}$ is the tissue half-time in minutes. Saturating He tensions and desaturating $N_2$ tensions were calculated and summed for discrete pairs of $N_2$ + He half-times as follows: 13 + 5, 22.5 + 9, 37.4 + 15, 60.2 + 25, 93 + 41, 139 + 63, 200 + 94, 273 + 138, 372 + 182, 480 + 240. The rationale for this procedure has been described by Smith (*11*). The excess gas concentration was calculated for all tissues by assuming an average fat composition of 15 percent by weight for all tissues and by finding the difference between the excess inert gas fraction and the same gas fraction at a saturation ratio of 1.00.
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26. We thank R. L. Stayton, J. Moore, M. Knowles, J. Mahoney, T. Baker, and S. Donaldson for expert technical assistance. Supported by grant N000129-76MB-498 from the Department of the Navy and by grant HL17503 from the Division of Lung Diseases of the National Heart, Lung, and Blood Institute.

27 December 1976; revised 14 February 1977

Abstract of Paper Presented at the 72nd Meeting of the Acoustical Society of America, November 2-5, 1966

# BREATHING MIXTURE AND DEPTH AS SEPARATE EFFECTS ON HELIUM SPEECH

Louis J. Gerstman
New York University, Bronx, New York

George R. Gamertsfelder and Arnold Goldberger
GPL Division, General Precision, Inc., Pleasantville, New York

Two divers made tape recordings of standard vocabularies while breathing several different helium-oxygen mixtures in a decompression chamber maintained at various simulated depths between sea level and 600 feet. Spectrographic analyses confirmed previous reports of non-linear formant-frequency shifts and changes in relative formant amplitudes, but failed to reveal improvements with time in talker intelligibility, especially at the lowest depths. A mathematical model, incorporating both the effects of helium concentration and of depth, was found to account successfully for the observed changes in formant frequencies. The model has also been employed in a real-time speech correction device, the output of which represents a significant improvement in helium speech intelligibility. (This work was supported by Ocean Systems, Inc.)

BA 874

# FINAL REPORT

# HYPERBARIC RESPIRATORY HEAT LOSS STUDY

Contract No. N00014-71-C-0099
Requisition No. NR101-840, Code 441

to

OFFICE OF NAVAL RESEARCH
DEPARTMENT OF THE NAVY
WASHINGTON, D.C.

October 31, 1971

WESTINGHOUSE ELECTRIC CORPORATION
UNDERSEAS DIVISION
OCEAN RESEARCH AND ENGINEERING CENTER
ANNAPOLIS, MARYLAND 21404



Maxwell W. Goodman
N. Eugene Smith
John W. Colston
Edward L. Rich III

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF FIGURES (Continued)



APPENDIXES

ABSTRACT

A multidepth saturation dive was performed as the vehicle for a study of respiratory heat loss during deep-depth, cold, helium-oxygen breathing. Respiratory heat loss was computed for each of the 137 combinations of depth and inhaled gas temperature for which ventilation and exhalation temperature were measured. Skin site temperatures and other respiratory parameters were also monitored, and the diver-subjects were under visual surveillance.

Exhalation gas temperature was always less than core temperature, regardless of the inhalation gas temperature (about 55, 45 and 35°F). The maximum rate of respiratory heat loss was observed with hard work (high ventilation rate) in 35°F water at 850 feet; about 400 watts (345 kilogram calories per hour). Respiratory symptoms of copious upper airway secretions, chest and back chilling and discomfort, and uncontrollable shaking and shivering reached peak severity during the 850 foot-35°F swims.

Conclusions having significance to operational diving without supplemental heating of the inhaled gas were formulated from the computations of respiratory heat loss, observations of falling core temperatures, and the subjective responses. These are as follows: (1) Dives to 850 feet for exposure durations in excess of 90 minutes in water of 45°F or colder are hazardous; (2) Dives to 650 feet or deeper for exposure durations in excess of 90 minutes in water of 35°F are liable to be characterized by significant task performance degradation.

SECTION 1

INTRODUCTION

The objective of these studies was to obtain, through immersion experiments with measurement of respiratory heat loss, information which is applicable in the estimation of depth and temperature operating limits for deep diving missions. The emphasis was upon immersion conditions encountered at a simulated depth of 850 feet. Actual mean temperature of inhaled gases approximated and was slightly warmer than that of ambient water temperature. At each experimental depth (450 ft., 650 ft., 850 ft. and 1,000 ft.) and at each controlled wet-pot water temperature (55°F, 45°F, 35°F) the divers were equipped with constant-flow hot water heated wet suits. These data are the first to be generated under conditions which thus mimic those of the operational scenario.

At sea level pressure the heat loss through respiration is relatively constant and is affected directly by the ventilatory air flow rate. Carlson, et. al. (9) estimated that this loss was equal to about 24% of the total body heat generated. Bribbia (4) determined that the heat loss of vaporization in men exercising in Arctic conditions was 9% of the total heat expended and that the water vapor loss was proportional to the ventilation rate. Day (14) computed respiratory heat loss (when the respiratory minute volume was 10 liters per minute and relative humidity was 50%) as follows:

| AIR TEMP. (°F) | SENSIBLE HEAT LOSS (BTU/HR.) | LATENT HEAT OF VAPORIZATION (BTU/HR.) | TOTAL R.H.L. (BTU/HR.) |
|---|---|---|---|
| 97 | 0 | 31 | 31 |
| 68 | 11 | 49 | 60 |
| 32 | 25 | 59 | 84 |

Numerous measurements of respiratory heat exchange have been made under comfortable, cool or hot conditions: Burch (5) (6), Cole (10) (11), Cramer (13), McCutcheon and Taylor (20) (21), Seeley (26) and Walker (31). For tabular resumes of the methods employed by most of the above investigators, as well as others, see the comprehensive review by Carlson (8). The following table of respiratory heat loss data is reproduced from his work:

## HEAT LOSS IN RESPIRED AIR

| Ambient Temperature | * | Belding et al. (1945) | Corlette (1942) | Day (1949) | Berg (1933) | Burch (1945) | Goodale (1896) | McCutchan & Taylor (1951) | Seeley (1940) |
|---|---|---|---|---|---|---|---|---|---|
| °C | | | kilogram calories per hour | | | | | | |
| 20 | 1. | | 2.0 | 2.87 | 0.76 | 1.9 | 2.5 | | |
| | 2. | | 9.5 | 12.27 | 8.72 | 7.9 | 8.94 | | |
| | 3. | | 11.5 | 15.14 | 9.48 | 9.8 | 11.44 | 11.9 | 12.0 |
| 0 | 1. | | 5.1 | 6.16 | | | 5.0 | | |
| | 2. | | 11.5 | 14.78 | | | 9.43 | | |
| | 3. | 18.5 | 10.6 | 20.94 | | | 14.43 | | 13.9 |
| -20 | 1. | | 8.2 | 9.25 | | | | | |
| | 2. | | 12.12 | 15.40 | | | | | |
| | 3. | 24.3 | 20.32 | 24.65 | | | | | |
| -40 | 1. | | 11.2 | 12.52 | | | | | |
| | 2. | | 12.23 | 15.43 | | | | | |
| | 3. | 28.3 | 23.43 | 27.95 | | | | | |

* Horizontal rows numbered 1., 2. and 3. are, respectively: the heat loss in warming inspired air (dry) and inspired water vapor; the heat loss in adding water vapor to the inspired air; the total heat loss, that is, the sum of the first two quantities.

Notes: a) Ambient relative humidity is taken as 50 per cent wherever possible. Exception — Berg dried the inspired air for his subjects.

b) The first three vertical columns represent values based on calculation. Day assumed expired air to be 37°C., saturated under all conditions. Corlette and Belding et al. took expired air to be 33°C, saturated.

c) It is assumed that the subject is at rest, comfortably clothed, and ventilating at the rate of 600 *l*/hr. Goodale did not record ventilation quantitatively.

Reproduced from Carlson (8)

Webb reported, in 1955 (34), that the relationship between ambient air and expired air temperatures approximates a linear function, as follows: "Starting at ambient temperature of 25°C, where the expired air temperature is 34°C, for every reduction of 5°C in ambient temperature there is a corresponding decrease of 1°C in the expired air temperature." Although this relationship was enunciated for conditions encountered at sea-level barometric pressure, the concept applied generally indicates that respiratory heat loss will be erroneously overestimated if the factor Δ(T exhaled - T inhaled) is computed by assuming equality of exhaled gas temperature to body temperature. The following table, adapted from Webb's report, compares respiratory heat loss according to his measurements ("B" values) with estimated values derived by assuming that exhaled air was at body temperature ("A" values). Heat loss data is in units of kilogram-calories.

| AIR TEMP. (°C) | SENSIBLE HEAT LOSS (A) | (B) | LATENT HEAT OF VAPORIZATION (A) | (B) | TOTAL R.H.L. (A) | (B) | TOTAL (A) HIGHER THAN TOTAL (B) BY |
|---|---|---|---|---|---|---|---|
| 20 | 2.87 | 2.42 | 12.27 | 9.40 | 15.14 | 11.81 | 28% |
| 0 | 6.16 | 5.39 | 14.78 | 8.35 | 20.94 | 13.75 | 52% |
| -20 | 9.25 | 8.37 | 15.40 | 6.96 | 24.65 | 15.33 | 61% |
| -40 | 12.58 | 11.35 | 15.43 | 5.92 | 28.01 | 17.26 | 62% |

Armstrong, et. al. (2) also reported on respiratory aspects of breathing very cold Arctic air at atmospheric pressure and under subatmospheric conditions as encountered during high altitude flight without the protection of a cockpit canopy. Exposures to ambient temperatures at 40°F to -80°F for 2 to 6 hours did not cause direct laryngeal injury. In this regard Rawlins and Tauber (25) have cautioned that, "Much work has been done on the effects of breathing cold air down to -55°C, but we know of no studies of the effect of prolonged breathing of cold helium mixtures at great depths. At high rates of ventilation with relatively dense gas mixtures of high heat capacity there is a very large heat loss effecting a limited area of the body, the upper respiratory tract. The possibility of laryngeal damage, edema or functional impairment, should be contemplated."

Spealman, et. al. (28) also observed subjects breathing cold (to -83°F) air at atmospheric pressure. These investigators, in contradistinction to Webb, found that the expired air temperature was approximately 36°C in all cases. They reported the following respiratory heat losses per 1,000 liters of respired air (assuming 90% water vapor saturation):

| AIR TEMP. (°C) | (°F) | SENSIBLE HEAT LOSS (KCAL.) | LATENT HEAT OF VAPORIZATION (KCAL.) | TOTAL R.H.L. (KCAL.) |
|---|---|---|---|---|
| 56 | 133 | +6.4 | +44.7 | +51.1 |
| 36 | 97 | 0.0 | 0.0 | 0.0 |
| 16 | 61 | 6.4 | 16.9 | 23.3 |
| -4 | 25 | 12.8 | 22.6 | 35.4 |
| -24 | -11 | 19.2 | 24.1 | 43.3 |
| -44 | -47 | 25.6 | 24.3 | 49.9 |
| -64 | -83 | 32.0 | 24.4 | 56.4 |

Note the net gain in respiratory heat for the initial condition (air temperature 133°F). By assuming that inhaled air is completely dry, however, there is a net respiratory heat loss in each instance:

| AIR TEMP (°C) | (°F) | TOTAL R.H.L. (KCAL.) |
|---|---|---|
| 56 | 133 | 18.0 |
| 36 | 97 | 24.4 |
| 16 | 61 | 30.8 |
| -4 | 25 | 37.2 |
| -24 | -11 | 43.6 |
| -44 | -47 | 50.0 |
| -64 | -83 | 56.4 |

Data on hyperbaric respiratory heat loss was reported in 1966 by Webb and Annis (37). Their study included a panel of diver-subjects during immersion experiments with an open-circuit demand breathing apparatus at simulated depths of 100 feet (4 atm. abs.) and 230 feet (8 atm. abs.). Mean data from their report is as follows:

| CONDITION | NO. OF EXPERIMENTS | INHALED TEMP. (°C) | (°F) | ΔT (°C) | R.H.L. (K CAL/MIN) | TOTAL HEAT LOSS (K CAL/MIN) | R.H.L. % of TOTAL |
|---|---|---|---|---|---|---|---|
| Air, 1 atm. | 35 | 20.9 | 69.6 | 13.4 | 0.56 | 5.5 | 9.5 |
| Air, 4 atm. | 4 | 17.0 | 62.6 | 16.3 | 0.90 | 4.8 | 17.7 |
| SF6, 1 atm.* | 37 | 20.2 | 68.4 | 13.7 | 0.71 | 5.0 | 13.5 |
| 80%He, 1 atm. | 40 | 22.7 | 72.9 | 11.1 | 0.48 | 5.4 | 9.0 |
| 80%He, 4 atm. | 8 | 15.3 | 59.5 | 15.4 | 0.48 | 3.1 | 16.3 |
| 96%He, 8 atm. | 8 | 16.5 | 61.7 | 16.0 | 0.90 | 3.8 | 25.1 |

* 80% sulfur hexafluoride - 20% oxygen

Albano (1), in his presentation of thermoanalysis in diving, states that, "In the respiratory tree, thermolysis takes place as a result of heating and humidification of the ventilated gas. Because of the effect of heating, air exhaled has a temperature of 37°C, regardless of the temperature of gas inhaled." Table VI of his monograph presents computed projections of respiratory heat loss at 15°C (59°F) and these reflect the influence of his assumption regarding exhalation temperature. For example, with air breathing at 25 liters per minute:

| DEPTH (ATM. ABS.) | RESPIRATORY HEAT LOSS (KCAL/MIN) | (KCAL/HR) |
|---|---|---|
| 1 | 0.78 | 46.6 |
| 2 | 0.93 | 55.6 |
| 4 | 1.23 | 73.7 |
| 8 | 1.83 | 109.8 |

In his excellent review of body heat loss in undersea gaseous environments Webb (35) states that, "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 returned to the respiratory tract as the warm moist air exits over the previously cooled tissues." In other words, to assume that gas is exhaled at body temperature is to ignore the counter-current heat exchange mechanism of the respiratory passages (19).

U.S. Navy studies (Naval Medical Research Institute - Navy Experimental Diving Unit) on respiratory heat loss from breathing cold gas at high pressures are in publication at this time. Preliminary findings have, however, been communicated. The investigators (Hoke, Jackson, Alexander and Flynn) reported significant problems during bicycle ergometer runs at 800 feet with inhaled gas at 32-35°F: excessive body heat loss, discomfort, shivering and acute respiratory difficulties. They measured respiratory heat loss as high as 780 watts during heavy work (respiratory minute volume = 64 lpm) at 1,000 feet when inhaled temperature was 45°F (7°C). Their conclusions noted that, "These experiments on respiratory heat

loss from breathing cold gases at high pressures show conclusively that at depths beyond 600 feet and water temperatures (i.e. inspired gas temperatures) of 40°F (4.2°C) or less, the results will be progressive negative thermal balance. The rate of heat loss will increase as respiratory minute volume increases at higher work rates. The data show that when respiratory heat loss exceeds about 350 watts the diver will be in danger sooner or later, depending on individual characteristics, because of excessive heat loss. In addition, a certain fraction of divers may exhibit sensitivity to the direct effects of cold gases and produce copious amounts of mucous which can cause acute respiratory difficulty. . . It is difficult to estimate how long any particular diver could withstand an RHL of greater than 350 watts. Therefore, our conclusion is that for safety, thermal comfort, and maximum efficiency, the diver's breathing gas should be heated for dives in excess of 500 feet . . ."

SECTION 2

METHODS AND PROCEDURES

## Hyperbaric Facility

All experiments were conducted with the subjects within the wet pot chamber of the Westinghouse hyperbaric facility (Figure 1). Monitoring and surveillance were by direct visual through-port observation and by closed circuit television. Dimensional characteristics of this three-compartment facility are as follows:

| CHAMBER | DIMENSIONS (FT) | VOLUME ($FT^3$) |
|---|---|---|
| Entrance Lock | dia 6 | 102 |
| Main Chamber | dia 8<br>length 10.3 | 396 |
| Wet Pot | dia 8.3<br>length 9.4 | 346 |

## Saturation Diving

These experiments were performed during the course of a thirteen-day long multi-level saturation dive, May 7- May 19, 1971. Initial compression, and time at 450 feet, was about 1 1/2 days, and just under two days were provided for runs at 650 feet. The remaining time, with excursion diving to 1,000 feet, was at 850 feet depth. The chamber atmosphere composition was 0.3 atm. abs. oxygen, 1.2 atm. abs. nitrogen, balance helium. The usual temperature in the main chamber was 88-90°F. Decompression was in accordance with the following:

DECOMPRESSION SUMMARY

| DEPTH (FEET) | TIME (HR. MIN.) | ELAPSED (HR. MIN.) | CLOCK TIME |
|---|---|---|---|
| 850-835 | 1.30 | 1.30 | 1600-1730 |
| 835-820 | 2.00 | 3.30 | 1730-1930 |
| 820 | 0.30 | 4.00 | 1930-2000 |
| 820-796 | 4.00 | 8.00 | 2000-2400 |
| 796 | 6.00 | 14.00 | 2400-0600 |

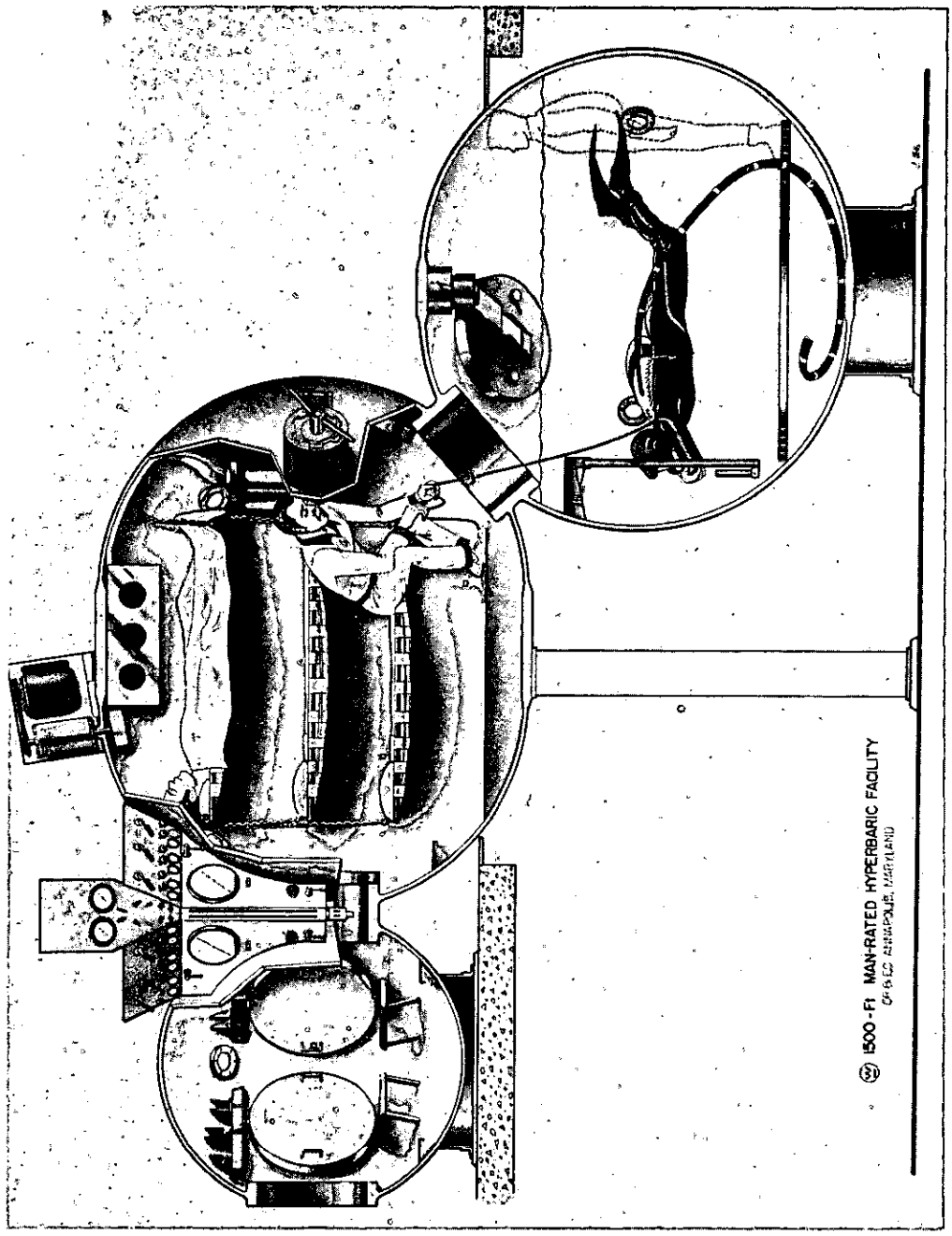


Figure 1. Westinghouse Hyperbaric Facility.

## DECOMPRESSION SUMMARY (CONTINUED)

| DEPTH (FEET) | TIME (HR. MIN.) | ELAPSED (HR. MIN.) | CLOCK TIME |
|---|---|---|---|
| 796-748 | 8.00 | 22.00 | 0600-1400 |
| 748 | 2.00 | 24.00 | 1400-1600 |
| 748-700 | 8.00 | 32.00 | 1600-2400 |
| 700 | 6.00 | 38.00 | 2400-0600 |
| 700-652 | 8.00 | 46.00 | 0600-1400 |
| 652 | 2.00 | 48.00 | 1400-1600 |
| 652-604 | 8.00 | 56.00 | 1600-2400 |
| 604 | 6.00 | 62.00 | 2400-0600 |
| 604-556 | 8.00 | 70.00 | 0600-1400 |
| 556 | 2.00 | 72.00 | 1400-1600 |
| 556-508 | 8.00 | 80.00 | 1600-2400 |
| 508 | 6.00 | 86.00 | 2400-0600 |
| 508-460 | 8.00 | 94.00 | 0600-1400 |
| 460 | 2.00 | 96.00 | 1400-1600 |
| 460-412 | 8.00 | 104.00 | 1600-2400 |
| 412 | 6.00 | 110.00 | 2400-0600 |
| 412-400 | 2.00 | 112.00 | 0600-0800 |
| 400-370 | 6.00 | 118.00 | 0800-1400 |
| 370 | 2.00 | 120.00 | 1400-1600 |
| 370-330 | 8.00 | 128.00 | 1600-2400 |
| 330 | 6.00 | 134.00 | 2400-0600 |
| 330-290 | 8.00 | 142.00 | 0600-1400 |
| 290 | 2.00 | 144.00 | 1400-1600 |
| 290-250 | 8.00 | 152.00 | 1600-2400 |
| 250 | 6.00 | 158.00 | 2400-0600 |
| 250-210 | 8.00 | 166.00 | 0600-1400 |
| 210 | 2.00 | 168.00 | 1400-1600 |
| 210-170 | 8.00 | 176.00 | 1600-2400 |
| 170 | 6.00 | 182.00 | 2400-0600 |
| 170-130 | 8.00 | 190.00 | 0600-1400 |
| 130 | 2.00 | 192.00 | 1400-1600 |
| 130-100 | 6.00 | 198.00 | 1600-2200 |
| 100-92 | 2.00 | 200.00 | 2200-2400 |
| 92 | 6.00 | 206.00 | 2400-0600 |
| 92-60 | 8.00 | 214.00 | 0600-1400 |
| 60 | 2.00 | 216.00 | 1400-1600 |
| 60-50 | 2.30 | 218.30 | 1600-1830 |
| 50-33 1/2 | 5.30 | 224.00 | 1830-2400 |
| 33 1/2 | 6.00 | 230.00 | 2400-0600 |
| 33 1/2-9 1/2 | 8.00 | 238.00 | 0600-1400 |
| 9 1/2 | 2.00 | 240.00 | 1400-1600 |
| 9 1/2-0 | 3.10 | 243.10 | 1600-1910 |

Subjects

The panel of diver-subjects was composed of two former U.S. Navy Sealab aquanauts, one of whom was a medical deep-sea diving technician, and a Westinghouse life support group engineer with a background in commercial diving.

| SUBJECT | AGE | HEIGHT (IN.) | WEIGHT (LB.) |
|---|---|---|---|
| KC | 39 | 69 | 170 |
| FA | 29 | 70 | 153 |
| SZ | 27 | 71 | 208 |

Procedure

Since the wet-pot water temperature served to control the temperature of inhaled gas, all swims on a given day at a particular depth were at the same temperature. Each diver-subject made at least one immersion run per full working day. Studies at 450 feet were performed first, followed by compression to, respectively, 650 feet and 850 feet. Runs at 1,000 feet were conducted as excursion dive maneuvers from a saturation level at 850 feet.

When fully dressed, checked out and ready for entry into the cold water in the wet pot the subject descended the ladder and then rigged it to function as an ergometer (described, following). A swim (work) - rest alternation pattern was employed, as follows: dress and enter water, 30 min.; rest and checkout equipment, 10 min.; resting ventilation measurements, 15 min.; light work, 20 min.; rest, 10 min.; moderate work, 20 min.; rest, 10 min.; heavy work, 20 minutes. All measured and derived parameters were referenced to the final portions of each of the four (rest and three work periods) activity levels. These parameters were: inhaled gas temperature, exhaled gas temperature, respiratory minute volume, tidal volume, respiratory frequency, inhalation and exhalation flow rate, exhalation pressure drop, mixed expired oxygen and carbon dioxide fraction, core temperature, skin site temperatures, water and equipment component temperatures.

Water temperatures of exposure were approximately 35°F for runs at 450, 650 and 850 feet, 45 °F for runs at 450, 650, 850 and 1,000 feet, and 55°F for runs at 850 feet only. Each combination of inhaled temperature-depth-activity level (ventilatory volume) was considered as a potential data point for respiratory heat loss. 137 such data points were obtained during the effort.

Breathing Gas Loop

The breathing gas supply was drawn from the main chamber atmosphere at a point about 6 feet from the carbon dioxide canister outflow and one foot above deck level. A positive displacement vane pump (Gast Manufacturing Corporation model 0740-P112A) was employed. The pump was driven by an explosion-proof, Dayton Manufacturing Company electric motor (model 6K040) rated at 0.75 horsepower. Both motor and pump were mounted in a sound-absorbing enclosure and the motor was continually flushed with dry helium. The gas stream was filtered at the pump intake and output (Gast Manufacturing Corporation model B343B and Wilkerson microalescer model 1206-4 filters, respectively). The filtered gas was pumped from the main chamber to the wet pot through approximately 6 feet of 1.5 inch polyethylene hose.

Underwater in the wet pot the gas passed through a submerged cooling coil consisting of 25 feet of 0.5 inch internal diameter copper tubing, a water trap (Bastian-Blessing Company model 8824) at the lowest point of the supply loop, three feet of 0.5 inch internal diameter copper tubing and a 1.5 inch polyvinyl chloride tee-fitting to which a flexible hose and breathing bag was attached.

The breathing bag (see Figure 2) which was inserted in the gas supply line to provide sufficient demand volume for peak inspirations was an Ohio Chemical and Surgical Equipment Company 5 liter rubber anesthesia bag (number 211-2800-100). The center of the breathing bag was at the approximate level of the diver's chest, about two feet below the water surface. It was secured there with a wire frame and rigid support. A flexible hose (Warren E. Collins, number P-521, 1.5 inch internal diameter reinforced polyethylene) connected it to the breathing loop and the gas supply.

The gas supply entered into the breathing gas circuit via a 1.5 inch polyvinyl chloride tee-fitting where it was divided into streams flowing through an exhaust flapper check valve and through a mushroom-type check valve to the mouthpiece breathing valve. The exhaust flapper valve was a Sadd valve (Warren E. Collins no. P-303-1) and the mouthpiece check valves were of the "V" type (Warren E. Collins no. P-315). A rubber mouthpiece (Warren E. Collins no. P-530) was also fitted to the mouthpiece breathing valve body which had been machined from a one inch internal diameter polyvinyl chloride tee-fitting. The inhalation-exhalation thermistor protruded downwards through the vertical aspect of the tee-fitting with

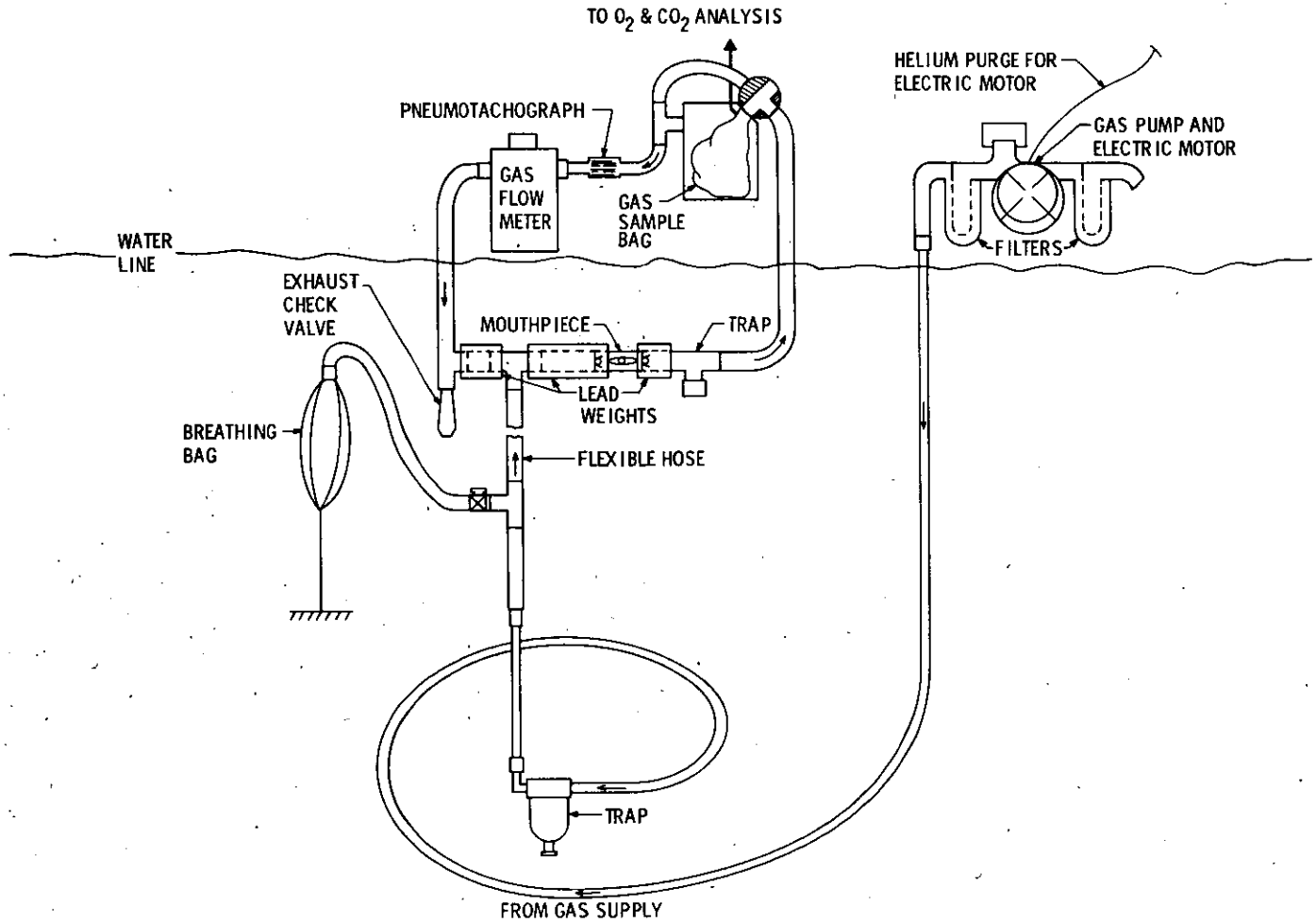


Figure 2. Gas Chilling, Delivery and Breathing System.

the thermistor bead itself exposed at a distance of 0.45 centimeters into the air stream. The maximum protrusion of the protective guard wires was 0.96 centimeters. The thermistor was located 2.2 centimeters from the inhalation and exhalation mushroom check valves and was at a distance of 5.2 centimeters from the cavity margin of the rubber mouthpiece. A saliva trap was placed about 10 centimeters downstream from the exhalation check valve. The mouthpiece breathing valve assembly was weighted with lead to maintain neutral buoyancy.

Suitable lengths of 1.5 inch internal diameter flexible hose conducted the exhalation gas stream vertically up into the main chamber and through the mixed expired gas sampling device, the pneumotachograph head and the dry gasometer (see below). Finally, the flow passed through the above-mentioned exhaust flapper check valve. This latter valve was on the same rigid mount as the divers' mouthpiece and was so placed that its location was at the divers chest level. Thus, the valve outlet was actually located about 2 feet below the water surface level and the entire breathing loop was thereby maintained at a slight positive pressure (about 1 pound per square inch gauge). A United States Gauge Company model 19693 pressure gauge at the pump outlet measured this pressure. (Also see Appendix 3).

Volume, Flow and Pressure Measurements in the Breathing Loop

The dry gasometer was a Parkinson-Cowan type CD-4 which had been modified (Figure 3) so that the inlet and outlet gas flow connections were oriented horizontally instead of vertically. The gasometer was fitted with a potentiometer and an electrical output corresponding to revolutions of the ten liter scale were obtained and recorded on a channel of a Electronic Instrumentation Associates model 1910 recorder. The gasometer was compared to standards at the Standardizing Laboratory at the Westinghouse Defense and Space Center, Baltimore, Maryland, using shop air in the range of 5 to 50 standard liters per minute. The uncertainty of measurement was reported as less than 0.5 standard liters per minute and of voltage as less than 1 millivolt.

The flow measuring system included a Fleisch pneumotachograph size 3, a Honeywell Accudata 113 bridge/DC amplifier and a channel on the Electronic Associates model 1910 recorder. The pneumotachograph was heated during operation. Gas temperature was monitored upstream and downstream of the pneumotachograph head using Yellow Springs Instrument Company type 421 thermistor probes. A Statham Instruments Inc. PM 97 TC-350 0.05 PSID pressure transducer was used to sense pressure drop across the pneumotachograph tubules. (Also see Appendix 4).

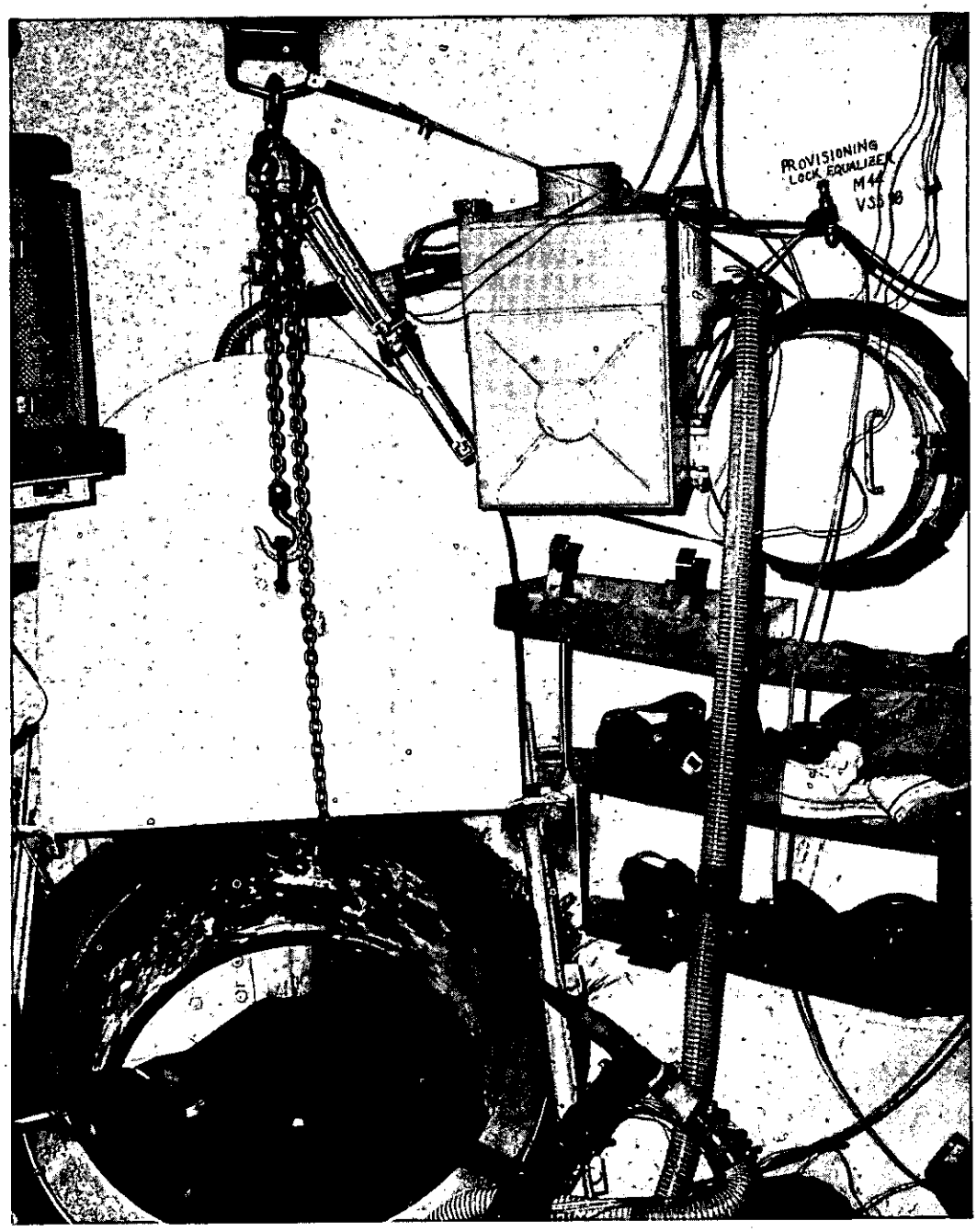


Figure 3. Interior of Main Chamber, Showing Modified Parkinson-Cowan Type CD-4 Gasometer.

2-8

One side of a Statham Instruments Inc. PM 60 TC-350 0.15 PSID differential pressure transducer was connected via a flush tap to the central cavity of the mouthpiece breathing valve. The other side, referenced to the same location on the external surface of the valve body, was kept free of water by means of a trickle flow of helium from the same source which supplied the pump and motor enclosure. This signal was processed with a Honeywell Accudata 113 bridge/DC amplifier and recorded with the Electronic Associates model 1910 recorder.

Oxygen - Carbon Dioxide Analysis

Mixed expired gas was collected during the final minutes of each of the 139 immersion tests. The gas sampling system (Figure 4) consisted of a 30 liter neoprene latex meteorological balloon (Warren E. Collins no. P-342-30) mounted inside a five gallon polyethylene container. The gas sample bag inlet valve (Warren E. Collins no. P-321) was normally open, allowing the gas stream to bypass the bag. During sampling the gas entering the bag displaced gas enclosed within the surrounding rigid container into the breathing gas loop, replacing the sampled volume. The outlet tee-fitting from the polyethylene container was a 1.5 inch polyvinylchloride fitting. The polyethylene container was also modified with a transparent lucite window for observing the degree of inflation of the enclosed balloon. Gas for analysis was withdrawn via tygon tubing affixed to the sampling port of the inlet stop-cock valve, through internal and external hull valves and fittings. A custom-manifold of needle valves, filters and rotometer flowmeters was used to divide the controlled flow through a Beckman Instruments Co. model E-2 oxygen analyzer and IR-315 carbon dioxide analyzer. Samples of this mixed expired effluent were also collected for Scholander microgasometric analysis.

Inhalation and Exhalation Temperature Measurement

A micro-bead thermistor (Victory Engineering Corporation type E31A401C) was used to measure the temperature of respired gas. The thermistor bead is about 0.005 inches in diameter and is mounted on 0.00075 inch diameter wires. Its time constant in still air is 0.12 seconds. The time constant in helium at 30 atmospheres absolute pressure with a flow of 100 feet per minute is 0.0102 seconds. Other characteristics of this thermistor are as follows: resistance approximately 1000 ohms at 25°C with a temperature coefficient of -3.2% per degree C at 25°C; dissipation constant approximately 0.045 MW/°C in still air. The

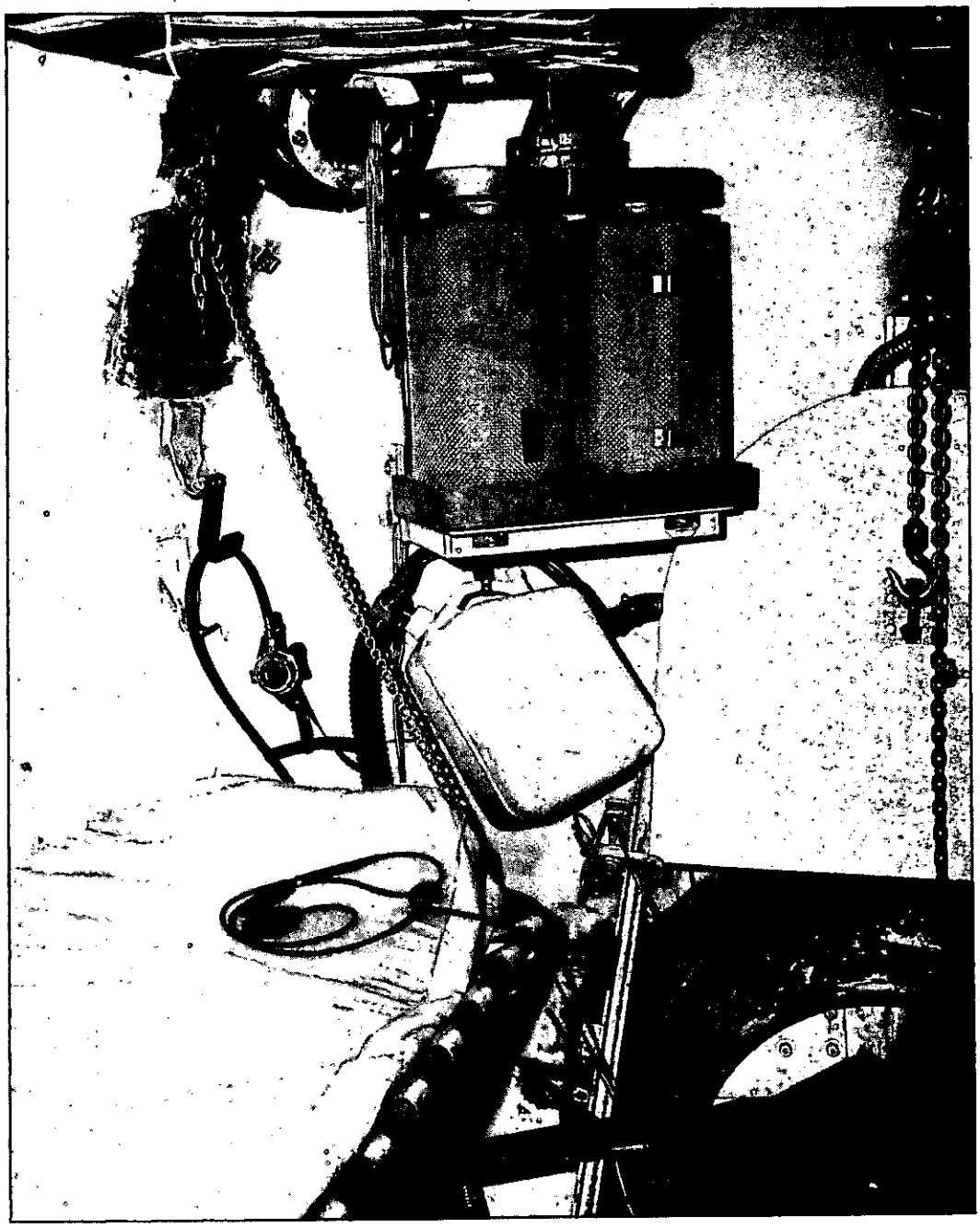

Figure 4. Interior Of Main Chamber, Showing Rigid Container for Mixed Expired Gas Collection Bag.

2-10

thermistor is mounted on a Victory Engineering Corporation TO-18 type header, and the thermistor-header was further protected by means of a pair of guard loops of number 24 gauge wire which crossed and surrounded the thermistor at a distance of not less than 16 diameters.

The signal conditioning bridge was designed to produce an output of 0-20 millivolts direct current for a temperature span of 0-40°C. Linearity was ±0.4°C over this range and was attained by means of the equal slope criterion and the linearity equation supplied by the manufacturer. The maximum self heating error, despite the low dissipation constant of the thermistor, was 0.1°C. A stabilized mercury cell (Mallory RM-12R) was used to obtain a constant voltage source for the bridge. Variations were less than ±0.1%.

The recorder was a Texas Instruments Company, Servo/Riter II model FS01N6B, and provided a 6-inch span for 0-20MV DC. The chart was readable to 0.1°C. For a span step response of 0.4 seconds the recorder accuracy was ±0.25% and linearity was ±0.1%. Recorder input impedance was matched to the load of the bridge.

Calibration of the complete system provided a correction curve which was applied to the raw data. Based on combined time response accuracies, a total step response of not less than 99.6% in 0.5 seconds was attained.

Thermistor mounting and location in the mouthpiece is described, preceding (see above), concurrently with other components of the breathing gas loop.

Appendix 2 provides further engineering documentation regarding the selection and use of the inhalation-exhalation thermistor.

Other Temperature Measurements

Skin site temperatures were obtained using Yellow Springs Instrument Company type 409 thermistors fastened to the divers with Band-Aid clear tape, as follows (Figure 5):

| Thermistor No. | | Location |
|---|---|---|
| 1. | - | Head - on the neck below the hairline and behind the right ear |
| 2. | - | Arm - on the lateral surface of the right biceps |
| 3. | | Chest - just above the right nipple |

Figure 5. Subject Being Outfitted With Thermistor Harness.

2-12

| Thermistor No. | | Location |
|---|---|---|
| 4. | - | Back - on the surface of the right scapula |
| 5. | - | Thigh - on the lateral surface of the right thigh |
| 6. | - | Calf - on the lateral surface of the right calf |
| 7. | - | Finger - on the medial surface of the right second phalange midway between the tip and the first joint |
| 8. | - | Toe - on the medial surface of the right large toe midway between the tip and the first joint |
| 10. | - | Forearm - on the lateral surface of the right forearm |

Mean weighted skin temperature was computed according to the method of Teichner (29):

Tmws = 1.5 (T chest + T back + T thigh +T calf/8 + T head/10 + T arm/14)

Additional temperature recording was done with thermistors placed in the following locations:

| Thermistor No. | | Location |
|---|---|---|
| 9. | - | Rectum - inserted approximately 9 centimeters beyond the anal verge |
| 11. | - | in the wet pot water approximately at diver level and 4 inches from the hull |
| 12. | - | in the hot water umbilical flow 1 inch from suit connection |
| 13. | - | inside the suits, various locations |
| 14. | - | on the gas pump housing |
| 15. | - | on the electric motor housing |
| 16. | - | in the gas stream immediately prior to the pneumotachograph |
| 17. | - | in the gas stream immediately after the pneumotachograph and prior to the gasometer |
| 18. | - | in the gas stream immediately after the gasometer |

The precise location for the wet pot thermistor was found through prior investigation not to be critical when the chiller pump was operating and circulating the water. Thermistor 12 was placed in the umbilical rather than switching it among the various suits. The function of thermistor 13 was to establish an exit temperature for the hot water leaving the suit. Thermistors 14 and 15 were used as safety monitors in the event the pump or motor began to fail and overheat.

Yellow Springs Instrument Company series 400 probes were employed for these measurements. The bridge was designed using linearization criteria and computer data processing in the same manner as the inhalation-exhalation thermistor bridge. Because of the higher dissipation constants of these probes an output of 0-40 millivolts DC was provided for a range of 0-40°C. Probes used to measure skin temperatures, gas temperatures (other than respired gas) and water temperature (YSI type 409) have a time constant of 1.7 seconds in stirred water. The rectal probe, YSI type 401, has a time constant of 7 seconds in stirred water.

A Hewlett-Packard model 2900D scanner selected the thermistor to be monitored and connected it to a digital voltmeter (Hewlett-Packard model 3460D). This provided a visual output and a signal to a Hewlett-Packard model 5050B digital printer which printed the temperature in 4 digits on a paper tape.

Calibration for Temperature Measurement

An Anschutz fractional degree, precision grade, Centigrade thermometer, range -12 to 61°C, certified by the National Bureau of Standards, and accurate to 0.2°C was used for calibration checks before and after the dive. Overall steady state accuracy of the thermistor-recorder systems after adjustment for calibration was within 0.3°C.

Ergometer

A spring-and-weight trapeeze ergometer was deployed underwater in the wet pot and provided the means of achieving serially increasing ventilatory volumes in response to the swimming work efforts thus applied. Since ventilatory volume, rather than simulated speed at thrust output was the parameter of interest, the assembled ergometer was not calibrated in units of work or work equivalents.

The variable, which was displayed to the swimming diver (Figure 6) and to topside (Figure 7) was displacement. A pointer, fastened to the ladder-trapeeze at the diver position, was situated several inches from the prone diver's face and indicated position in inches from the wall. A light cable directed vertically across a porthole, counter-weighted and with a pointer displayed the trapeeze position to topside supervisors. The movement of the ladder-trapeeze, as the diver pressed against the horizontal swim bar, was from a vertical, free-hanging position to a small angle where the base of the ladder contacted the chamber hull. The zero position was thus established at this hard-into-the-hull position, and displacement was marked in inches from the hull at the swim bar, 29 inches from the pivot.

The weight and spring loadings were applied at a greater distance, 41 inches from the pivot, thus causing an amplification of (41/29 = 1.41) force to the diver. For this application 5 lbs. of lead divers' weight-belt weights were used in a reverse pull arrangement (see Figure 8). A spring (K=1 lb./inch) was mounted at the end of the trapeeze to provide an increase in load such that it was the maximum at maximum displacement from the vertical. The operating range was thus measured from the hull, beginning with an arbitrary zero in that position and the load decreased as the distance from the hull increased. The divers were thus swimming against a force that was a combination of the amplified weight loading and the horizontal component of the spring. It was felt that the divers could better regulate their swimming thrust output by working against an increase in load over a short displacement. In operation, the divers swim at a rate to displace the ladder to markings on the indicator.

Suit Description

The suits worn during all tests were free flooding hot water suits style Diving Unlimited Mk XAD. The suit is of one piece construction which includes torso, hood, arms, and legs sections. Boots and gloves are worn as separate items. The suit is a nominal 1/4 inch neoprene foam with nylon on each side.

Hot water enters the suit at a manifold block on the right hip, from which it is directed into six outlet tubes. One tube leads to each of the arms and legs, one to the front of the body, and one to the back and head (Figure 9). Each tube has exhaust ports which vary in

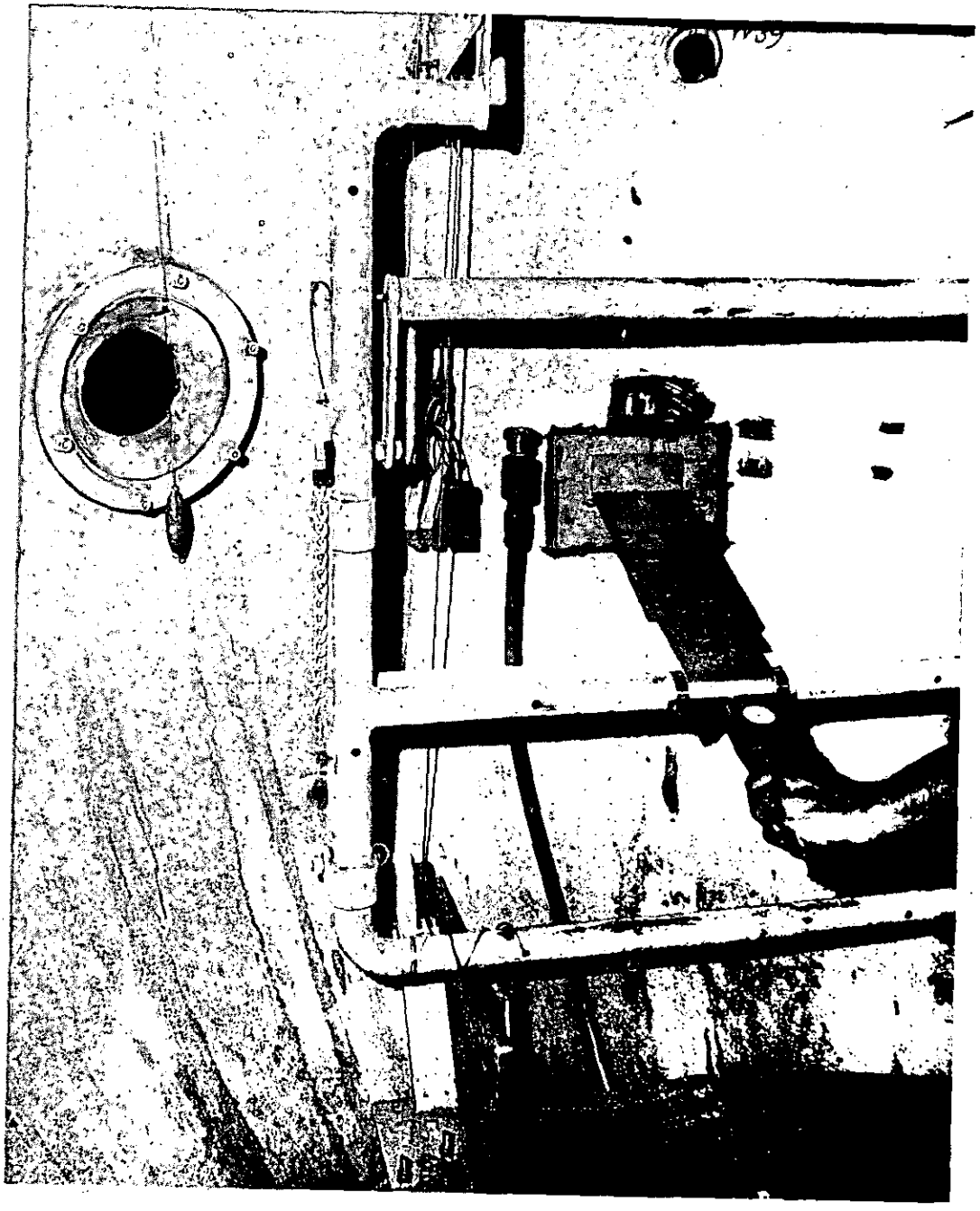

Figure 6. Interior Of Wet Pot, Showing Ergometer And Diver Display Device.

2-16

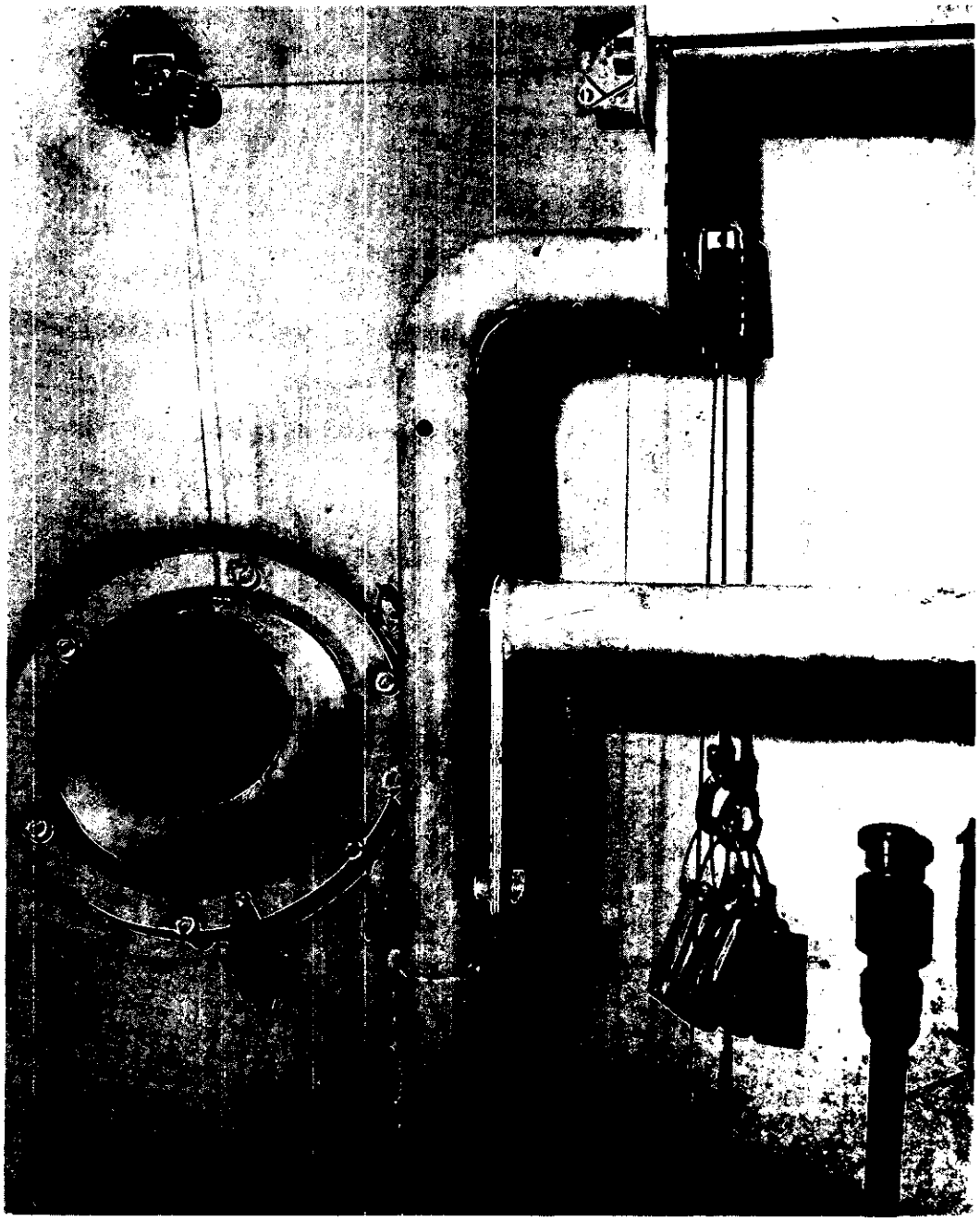

Figure 7. Interior Of Wet Pot, Showing Ergometer and Topside Display Method.

2-17

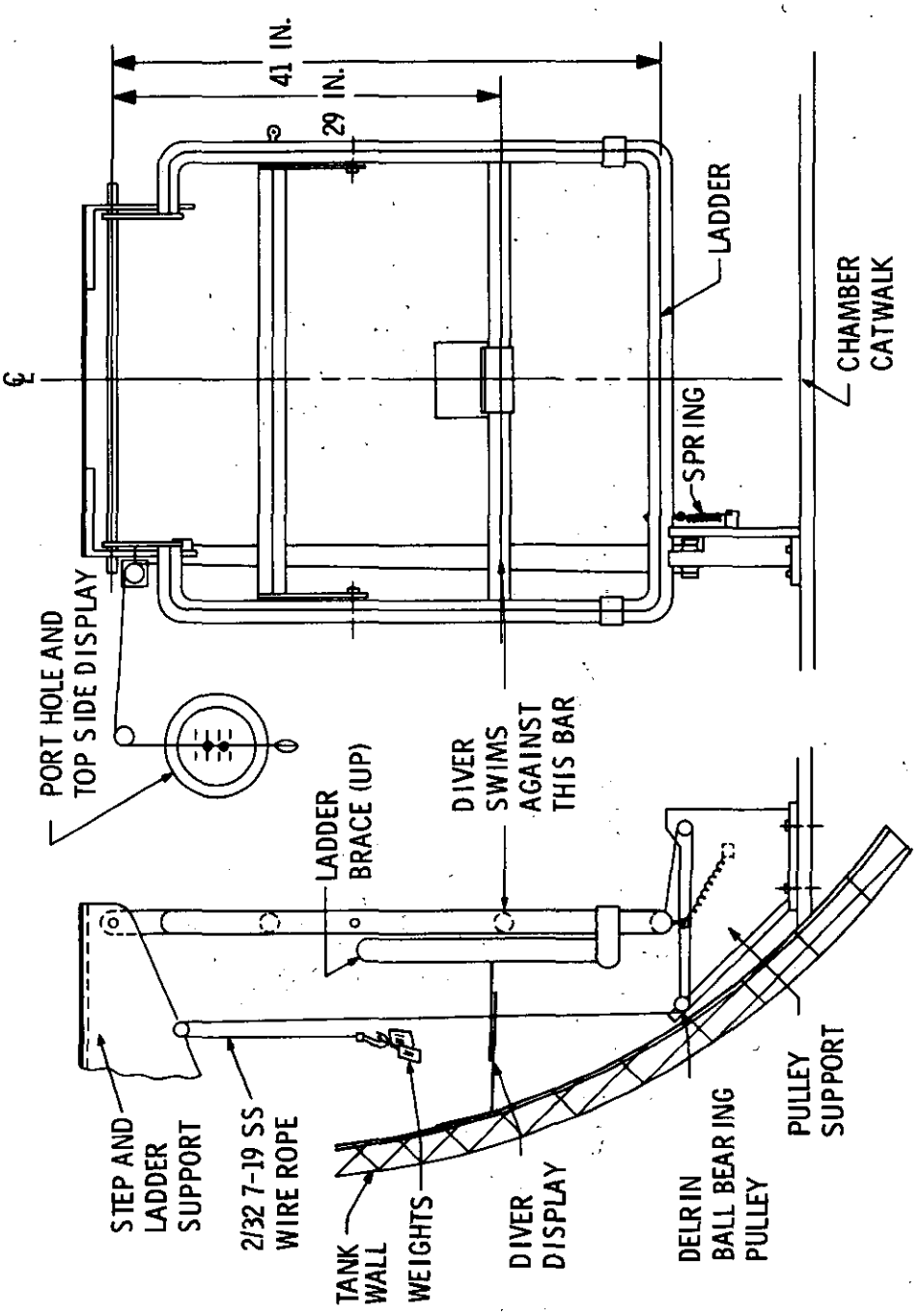


Figure 8. Ergometer Layout Drawings.

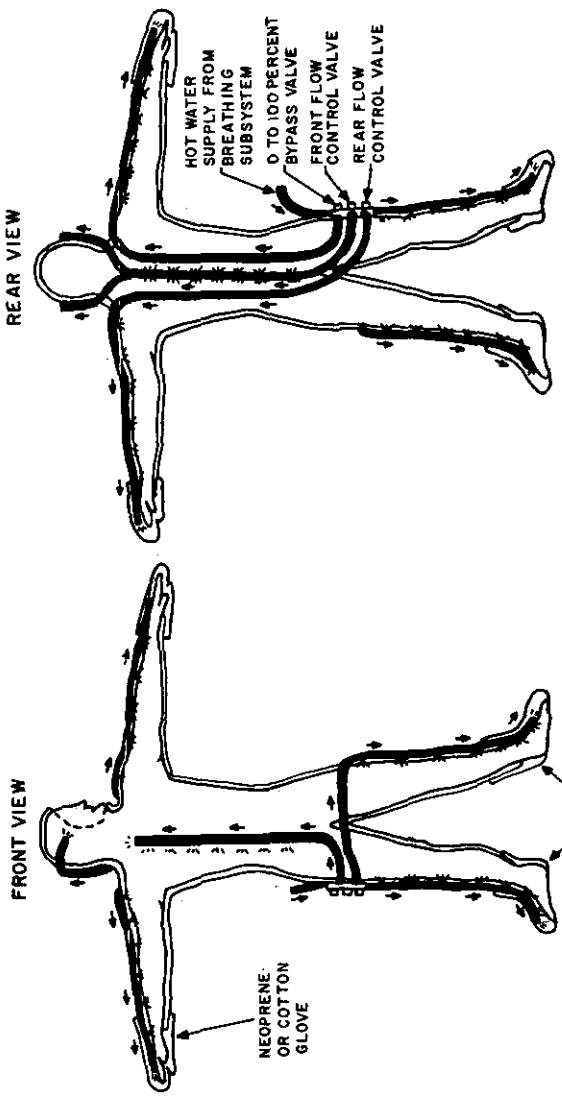


Figure 9. Hot Water Suit Flow Distribution.

size according to regional body hot water requirements. Soft flexible tubes extend beyond the wrists and ankles, and feed water to the hands and feet. The water exits the suit at the wrist, ankles, and neck in undetermined proportions.

Approximately 1/2 inch of clearance is required between the suit and the diver's body for efficient circulation of the hot water. Diver subjects were measured and suits ordered which would provide adequate clearance after a 5% shrinkage with compression. A nominal 1/8 inch neoprene foam suit consisting of pants and jacket was worn under the free flooding suit.

The suit manifold block consists of three valves for regulating the amount of umbilical water flow into the suit, to the front of the body, and to the back and head, respectively. During the test swims the valves were maintained in full open position. Hot water flow into the suit was maintained at 2.0-2.25 gallons per minute and inlet temperature to the suit at 105-107°F for the 450 and 650 feet runs and at 110°F for the 850 and 1000 feet runs. These water flow rates and temperatures were controlled topside.

Calculation of Respiratory Heat Loss

Heat lost from the respiratory tract due to heating and humidification of the breathing gas can be calculated using the following equation:

$$Q_r = V_g \quad \rho_g \, Cp_g \, (Te-Ti) + V_g \quad \rho_g \, h_{fg} \, (We-Wi) \qquad (1)$$

$Q_r$ = respiratory heat loss, Btu/hr.
$V_g$ = Respiratory rate, $ft^3/hr$.
$\rho_g$ = gas density, $lbm/ft^3$
$Cp_g$ = gas specific heat, Btu/lbm °F
Te = temperature of expired gas, °F
Ti = temperature of inspired gas, °F
$h_{fg}$ = latent heat of vaporization, $Btu/lb_w$
We = humidity ratio of expired gas, $lb_w/lb_g$
Wi = humidity ratio of inspired gas, $lb_w/lb_g$
$lb_w$ = pounds of water vapor
$lb_g$ = pounds of dry gas

*The first group of terms,* $V_g \rho_g Cp_g (Te-Ti)$, *is the heat required to raise the temperature of the inspired gas to the expired temperature, and is known as sensible heat.* The second group of terms, $V_g \rho_g h_{fg} (We-Wi)$, is the heat required to vaporize the water which is added to the gas from the respiratory epithelium and is known as insensible heat.

The humidity ratio, W, can also be expressed as a ratio of the products of the molecular weights and partial pressures of the water vapor and dry gas.

$$W = \frac{M_{H_2O} \; P_{H_2O}}{M_g \quad P_g} \quad \text{and,} \tag{2}$$

$$We-Wi = \frac{M_{H_2O} \; (P_{H_2O_e} - P_{H_2O_i})}{M_g \quad P_g} \tag{3}$$

Where

$M_{H_2O}$ = molecular weight of water vapor

$M_g$ = *molecular weight of gas*

$P_{H_2O_e}$ = expired vapor pressure, psi

$P_{H_2O_i}$ = inspired vapor pressure, psi

$P_g$ = pressure of dry gas, psi

To utilize the quick response of the computer system (Univac 1108 and teletype terminals), and to facilitate computer program writing and debugging basic language), equation (1) was rewritten into three parts (1) sensible gas, (2) sensible water vapor, and (3) insensible water vapor:

$$Q_r = \underset{(1)}{V_g \; \rho_g \, Cp_g (Te-Ti)} + \underset{(2)}{V_g \; \rho_g \; W_i \; Cp_{H_2O} (Te-Ti)} +$$

$$\underset{(3)}{\frac{h_{fg} \; V_g \; \rho_g \; M_{H_2O} \; (P_{H_2O_e} - P_{H_2O_i})}{M_g \quad P_g}} \tag{4}$$

The composition of inhaled and exhaled gas was calculated using measured values for oxygen and carbon dioxide.

The nitrogen component of chamber atmospheric gas was estimated at 1.11 atmospheres absolute partial pressure. This was based upon an initial pressurization to 15 feet using air. This resulted in an oxygen partial pressure of 0.3 ata and a corresponding nitrogen partial pressure of 1.2 ata. During the dive the provisioning lock was pressurized using helium resulting in a loss of 0.4 ata nitrogen for the volume of gas in the lock. Make-up gas for the chamber was 100% helium. A main chamber atmosphere gas sample obtained on the final day at 850 feet showed an oxygen plus nitrogen percentage of 5.28%. Since chamber atmosphere oxygen composition was 1.12%, the nitrogen composition was 5.28 - 1.12 = 4.16%, and, at 850 feet, the nitrogen partial pressure therefore was 1.11 atmospheres absolute.

The density of the expired gas was calculated using:

$$\rho_g = \frac{(P_e - P_{H_2O_e})\,144}{T_e\,R_e}, \tag{5}$$

in which the subscript e stands for expired values, and Re is the expired gas constant which was calculated as follows:

$$R_e = \frac{\%O_2\,M_{O_2}\,R_{O_2} + \%CO_2\,M_{CO_2}\,R_{CO_2} + \%N_2\,M_{N_2}\,R_{N_2} + \%He\,M_{H_e}\,R_{H_e}}{\%O_2\,M_{O_2} + \%CO_2\,M_{CO_2} + \%N_2\,M_{N_2} + \%He\,M_{He}} \tag{6}$$

The expired gas specific heat is:

$$Cp_e = \frac{\%O_2\,M_{O_2}\,Cp_{O_2} + \%CO_2\,M_{CO_2}\,Cp_{CO_2} + \%N_2\,M_{N_2}\,Cp_{N_2} + \%He\,M_{He}\,Cp_{He}}{\%O_2\,M_{O_2} + \%CO_2\,M_{CO_2} + \%N_2\,M_{N_2} + \%He\,M_{He}} \tag{7}$$

Equations (6) and (7) convert volume percent to mass fraction.

The latent heat of vaporization was taken as 1045 Btu/lbm, corresponding to a vaporization temperature of 85°F.

Equations (8), (9), and (10) for specific heat of $O_2$, $CO_2$, and $H_2O$ as a function of temperature were taken from Van Wylen (30). These equations were determined

for one atmosphere of pressure, and although they will change with pressure the overall effect on the specific heat of the gas mix is small:

$$Cp_{O_2} = \frac{1}{32}\left(11.515 - \frac{172}{\sqrt{T}} + \frac{1530}{T}\right) \quad (8)$$

$$Cp_{CO_2} = \frac{1}{44.01}\left(16.2 - \frac{6.53 \cdot 10^3}{T} + \frac{1.41 \cdot 10^6}{T^2}\right) \quad (9)$$

$$Cp_{H_2O} = \frac{1}{18.016}\left(19.86 - \frac{597}{\sqrt{T}} + \frac{7500}{T}\right) \quad (10)$$

A similar equation was given for nitrogen, but values calculated for low temperatures did not agree with corresponding values from other sources. Assuming a constant value of 0.247 Btu/lbm°F results in an error of less than 1% for the nitrogen fraction, or 0.04% for the mixture. The specific heat of helium is essentially constant at 1.24 Btu/lbm°F.

Since expired volume was measured with a dry gasometer a correction was made for the difference between the gasometer temperature and the expired temperature.

Vapor pressure was calculated using the formula for saturation pressure versus temperature from Smith, Keyes and Gerry (25):

$$\log_{10}\frac{218.167}{P_{H_2O}} = \frac{X}{T}\left[\frac{3.2437814 + 5.86826\ 10^{-3}\ X + 1.1702379.10^{-8}X^3}{1 + 2.1878462.10^{-3}X}\right] \quad (11)$$

where X = (647.27-T), °K P is in int. atm.

The computer could not solve this directly and an iteration procedure was used.

Units of the British Technical System were used for this calculation because of the abundance of data in engineering texts and references. Once heat loss is calculated in Btu/hr multiplying by 0.292833 converts the answer to watts, and mutiplying by 0.253 converts the answer to Kcal/hr. Similar conversions could be applied for density or specific heat if required.

The following assumptions were made:

1. Ideal gas laws apply for individual gases and ideal solutions are formed at every temperature and pressure. No data were found for thermodynamic properties of helium-oxygen mixtures and especially not for mixtures of helium-oxygen-nitrogen-carbon dioxide-water vapor.
2. Inspired gas is saturated at the inspired temperature. The temperature in the chamber was approximately 90°F and the relative humidity estimated at 50-80%. The resultant dew point was well above 55°F, the temperature of the warmest inspired gas.
3. Expired gas is saturated at the expired temperature.
4. Expired temperature is the mean expired temperature.

The complete computer program for calculating respiratory heat loss is included in Appendix 1.

SECTION 3

RESULTS

Respiratory Heat Loss

The 137 sets of measurements and the computed magnitudes of respiratory heat loss are listed consecutively, in Table I, in the order in which the data was obtained. Three sets of data are missing because the exposures were aborted voluntarily by the divers. The data number indicates the sequential data point in the total experiment and the run number indicates a diver-subject in the water. The next two columns index the data by depth in feet of seawater and by nominal water temperature in °F. TI and TE denote inhalation and exhalation temperature, respectively. Respiratory minute volume (RMV) is in liters per minute (BTPS). These values are slightly higher than the measured volumes exhaled, due to the correction to 37°C. Values of respiratory heat loss (RHL) were calculated using the respiratory minute volume at exhalation temperature. That portion of respiratory heat loss due to vaporization of water is shown as insensible heat loss in Kcal/hr. The final three columns are respiratory heat loss in units of Kcal/hr, Btu/hr and Watts.

Table I shows the essential components of the heat loss equation previously explained. The notable exceptions are the densities and specific heats of the breathing gases. Since these are relatively constant for a given depth, typical values are included below for the helium-oxygen-nitrogen-carbon dioxide mixes exhaled:

| Depth (feet) | $\rho$ ($lb_m/ft^3$) | Cp (Btu/$lb_m$-°F) | $\rho$ Cp (Btu/$ft^3$-°F) |
|---|---|---|---|
| 450 | .292 | .684 | .199 |
| 650 | .391 | .715 | .280 |
| 850 | .491 | .731 | .358 |
| 1000 | .565 | .735 | .415 |

Respiratory heat loss in Kcal/hr is illustrated as a function of respiratory minute volume in figures 10, 12, and 14. Figure 10 shows the calculated values derived from data acquired during the swims in 35°F water at depths of 450, 650, and 850 feet. Since the exhalation temperature did not vary significantly with depth, and the gas mixture was constant for a given depth, the relationship between RHL and RMV was expected to be linear. The magnitude of heat loss for a given RMV will be proportional to the density and specific heat of the gas mixture. This can be seen more clearly in Figure 11 which is the least squares regression for the data at each depth. The difference in heat capacity of the gas respired at 450 feet and at 650 feet is approximately the same as the heat capacity difference between the gas at 650 feet and 850 feet. This is seen in the regression coefficients for the different depths.

Figure 12 presents respiratory heat loss as a function of respiratory minute volume for data taken during swims in 45°F water. All data runs at 1000 ft were in 45°F water and these results are included in this figure. As anticipated, the difference between the slope of the 1000 ft data regression and the 850 ft data regression is less than slope differences for the other pairs of depths. The regression coefficients are shown in Figure 13.

Results at 850 feet are seen in Figure 14. The influence of changes in water (inhaled) temperature is also shown in Figure 15 (regression coefficients for RHL at 850 ft).

The insensible heat loss due to vaporization of water in the respiratory tract ranged between 5 and 26 Kcal/hr. This is plotted as percent of total respiratory heat loss (Figure 16). The respired gas was saturated at the inhalation temperature and assumed to be saturated at the exhalation temperature, which was considerably less than body core temperature. The variations in insensible heat loss with inhalation temperatures can be seen in Table I. Because the ranges of the different temperatures overlap considerably, the median and extreme values are marked for each depth.

Exhalation temperature as a function of inhalation temperature is shown in Figure 17. The exhalation temperature does not vary appreciably with depth and the total regression equation is TE = 22 + 0.649 TI. Figure 18 shows the inhalation-exhalation temperatures at 850 ft.

The mean respiratory minute volume for each diver-subject run was determined by dividing the total measured exhalation volume by the total elapsed time of the run. Since mean values of oxygen uptake and inhalation-exhalation temperature difference were required it was necessary to determine weighting factors for each of the four measurement periods, and for the rest periods during which no measurements were taken. The best correlation between measured mean RMV and the mean RMV calculated using weighting factors was found when the mean respiratory volume for the second and third rest periods equaled the respiratory volume for the light work period. Table II lists averaged measurements calculated using this weighting technique. The first three columns index the exposure according to run number, depth in feet and water temperature in °F and °C. Average Δ (TE-TI) is listed in column 5. The next three columns show the thermal imbalance of the diver's body as indicated by change in temperature. An average total body temperature is calculated using one third of the mean weighted skin temperature (Tmws) and two thirds of the rectal (core) temperature (Tr) (Burton, ref. 7 ). The change in total body temperature then becomes $\Delta T_b = 1/3\ \Delta Tmws + 2/3\ \Delta Tr$. The change in Tmws is listed in column 6, the change in Tr in column 7, and the change in $T_b$ in column 8. The last two columns show the mean respiratory minute volume (LPM, BTPS) and mean respiratory heat loss in kilogram-calories per hour.

Body Heat Balance

The mean weighted skin temperatures for each diver exposure are presented in Table III. These were calculated according to the method of Teichner, described earlier.

TABLE I

Results Of Respiratory Heat Loss Calculations

| DATA NO | RUN NO | DEPTH FT | TW F | TI C | TE C | RMV LPM | INSEN Q KCAL/HR | RHL KCAL/HR | RHL BTU/HR | RHL WATTS |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1 | 450 | 45 | 7.1 | 24.5 | 11.2 | 5 | 40 | 159 | 47 |
| 2 | 1 | 450 | 45 | 6.7 | 23.8 | 20.1 | 9 | 71 | 279 | 82 |
| 3 | 1 | 450 | 45 | 6.7 | 24.5 | 22.8 | 11 | 83 | 329 | 96 |
| 4 | 1 | 450 | 45 | 6.5 | 23.8 | 35.1 | 16 | 124 | 489 | 143 |
| 5 | 2 | 450 | 45 | 6.3 | 23.0 | 15.8 | 7 | 54 | 214 | 63 |
| 6 | 2 | 450 | 45 | 6.3 | 23.6 | 23.5 | 11 | 85 | 334 | 98 |
| 7 | 2 | 450 | 45 | 6.1 | 23.8 | 26.5 | 12 | 97 | 382 | 112 |
| 8 | 2 | 450 | 45 | 6.1 | 23.8 | 28.4 | 13 | 103 | 407 | 119 |
| 9 | 3 | 450 | 45 | 5.9 | 25.7 | 22.0 | 12 | 90 | 356 | 104 |
| 10 | 3 | 450 | 45 | 5.9 | 27.6 | 27.7 | 18 | 125 | 495 | 145 |
| 11 | 3 | 450 | 45 | 5.9 | 26.0 | 34.6 | 19 | 143 | 567 | 166 |
| 12 | 3 | 450 | 45 | 5.9 | 26.0 | 44.6 | 25 | 184 | 729 | 213 |
| 13 | 4 | 450 | 35 | 2.1 | 22.3 | 7.1 | 3 | 29 | 114 | 33 |
| 14 | 4 | 450 | 35 | 2.3 | 23.8 | 14.8 | 8 | 64 | 254 | 75 |
| 15 | 4 | 450 | 35 | 2.3 | 24.5 | 29.0 | 16 | 130 | 512 | 150 |
| 16 | 4 | 450 | 35 | 2.1 | 26.0 | 42.1 | 26 | 203 | 802 | 235 |
| 17 | 5 | 450 | 35 | 1.7 | 26.0 | 14.1 | 9 | 71 | 279 | 82 |
| 18 | 5 | 450 | 35 | 1.7 | 27.6 | 17.1 | 12 | 91 | 361 | 106 |
| 19 | 5 | 450 | 35 | 1.9 | 26.0 | 18.1 | 11 | 89 | 353 | 103 |
| 20 | 5 | 450 | 35 | 1.9 | 26.0 | 23.9 | 14 | 118 | 467 | 137 |
| 21 | 6 | 450 | 35 | 2.1 | 21.5 | 24.0 | 10 | 93 | 369 | 108 |
| 22 | 6 | 450 | 35 | 2.1 | 20.8 | 30.5 | 12 | 115 | 454 | 133 |
| 23 | 6 | 450 | 35 | 2.1 | 20.8 | 32.5 | 13 | 122 | 483 | 141 |
| 24 | 6 | 450 | 35 | 1.7 | 23.8 | 36.3 | 18 | 162 | 641 | 188 |
| 25 | 7 | 650 | 35 | 1.9 | 23.8 | 11.7 | 6 | 70 | 279 | 82 |
| 26 | 7 | 650 | 35 | 2.6 | 24.5 | 19.5 | 10 | 119 | 468 | 137 |
| 27 | 7 | 650 | 35 | 1.7 | 24.5 | 35.5 | 19 | 222 | 879 | 256 |
| 28 | 7 | 650 | 35 | 2.1 | 25.3 | 39.1 | 22 | 250 | 988 | 289 |
| 29 | 8 | 650 | 35 | 2.3 | 23.8 | 16.8 | 8 | 99 | 392 | 115 |
| 30 | 8 | 650 | 35 | 3.0 | 22.3 | 20.5 | 9 | 108 | 429 | 126 |
| 31 | 8 | 650 | 35 | 3.4 | 21.5 | 23.1 | 9 | 114 | 452 | 132 |
| 32 | 8 | 650 | 35 | 3.0 | 23.0 | 26.5 | 12 | 146 | 576 | 169 |
| 33 | 9 | 650 | 35 | 2.6 | 26.0 | 14.1 | 8 | 91 | 361 | 106 |
| 34 | 9 | 650 | 35 | 2.6 | 26.0 | 22.8 | 14 | 148 | 585 | 171 |
| 35 | 9 | 650 | 35 | 2.1 | 25.3 | 28.0 | 16 | 178 | 704 | 206 |
| 36 | 9 | 650 | 35 | 2.6 | 24.5 | 34.4 | 18 | 207 | 818 | 239 |
| 37 | 10 | 650 | 45 | 6.7 | 26.0 | 9.2 | 5 | 50 | 197 | 58 |
| 38 | 10 | 650 | 45 | 7.1 | 25.3 | 17.6 | 9 | 89 | 353 | 103 |
| 39 | 10 | 650 | 45 | 6.5 | 26.0 | 29.2 | 16 | 159 | 627 | 184 |
| 40 | 10 | 650 | 45 | 7.9 | 28.0 | 40.3 | 25 | 228 | 900 | 263 |
| 41 | 11 | 650 | 45 | 5.9 | 27.6 | 13.6 | 9 | 83 | 327 | 96 |
| 42 | 11 | 650 | 45 | 6.7 | 26.0 | 18.5 | 10 | 100 | 394 | 116 |
| 43 | 11 | 650 | 45 | 6.7 | 26.0 | 19.1 | 10 | 104 | 410 | 120 |
| 44 | 11 | 650 | 45 | 6.3 | 26.0 | 24.6 | 13 | 135 | 536 | 157 |
| 45 | 12 | 650 | 45 | 6.7 | 26.8 | 18.0 | 10 | 101 | 400 | 117 |

TABLE I

Results Of Respiratory Heat Loss Calculations (Continued)

| DATA NO | RUN NO | DEPTH FT | TW F | TI C | TE C | RMV LPM | INSEN Q KCAL/HR | RHL KCAL/HR | RHL BTU/HR | RHL WATTS |
|---|---|---|---|---|---|---|---|---|---|---|
| 46 | 12 | 650 | 45 | 6.9 | 27.6 | 24.7 | 15 | 144 | 567 | 166 |
| 47 | 12 | 650 | 45 | 6.7 | 26.8 | 30.2 | 17 | 170 | 673 | 197 |
| 48 | 12 | 650 | 45 | 7.7 | 26.0 | 36.4 | 19 | 186 | 736 | 216 |
| 49 | 13 | 850 | 55 | 12.5 | 28.4 | 8.2 | 5 | 47 | 186 | 55 |
| 50 | 13 | 850 | 55 | 12.7 | 28.4 | 16.5 | 9 | 92 | 366 | 107 |
| 51 | 13 | 850 | 55 | 13.0 | 29.2 | 27.7 | 16 | 160 | 634 | 186 |
| 52 | 13 | 850 | 55 | 12.5 | 29.2 | 33.7 | 20 | 200 | 792 | 232 |
| 53 | 14 | 850 | 55 | 12.7 | 28.4 | 12.5 | 7 | 71 | 279 | 82 |
| 54 | 14 | 850 | 55 | 13.0 | 27.6 | 20.7 | 10 | 109 | 430 | 126 |
| 55 | 14 | 850 | 55 | 13.0 | 28.4 | 22.1 | 12 | 123 | 485 | 142 |
| 56 | 14 | 850 | 55 | 13.0 | 28.4 | 24.4 | 13 | 135 | 535 | 157 |
| 57 | 15 | 850 | 55 | 12.3 | 29.2 | 15.3 | 9 | 93 | 369 | 108 |
| 58 | 15 | 850 | 55 | 12.3 | 28.4 | 22.2 | 12 | 129 | 510 | 149 |
| 59 | 15 | 850 | 55 | 12.7 | 28.4 | 22.6 | 12 | 128 | 507 | 148 |
| 60 | 15 | 850 | 55 | 12.7 | 29.2 | 24.5 | 14 | 147 | 581 | 170 |
| 61 | 16 | 850 | 45 | 7.9 | 26.0 | 11.0 | 6 | 70 | 278 | 81 |
| 62 | 16 | 850 | 45 | 7.7 | 27.6 | 25.6 | 15 | 181 | 714 | 209 |
| 63 | 16 | 850 | 45 | 7.5 | 27.6 | 34.8 | 21 | 248 | 979 | 287 |
| 64 | 16 | 850 | 45 | 7.5 | 27.6 | 39.1 | 23 | 278 | 1098 | 321 |
| 65 | 17 | 850 | 45 | 7.3 | 27.6 | 16.7 | 10 | 120 | 475 | 139 |
| 66 | 17 | 850 | 45 | 7.3 | 26.8 | 28.0 | 16 | 193 | 761 | 223 |
| 67 | 17 | 850 | 45 | 7.3 | 26.8 | 31.8 | 18 | 219 | 864 | 253 |
| 68 | 17 | 850 | 45 | 6.9 | 26.0 | 34.8 | 18 | 234 | 924 | 271 |
| 69 | 18 | 850 | 45 | 7.1 | 28.4 | 19.5 | 13 | 147 | 582 | 170 |
| 70 | 18 | 850 | 45 | 6.9 | 28.4 | 28.0 | 18 | 213 | 842 | 247 |
| 71 | 18 | 850 | 45 | 7.5 | 27.6 | 35.0 | 21 | 248 | 979 | 287 |
| 72 | 18 | 850 | 45 | 6.7 | 26.8 | 36.0 | 21 | 254 | 1004 | 294 |
| 73 | 19 | 1000 | 45 | 7.1 | 26.8 | 11.1 | 6 | 89 | 354 | 104 |
| 74 | 19 | 1000 | 45 | 7.5 | 27.6 | 18.4 | 11 | 152 | 600 | 176 |
| 75 | 19 | 1000 | 45 | 6.9 | 28.4 | 30.3 | 20 | 265 | 1047 | 307 |
| 76 | 19 | 1000 | 45 | 7.5 | 28.4 | 34.0 | 22 | 290 | 1146 | 336 |
| 77 | 20 | 1000 | 45 | 7.5 | 26.8 | 15.3 | 9 | 120 | 475 | 139 |
| 78 | 20 | 1000 | 45 | 7.1 | 26.0 | 25.0 | 13 | 191 | 755 | 221 |
| 79 | 20 | 1000 | 45 | 7.1 | 26.8 | 28.8 | 16 | 231 | 913 | 267 |
| 80 | 20 | 1000 | 45 | 7.3 | 26.0 | 28.5 | 15 | 216 | 855 | 250 |
| 81 | 21 | 1000 | 45 | 6.7 | 28.4 | 19.9 | 13 | 177 | 698 | 205 |
| 82 | 21 | 1000 | 45 | 6.9 | 27.6 | 26.8 | 16 | 225 | 891 | 261 |
| 83 | 21 | 1000 | 45 | 7.1 | 28.4 | 29.2 | 19 | 254 | 1005 | 294 |
| 84 | 21 | 1000 | 45 | 7.1 | 28.4 | 36.4 | 23 | 316 | 1250 | 366 |
| 85 | 22 | 850 | 35 | 3.2 | 26.0 | 8.3 | 5 | 67 | 263 | 77 |
| 86 | 22 | 850 | 35 | 3.0 | 26.0 | 13.5 | 8 | 109 | 432 | 127 |
| 87 | 22 | 850 | 35 | 3.2 | 26.0 | 20.7 | 12 | 165 | 654 | 192 |
| 88 | 22 | 850 | 35 | 3.2 | 26.0 | 28.6 | 17 | 228 | 901 | 264 |
| 89 | 23 | 850 | 35 | 3.2 | 26.0 | 17.5 | 10 | 139 | 550 | 161 |
| 90 | 23 | 850 | 35 | 3.0 | 25.3 | 30.4 | 17 | 236 | 933 | 273 |

TABLE I

Results Of Respiratory Heat Loss Calculations (Continued)

| DATA NO | RUN NO | DEPTH FT | TW F | TI C | TE C | RMV LPM | INSEN @ KCAL/HR | RHL KCAL/HR | RHL BTU/HR | RHL WATTS |
|---|---|---|---|---|---|---|---|---|---|---|
| 91 | 23 | 850 | 35 | 3.0 | 26.8 | 41.0 | 26 | 341 | 1347 | 394 |
| 92 | 23 | 850 | 35 | .0 | .0 | .0 | 0 | 0 | 0 | 0 |
| 93 | 24 | 850 | 35 | 2.7 | 27.6 | 19.6 | 13 | 172 | 679 | 199 |
| 94 | 24 | 850 | 35 | 2.7 | 26.8 | 31.1 | 19 | 262 | 1035 | 303 |
| 95 | 24 | 850 | 35 | 3.0 | 26.0 | 38.1 | 22 | 305 | 1207 | 353 |
| 96 | 24 | 850 | 35 | .0 | .0 | 10.1 | 0 | 0 | 0 | 0 |
| 97 | 25 | 850 | 35 | 2.7 | 26.0 | .0 | 6 | 82 | 324 | 95 |
| 98 | 25 | 850 | 35 | 3.4 | 25.3 | 15.7 | 9 | 121 | 477 | 140 |
| 99 | 25 | 850 | 35 | 3.2 | 26.0 | 23.0 | 13 | 183 | 722 | 211 |
| 100 | 25 | 850 | 35 | 2.6 | 26.0 | 29.0 | 17 | 237 | 935 | 274 |
| 101 | 26 | 850 | 35 | 2.7 | 25.3 | 21.0 | 12 | 165 | 652 | 191 |
| 102 | 26 | 850 | 35 | 3.0 | 25.3 | 24.5 | 14 | 190 | 752 | 220 |
| 103 | 26 | 850 | 35 | 3.2 | 25.3 | 32.7 | 18 | 252 | 996 | 292 |
| 104 | 26 | 850 | 35 | 3.2 | 25.3 | 36.5 | 20 | 281 | 1111 | 325 |
| 105 | 27 | 850 | 35 | 2.7 | 27.6 | 22.8 | 15 | 200 | 788 | 231 |
| 106 | 27 | 850 | 35 | 3.2 | 27.6 | 35.4 | 23 | 303 | 1197 | 350 |
| 107 | 27 | 850 | 35 | 3.4 | 26.8 | 41.7 | 26 | 341 | 1349 | 395 |
| 108 | 27 | 850 | 35 | .0 | .0 | 7.7 | 0 | 0 | 0 | 0 |
| 109 | 28 | 850 | 35 | 3.8 | 26.0 | 13.3 | 4 | 60 | 237 | 69 |
| 110 | 28 | 850 | 35 | 3.0 | 25.3 | .0 | 7 | 104 | 411 | 120 |
| 111 | 28 | 850 | 35 | 3.2 | 26.0 | 21.6 | 13 | 172 | 679 | 199 |
| 112 | 28 | 850 | 35 | 3.0 | 26.0 | 34.5 | 20 | 276 | 1092 | 320 |
| 113 | 29 | 850 | 35 | 3.4 | 26.0 | 24.4 | 14 | 191 | 755 | 221 |
| 114 | 29 | 850 | 35 | 3.2 | 25.3 | 24.3 | 14 | 187 | 739 | 216 |
| 115 | 29 | 850 | 35 | 3.2 | 25.3 | 31.7 | 18 | 243 | 959 | 281 |
| 116 | 29 | 850 | 35 | 2.6 | 24.5 | 37.7 | 20 | 286 | 1130 | 331 |
| 117 | 30 | 850 | 35 | 3.2 | 26.8 | 13.3 | 8 | 110 | 433 | 127 |
| 118 | 30 | 850 | 35 | 3.0 | 26.0 | 24.6 | 14 | 197 | 778 | 228 |
| 119 | 30 | 850 | 35 | 3.0 | 26.8 | 28.7 | 18 | 239 | 944 | 277 |
| 120 | 30 | 850 | 35 | 3.0 | 26.4 | 37.7 | 23 | 307 | 1212 | 355 |
| 121 | 31 | 850 | 45 | 7.9 | 27.6 | 4.7 | 3 | 33 | 132 | 39 |
| 122 | 31 | 850 | 45 | 7.9 | 26.8 | 11.9 | 7 | 80 | 315 | 92 |
| 123 | 31 | 850 | 45 | 7.9 | 26.8 | 18.8 | 10 | 125 | 495 | 145 |
| 124 | 31 | 850 | 45 | 7.5 | 26.8 | 21.4 | 12 | 145 | 575 | 168 |
| 125 | 32 | 850 | 45 | 7.3 | 28.4 | 9.9 | 6 | 75 | 295 | 86 |
| 126 | 32 | 850 | 45 | 7.1 | 26.8 | 19.8 | 11 | 138 | 544 | 159 |
| 127 | 32 | 850 | 45 | 7.1 | 26.8 | 24.7 | 14 | 172 | 679 | 199 |
| 128 | 32 | 850 | 45 | 7.5 | 27.6 | 29.9 | 18 | 213 | 841 | 246 |
| 129 | 33 | 850 | 35 | 3.0 | 25.3 | 8.5 | 5 | 66 | 262 | 77 |
| 130 | 33 | 850 | 35 | 3.0 | 25.3 | 17.2 | 10 | 133 | 526 | 154 |
| 131 | 33 | 850 | 35 | 3.0 | 26.0 | 25.8 | 15 | 207 | 819 | 240 |
| 132 | 33 | 850 | 35 | 3.0 | 26.0 | 30.7 | 18 | 246 | 973 | 285 |
| 133 | 34 | 850 | 35 | 3.2 | 26.0 | 15.0 | 9 | 120 | 474 | 139 |
| 134 | 34 | 850 | 35 | 3.2 | 25.3 | 25.0 | 14 | 192 | 758 | 222 |
| 135 | 34 | 850 | 35 | 3.2 | 25.3 | 21.5 | 12 | 165 | 653 | 191 |

TABLE I

*Results of Respiratory Heat Loss Calculations (Continued)*

| DATA NO | RUN NO | DEPTH FT | TW F | TI C | TE C | RMV LPM | INSEN Q KCAL/HR | RHL KCAL/HR | RHL BTU/HR | RHL WATTS |
|---|---|---|---|---|---|---|---|---|---|---|
| 136 | 34 | 850 | 35 | 3.2 | 25.3 | 28.1 | 15 | 217 | 856 | 251 |
| 137 | 35 | 850 | 35 | 2.6 | 27.6 | 16.1 | 11 | 141 | 559 | 164 |
| 138 | 35 | 850 | 35 | 3.0 | 26.0 | 26.6 | 16 | 213 | 842 | 247 |
| 139 | 35 | 850 | 35 | 3.2 | 26.0 | 35.6 | 21 | 282 | 1115 | 327 |
| 140 | 35 | 850 | 35 | 3.0 | 25.3 | 42.7 | 25 | 342 | 1350 | 395 |

NOW AT 130

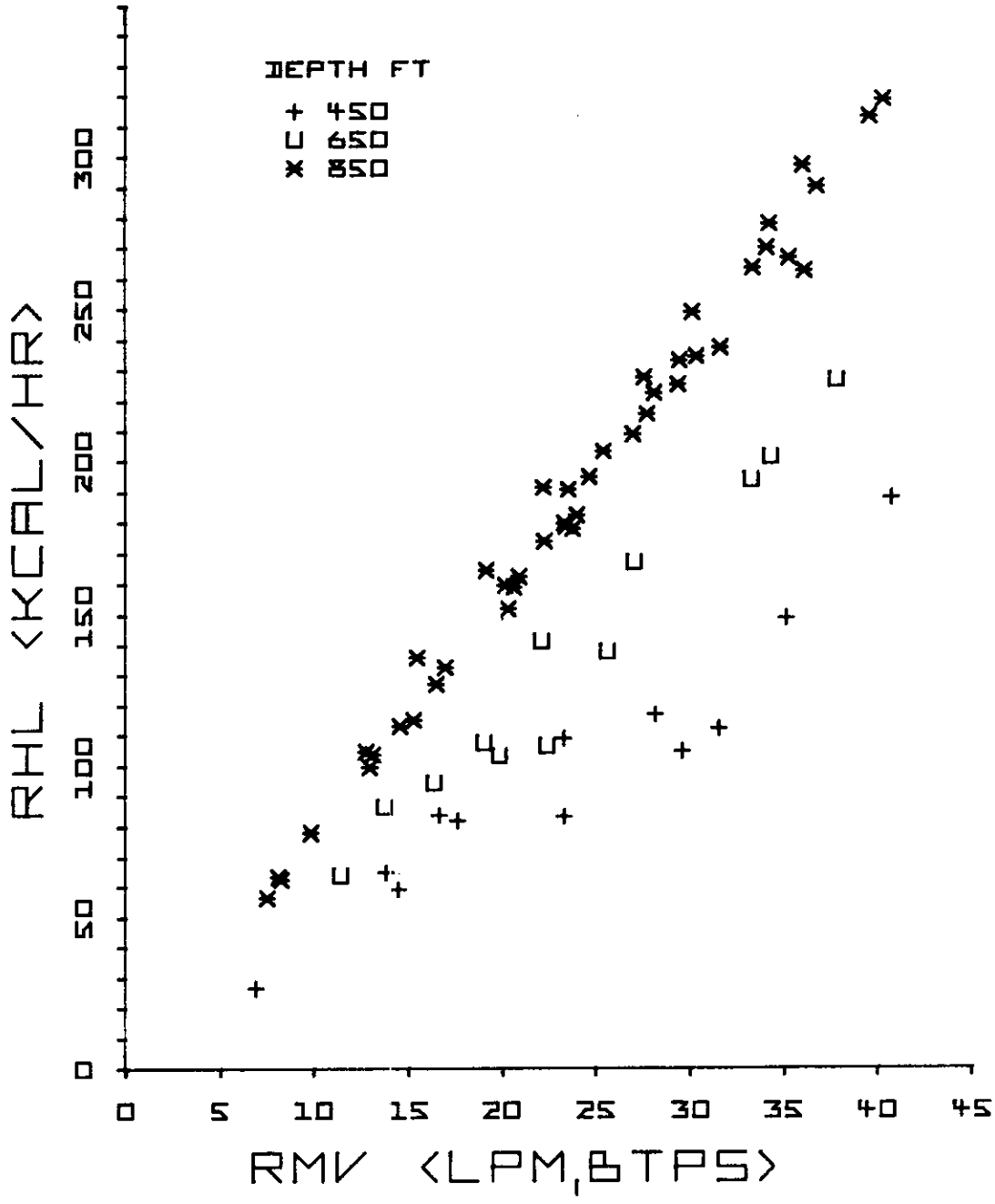


Figure 10. Water Temperature 35°F: Respiratory Heat Loss As A Function Of Ventilation During Data Runs At 450, 650, and 850 Feet.

3-7

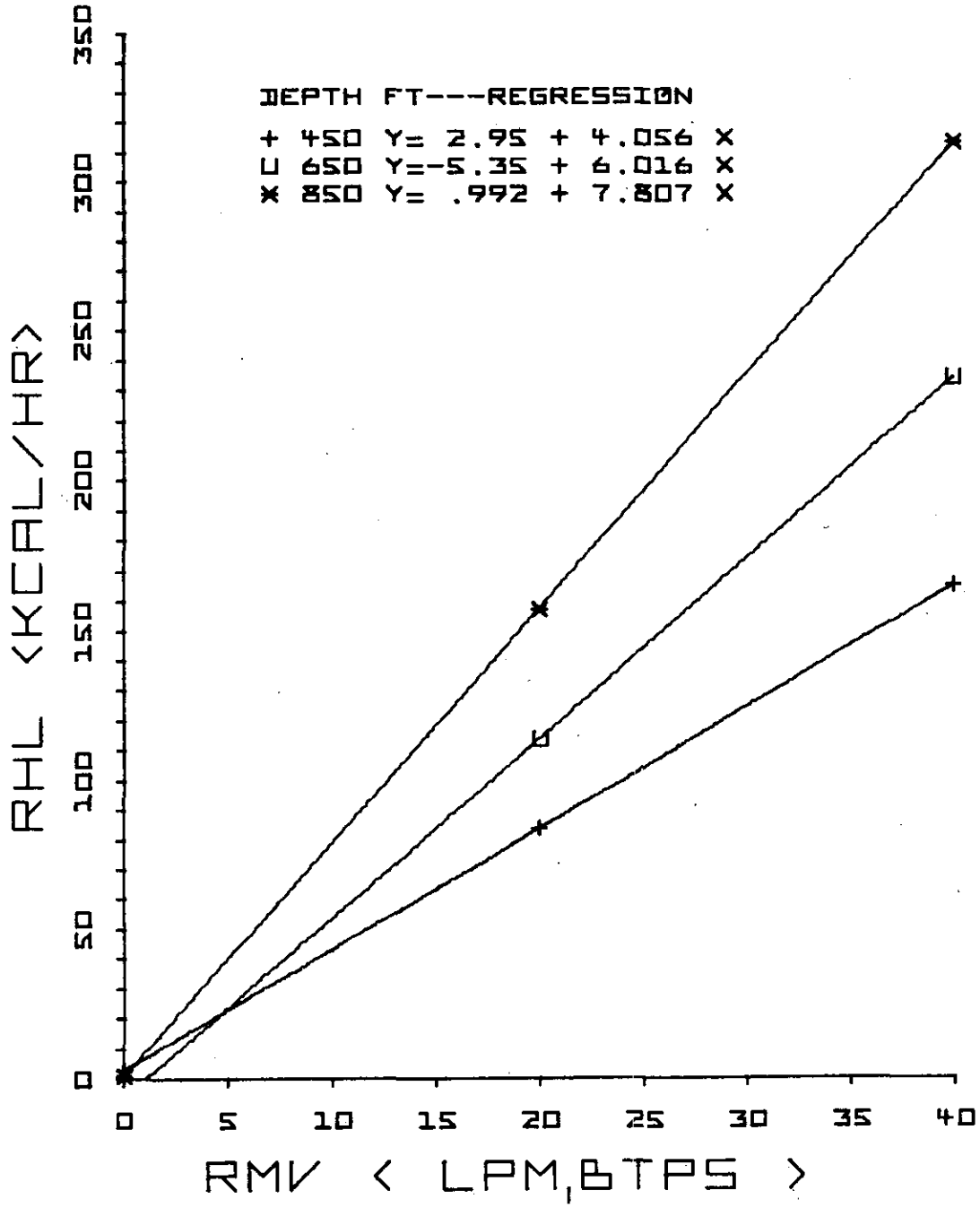


Figure 11. Water Temperature 35°F: Regression Lines For Respiratory Heat Loss As A Function Of Ventilation During Data Runs At 450, 650, and 850 Feet.

3-8

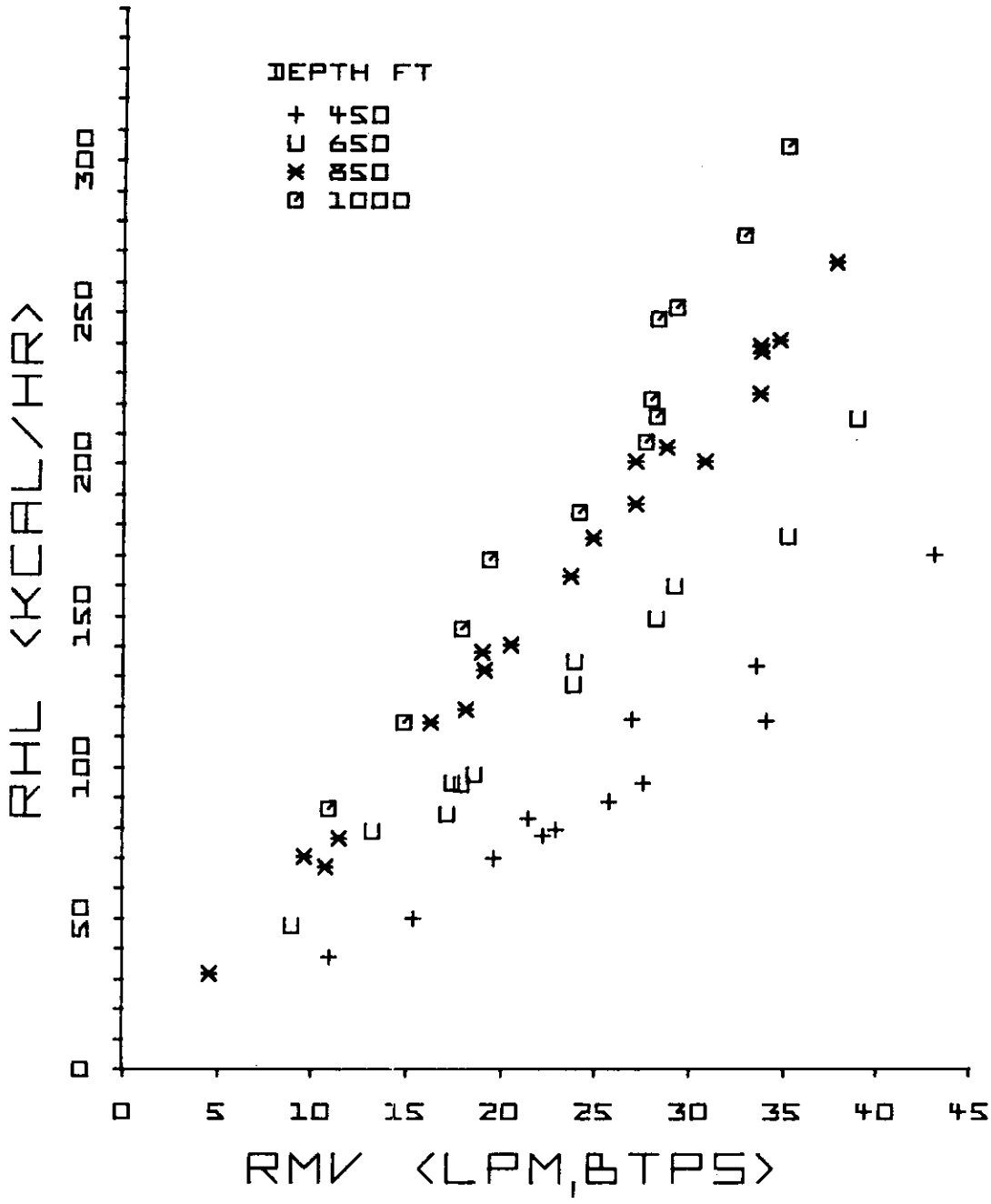


Figure 12. Water Temperature 45°F: Respiratory Heat Loss As A Function Of Ventilation During Data Runs at 450, 650 and 1,000 Feet.

3-9

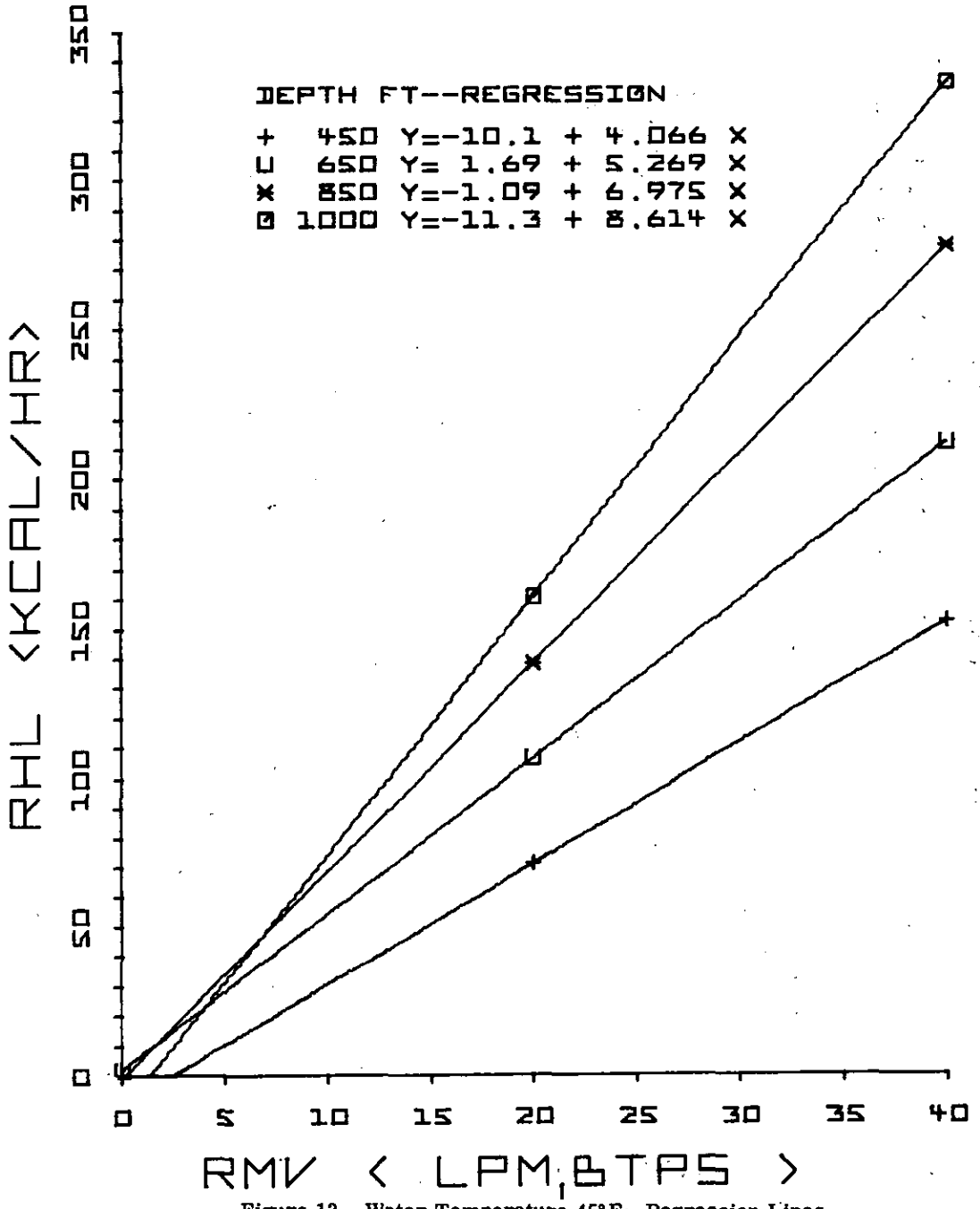


Figure 13. Water Temperature 45°F: Regression Lines For Respiratory Heat Loss As A Function Of Ventilation During Data Runs At 450, 650, 850 and 1,000 Feet.

3-10

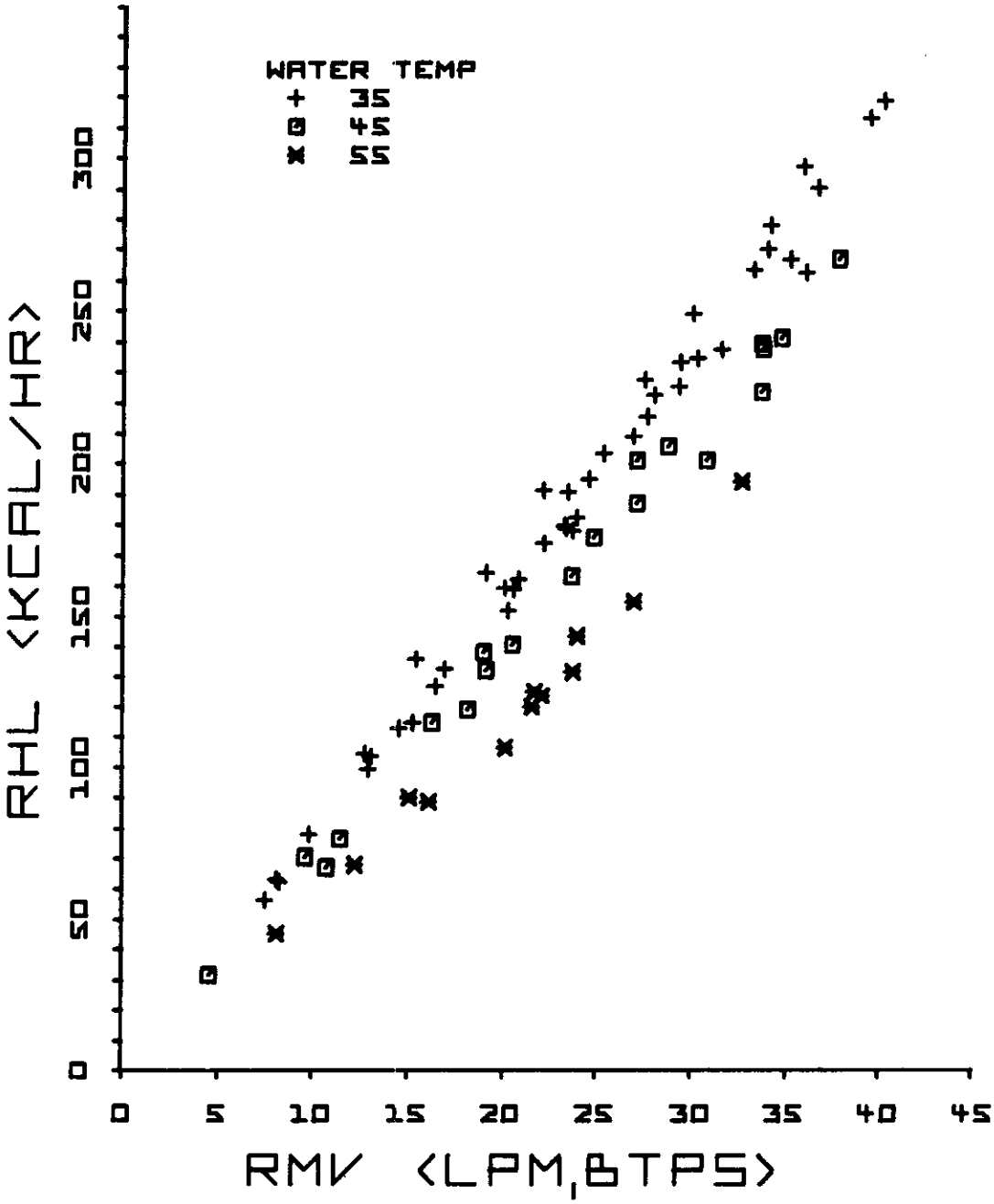


Figure 14. Depth 850 Feet: Respiratory Heat Loss As A Function Of Ventilation During Data Runs At Nominal Water Temperatures of 35°F, 45°F and 55°F.

3-11

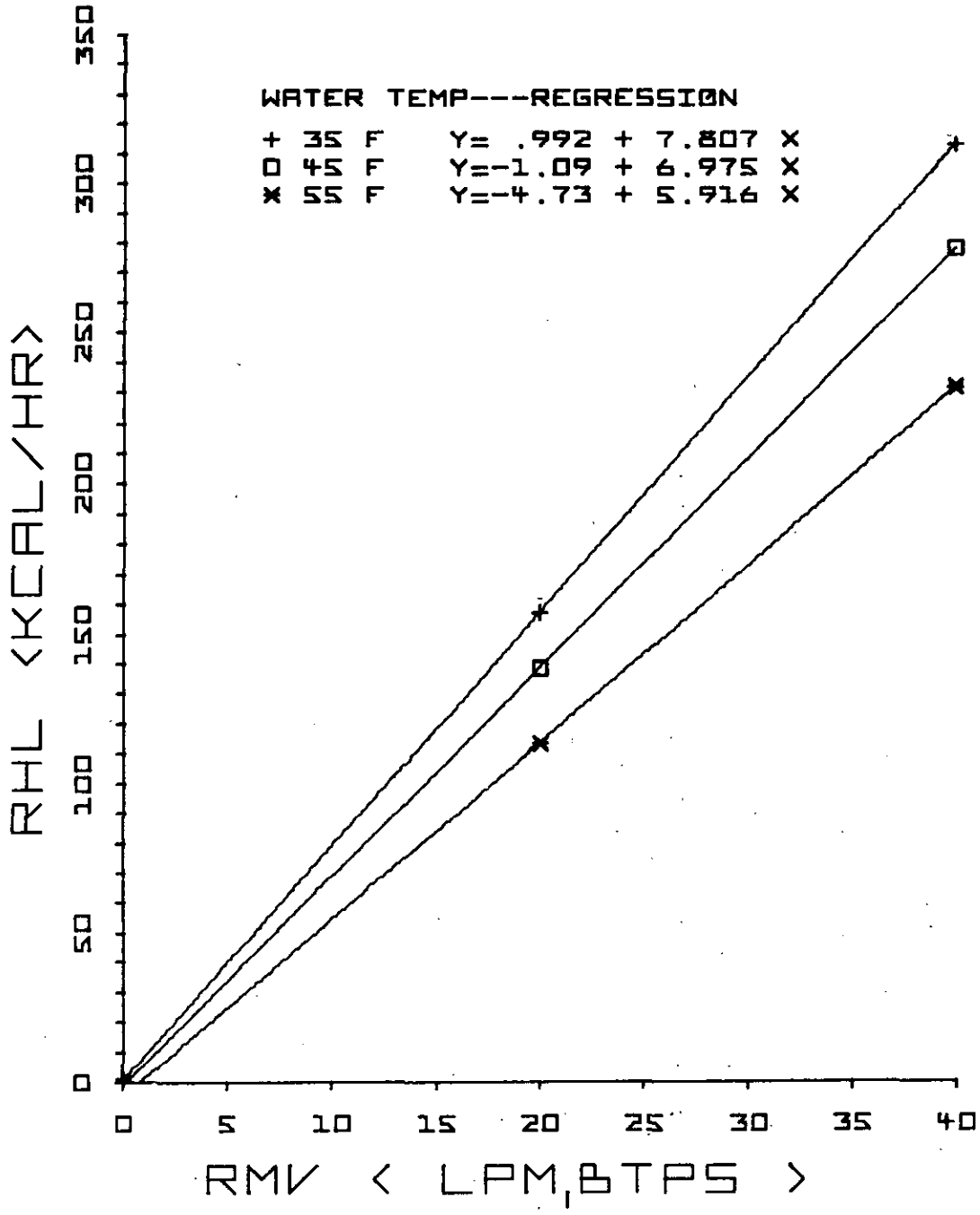


Figure 15. Depth 850 Feet: Regression Lines For Respiratory Heat Loss As A Function Of Ventilation During Data Runs At Nominal Water Temperatures of 35°F, 45° F and 55°F.

3-12

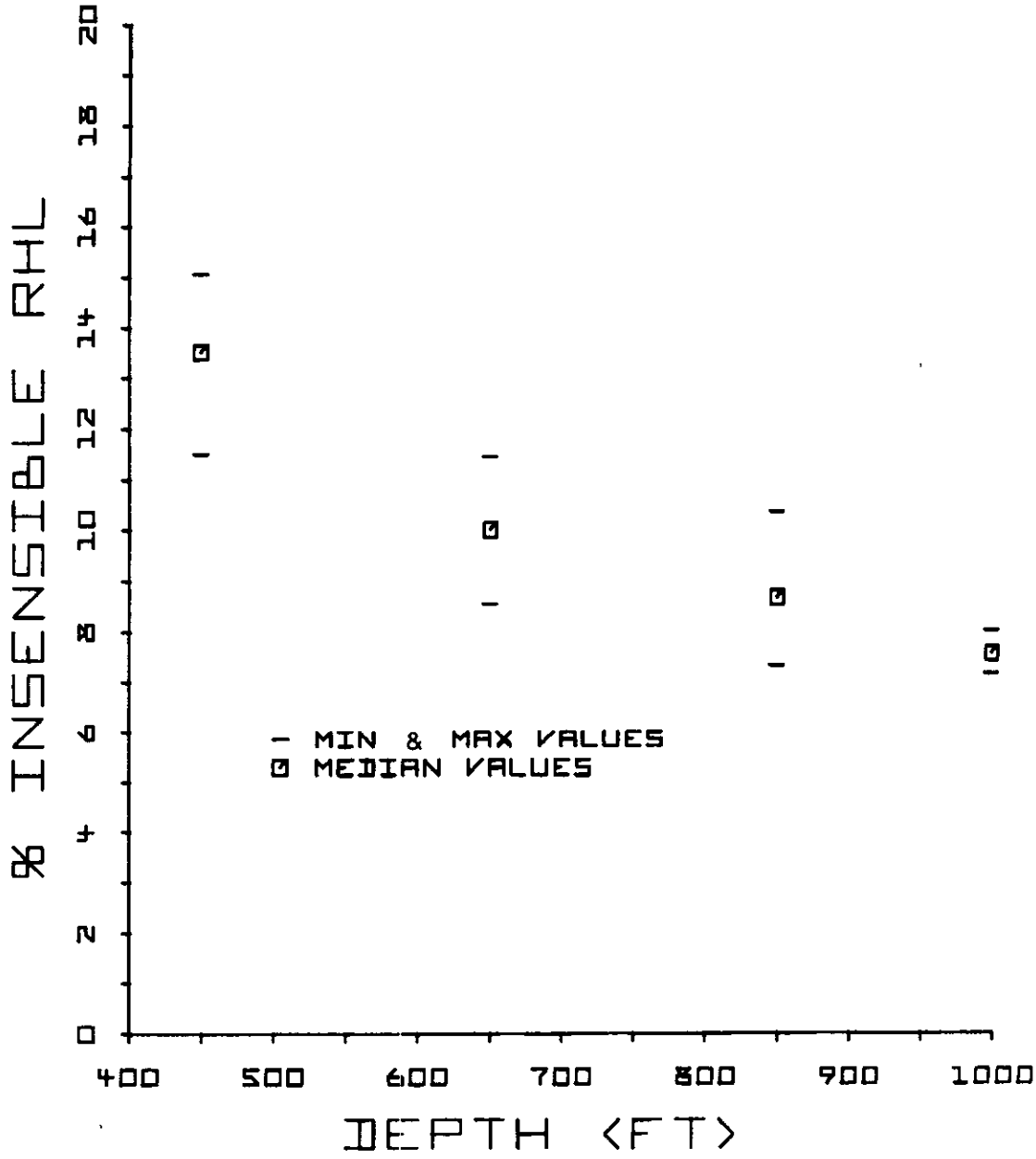


Figure 16. Insensible Heat Loss Fraction of Total Respiratory Heat Loss.

3-13

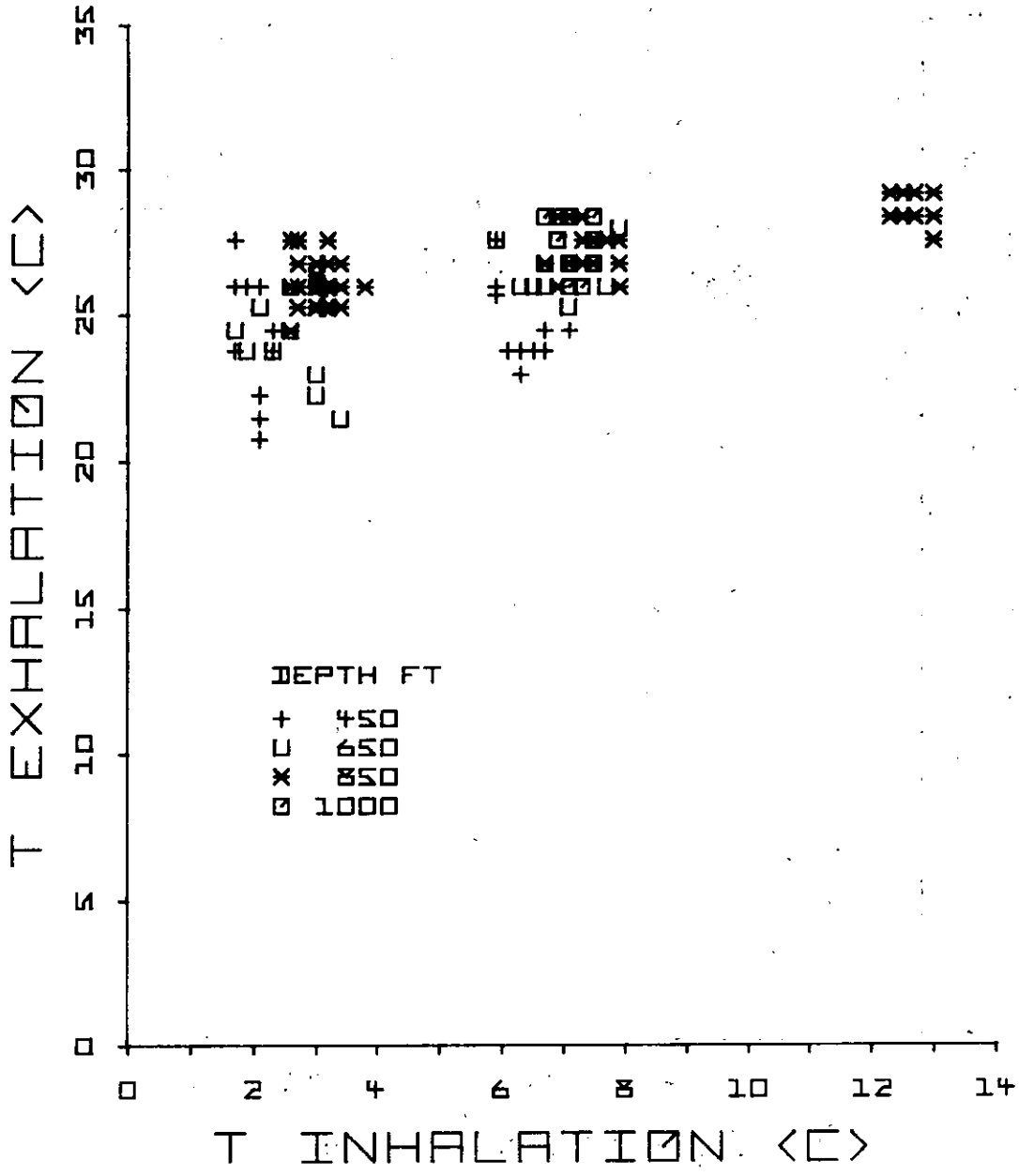


Figure 17. Relationship Between Observed Temperatures (°C) Of Inhaled and Exhaled Gases.

3-14

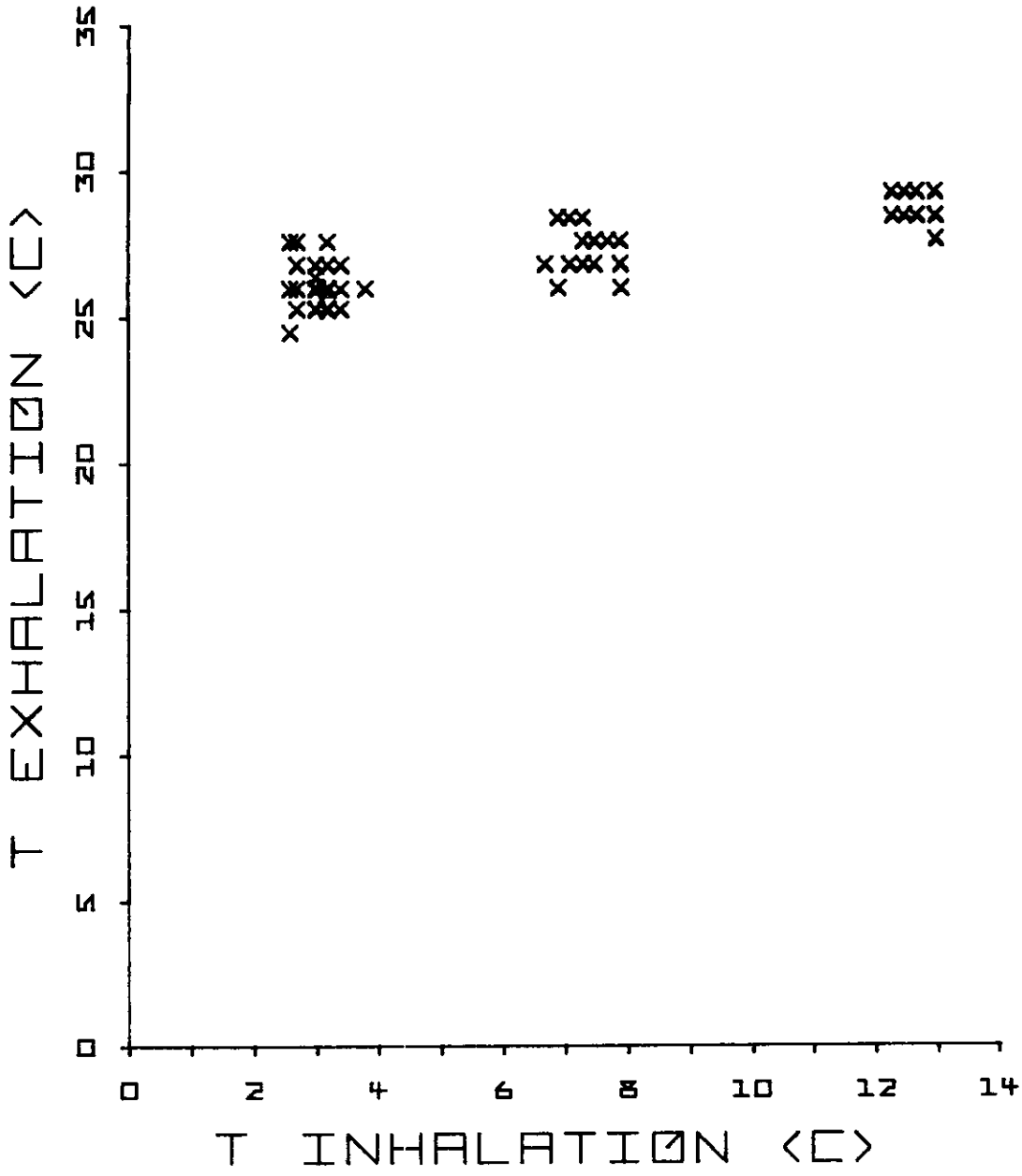


Figure 18. Depth 850 Feet: Relationship Between Observed Temperatures (°C) Of Inhaled And Exhaled Gases.

3-15

## TABLE II

### Averaged Parameters Of Respiratory Heat Loss And Thermal Balance For Each Immersion Exposure.

| Run No | Depth Ft | T Water °F | T Water °C | TE-TI AVG °C | Δ T MWS °C | Δ T Rectal °C | Δ T Body °C | RMV-AVG LPM | RHL AVG Kcal/hr |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 450 | 45 | 7.2 | 17.3 | +0.27 | xx | xx | 22.4 | 80 |
| 2 | 450 | 45 | 7.2 | 17.5 | -0.38 | -0.44 | - .42 | 23.9 | 86 |
| 3 | 450 | 45 | 7.2 | 20.7 | -1.29 | -1.66 | -1.53 | 31.2 | 136 |
| 4 | 450 | 35 | 1.7 | 21.9 | -2.02 | -0.32 | -0.88 | 22.1 | 102 |
| 5 | 450 | 35 | 1.7 | 24.9 | -1.56 | -0.81 | -1.04 | 18.1 | 93 |
| 6 | 450 | 35 | 1.7 | 19.5 | -2.20 | -1.61 | -1.80 | 31.0 | 123 |
| 7 | 650 | 35 | 1.7 | 22.4 | -3.22 | -0.73 | -1.55 | 25.4 | 161 |
| 8 | 650 | 35 | 1.7 | 19.5 | -2.61 | -0.49 | - .90 | 21.6 | 116 |
| 9 | 650 | 35 | 1.7 | 23.0 | -1.57 | -1.44 | -1.48 | 24.5 | 158 |
| 10 | 650 | 45 | 7.2 | 19.0 | - .73 | -0.31 | -0.45 | 23.0 | 127 |
| 11 | 650 | 45 | 7.2 | 19.8 | -2.20 | -0.53 | -1.09 | 18.8 | 105 |
| 12 | 650 | 45 | 7.2 | 20.0 | -2.14 | -1.21 | -1.52 | 26.6 | 151 |
| 13 | 850 | 55 | 12.8 | 16.0 | -1.22 | -0.50 | -0.74 | 20.7 | 122 |
| 14 | 850 | 55 | 12.8 | 15.1 | -2.01 | -0.81 | -1.21 | 20.2 | 111 |
| 15 | 850 | 55 | 12.8 | 16.2 | -0.85 | -0.80 | -0.82 | 21.6 | 127 |
| 16 | 850 | 45 | 7.2 | 19.7 | -3.29 | -0.47 | -1.48 | 27.3 | 198 |
| 17 | 850 | 45 | 7.2 | 19.5 | -1.83 | -0.89 | -1.20 | 27.7 | 195 |
| 18 | 850 | 45 | 7.2 | 20.9 | -1.82 | -0.93 | -1.23 | 28.9 | 219 |
| 19 | 1000 | 45 | 7.2 | 20.5 | -2.24 | -0.46 | -1.05 | 22.5 | 195 |
| 20 | 1000 | 45 | 7.2 | 19.1 | -1.48 | -0.94 | -1.12 | 24.5 | 194 |
| 21 | 1000 | 45 | 7.2 | 21.1 | -1.87 | -0.84 | -1.25 | 27.4 | 243 |
| 22 | 850 | 35 | 1.7 | 22.9 | +0.84 | -0.46 | -0.59 | 17.1 | 139 |
| 23 | 850 | 35 | 1.7 | 22.6 | -1.66 | -0.71 | -1.03 | 29.9 | 246 |
| 24 | 850 | 35 | 1.7 | 23.7 | -0.87 | -1.52 | -1.29 | 29.8 | 254 |
| 25 | 850 | 35 | 1.7 | 22.6 | -1.35 | -0.62 | -0.86 | 18.8 | 152 |
| 26 | 850 | 35 | 1.7 | 22.3 | 2.11 | -1.00 | -1.37 | 27.5 | 218 |
| 27 | 850 | 35 | 1.7 | 24.0 | -1.96 | -1.12 | -1.40 | 33.4 | 291 |
| 28 | 850 | 35 | 1.7 | 22.5 | -0.80 | -0.91 | -0.87 | 18.3 | 148 |
| 29 | 850 | 35 | 1.7 | 22.1 | -1.44 | -0.65 | -0.91 | 27.9 | 220 |
| 30 | 850 | 35 | 1.7 | 23.3 | -0.33 | -1.21 | -1.90 | 25.7 | 215 |
| 31 | 850 | 45 | 7.2 | 19.1 | -0.61 | -0.59 | -0.60 | 14.0 | 96 |
| 32 | 850 | 45 | 7.2 | 20.0 | -1.16 | -0.70 | -0.85 | 20.9 | 151 |
| 33 | 850 | 35 | 1.7 | 22.6 | -2.41 | -1.14 | -1.56 | 20.0 | 162 |
| 34 | 850 | 35 | 1.7 | 22.2 | -1.52 | -0.82 | -1.05 | 22.8 | 180 |
| 35 | 850 | 35 | 1.7 | 23.1 | -2.46 | -1.55 | -1.85 | 29.7 | 243 |

TABLE III

Time Sequence For Mean Weighted Skin Temperature

| RUN NO. | DEPTH FT | TW F | SUB | REST 1 | LIGHT WORK 2 | REST 3 | MEDIUM WORK 4 | REST 5 | HARD WORK 6 | 7 | MEAN TMWS F | C |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 450 | 45 | KC | 88.1 | 90.2 | 87.9 | 89.0 | 88.9 | 88.1 | 88.6 | 88.3 | 31.3 |
| 2 | 450 | 45 | SZ | 93.9 | 95.7 | 91.9 | 92.7 | 92.0 | 91.2 | 93.2 | 93.5 | 34.2 |
| 3 | 450 | 45 | FA | 94.4 | 92.3 | 91.6 | 91.3 | 92.3 | 91.7 | 92.1 | 93.2 | 34.0 |
| 4 | 450 | 35 | KC | 93.5 | 93.5 | 90.3 | 90.7 | 89.9 | 89.7 | 89.8 | 91.7 | 33.2 |
| 5 | 450 | 35 | SZ | 94.1 | 95.8 | 93.4 | 93.9 | 91.3 | 91.5 | 91.3 | 92.7 | 33.7 |
| 6 | 450 | 35 | FA | 93.8 | 93.1 | 91.4 | 91.8 | 90.2 | 91.5 | 89.9 | 91.8 | 33.2 |
| 7 | 650 | 35 | KC | 93.7 | 91.0 | 89.0 | 91.5 | 89.2 | 90.0 | 87.9 | 90.7 | 32.6 |
| 8 | 650 | 35 | SZ | 96.5 | 94.6 | 92.7 | 93.8 | 93.3 | 94.6 | 91.7 | 94.1 | 34.5 |
| 9 | 650 | 35 | FA | 96.1 | 96.9 | 95.5 | 96.7 | 94.9 | 95.6 | 93.2 | 94.7 | 34.8 |
| 10 | 650 | 45 | KC | 93.7 | 93.8 | 91.4 | 92.2 | 92.5 | 93.6 | 92.4 | 93.1 | 33.9 |
| 11 | 650 | 45 | SZ | 94.2 | 94.7 | 92.4 | 93.0 | 91.8 | 93.1 | 90.3 | 92.2 | 33.4 |
| 12 | 650 | 45 | FA | 95.8 | 95.3 | 92.4 | 92.5 | 92.3 | 94.3 | 92.0 | 93.9 | 34.4 |
| 13 | 850 | 55 | KC | 94.0 | 94.1 | 93.3 | 94.2 | 92.7 | 93.3 | 91.8 | 92.9 | 33.8 |
| 14 | 850 | 55 | SZ | 93.9 | 92.3 | 90.1 | 91.0 | 90.8 | 91.1 | 90.2 | 92.1 | 33.4 |
| 15 | 850 | 55 | FA | 97.0 | 99.2 | 96.6 | 98.6 | 96.9 | 98.5 | 95.4 | 96.1 | 35.6 |
| 16 | 650 | 45 | KC | 96.4 | 92.5 | 90.7 | 91.2 | 89.5 | 91.2 | 90.5 | 93.4 | 34.1 |
| 17 | 650 | 45 | SZ | 92.8 | 90.6 | 89.3 | 92.0 | 91.1 | 92.2 | 89.6 | 91.2 | 32.9 |
| 18 | 650 | 45 | FA | 94.3 | 95.5 | 92.6 | 95.1 | 91.2 | 93.5 | 91.0 | 92.7 | 33.7 |
| 19 | 1000 | 45 | KC | 99.1 | 98.0 | 95.8 | 97.4 | 95.7 | 96.4 | 95.1 | 97.1 | 36.2 |
| 20 | 1000 | 45 | SZ | 95.0 | 95.8 | 93.2 | 94.6 | 92.9 | 94.0 | 92.4 | 93.7 | 34.3 |
| 21 | 1000 | 45 | FA | 95.6 | 95.8 | 95.2 | 95.2 | 92.9 | 94.1 | 92.2 | 93.9 | 34.4 |
| 22 | 850 | 35 | KC | 92.1 | 94.3 | 92.6 | 93.2 | 95.0 | 95.8 | 93.6 | 92.8 | 33.8 |
| 23 | 850 | 35 | SZ | 94.5 | 92.4 | 93.6 | 91.5 | | | | 93.0 | 33.9 |
| 24 | 850 | 35 | FA | 91.9 | 92.3 | 88.2 | 89.2 | 90.3 | | | 91.1 | 32.8 |
| 25 | 850 | 35 | KC | 93.9 | 92.5 | 93.4 | 92.1 | 92.8 | 92.9 | 91.5 | 92.7 | 33.7 |
| 26 | 850 | 35 | SZ | 93.6 | 96.1 | 93.0 | 95.4 | 93.6 | 91.3 | 89.8 | 91.7 | 33.2 |
| 27 | 850 | 35 | FA | 93.9 | 94.2 | 90.9 | 91.8 | 90.3 | | | 92.1 | 33.4 |
| 28 | 850 | 35 | KC | 94.8 | 95.5 | 93.6 | 93.7 | 93.2 | 92.3 | 93.4 | 94.1 | 34.5 |
| 29 | 850 | 35 | SZ | 93.3 | 91.4 | 90.8 | 90.3 | 90.6 | 90.6 | 90.7 | 92.0 | 33.3 |
| 30 | 850 | 35 | FA | 94.1 | 96.3 | 94.2 | 94.8 | 92.5 | 94.5 | 93.5 | 93.8 | 34.3 |
| 31 | 850 | 45 | KC | 95.3 | 96.8 | 94.5 | 96.7 | 95.1 | 95.6 | 94.2 | 94.7 | 34.8 |
| 32 | 850 | 45 | FA | 97.6 | 99.3 | 97.9 | 100.3 | 96.4 | 98.5 | 95.6 | 96.6 | 35.9 |
| 33 | 850 | 35 | KC | 97.6 | 97.2 | 95.0 | 95.2 | 94.2 | 94.6 | 93.3 | 95.4 | 35.2 |
| 34 | 850 | 35 | SZ | 93.8 | 91.8 | 91.5 | 91.0 | 95.2 | 91.1 | 91.1 | 92.3 | 33.5 |

NOW AT 540

15:51 RAN 0 MINS 0.75 SECS

READY

Oxygen consumption and carbon dioxide production were computed from the inhaled and exhaled gas composition and the exhalation volume. Oxygen consumption (STPD) is shown as a function of respiratory minute volume (BTPS) in Figures 19-22. The reasons for the scatter of this data at 850 feet are not evident. Carbon dioxide production (STPD) as a function of respiratory minute volume (BTPS) is plotted in Figures 23-28. The data at 850 feet, Figure 26, is again completely random. Without the 850 feet data there is a trend: $\dot{V}CO_2 = .045$ RMV (Fig. 28). Figures 29-33 are plots of oxygen consumption-carbon dioxide production. The 850 feet data (Fig. 32) which was scattered for both $\dot{V}CO_2$ and $\dot{V}O_2$ appear to correlate along a line of $\dot{V}CO_2 = 0.9\dot{V}O_2$. This correlation line also appears to be the best representation of the total data shown in Figure 29.

Other Ventilatory Data

Tidal volumes, respiratory frequency, inhalation and exhalation pressure drop and exhalation peak flow rate, as well as $\dot{V}O_2$, $\dot{V}CO_2$, and respiratory exchange ratio are presented in Table IV. Neither pressure drop, flow, nor respiratory resistance during exhalation appear to vary consistently as functions of depth (density) or inhalation temperature. The applicability of pneumotachography to diving research is the subject of Appendix 3.

Subjective Effects of Breathing Cold Hyperbaric Gas

The following paragraphs, and Table V, are from the test subjects' reports, and are, in fact, directly quoted (author: subject SSZ).

"The respiratory heat loss effects reported here are those noted by one test subject, myself, and partly those reported or observed from the other two test subjects. The data summarized in Table V are from 850 feet, 35°F water dives of May 12, 14, 15, 16, and 18, 1971. Factors which affected the heating and cooling of each test subject were the ability of the inner and outer wet suits to heat the subject and the level of muscular activity of the subject. These factors are discussed below. Both the sequence of appearance of the effects of respiratory heat loss and the magnitude of these effects were consistent in several of the experiments, despite variations in heating from the wet suits and in work rates used.

"Early in the experiments, loosely fitting inner wet suits caused cold skin areas on all the test subjects and inadequate hot water circulation from the outer wet suit caused cold skin areas on two subjects, FA and KC, throughout the experiments. Table V shows a correlation of cold skin areas with early onset of shivering, usually within the first few minutes of the first rest period. The third subject, myself, noted fewer cold skin areas and had a later onset of shivering. These data indicate that the onset of heat loss effects is somewhat dependent on external heating.

"Another effect of the inadequate circulation of the wet suits was that the feet and hands became cold if they were not in at least intermittent movement. Thus, the rest periods were actually periods of activity of about 30-50% of work rate 3 (lightest effort).

"Where heating from the wet suits was sufficient, the onset of chest muscle shivering occurred during either work rate 3 or the second rest period. Work rate 3 was a very light work rate, requiring only a slow, easy kick with the fins. This work rate was sufficient to increase the subjects' heart rate and breathing rate and to create some warmth from exercise.

"All test subjects had chest muscle shivering during the second rest period, indicating that the warmth lost from cessation of exercise, or the continued exposure caused the onset of shivering.

"A decrease in shivering in both limbs and torso occurred with the increased activity of the moderate and the heavy work rates, indicating that the warmth produced by exercise somewhat affects the heat lost to the large volumes of cold gas that are breathed at these work rates.

"The first respiratory symptom was a flow of saliva, starting within the first minute of exposure and increasing to a steady rate within a few minutes at each work rate. These steady rates seemed to be proportional to the volumes of gas breathed. The total flow was about four to eight ounces of saliva per subject per dive, estimated from the drainage from the water trap and transparent hose for all three subjects.

"The second symptom was nasal drainage, beginning in the first work period and continuing at a slow, steady rate throughout each dive. The total flow was about 0.5 to 1 ounce per subject per dive. This flow is estimated from observations of all three subjects.

"Another symptom was shivering in the torso, beginning in the skeletal chest muscles. The following estimates of frequency and magnitude of shivering are only for one test subject, myself. The initial frequency of shivering was about once every three breaths, or approximately every 9 to 12 seconds, for a duration of about two seconds. The frequency would decrease to once every four or five breaths during heavy work with about the same duration.

" Shivering would usually spread over the skeletal muscles of the chest and abdomen, then over the back muscles from shoulders to thighs. This shivering was involuntary and uncontrollable.

"The fourth symptom was shivering of the muscles of the limbs, starting with the upper arms and thighs. This symptom usually began in the second rest period, decreased or stopped during the second work period, recurred in the third rest period, and usually stopped during heavy work. Thus, warmth from exercise apparently decreased this shivering.

"The shivering of the upper limbs spread to the hands and feet during two of the five dives, during the second and third rest periods. The rate of shivering was approximately

once every three breaths, for a duration of about two seconds. This shivering was involuntary and uncontrollable. The amplitude at the fingers was about one-quarter inch, estimated by holding the trapeze firmly and watching the work rate indicator. This symptom also includes shivering of the jaw and neck muscles, which caused difficulty retaining the mouthpiece. Shivering of the hands never became severe enough to prevent holding any object.

"Other symptoms, such as chest pain, headache, coughing, visual disturbance and breathing difficulty occured occasionally, with no appreciable repeatability or consistency among all three subjects."

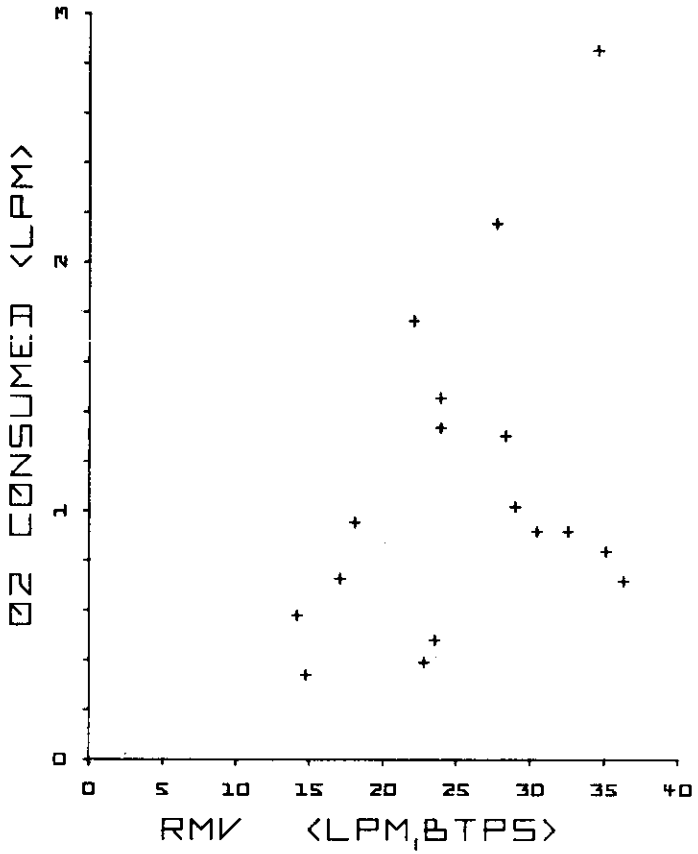


Figure 19. Oxygen Consumption (LPM, STPD) During Data Runs At 450 Feet.

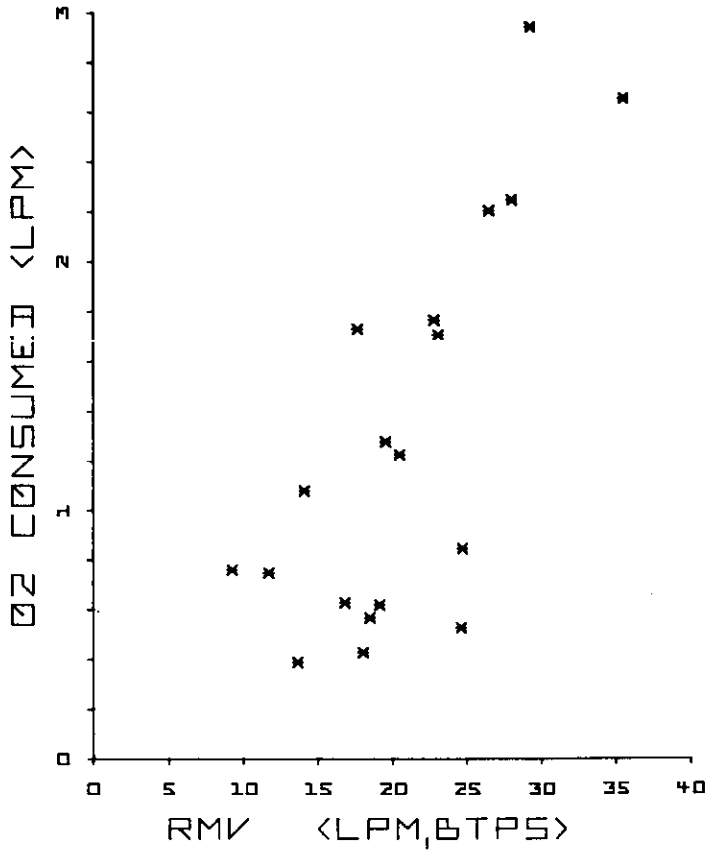


Figure 20. Oxygen Consumption (LPM, STPD) During Data Runs At 650 Feet.

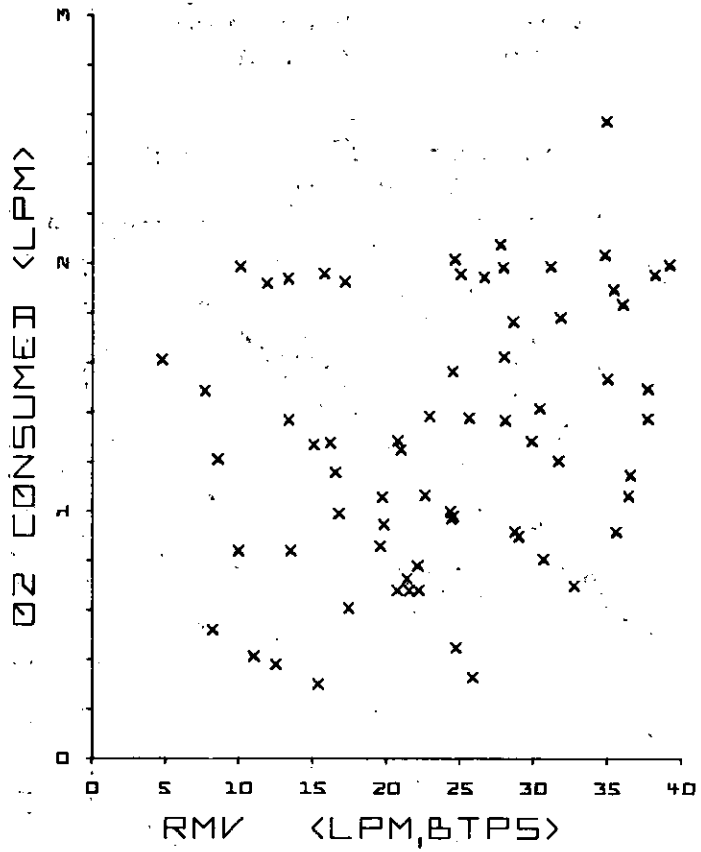


Figure 21. Oxygen Consumption (LPM, STPD) During Data Runs At 850 Feet.

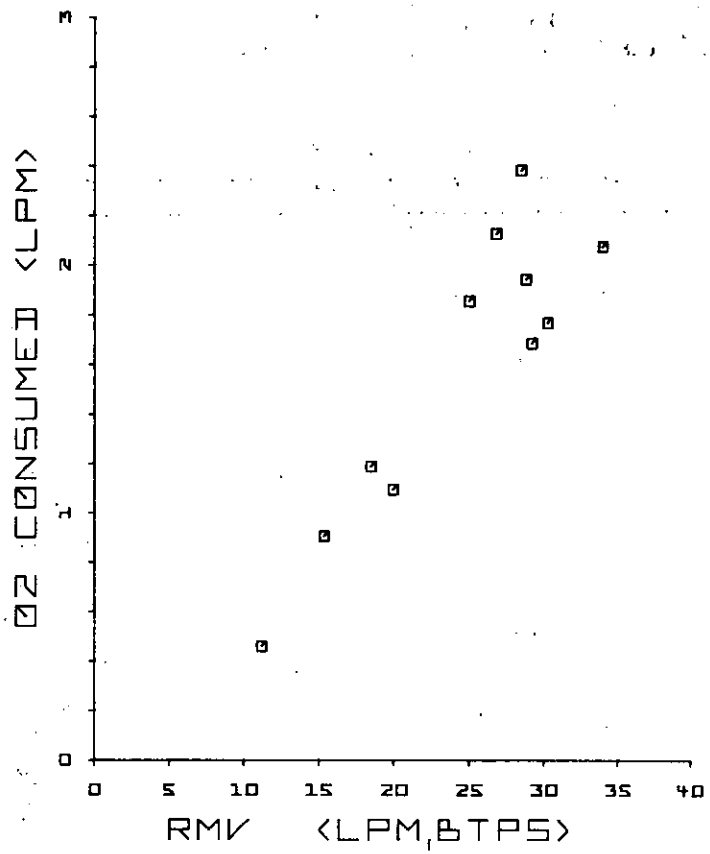


Figure 22. Oxygen Consumption (LPM, STPD) During Data Runs At 1,000 Feet.

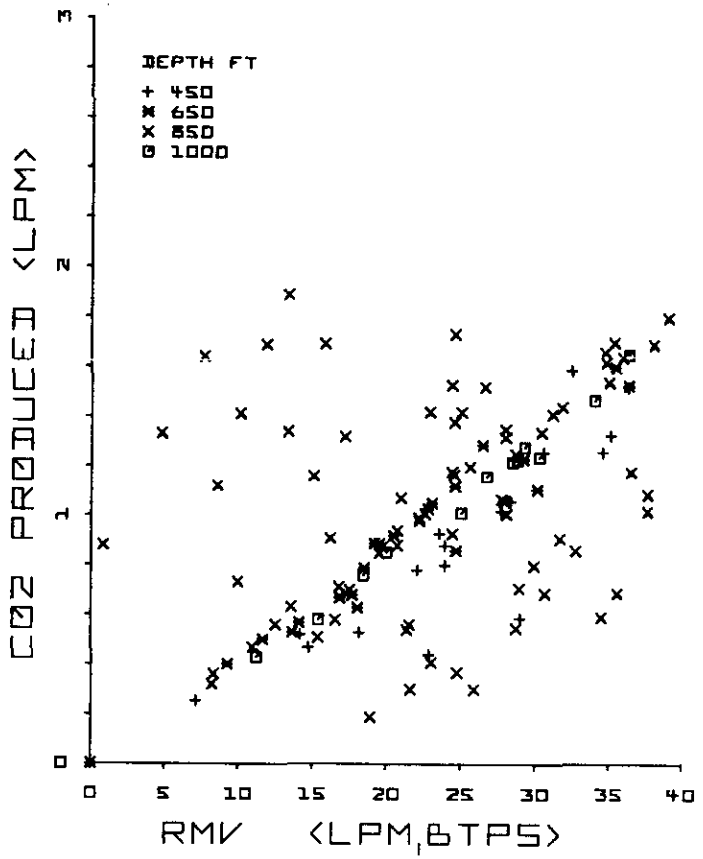


Figure 23. Plot Of All Values For Carbon Dioxide Production (LPM, STPD), As Functions Of Respiratory Minute Volume.

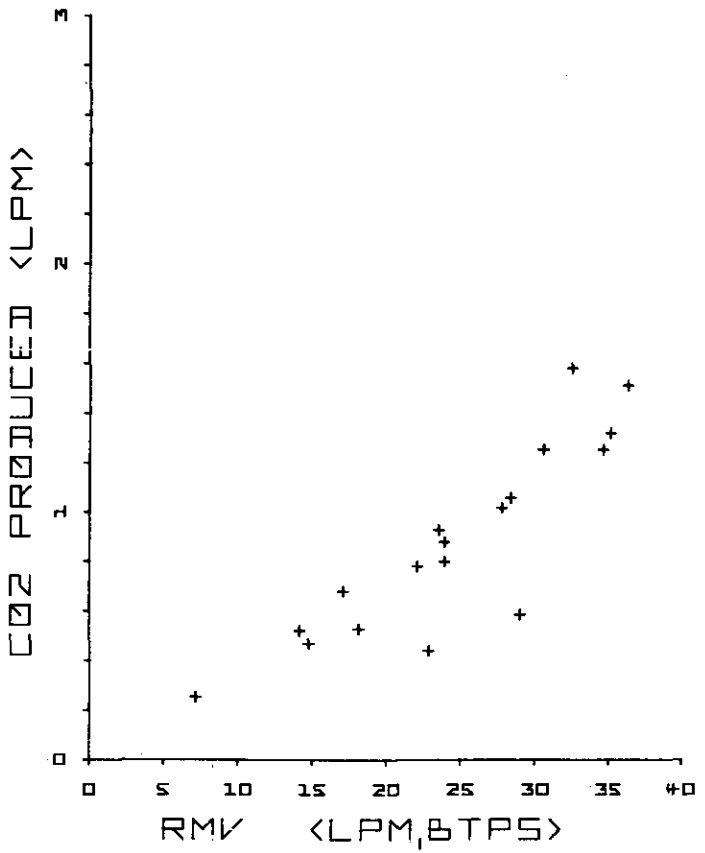


Figure 24. Carbon Dioxide Production (LPM, STPD) During Data Runs At 450 Feet.

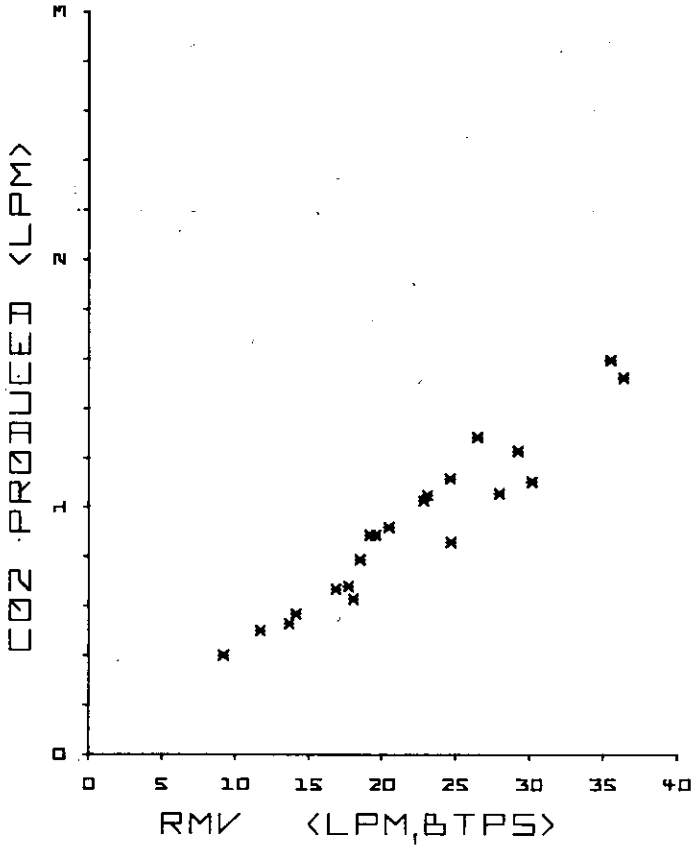


Figure 25. Carbon Dioxide Production (LPM, STPD) During Data Runs At 650 Feet.

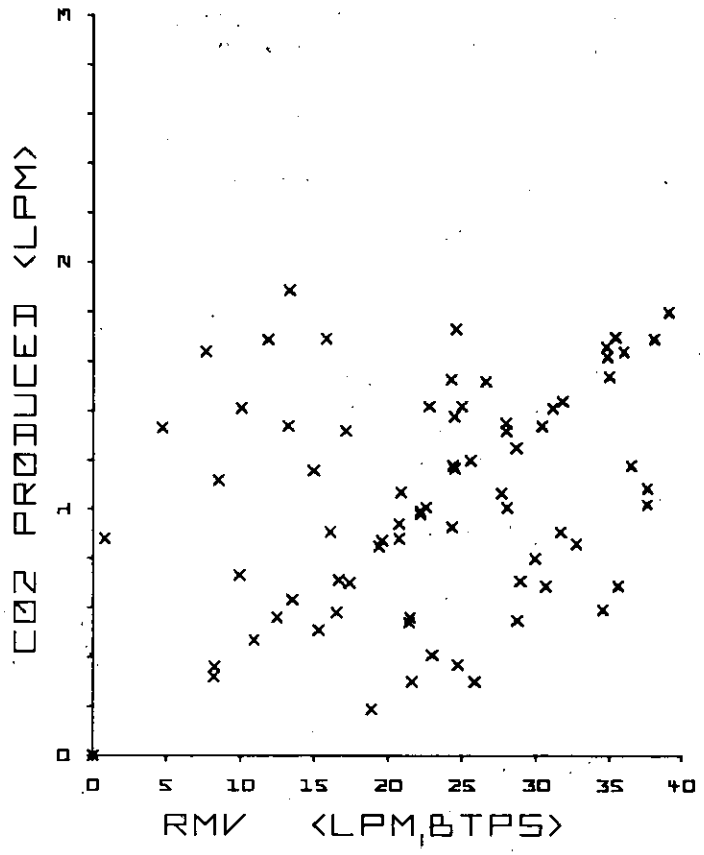


Figure 26. Carbon Dioxide Production (LPM, STPD) During Data Runs At 852 Feet.

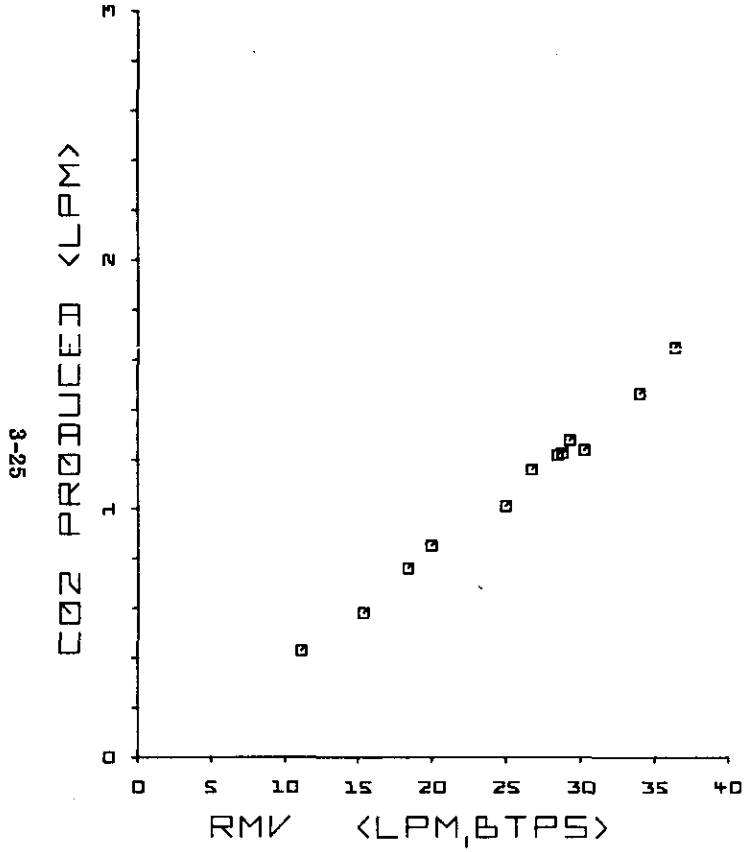


Figure 27. Carbon Dioxide Production (LPM, STPD) During Data Runs At 1,000 Feet.

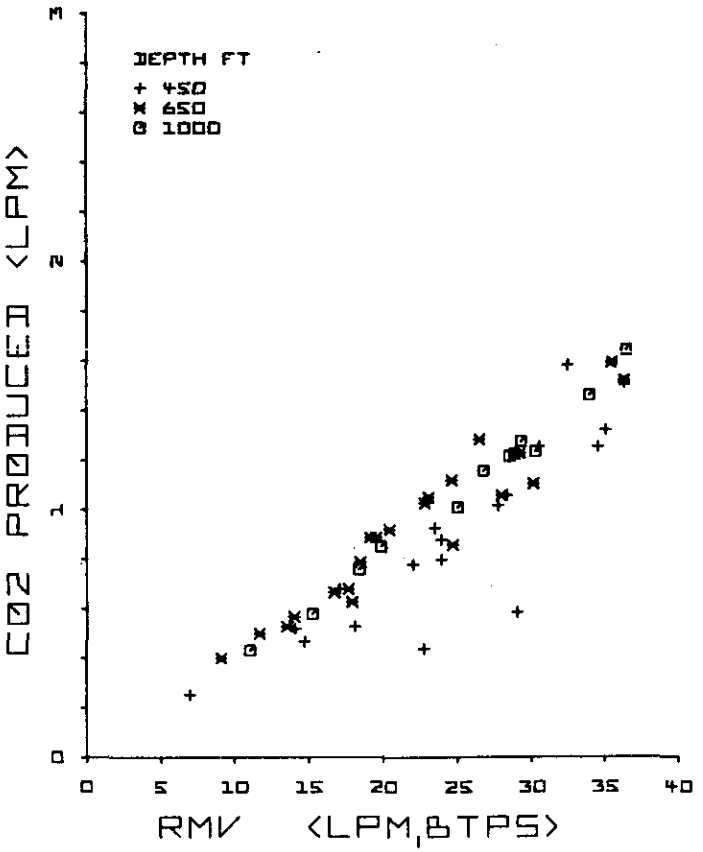


Figure 28. Carbon Dioxide Production As A Function Of Ventilation: Same As Figure 23, Without Data For 852 Feet.

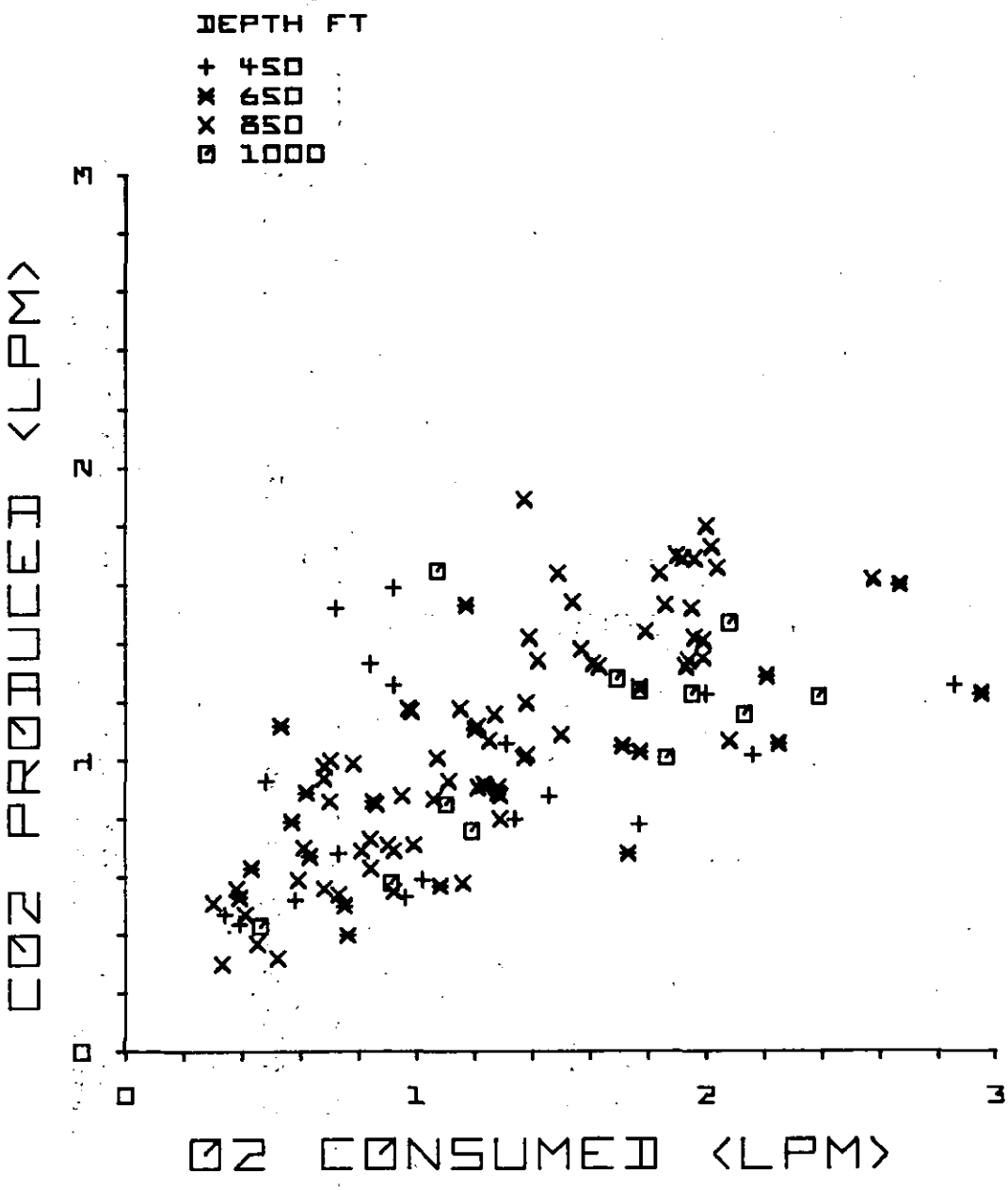


Figure 29. Relationship Of Oxygen Consumed To Carbon Dioxide Produced ($V_{CO_2}/V_{O_2}$ = Respiratory Exchange Ratio)

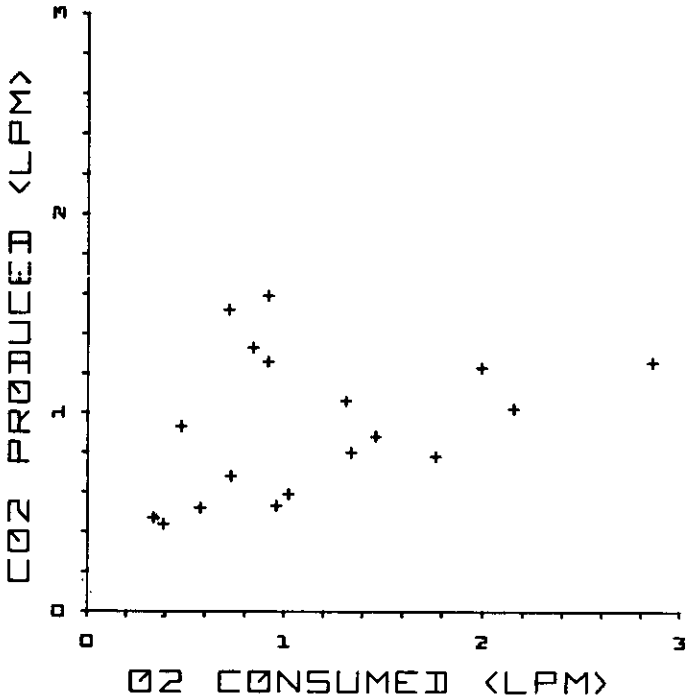


Figure 30. Depth 450 Feet: Relationship Of Oxygen Consumption And Carbon Dioxide Production.

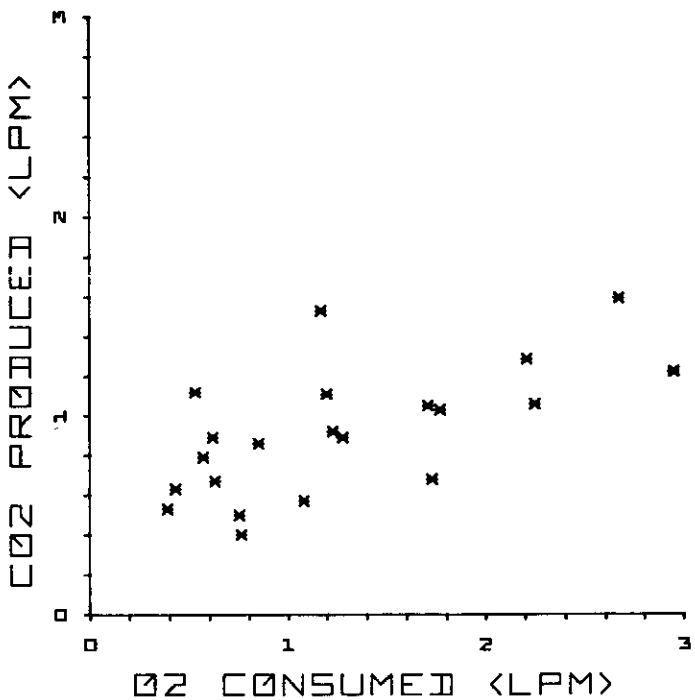


Figure 31. Depth 650 Feet: Relationship Of Oxygen Consumption and Carbon Dioxide Production.

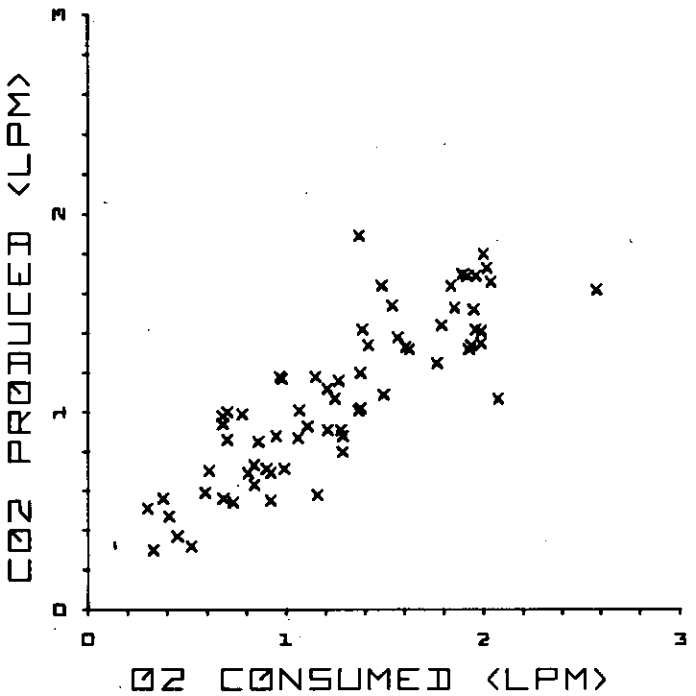


Figure 32. Depth 850 Feet: Relationship Of Oxygen Consumption and Carbon Dioxide Production.

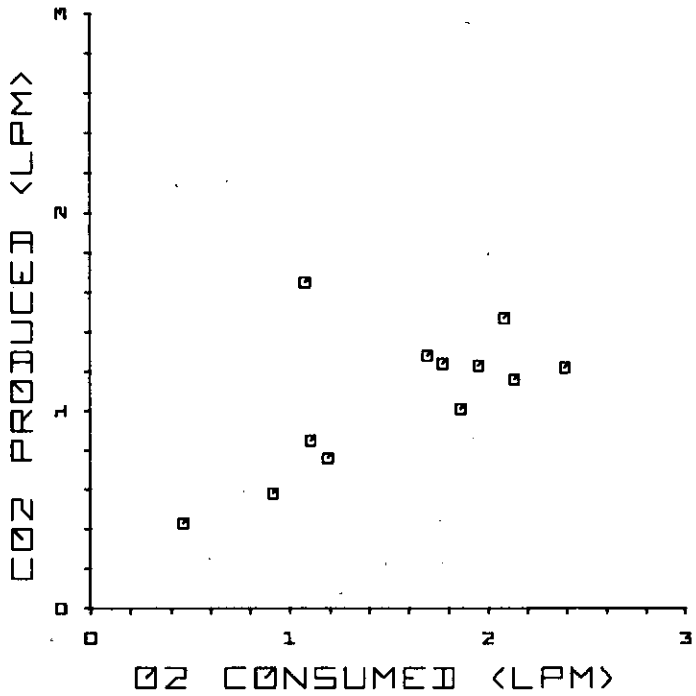


Figure 33. Depth 1,000 Feet Relationship of Oxygen Consumption and Carbon Dioxide Production.

TABLE IV

Ventilatory Parameters

| DATA NO | RMV LPM,BTPS | VT L,BTPS | F | P(CMH2O) IN | P(CMH2O) EX | FLOW L,SEC | V02 LPM | VC02 LPM | RER |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 11.189 | .9 | 13.0 | 0 | 0 | .5 | 2.283 | .280 | .12 |
| 2 | 20.138 | 1.4 | 14.4 | 3 | 5 | .7 | 4.010 | .520 | .13 |
| 3 | 22.816 | 1.4 | 16.6 | 8 | 8 | 1.2 | .393 | .437 | 1.11 |
| 4 | 35.136 | 1.6 | 21.3 | 8 | 10 | 1.8 | .844 | 1.328 | 1.57 |
| 5 | 15.778 | .8 | 19.6 | 2 | 3 | .6 | 2.584 | .564 | .22 |
| 6 | 23.543 | 1.4 | 17.4 | 2 | 5 | 1.0 | .479 | .925 | 1.93 |
| 7 | 26.537 | 1.6 | 17.0 | 4 | 6 | 1.2 | 3.977 | 1.016 | .26 |
| 8 | 28.359 | 1.8 | 16.2 | 7 | 8 | 1.2 | 1.313 | 1.057 | .80 |
| 9 | 22.035 | 1.9 | 11.9 | 4 | 4 | .7 | 1.768 | .775 | .44 |
| 10 | 27.722 | 1.9 | 14.3 | 6 | 8 | 1.0 | 2.164 | 1.017 | .47 |
| 11 | 34.573 | 1.7 | 20.4 | 7 | 10 | 1.2 | 2.864 | 1.257 | .44 |
| 12 | 44.610 | 1.8 | 24.3 | 8 | 12 | 1.8 | 3.220 | 1.671 | .52 |
| 13 | 7.052 | .6 | 12.0 | 0 | 0 | .4 | .235 | .252 | 1.07 |
| 14 | 14.751 | 1.1 | 13.7 | 3 | 4 | .8 | .341 | .466 | 1.37 |
| 15 | 29.033 | 1.8 | 16.4 | 14 | 17 | 2.2 | 1.015 | .586 | .58 |
| 16 | 42.103 | 3.6 | 11.8 | 15 | 35 | 2.5 | 2.000 | 1.235 | .62 |
| 17 | 14.148 | .7 | 19.0 | 3 | 3 | .4 | .575 | .520 | .90 |
| 18 | 17.092 | .9 | 18.8 | 3 | 3 | .7 | .733 | .680 | .93 |
| 19 | 16.087 | 1.1 | 17.2 | 3 | 5 | .9 | .964 | .534 | .55 |
| 20 | 23.946 | 1.6 | 15.0 | 6 | 12 | 1.3 | 1.456 | .882 | .61 |
| 21 | 23.959 | 1.7 | 14.0 | 0 | 0 | 1.0 | 1.344 | .804 | .60 |
| 22 | 30.498 | 1.9 | 15.8 | 6 | 8 | 1.4 | .917 | 1.261 | 1.37 |
| 23 | 32.505 | 1.8 | 18.2 | 0 | 8 | 1.6 | .924 | 1.586 | 1.72 |
| 24 | 36.299 | 1.7 | 21.0 | 0 | 0 | 1.8 | .724 | 1.520 | 2.10 |
| 25 | 11.656 | .7 | 16.5 | 0 | 0 | .6 | .749 | .503 | .67 |
| 26 | 19.545 | 1.0 | 19.4 | 0 | 0 | .9 | 1.283 | .888 | .69 |
| 27 | 35.471 | 2.1 | 17.0 | 7 | 10 | 1.8 | 2.672 | 1.604 | .60 |
| 28 | 39.111 | 3.1 | 12.8 | 11 | 18 | 3.5 | 3.111 | 1.106 | .36 |
| 29 | 16.816 | .7 | 22.8 | 4 | 4 | .6 | .635 | .668 | 1.05 |
| 30 | 20.466 | .9 | 22.9 | 2 | 8 | .9 | 1.231 | .918 | .75 |
| 31 | 23.062 | 1.0 | 22.8 | 4 | 5 | 1.0 | 1.706 | 1.053 | .62 |
| 32 | 26.465 | 1.2 | 23.0 | 4 | 4 | 1.0 | 2.209 | 1.292 | .58 |
| 33 | 14.080 | 1.2 | 11.8 | 0 | 0 | .8 | 1.077 | .571 | .53 |
| 34 | 22.809 | 1.6 | 14.6 | 0 | 0 | 1.0 | 1.772 | 1.027 | .58 |
| 35 | 27.964 | 1.5 | 18.5 | 0 | 0 | 1.2 | 2.251 | 1.061 | .47 |
| 36 | 34.378 | 1.5 | 22.2 | 10 | 12 | 1.6 | 3.112 | 1.447 | .46 |
| 37 | 9.170 | .7 | 13.0 | 2 | 3 | .5 | .758 | .395 | .52 |
| 38 | 17.644 | 1.4 | 13.0 | 4 | 5 | 1.0 | 1.729 | .678 | .39 |
| 39 | 29.184 | 2.8 | 10.4 | 10 | 12 | 3.0 | 2.952 | 1.227 | .42 |
| 40 | 40.277 | 3.4 | 12.0 | 12 | 35 | 3.6 | 4.325 | 1.650 | .38 |
| 41 | 13.632 | .6 | 21.0 | 4 | 4 | .5 | .394 | .526 | 1.34 |
| 42 | 18.476 | 1.0 | 18.6 | 3 | 7 | .8 | .565 | .795 | 1.41 |
| 43 | 19.133 | 1.1 | 18.2 | 4 | 5 | .9 | .617 | .888 | 1.44 |
| 44 | 24.566 | 1.3 | 19.4 | 6 | 8 | 1.2 | .533 | 1.119 | 2.10 |
| 45 | 18.031 | 1.4 | 12.7 | 3 | 4 | .7 | .425 | .629 | 1.48 |
| 46 | 24.678 | 1.6 | 15.1 | 5 | 8 | 1.0 | .849 | .864 | 1.02 |

TABLE IV

Ventilatory Parameters (Continued)

| DATA NO | RMV L,BTPS | VT L,BTPS | F | P(CMH2O) IN | P(CMH2O) EX | FLOW L,SEC | V02 LPM | VC02 LPM | RER |
|---|---|---|---|---|---|---|---|---|---|
| 47 | 30.159 | 1.8 | 17.0 | 0 | 0 | 1.2 | 1.201 | 1.110 | .92 |
| 48 | 36.364 | 1.9 | 18.7 | 0 | 10 | 1.8 | 1.174 | 1.534 | 1.31 |
| 49 | 8.213 | .7 | 11.5 | 2 | 2 | .4 | .516 | .319 | .62 |
| 50 | 16.520 | 1.4 | 11.5 | 3 | 4 | .8 | 1.165 | .580 | .50 |
| 51 | 27.750 | 3.3 | 8.4 | 7 | 15 | 2.0 | 2.083 | 1.066 | .51 |
| 52 | 33.686 | 4.1 | 8.3 | 10 | 25 | 3.0 | 1.732 | 1.532 | .88 |
| 53 | 12.434 | .8 | 16.0 | 0 | 0 | .6 | .382 | .556 | 1.45 |
| 54 | 20.732 | 1.0 | 21.0 | 6 | 7 | .9 | .681 | .940 | 1.38 |
| 55 | 22.148 | 1.0 | 22.0 | 10 | 12 | 1.1 | .779 | .994 | 1.28 |
| 56 | 24.366 | 1.1 | 22.5 | 10 | 20 | 1.2 | .967 | 1.176 | 1.22 |
| 57 | 15.315 | 1.3 | 11.6 | 0 | 0 | .7 | .303 | .512 | 1.69 |
| 58 | 22.176 | 1.7 | 12.8 | 0 | 0 | 1.0 | .682 | .981 | 1.44 |
| 59 | 22.583 | 1.9 | 11.7 | 0 | 0 | 1.3 | 1.069 | 1.009 | .94 |
| 60 | 24.526 | 1.6 | 15.8 | 9 | 22 | 1.6 | .977 | 1.165 | 1.19 |
| 61 | 10.978 | .7 | 15.2 | 2 | 2 | .6 | .413 | .470 | 1.14 |
| 62 | 25.606 | 2.0 | 13.0 | 4 | 6 | 1.2 | 1.376 | 1.203 | .87 |
| 63 | 34.826 | 3.0 | 11.5 | 5 | 8 | 2.2 | 2.035 | 1.661 | .82 |
| 64 | 39.140 | 3.6 | 10.8 | 6 | 12 | 3.1 | 2.004 | 1.801 | .90 |
| 65 | 16.708 | 1.0 | 16.6 | 2 | 3 | .9 | .990 | .707 | .71 |
| 66 | 27.975 | 1.5 | 18.2 | 5 | 6 | 1.6 | 1.990 | 1.347 | .68 |
| 67 | 31.805 | 1.6 | 20.2 | 0 | 0 | 1.9 | 1.791 | 1.439 | .80 |
| 68 | 34.843 | 1.5 | 23.0 | 0 | 0 | 2.0 | 2.579 | 1.623 | .63 |
| 69 | 19.508 | 1.6 | 12.2 | 2 | 4 | 1.2 | .863 | .850 | .98 |
| 70 | 28.006 | 1.8 | 15.5 | 3 | 5 | 1.4 | 1.633 | 1.321 | .81 |
| 71 | 35.002 | 2.2 | 16.1 | 8 | 13 | 2.0 | 1.544 | 1.536 | .99 |
| 72 | 35.974 | 2.1 | 17.1 | 8 | 13 | 2.4 | 1.843 | 1.641 | .89 |
| 73 | 11.118 | .8 | 14.7 | 0 | 0 | .4 | .464 | .430 | .93 |
| 74 | 18.431 | 2.2 | 8.5 | 0 | 0 | .9 | 1.195 | .761 | .64 |
| 75 | 30.261 | 3.4 | 8.8 | 5 | 16 | 2.6 | 1.765 | 1.243 | .70 |
| 76 | 34.022 | 3.8 | 9.0 | 9 | 21 | 3.5 | 2.076 | 1.465 | .71 |
| 77 | 15.339 | .7 | 21.0 | 0 | 0 | .7 | .910 | .576 | .63 |
| 78 | 24.975 | 1.1 | 23.3 | 5 | 5 | 1.1 | 1.860 | 1.011 | .54 |
| 79 | 28.834 | 1.3 | 22.0 | 0 | 0 | 1.4 | 1.952 | 1.226 | .63 |
| 80 | 28.469 | 1.4 | 21.0 | 5 | 9 | 1.3 | 2.395 | 1.224 | .51 |
| 81 | 19.921 | 1.5 | 13.0 | 3 | 5 | .7 | 1.099 | .850 | .77 |
| 82 | 26.750 | 1.8 | 14.5 | 0 | 0 | 1.1 | 2.134 | 1.163 | .54 |
| 83 | 29.249 | 2.0 | 14.3 | 0 | 0 | 1.3 | 1.688 | 1.280 | .76 |
| 84 | 36.401 | 2.2 | 16.5 | 0 | 0 | 1.9 | 1.072 | 1.650 | 1.54 |
| 85 | 8.283 | .8 | 10.8 | 0 | 0 | .4 | .213 | .364 | 1.71 |
| 86 | 13.498 | 1.2 | 11.0 | 3 | 3 | .7 | .837 | .626 | .75 |
| 87 | 20.735 | 2.6 | 8.0 | 7 | 11 | 2.3 | 1.292 | .882 | .68 |
| 88 | 28.632 | 3.0 | 9.5 | 8 | 14 | 2.7 | 1.771 | 1.248 | .70 |
| 89 | 17.451 | 1.1 | 16.2 | 2 | 3 | .7 | .615 | .700 | 1.14 |
| 90 | 30.413 | 1.6 | 18.5 | 3 | 6 | 1.4 | 1.421 | 1.341 | .94 |
| 91 | 41.017 | 1.7 | 24.3 | 5 | 7 | 2.2 | 5.736 | .336 | .06 |
| 92 | .000 | .0 | .0 | 0 | 0 | .0 | .000 | .000 | .00 |

TABLE IV

Ventilatory Parameters (Continued)

| DATA NO | RMV LPM,BTPS | VT L,BTPS | F | P(CMH2O) IN | P(CMH2O) EX | FLOW L,SEC | VO2 LPM | VCO2 LPM | RER |
|---|---|---|---|---|---|---|---|---|---|
| 93 | 19.641 | 1.7 | 11.3 | 4 | 4 | 1.0 | 1.062 | .874 | .82 |
| 94 | 31.097 | 2.0 | 15.3 | 5 | 7 | 1.6 | 1.988 | 1.407 | .71 |
| 95 | 38.120 | 2.4 | 16.0 | 0 | 0 | 2.2 | 1.961 | 1.693 | .86 |
| 96 | 10.052 | .0 | .0 | 0 | 0 | .0 | 1.988 | 1.407 | .71 |
| 97 | .000 | .0 | 12.8 | 2 | 3 | .4 | .000 | .000 | .00 |
| 98 | 15.745 | 1.3 | 11.8 | 3 | 4 | .7 | 1.961 | 1.693 | .86 |
| 99 | 22.976 | 2.9 | 7.8 | 7 | 16 | 2.1 | .174 | .409 | 2.35 |
| 100 | 23.992 | 2.6 | 11.0 | 6 | 20 | 2.3 | .904 | .706 | .78 |
| 101 | 20.956 | .9 | 23.9 | 3 | 4 | .8 | 1.251 | 1.074 | .86 |
| 102 | 24.503 | 1.2 | 21.0 | 4 | 6 | 1.2 | 1.575 | 1.378 | .87 |
| 103 | 32.726 | 1.3 | 24.6 | 5 | 7 | 1.4 | .699 | .858 | 1.23 |
| 104 | 36.531 | 1.6 | 23.2 | 7 | 14 | 1.8 | 1.153 | 1.175 | 1.02 |
| 105 | 22.844 | 1.8 | 12.4 | 4 | 5 | 1.1 | 1.391 | 1.417 | 1.02 |
| 106 | 35.400 | 2.2 | 16.2 | 5 | 8 | 1.8 | 1.898 | 1.701 | .90 |
| 107 | 41.749 | 2.2 | 19.2 | 5 | 8 | 1.9 | .700 | .998 | 1.43 |
| 108 | 7.694 | .0 | .0 | 0 | 0 | .0 | 1.488 | 1.644 | 1.11 |
| 109 | 13.344 | 1.2 | 11.3 | 0 | 0 | .4 | 1.369 | 1.889 | 1.38 |
| 110 | .000 | .0 | 11.2 | 0 | 0 | .7 | .000 | .000 | .00 |
| 111 | 21.597 | 2.6 | 8.4 | 4 | 9 | 2.6 | .184 | .299 | 1.63 |
| 112 | 34.513 | 3.1 | 11.0 | 8 | 14 | 2.4 | .594 | .590 | .99 |
| 113 | 24.387 | 1.1 | 22.4 | 3 | 6 | 1.2 | 1.114 | .934 | .84 |
| 114 | 24.349 | 1.1 | 21.8 | 3 | 7 | 1.4 | 1.856 | 1.531 | .83 |
| 115 | 31.672 | 1.4 | 22.9 | 4 | 8 | 1.6 | 1.208 | .910 | .75 |
| 116 | 37.682 | 1.7 | 22.8 | 5 | 9 | 2.2 | 1.378 | 1.020 | .74 |
| 117 | 13.266 | 1.3 | 10.6 | 0 | 0 | .7 | 1.944 | 1.338 | .69 |
| 118 | 24.560 | 1.7 | 14.6 | 5 | 6 | 1.3 | 2.023 | 1.733 | .86 |
| 119 | 28.743 | 1.9 | 15.1 | 7 | 9 | 1.7 | .922 | .550 | .60 |
| 120 | 37.673 | 1.8 | 21.2 | 8 | 11 | 1.9 | 1.503 | 1.089 | .72 |
| 121 | 4.747 | .4 | 10.7 | 0 | 0 | .4 | 1.605 | 1.329 | .83 |
| 122 | 11.874 | 1.0 | 11.4 | 0 | 0 | .6 | 1.924 | 1.694 | .88 |
| 123 | 18.828 | 2.7 | 7.0 | 0 | 0 | 2.3 | .146 | .188 | 1.29 |
| 124 | 21.384 | 3.1 | 6.9 | 0 | 0 | 2.6 | .730 | .538 | .74 |
| 125 | 9.947 | 1.2 | 8.2 | 0 | 0 | .7 | .841 | .727 | .86 |
| 126 | 19.832 | 1.6 | 12.3 | 0 | 0 | 1.0 | .951 | .878 | .92 |
| 127 | 24.714 | 1.8 | 14.0 | 0 | 0 | 1.5 | .448 | .368 | .82 |
| 128 | 29.897 | 1.6 | 18.2 | 0 | 0 | 1.7 | 1.289 | .800 | .62 |
| 129 | 8.511 | .7 | 11.7 | 0 | 0 | .4 | 1.211 | 1.117 | .92 |
| 130 | 17.160 | 1.3 | 12.8 | 0 | 0 | .8 | 1.926 | 1.324 | .69 |
| 131 | 25.843 | 2.8 | 9.3 | 0 | 0 | 1.7 | .326 | .305 | .94 |
| 132 | 30.655 | 2.9 | 10.5 | 0 | 0 | 2.0 | .812 | .689 | .85 |
| 133 | 15.012 | 1.0 | 14.7 | 0 | 0 | .8 | 1.269 | 1.161 | .92 |
| 134 | 24.976 | 1.2 | 20.6 | 0 | 0 | 1.7 | 1.963 | 1.417 | .72 |
| 135 | 21.528 | 1.4 | 15.2 | 0 | 0 | 1.9 | .681 | .562 | .83 |

TABLE IV

Ventilatory Parameters (Continued)

| DATA NO | RMV LPM,BTPS | VT L,BTPS | F F | P(CMH2O) IN | P(CMH2O) EX | FLOW L,SEC | V02 LPM | VC02 LPM | RER |
|---|---|---|---|---|---|---|---|---|---|
| 136 | 28.079 | 1.3 | 22.3 | 0 | 0 | 1.7 | 1.366 | 1.012 | .74 |
| 137 | 16.140 | 1.5 | 10.7 | 0 | 0 | 1.2 | 1.280 | .906 | .71 |
| 138 | 26.595 | 1.9 | 14.0 | 0 | 0 | 2.1 | 1.949 | 1.517 | .78 |
| 139 | 35.569 | 2.0 | 18.0 | 7 | 13 | 1.9 | .917 | .685 | .75 |
| 140 | 42.710 | 2.0 | 21.2 | 9 | 15 | 2.3 | 1.775 | 1.172 | .66 |

TABLE V

TEST SUBJECT RESPONSES TO COLD WATER - COLD GAS EXPOSURES

| ACTIVITY | RESTING | | | LIGHT WORK | | | RESTING | | | MODERATE WORK | | | RESTING | | | HEAVIEST WORK | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SUBJECT | F.A. | K.C. | S.Z | F.A. | K.C. | S.Z. | F.A. | K.C. | S.Z. | F.A. | K.C. | S.Z. | F.A. | K.C. | S.Z. | F.A. | K.C. | S.Z. |
| Cold Torso, Skin | 100 | 100 | 50 | 100 | 100 | 50 | 100 | 100 | 50 | 100 | 100 | 25 | 100 | 100 | 0 | 100 | 75 | 0 |
| Cold Extremity, Skin | 100 | 100 | 50 | 100 | 100 | 50 | 100 | 75 | 25 | 100 | 75 | 25 | 100 | 75 | 0 | 100 | 25 | 0 |
| Headache | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 25 | 0 | 0 | 25 | 0 | 0 | 25 |
| Chest Pain | 0 | 0 | 0 | 0 | 0 | 50 | 0 | 0 | 0 | 0 | 0 | 75 | 0 | 0 | 0 | 0 | 0 | 75 |
| Shivering, Chest | 100 | 100 | 75 | 100 | 100 | 75 | 100 | 100 | 100 | 100 | 100 | 75 | 100 | 100 | 100 | 100 | 75 | 50 |
| Shivering, Limbs | 100 | 75 | 25 | 100 | 75 | 0 | 100 | 75 | 100 | 100 | 75 | 50 | 100 | 75 | 75 | 100 | 75 | 50 |
| Salivating | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Nasal Drainage | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Coughing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 25 | 0 |
| Breathing Difficulty | 0 | 0 | 0 | 25 | 0 | 0 | 0 | 0 | 0 | 100 | 0 | 0 | 0 | 0 | 0 | 100 | 25 | 0 |

## SECTION 4

## DISCUSSION

### Temperature of Exhaled Gas

Unless there are reliable measurements of the temperature of the gas as it is exhaled, projections of the heat loss through respiration remain speculative. With respect to the mathematical expressions for respiratory heat loss, one can define the magnitudes of the gas properties, density and specific heat, and assign sample values to inhaled gas temperature and pulmonary ventilatory rate, but, as Webb (35) has stated, "the only unknown is the temperature of the air as it leaves the oronasal portal in expiration." The effect of presuming that the exhaled air is at core temperature has already been reviewed (see Introduction). Thus, the most important quantitative information acquired during this study is the temperature data for exhaled gas. The extensive engineering efforts in support of this data acquisition have been documented in Appendix 2.

The results listed herein for respiratory heat loss will be approximately 60 - 80% of theoretical values calculated assuming exhalation temperature equals core temperature. Also, these results are based upon a gas saturated at inhalation temperature and saturated at exhalation temperature, not core temperature. This will produce a lower value of insensible heat loss of 30 to 60% depending upon the water temperature.

### Diver-Subject Heat Balance

The energy generated by metabolism is thermally stored in the body or lost to the environment by work and thermal conduction, convection, evaporation, and radiation heat transfer. The rates of energy flow are given in the energy flow equation for a body, as shown by Nevins (23)

$$M = S + W + K + C + E + R$$

where:

M is rate of metabolic energy produced within the body. It varies with the level of physical activity and is calculated using the measured oxygen consumption.

S is rate of heat stored into the body. It is calculated by the technique of Burton described earlier

$$S = m_b \; Cp_b \; (2/3 \; \Delta T_r + 1/3 \; \Delta T_{mws})$$

$m_b$ is mass of the body

$Cp_b$ = .83 Btu/lb - °F (0.83 Kcal/Kgm °C) is the most acceptable mean value of specific heat of the body (17).

$\Delta T_r$ is change in rectal temperature

$\Delta T_{mws}$ is change in mean weighted skin temperature

In this study the temperatures decrease so we have a negative value of stored heat, S, or a positive value of (-S).

W is rate of work done by the body on the environment. For the swimmer working against the ergometer described herein, his body motion work energy is converted into ambient water kinetic energy and finally dissipated in the ambient water as viscous energy loss.

K is rate of heat loss conducted into a solid surface touching the skin.

$C = C_s + C_r$ is rate of heat conducted and convected away from the body by a gas or a liquid medium touching the skin, $C_s$, or breathing gas in the respiratory tract, $C_r$.

$E = E_s + E_r$ is rate of heat loss by evaporation from the skin, $E_s$, and from the respiratory tract, $E_r$.

R is net rate of heat radiated from the skin.

The total heat loss through the skin ($Q_s$) is

$$Q_s = + K_s + C_s + E_s + R$$

and, the heat loss from the respiratory tract (Qr) is

$$Q_r = C_r + E_r$$

$C_r$ and $E_r$ are calculated from changes in temperature and composition of the breathing gas, utilizing the equation shown in Section 2 and Appendix 1.

In the case of a fully submerged diver wearing a free flooding hot water suit the radiation term, R, and skin evaporation term, $E_s$, are assumed to be zero, and the energy flow equation for the diver subjects of this study becomes

$$M = S + W + Q_s + Q_r.$$

The heat balance, thus computed on a run basis, is shown in Table VI.

A rough estimate of the diver-subjects mean work rate is W = 0.1 hp or 64 Kcal/hr. This value was obtained assuming a maximum work rate of 0.4 hp and scaling the work rates according to the diver-subjects reported effort levels. The reference for this estimate is the Bioastronautics Data Book (36) which summarizes the sustainable work levels on a time and subject fitness basis. This value is used to calculate $Q_s$ in Table VI.

Metabolic rates of the diver subjects were calculated from measured compositions of mixed exhaled gas. To obtain an average value for each diver-subject run the values of oxygen uptake were averaged using the technique described earlier for respiratory minute volume. These values were then converted to units of energy (1 liter per minute $O_2$ uptake = 1158 Btu/hr or 293 Kcal/hr) and are listed in column 2 of Table VI. The wide range in metabolic rates for the individual data points resulted in average metabolic rates which did not allow a heat balance analysis of any consistency. Therefore two assumptions were made: (1) that the average respiratory quotient for all data was 0.9; (2) that $CO_2$ production was 0.045 liters $CO_2$ produced per liter exhaled gas. Oxygen consumption was then estimated by assuming that 0.05 liters of $O_2$ were produced per liter of gas exhaled. The metabolic rates thus calculated ($M_c$) are listed in column 3 of Table VI.

Columns 4 and 5 of Table VI list respiratory heat loss and body heat storage respectively. The storage term is negative indicating that the body is in negative thermal balance. The magnitude of the storage term indicates the rate that the energy leaving the body exceeds the metabolic rate.

TABLE VI

| HEAT BALANCE ANALYSIS | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Run No. | Metabolic Rate M Kcal/hr | Adjusted Metabolic Rate Mc Kcal/hr | RHL (Qr) Kcal/hr | S Storage Kcal/hr | Qr/Mc % | $Q_s$ | Heat Transfer Coefficient $H_s$ Kcal/hr $M^2C$ | W Kcal/hr |
| 1 | 180 | 328 | 79 | -- | 24 | — | -- | 64 |
| 2 | 262 | 350 | 86 | -21 | 25 | 221 | 42.2* | 64 |
| 3 | 721 | 457 | 135 | -48 | 30 | 306 | 50.6* | 64 |
| 4 | 238 | 324 | 101 | -37 | 31 | 196 | 25.3 | 64 |
| 5 | 265 | 265 | 93 | -53 | 35 | 161 | 21.5 | 64 |
| 6 | 276 | 454 | 122 | -64 | 27 | 332 | 49.0* | 64 |
| 7 | 547 | 372 | 160 | -65 | 43 | 213 | 25.3 | 64 |
| 8 | 421 | 316 | 116 | -60 | 37 | 196 | 31.7 | 64 |
| 9 | 597 | 359 | 157 | -53 | 44 | 191 | 49.0* | 64 |
| 10 | 694 | 337 | 126 | -19 | 37 | 166 | 26.5 | 64 |
| 11 | 158 | 275 | 105 | -54 | 38 | 160 | 18.7 | 64 |
| 12 | 270 | 390 | 151 | -54 | 39 | 228 | 46.4* | 64 |
| 13 | 374 | 303 | 122 | -31 | 40 | 148 | 23.3 | 64 |
| 14 | 208 | 295 | 111 | -61 | 38 | 182 | 22.4 | 64 |
| 15 | 223 | 316 | 127 | -29 | 40 | 154 | — | 64 |
| 16 | 436 | 400 | 197 | -62 | 49 | 201 | 35.1 | 64 |
| 17 | 558 | 406 | 195 | -60 | 48 | 207 | 22.5 | 64 |
| 18 | 448 | 423 | 218 | -44 | 51 | 185 | 29.1 | 64 |
| 19 | 404 | 330 | 194 | -44 | 59 | 116 | 53.6* | 64 |
| 20 | 548 | 359 | 193 | -56 | 54 | 158 | 26.0 | 64 |
| 21 | 482 | 401 | 242 | -54 | 60 | 150 | 27.0 | 64 |
| 22 | 301 | 250 | 139 | -11 | 55 | | 9.2 | 64 |
| 23 | 334 | 438 | 245 | -75 | 56 | 204 | 27.2 | 64 |
| 24 | 510 | 437 | 254 | -68 | 58 | 186 | 25.0 | 64 |
| 25 | 293 | 275 | 152 | -36 | 55 | 95 | 13.4 | 64 |
| 26 | 376 | 403 | 218 | -68 | 54 | 189 | 24.4 | 64 |

TABLE VI (Continued)

| Run No. | Metabolic Rate M Kcal/hr | Adjusted Metabolic Rate Mc Kcal/hr | RHL (Qr) Kcal/hr | S Storage Kcal/hr | Qr/Mc % | $Q_s$ | Heat Transfer Coefficient $H_S$ Kcal/hr $M^2C$ | W Kcal/hr |
|---|---|---|---|---|---|---|---|---|
| 27 | 367 | 490 | 290 | -73 | 59 | 208 | 29.9 | 64 |
| 28 | 264 | 268 | 147 | -36 | 55 | 175 | 39.6 | 64 |
| 29 | 469 | 408 | 219 | -46 | 54 | 172 | 21.6 | 64 |
| 30 | 444 | 376 | 214 | -68 | 57 | 166 | 33.8 | 64 |
| 31 | 206 | 205 | 96 | -25 | 47 | 70 | 16.3 | 64 |
| 32 | 372 | 306 | 159 | -31 | 49 | 123 | 75.0* | 64 |
| 33 | 313 | 293 | 161 | -65 | 55 | 133 | 38.6 | 64 |
| 34 | 397 | 334 | 179 | -52 | 54 | 143 | 19.4 | 64 |
| 35 | 548 | 435 | 242 | -66 | 56 | 195 | 158.5* | 64 |

The percentage of metabolic heat lost through respiratory heat loss is shown in column 6. In all cases but two at 850 feet and deeper this value exceeds 50%, including each case that was diver aborted.

Theoretically, reducing the respiratory heat loss by an amount equal to or greater than the value of negative thermal storage would restore thermal balance. Unpublished results of prior dives in 35°F water at 650 ft. with the diver subject wearing the identical hot water suit described herein showed divers in thermal balance over a four-hour period. The breathing apparatus worn by the diver was semi-closed circuit and featured a hot-water-heated $CO_2$ absorbent canister. These divers also used full face masks with inner oro-nasal masks. At that time the inhalation temperature (not measured) was estimated to be water temperature. Subsequent unpublished tests with this breathing apparatus and face mask indicate that actual inhalation temperature was much higher, possibly 65°F. This, of course, has a considerable influence on the magnitude of respiratory heat loss, and evidently allowed thermal balance.

The remaining factor in the heat balance expression is the heat lost through the skin. Heat lost through the skin of the diver-subjects depended on mean temperatures, and on characteristics of the diver, the water heated suit, and the ambient wet pot water. Figure 34 shows a schematic cross section of diver's skin, suit, and wet pot water with a hypothetical mean temperature profile and mean heat flows. The complex shape of the human body and the unknown distribution of hot water within the suit make it difficult to directly calculate this heat loss. However, since the other components of the heat balance are measured, the energy loss through the skin can be calculated indirectly. The results of solving the equation, $Q_s = M-S-W-Q_r$, are shown in column 8 of Table VI. The amount of heat lost by the body at the skin surface must equal the heat flowing to the skin from the deep body tissues. This heat flow can be expressed as follows:

$$Q_s = h_s A_b (T_r - T_{mws})$$

where

$h_s$ = mean heat transfer coefficient for the skin and body tissues, and

$A_b$ = body surface area according to the method of Dubois (15):

$$A_b = \left[0.108\right] \left[W^{0.425}\right] \left[H^{0.725}\right] ,$$

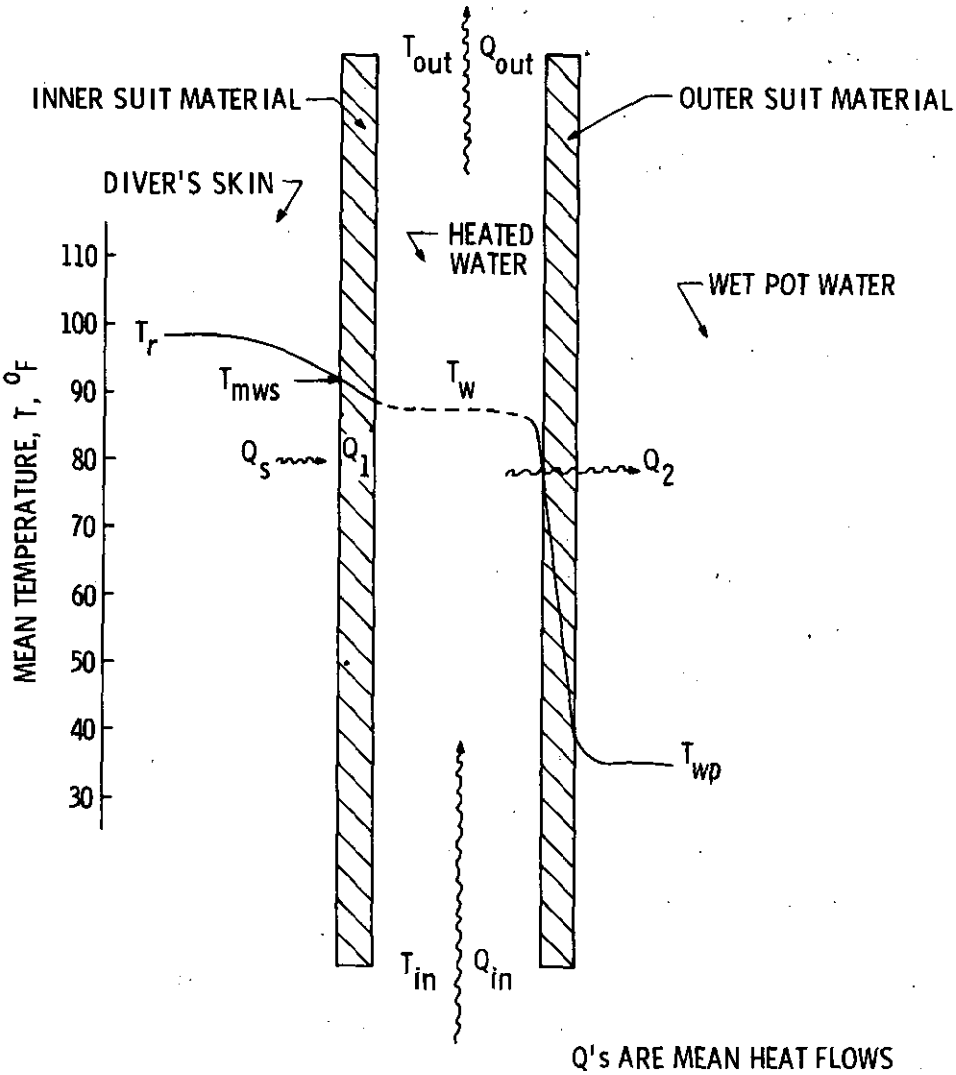


Figure 34. Hypothetical Mean Temperature Profile Across A Diver's Skin And Water Heated Suit.

with weight (W) in pounds and height (H) in inches.

The values for BSA as computed for our subjects are as follows:

| Subject | Body Surface Area ($M^2$) | Data Runs |
|---|---|---|
| SZ | 2.14 | 2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 34 |
| KC | 1.93 | 1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 33 |
| FA | 1.84 | 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 32, 35 |

This equation can be rearranged, and the unknown term $h_s$ calculated using

$$h_s = \frac{Q_s}{A_b (T_r - T_{mws})} = \frac{M-S-E-W}{A_b (T_r - T_{mws})}$$

Results of this equation are given in Table VI for all runs except the first, for which a value of mean corrected heat flow out of the skin was not obtainable.

Calculated values of heat transfer coefficient, $h_s$, show 24 of the 33 values are grouped between $h_s$ = 9.2 and 38.6 Kcal/hr $m^2$°C. The remaining values seemed higher than possible. Nine of the calculated values of $h_s$ are much greater than the approximate range of skin heat transfer coefficients found in the literature. For example, an approximate range of skin conductance is given as 9-30 Kcal/hr $m^2$°C by Webb (36). References (9) (24) indicate that heat transfer coefficients are greatest for high work rates, high skin temperatures, and thin subjects. These sources report variation in $h_s$ between 2.2 and 33 Kcal/hr $m^2$°C, for immersed subjects. The variation in skin heat transfer coefficient is mainly due to differences in fat skin fold thicknesses and the variation in vasoconstriction of the peripheral blood vessels. It is not surprising therefore that six of the nine high values of $h_s$ were for runs by the thinnest diver, F.A.

The divers mean weighted skin temperatures were in the range normally considered to be comfortable (38) (39). This indicates that the peripheral vessels were not constricted, and that the heat transfer coefficient was high.

The measured mean weighted skin temperatures and their correlation with reported comfort zones are contradictory to the divers subjective reports. The method of Teichner, which was selected for calculating mean weighted skin temperatures to allow direct

comparisons with earlier results (3), does not include extremity temperatures. Some sample calculations were made with the DuBois formula which includes extremity temperatures, and the results for mean weighted skin were about 0.8°C (1.4°F) lower. Also it is characteristic of this hot water suit that the extremities are maintained warmer than they are under conditions of thermal comfort in air. A 1°C lower skin temperature is not significant since all the measurements except one indicate that skin temperature is in the comfort range. Also the drop in skin temperatures is much less than would be expected from either the subjective responses or the fall in rectal temperature. Two of the exceptions are runs 23 and 27, which were aborted by the divers.

One explanation for the discrepancy between reported comfort levels and that indicated by the skin temperatures is that the extreme local discomfort of breathing the cold gas interferes with appreciation of warm skin areas. Another may be that sections of the diver's suits trapped and held water, causing cold skin temperatures in areas not under thermistor monitoring. This would cause the measured mean skin temperature to be greater than actual skin temperature, thus producing unreasonably high calculated values of $h_s$. Cold water within the suit could be due to wet pot water flushing in and out, or to low flow of heating water as a result of flow restrictions.

To determine the effectiveness of the water heated diving suit, the heat flow, $Q_s$, through the diver's skin for a typical run is compared to the theoretical heat flow, $Q'_s$, if the diver had been wearing a hypothetical suit with a uniform flow of heating water in it. The hypothetical suit is assumed to have rectangular shape with a length of L, a breadth of B, and a heating water gap of $D_1$. The heated water is assumed to have a uniform velocity and a constant temperature at each distance, x, of the total flow length, L. The typical run chosen for the comparison is run 29. The value of $h_s$ for this run is 21.6 Kcal/hr $m^2$°C, which is about the mean value of the grouped values of $h_s$. The heat flow out through the skin, calculated from test data is 681 Kcal/hr as compared to the heat flow into the skin from the hypothetical suit, 43 Kcal/hr. The heat flow into the hypothetical suit is found from

$$Q'_s = \frac{1}{\frac{1}{h_s} + \frac{D_1}{K_m}} \quad A_b (T_r - T_w) = -170 \text{ Btu/hr } (-43 \text{ Kcal/hr})$$

where

$D_1$ = thickness of inner suit

$K_m$ = thermal conductivity of inner suit material, Btu/hr $ft^2$•F

$T_w$ = mean water temperature inside the suit

The heat transfer coefficient of the skin, $h_s = 4.4$ Btu/hr $ft^2$°F, for run 29 is considerably less than the heat transfer coefficient of the inner suit material, $K_m/D_1 = .1/.00833 = 12$ Btu/hr $ft^2$°F. This indicates that the inner suit material does not significantly contribute to the thermal insulation.

The mean water temperature ($T_w$) used to calculate the heat flow through the skin of the diver with the hypothetical suit is 101°F. This was calculated by assuming heat flow only across the outer suit material. Such a simplification results in little error because the heat flow across the outer suit material is much greater than the heat flow across the inner suit material. Heat flow across an incremental length, dx, of the outer suit material would be

$$dQ_2 = K_m (T - T_{wp}) B dx/D_0$$

in which

$T_{wp}$ = wet pot water temperature.

Heat flow from an incremental length of water in the suit would be

$$dQ_2 = Cp\rho\ V\ dT$$

Equating the heat flows,

$$K_m (T - T_{wp})\ B\ dx/D_0 = -Cp\rho\ V\ dT \qquad \frac{K_m B}{D_2\ Cp\rho V}\ dx = \frac{dT}{T-T_{wp}}$$

Integrating across the water flow length, L,

$$\int_0^L \frac{K_m B}{D_2\ Cp\rho\ V}\ dx = -\int_{T_{in}}^{T_{out}} \frac{dT}{T-T_{wp}}$$

Since

$\rho V = w$, i.e., density multiplied by volume flow equals mass flow,

$$\frac{K_m}{D_2 \, Cp \, w} + -1n \frac{T_{out} - T_{wp}}{T_{in} - T_{wp}}$$

Using (area) A = BL (breadth - length) and rearranging in exponential form, results in the equation of outlet water temperature:

$$T_{out} = T_{wp} + (T_{in} - T_{wp}) \, e^{-\frac{K_m A}{D_2 \, Cp \, w}}$$

Evaluating $T_{out}$:

$$T_{out} = 35 + (110 - 35) \, e^{-\frac{.1 \, (23.0)}{.00833 \, (1.0) \, 1044}}$$

$$= 92.5°F$$

The temperature distribution is a function of water flow path length and surface area, resulting in a mean water temperature in the suit of

$$T_w = \frac{1}{A} \int_0^A T dA$$

For the case of even distribution, $T_w$ can be approximated by $T_w = (T_{in} + T_{out})/2$. For the example just described $T_w = 101°F$.

The mean skin temperature for the diver wearing the hypothetical suit is about 100°F and the suit is adding heat to the diver's body. This was not the case during this study since the skin temperatures were always below core temperature, and the thermal gradient indicates heat flow from the body. This is corroborated by the correlation between values of $h_s$ derived from the heat balance and those reported in the literature. The suits therefore did not heat the body, but by maintaining a warm skin temperature did decrease the magnitude of heat flow from the body core.

Respiratory Effects

It must not be thought that the subjects were able, uniformly, to swim and endure their exposures in 35°F water at 850 feet to completion. In three such instances the diver elected to discontinue the run, and thus we present 137 sets of data rather than 140. Often it was necessary for the divers to interrupt the swimming tasks because the accumulating fluids within the breathing valve and their mouths inhibited respiration gas flow. Of course, in the simulation scenario of a wet pot, in contradistinction to a real operation in the water, the diver is never more than a few feet away from a refuge. And the applied stresses of these experiments repeatedly forced them to utilize it, even in the runs which they swam to completion.

Diver reports (also refer to Table V) filed subsequent to the aborted runs are of particular interest in this context. Following are brief exerpts:

(1) "By the end of work no. 2 it was constant moderate to severe shaking. During the *rest period it remained same. Right after start of work number 1 I started constant* severe shaking with difficulty in holding work load. When I quit I was unable to even come close to holding work load and was experiencing difficulty in taking breaths."

(2) "At the time I aborted today's dive I was in bad shape. Due to neck and jaw hurting I was having a very hard time holding the mouthpiece. Experiencing severe shakes *with ice cold back and chest.*"

(3) "Torso shivering on work number 3 and rest period, stopped as I started work rate 2. Began shivering while cleaning thermistor, waited for a couple of minutes while shivering, decided the situation was unhealthy at least and possibly dangerous, and bailed out. I really thought I was in jeopardy."

Miscellaneous Discussion

The chamber atmosphere oxygen partial pressure was increased to 0.5 atm. abs. just prior to the excursion dive to 1,000 feet. The length of the swimming-work periods and

interspersed rests was reduced to 15 and 5 minutes, respectively, so that all three subject immersion exposures could be completed within the allotted four hour span of the excursion. Subsequent decompression to 850 feet was gradual, over a period of 10 hours, and was uneventful. There were, likewise, no incidents of decompression sickness during the final ascent from 850 feet to the surface.

SECTION 5

# CONCLUSIONS

Computed magnitudes of respiratory heat loss, observations of progressively decreasing core (rectal) temperatures, and subjective responses (diver reports and observations of their behavior) have been used in formulating the following conclusions which relate to operational diving:

(1) Dives to 850 feet for exposure durations in excess of 90 minutes in water of 45°F (or colder), i.e., with 215 kilogram-calories/hour (250 watts) respiratory heat loss are, in this context, hazardous without supplemental heating of the inhaled gas;

(2) Dives to 650 feet, or deeper, for exposure durations in excess of 90 minutes in water of 35°F, i.e., with 150 kilogram-calories/hour (about 175 watts) respiratory heat loss are, in this context, liable to be discomforting to the point of distraction and task performance degradation.

## SECTION 6

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# Bubble Formation in Physical and Biological Systems: A Manifestation of Counterdiffusion in Composite Media

Abstract. *The counterdiffusion of gases across a composite layer can lead to supersaturation and development of bubbles within the layer. A physicochemical model has been derived to predict the extent of such supersaturation; experiments with inert liquid layers confirm predictions. These findings explain the evolution of cutaneous lesions observed in man during simulated deep-sea dives and the cutaneous lesions and intravascular bubbles experimentally induced in pigs by exchanging certain inert gases across the skin. The phenomena associated with counterdiffusion have widespread physical and biological implications.*

In an attempt to explain several puzzling physiological phenomena observed during simulated diving experiments, we have performed studies of gas counterdiffusion in composite layers. The theoretical analysis and experimental work which followed this line of inquiry have uncovered a variety of effects concerning gas exchange with potential applications in diverse fields, including hyperbaric and underwater physiology, anesthesiology, and membrane biophysics, and in studies of membrane separations and nucleation phenomena.

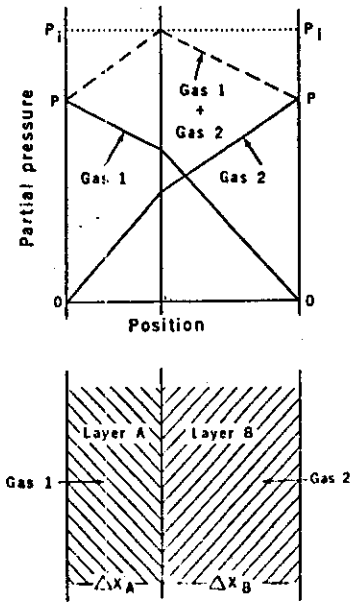


Fig. 1. Gas partial pressure profiles resulting from steady counterdiffusion of two inert gases through a two-layer composite of materials having different permeabilities for the two gases (see text).

The initial observations were made during a series of experiments carried out at the Institute for Environmental Medicine, University of Pennsylvania (Predictive Studies III) (*1*). Subjects in a helium-oxygen environment at a constant elevated pressure developed intense itching; gross, confluent maculopapular skin lesions (*2*); and an incapacitating vestibular derangement including vertigo, nausea, and nystagmus (*3*) within an hour after beginning to breathe a nitrogen-oxygen or neon-oxygen mixture through a mask or mouthpiece. Itching and skin lesions in man under related circumstances had been reported by investigators at Duke University (*4*). The skin manifestations could be prevented by covering exposed skin areas with a relatively impermeable suit ventilated with the same gas mixture that was being breathed.

The investigators at Duke had postulated osmotic gradients and the water flux produced by these gradients (*5*) as a causative mechanism for the skin lesions. We examined the counterdiffusion of two gaseous species through a two-layer structure and concluded (*6*) that, under the proper conditions, supersaturation with the attendant possibility of bubble development would exist in some region within the two-layer system (that is, the sum

of the two gas partial pressures would exceed the ambient pressure, which is equivalent to the statement that the amount of gas dissolved would exceed that corresponding to equilibrium at the ambient pressure).

The counterdiffusion supersaturation phenomenon is most readily illustrated by assuming constant diffusivities and ideal solubility relationships for the gases. These restrictions are not necessary, but they simplify the analysis and lead to the possibility of developing quantitative conclusions and criteria through a mathematical model. Figure 1 illustrates the linear partial pressure profiles which are calculated to result during gas counterdiffusion under the conditions described. The properties of the layers and permeants have been chosen in such a way that the resistance to transport is low in the first layer that a permeant traverses and high in the second layer. The sum of the partial pressures is shown as a broken line which in this case is always above the ambient pressure and is a maximum at the interface of the two layers. More specific information can be gained by starting with a flux equation based on a combination of Fick's law for diffusive flux and Henry's law for the gas solubilities (*7*)

$$J_{1A} = -K_{1A}\frac{\Delta P_{1A}}{\Delta X_A} \qquad (1)$$

where $J_{1A}$ is the flux of species 1 through layer A, $K_{1A}$ is the permeability coefficient of 1 in A (the product of diffusivity and solubility), $\Delta P_{1A}$ is the partial pressure difference of 1 across layer A, and $\Delta X_A$ is the thickness of A. By writing the four equations of this type for the two permeants and the two layers and invoking restrictions such as the continuity of fluxes, one can find an expression for the sum of the partial pressures at the interface between the two layers ($P_i$). For pure permeants 1 and 2 at equal pressure $P$ on opposite sides of layers A and B, the following result is obtained:

$$\frac{P_i}{P} = \frac{\Delta X_B K_{1A}}{\Delta X_B K_{1A} + \Delta X_A K_{1B}} + \frac{\Delta X_A K_{2B}}{\Delta X_A K_{2B} + \Delta X_B K_{2A}} \qquad (2)$$

The first term in Eq. 2 is the relative partial pressure of component 1 and the second term that of component 2.

Two consequences of this model are particularly interesting. The first is that the two layers do not have to exhibit opposite semipermeabilities for the two gases to produce supersaturation ($P_i/P > 1$). A necessary and sufficient condition is simply that the layers exhibit different semipermeabilities and that they be arranged in the proper sequence. Specifically, the condition is given by

$$\frac{K_{1A}}{K_{2A}} > \frac{K_{1B}}{K_{2B}} \qquad (3)$$

The second consequence is that, for a particular pair of permeants and of materials, a maximum supersaturation is obtained at a certain ratio of layer thicknesses:

$$\frac{\Delta X_A}{\Delta X_B} = \left(\frac{K_{1A}}{K_{1B}}\frac{K_{2A}}{K_{2B}}\right)^{1/2} \qquad (4)$$

The absolute thicknesses are immaterial at steady state. If at least one of the layers is liquid and if suitable nuclei are present, bubbles will form and grow continuously. With poorly adherent solid layers, blebs or gross separation could result. If mechanical restraints are imposed which prevent layer separation, an increase in pressure in the gas phase within the layers will be seen.

Although this analysis has been presented for dissolved gaseous permeants, it is by no means limited to them. For example, in the case of two solutes which participate in a common chemical reaction, the product of chemical activities (or, in the ideal case, concentrations) may be of primary importance rather than the sum of partial pressures. Counterdiffusion in this instance might drastically alter the velocity of a chemical reaction. Specifically, consider a case where two different reactants are maintained at equal concentrations in separate compartments (for example, intracellular and extracellular) and that a reaction involving them takes place between two sequential membranes separating the compartments. If each membrane is perfectly permeable to the reactant in contact with it and impermeable to the second reactant, the concentrations within the intramembrane space would be the same as in each external compartment. If we prepare a second system having two identical membranes with some finite permeability, however, the intramembrane concentrations would be half those in the two compartments. For a reaction which is first order in each reactant, the rates in those two cases would differ by a factor of 4. This illustrates how reaction rates in a multimembrane system such as a cell might be quite different from those anticipated.

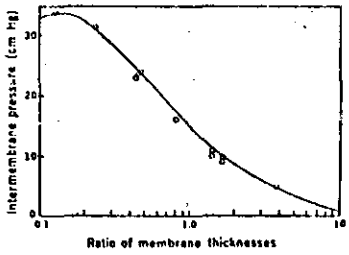


Fig. 2. Confirmation of Eq. 2 (solid curve) with an ethyl cellulose–silicone copolymer two-membrane system (data points). The ordinate represents the steady-state pressure buildup (between the membranes) over ambient pressure (outside the membranes) as a function of the thickness ratio of ethyl cellulose to silicone. The solid curve was calculated from measured permeabilities by using Eq. 2; the data points were measured in a dual-membrane cell. Note that the pressure goes through a maximum as predicted by Eq. 3.

The prediction of counterdiffusion supersaturation leading to bubble formation has been confirmed through a series of related experimental studies, both in model physical systems (*6*) and in vivo with young pigs (*8*). With the physical model we have demonstrated bubble evolution in an oil-water system seeded with crushed glass for nuclei with counterdiffusing nitrogen and helium (helium on the water side) (*6*). We also used two solid membranes as the layers [General Electric XD1 silicone copolymer (*9*), and ethyl cellulose or polyethylene] with the same counterdiffusing gases (nitrogen on the silicone side). A small gas space was provided between the two membranes with an outlet so that flow into the space or pressure buildup could be monitored. Even with a relatively crude apparatus, we measured both a continual flow of gas into the space and a pressure buildup to 25 torr ($3.4 \times 10^4$ dyne/cm$^2$) when the outlet was closed off in the silicone-polyethylene system. A very satisfactory confirmation of Eq. 2 was obtained in the silicone–ethyl cellulose system (see Fig. 2). A substantial pressure of 336 torr was measured in one case. In the physiological studies, young pigs anesthetized with pentobarbital breathed a mixture of one inert gas such as nitrogen or nitrous oxide with oxygen at its normal 0.21-atm pressure while they were surrounded by a second inert gas, helium (*8*). In this in vivo situation the specific inert gas atmosphere surrounding the skin of the pig (source 1) contained a gas which diffused through the skin to the blood capillary (sink 1). The blood itself contained the highest tension of a second inert gas (source 2) which diffused out-

ward through the skin to the atmosphere (sink 2). These exposures led to formation of gas bubbles in the skin and in cutaneous blood vessels.

In the physiological studies (*8*), more than 50 such animals were exposed to counterdiffusion conditions for periods of at least 6 hours. In 43 cases where the pig was surrounded by helium and the normoxic (0.21 atm) breathing mixture contained nitrous oxide at atmospheric pressure, or argon or nitrogen at pressures ranging from 1 to 10 atmospheres absolute, skin lesions occurred after an average exposure time of 80 minutes. In the animals where conditions were reversed (argon or nitrous oxide surrounded the pig while the inspired gas was a helium-oxygen mixture), no lesions were observed in any animal throughout the 6-hour duration of the experiment. In the "reversal" experiments we selected those conditions of gas and pressure which had produced the most severe lesions, but reversed the direction of the gas gradients. The most pronounced effects were seen with a nitrous oxide–oxygen mixture for the breathing gas at atmospheric pressure and with an argon-oxygen mixture at 10 atm pressure. Details of the in vivo studies, including implications for gaseous anesthesia, will be described elsewhere (*8*).

The tissue layers involved in the development of lesions were found to include the adipose subcutaneous tissue, the capillary plexus, and the keratinized outermost layers of the skin, each of which is traversed by the permeating gases (*8*). Constituents of such structures include lipids, lipoprotein membranes, and aqueous solutions, and we have demonstrated bubble formation in a lipid-aqueous system. Finally, the in vivo experiments with pigs were found to obey the condition demanded by Eq. 3, namely, lesions form when the gases counterdiffuse in one direction but do not form when the gases are reversed.

The consequences for physiology and anesthesiology of bubble formation in tissues and vessels are apparent. Less obvious, perhaps, is how membrane transport phenomena might be affected by factors such as the increased reaction rates suggested above. These brief examples should alert specialists in various disciplines to a few of the unusual properties of countertransport in composites. We suggest three potential applications. The study of nucleation phenomena should profit from the opportunity now presented to achieve known steady-state supersaturation levels in specific regions of a system. The conversion of free energy of mixing to work has already been achieved in our crude two-membrane device and remains to be further exploited. By operating the two-membrane device "backward" (that is, supplying a gas mixture to the intramembrane space and removing two relatively purified product streams from either side of the membranes), a separation device with interesting properties can be constructed.

D. J. GRAVES
*School of Chemical Engineering, University of Pennsylvania, Philadelphia*
J. IDICULA, C. J. LAMBERTSEN
*Institute for Environmental Medicine, University of Pennsylvania Medical Center*
J. A. QUINN
*School of Chemical Engineering, University of Pennsylvania*

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# REPORT

# ON USE OF

# HELIUM OXYGEN MIXTURES

# FOR DIVING

REPORT NO. 2

Apr 1939, Rev. OCT 1942

EXPERIMENTAL DIVING UNIT
NAVY YARD, WASHINGTON, D.C.
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## GENERAL DISCUSSION OF THE DEVELOPMENT OF THE PROJECT

Lieutenant Commander C. B. Momsen, USN.

The diving suit of the present day is essentially the same as the one that Siebe, an Englishman invented in 1837. It is a closed dress made of heavy water proof canvas. This is attached to a breast plate which is a saddle shaped metal plate which fits around the neck and rests on the shoulders. The helmet is attached to the breast plate by an interrupted screw thread. Air supply hose and telephone cable and life line combined are attached to the helmet, being passed around under the left arm so that the left hand can manipulate the air supply through the control valve. On the helmet at the point where the supply air enters, an automatic non-return valve is installed so that if the air hose is ruptured air will not escape from the helmet. On the right side of the helmet an exhaust valve is provided. This has a spring loaded valve in it, the action of which is to allow the pressure in the helmet to be slightly greater than the surrounding water pressure so as to keep the suit partially inflated and thus keep the weight of the helmet and breast plate off of the diver's body. The exhaust valve opening can be adjusted for the amount of air that is desired to have excape in order to insure proper ventilation. About 41/2 cubic feet of air per minute per atmosphere is considered sufficient for working conditions. The main purpose of having this ventilation is to keep the carbon dioxide and moisture content in the helmet at a low level. While it is also essential to provide make up oxygen, this can be accomplished with a very much smaller supply.

While some divers do not use gloves, it is the usual practice in the U.S. Navy to have canvas gloves cemented to the sleeves. These gloves are a split mitten, two fingers in each partition. A heavy leather belt with lead weights fastened to it is placed around the waist outside of the suit. There are straps over each shoulder to take the weight and a jock strap through the crotch to hold the suit down and close to the body. The legs are tightly laced so that they will not fill with air and upset the distribution of buoyancy. On the feet heavy lead soled shoes are worn. The entire equipment weighs about two hundred pounds.

From the earliest days of diving, man has dreaded the disease of divers known as bends. History is filled with cases where men have come up from the depths paralyzed, blind, cramped with pain, or even totally unconscious. For years they did not understand the reasons for bends. They prayed for relief, took hot baths, and even partook of magic in one form or another. The problem has been studied by many prominent physicians and physiologists. The application of the laws of physics and the method of trial and error have gone a long way toward the solution.

Haldane, a prominent English physiologist, in association with Boycott and Damant, made the greatest contribution to the art of diving when he introduced the stage method of decompressing after a dive. It was he, too, who classified the various tissues of the body according to the time that it takes the blood stream to fill them with gas. He published tables up to a depth of 204 feet which were generally safe. These tables have been extended by others, but since Haldane did not publish his exact method of calculating his tables, the extension has been made the hard way, e.g., by trial and error.

Nitrogen is a very stubborn gas with a great affinity for fat and a hundred successful dives might be made using the same decompression table without the slightest symptom and yet the one hundred and first dive on the same schedule may develop a serious case of bends.

Experts have been casting curious eyes in the direction of helium as a substitute for this nitrogen for years, in fact ever since it was first suggested by (Sayers, Hildebrant and Yant) in 1921.

The U. S. Navy took steps to investigate Helium, starting in 1925. It was found that mixed with the proper amounts of oxygen it was absolutely harmless at atmospheric pressures and that under pressure it seemed to be better than air. They found also, that a diver can get bends from helium just as badly if not worse than from air. The studies were interrupted for a number of reasons and the problem lay more or less dormant until 1937. In the past year considerable progress has been made. Divers have reached a depth of 500 feet in tanks and 400 feet in the open sea. Promise of even greater depths has been indicated.

Older divers and pioneers in the diving art simply cannot believe that such depths are within the grasp of man. The unravelling of the mysteries of the theory of decompression from a helium dive has been quite complicated and at time disappointing, but at no time without interest. New equipment must, of course, go hand in hand with the development of the theory. Both have led the investigators up many blind alleys.

For instance, it was found that a man suffers more from cold when breathing helium than when breathing air. Electrically heated under clothing was provided and it was found that about twice the heat was required to keep a diver warm in cold water when breathing helium as compared with when breathing air. Temperatures at great depths in the sea are very low, in fact they may be well below freezing.

Substances which are not ordinarily combustible under atmospheric conditions might become highly combustible when exposed to high oxygen. Consequently the ordinary insulation of diving underwear which might be considered safe in every-day life would become dangerous to a diver when he is exposed to high oxygen pressures. To meet this condition steps have been taken to have the wires used in the heating elements in the diving underwear insulated with glass thread and the wire pads enclosed with glass cloth.

Another problem which develops when divers go to great depths is the matter of handling his hose, life line and telephone cable. Aslight current on a long scope of these lines might very well pull the diver off of his descending line.

Stronger hoses and fittings than heretofore used have to be developed. Several changes in the standard diving dress have had to be made.

To use synthetic mixtures at the rate of 4 1/2 cubic feet per atmosphere, per minute, would require very large storages of gas aboard ship. In order to reduce the amount used in the suit, it was necessary to develop an apparatus that would first, remove the excess carbon dioxide, second, remove the excess moisture and third, provide make up oxygen for that consumed by the body. The first consideration was the oxygen, for in addition to making certain that the diver has enough oxygen to sustain life, it was highly desirable to keep up the oxygen partial pressure so as to prevent the increase of partial pressure of the helium that controls the decompression requirements. It was calculated that a half a cubic foot (14 liters) of gas containing not less than 15% oxygen would provide about 2.1 liters of make up oxygen per minute, which is enough to sustain life in a man doing fairly hard work. A closed circuit which would return the exhaust gas to the surface for revitilization would be impracticable. It was first thought that it would be necessary to provide the diver with supplementary equipment somewhat resembling the rescue breathing apparatus, including a compressed supply of oxygen-helium mixture. This idea was, however, abandoned. The gas contained in the diver's dress must be revitalized by forcing it through a chemical absorbent. In the rescue breathing apparatus a mouthpiece is employed whereby the lung pressure is used to accomplish the circulation. In order to avoid the use of a mouthpiece and yet maintain a forced circulation it was suggested by the late Dr. J. A. Hawkins of the Experimental Diving Unit that the oxygen-helium supply which provides the make up oxygen to be used as a driving agent in an aspirator to force the diver's gas through the absorbent without effort or attention on his part.

It has been found that the standard hose and fittings should be retained. A small hose is led from the regular hose on the supply source or surface side of the control valve. With this arrangement the driving gas is led to the jet described below, with the control valve closed, yet should the diver require a sudden additional supply of gas, as for instance when descending, he has merely to open his control valve.

The aspirator, or circulator as it is called by the divers, is a venturi tube, into the throat of which a jet is fitted, having an orifice so proportioned that with 50 pounds per square inch differential pressure, a volume of gas, which contains oxygen, is introduced in any given time, which is sufficient to replace the oxygen consumed by respiration and, at the same time, the venturi tube forces a total volume from the helmet through a cannister containing moisture and $CO_2$ absorbent, and back into the helmet, which is equal to the volume exhaled by the diver in the same time interval. The excess gas that tends to accumulate escapes through the exhaust valve. By means of this circulator, the diver is given sufficient ventilation and uses only about one fifth the amount of gas that would be required using normal ventilation.

In the beginning of the work, soda lime was used as the absorbent, but it was found that it did not absorb the moisture and the excess moisture not only fogged the face plates of the helmet, but dampened the soda lime which reduced the effectiveness, allowing the carbon dioxide to build up.

Shell Natron, a caustic potash mixture, is now used and is quite satisfactory. It has a tremendous affinity for moisture and even when exposed to the air will deteriorate rapidly for this reason. This chemical was at first purchased in 50 pound drums, but it was found that in opening the drum from day to day, moist air entered the drum with the result that the last part of the material was spoiled. It is now supplied in three pound cartons and one pounds is used in the cannister for each dive. One pound has been found to last three hours provided the diver does no hard work, and 30 minutes doing hard work.

The method of attaching the breast plate to the suit of standard dress is accomplished by bolting. Twelve equally spaced holes moulded in the rubber collar of the suit fit over twelve studs in the breast plate. Four strips of metal, two in front and two behind, fit over the studs to hold the collar securely. Wing nuts clamp the strips into place.

While the standard method of attaching the breast plate to the dress is satisfactory when diving on air, it has undesirable features when using helium-oxygen mixtures. In the first place the old attachment is not always gas tight and it is more important to keep the suit tight when using helium because a small amount of gas is used. In the second place, it is desirable to have the suit so built that the diver can be quickly undressed by one man for reasons that will be explained elsewhere. A mean of attaching the breast plate to the suit by quick operating wire cables invented by Mr. William Scrimgeour, was developed by the Navy Yard, Washington, D.C. and suits without the moulded holes in the rubber collars were obtained. The new method of attachment makes the suit tight and does not detract from the comfort of the diver. By suspending the weight of the helmet and breast plate from overhead one man may remove them as a single unit from the diver quite easily.

When decompressing a diver after an exposure to helium-oxygen mixtures many hours time can be saved by using oxygen instead of continuing on the same helium-oxygen mixtures. It is however, feasible to decompress on air or on the helium-oxygen mixtures. It was found that the body cannot stand a direct change from helium to nitrogen at depths beyond six atmospheres without discomfort. The adverse effects may be caused by the sudden increase of weight of the nitrogen, because nitrogen is seven times the weight of helium. If, however, the air is supplied gradually, at the approximate rate of 3% increase per minute, the diver is unaffected, except for the usual sense of depth caused by the nitrogen. In actual practice gradual shift from helium to air is accomplished through use of the circulator for the first 20 minutes decompression time. After this air may be ventilated through the helmet in the usual manner. Using air for decompression is more economical than using oxygen or helium-oxygen. It is much slower and not as reliable as oxygen. Since pure oxygen should not be used at depths greater than 60 feet, the decompression must be made on helium-oxygen mixtures up to that point. It is desirable when doing this to keep the oxygen tension as near to 2 5 atmospheres effective as practicable.

It is not desirable to have the diver suspended over the side of the ship for long periods waiting for decompression. In the first place it entails more lines in the water and more tenders on deck, thus adding confusion to a job when it is desired to have work on the bottom proceed by using relief divers, in the second place it is uncomfortable for the diver, and finally it places the ship and the diver in a precarious position should it become necessary to move because of stress of weather.

For these reasons a submersible decompression chamber has been built somewhat similar to the rescue chamber which has been in use for many years. This chamber, containing one operator, is lowered in the water, being guided down the descending line by a large ring bolt welded to its side. A telephone and other essential equipment are inside. Upon reaching the depth of the diver's first stop, the pressure in the chamber is built up to an amount equal to surrounding sea pressure by admitting compressed air. The hatch at the bottom is opened and the descending line is fished into the hatch opening. The diver coming up enters the hatch opening by ascending a ladder attached to the bottom of the chamber. The operator passes a safety line around the diver, fastens another line to the helmet and then unfastens the breastplate wire. This permits the diver to duck out of his helmet and breast plate. The diver then puts on a breathing mask and decompression begins. The operator, after covering the breast plate with a canvas cover drops the entire apparatus out of the bottom of the chamber so that it can be hauled to the surface. He then closes the hatch and undresses the diver as necessary. The chamber can now be hoisted clear of the water and placed out of the way on deck. Decompression is controlled from this point on by the operator by means of regulating the air pressure inside the chamber.

It is contemplated having a means of locking the diver and operator from the submersible chamber to the main decompression chamber so as to render the submersible chamber available for the next diver.

When a diver is exposed to an increased pressure and is breathing air, the pressure is immediately transmitted throughout the entire body. Since the body is largely liquid and is for all practical consideration incompressible there is no sense of pressure as a physical force, except in certain small passages. The eustachian tubes and sinus canals are such small air passages which might be blocked by slight infection or by mucous. When this occurs the pressure tending to collapse these spaces may produce pain.

The body of a normal healthy man, such as a diver has to be, consists of about 80% water, about 15% fat, and the rest solids. It is a well known fact that fat and water will hold in solution definite amounts of gas. The amounts vary with the solubilities of the different gases and also vary directly as the pressure to which the liquids are exposed. While the amounts do also vary with temperature changes, the body's temperature is nearly constant and need not be considered.

Consequently when the body is exposed to increased pressures these physical laws cause the body liquids to have a greater absorption capacity for the gases. The process of increasing the saturation of the body is accomplished in the main through the blood stream. The increased pressure is first introduced into the lungs by breathing. The blood is distributed through tiny vessels, capillaries, over a tremendous area, approximately 1000 square feet, in the many folds and irregular surfaces in the lungs. These small vessels have very thin walls and the gases taken into the lungs diffuse through the walls into the blood. The capillaries flow into a larger vessel and the blood is assembled into a large artery where it starts on its journey through the body. When it leaves the lungs it is saturated with the gases which were present in the lungs to an amount corresponding to the solubilities of the various gases, the percentages of each gas present and the pressure to which the gases are exposed. The term partial pressure is used so much and can be so confusing that a definition of its meaning is in order. The partial pressure of a gas is the actual pressure multiplied by its percent of the total. Thus if air is 79% nitrogen, at a pressure of 100 pounds the partial pressure of nitrogen would be 79 pounds. It is customary to express the partial pressure (pp) in terms of feet depth of salt water when using the term in diving. An atmosphere of pressure (14.7 pounds per square inch) is very close to the pressure exerted by a column of sea water 33 feet high. Thus for rough calculating it is a close approximation to assume that each hundred feet of salt water will result in 3 atmospheres of excess pressure. To return to the blood stream which is saturated with gases from the lungs, the circulatory system now distributes the blood to every part of the body and when the blood is again spread out by means of capillaries these gases are exposed to the tissues and the partial pressure of gas builds up in the tissues while the partial pressure in the blood is lowered a corresponding amount. Of course, one of the main purposes of the blood circulation system is to supply the oxygen to and remove the carbon dioxide from the tissues. When the blood leaves the capillaries the gas pressure in the blood of each capillary is in a state of equilibrium with the tissues which it supplied. The blood is collected in veins and finally returns to the lungs. When the blood is returned to the lungs it has lost some of its partial pressure as a result of its distribution throughout the body and a new load of gas is picked up in the lungs. This process is continuous and when all of the tissues are saturated with the gases which are being breathed, the body is said to be in a state of saturation corresponding to this pressure. With every change in barometer and every change in altitude a readjustment of the amount of gas in the body follows.

An average persons' body contains about one liter of nitrogen in solution. This amount increases if the barometer increases and of course, decreases when it is lowered. The ability of the body to thus accommodate itself to changes of pressure causes the complicated problems of deep sea diving, for when a man has become saturated with gas at a great pressure, the process of elimination of this gas is slow and the lowering of the pressure must be slow so as to prevent the gas from forming as bubbles before the blood stream can carry it off through the lungs. It is hardly necessary to say that the formation of gas bubbles in the blood stream might be extremely dangerous if not fatal, for this condition is bends.

Gingerale is prepared with carbon dioxide gas in solution at a pressure of a few pounds more than atmospheric pressure. It has this gas in solution and the gas is, therefore, not visible. If, however, the bottle is uncapped the excess pressure is imediately removed and the liquid cannot hold as much gas in solution. Bubbles form and the gas escapes. (If the bottle were opened very slowly no bubbles would excape into the air). After several hours the gingerale would cease to bubble, that is to say the partial pressure of the gas in the liquid would be in equilibrium with the surrounding atmosphere and no more gas will come off. Liquids will hold a greater amount of gas than the solubility laws permit, without bubbling. The excess will begin to diffuse out, however, when a small pressure decrease is made. When a liquid contains in solution an excess of gas and yet this amount is insufficient to cause it to bubble it is considered to be super-saturated. This condition is utilized in providing decompression for divers.

To return to the example of the gingerale. If the bottle is uncapped and allowed to stand the bubbles will form and escape. At the moment that bubbles cease to come off the gingerale is super-saturated to its maximum. That it is super-saturated may be demonstrated by stirring the gingerale or shaking the bottle. The gas in super-saturation being in an unstable condition will again start to bubble. If the gingerale is supersaturated and the bottle is re-capped, the pressure will build up above the fluid in the bottle to an amount equal to the super-saturation pressure.

It has been found that the pressure on the body of a diver may be reduced a certain percentage of the total without causing bubbles to form. The relation of the total partial

pressures of the gases in the body to the pressure to which it can be reduced with safety is called the safe ascent ratio. It naturally follows that the greater this ratio the more rapid will be the elimination of excess gas from the tissues.

When a man takes a breath of ordinary air it contains about 78% nitrogen, about 20.9% oxygen, .03% carbon-dioxide, various amounts of water vapor, .94% argon and minute quantities of the several rare gases. All of these are nearly constant except the water vapor and when the air is adjusted to the body temperatures in the lungs the water vapor percentage is constant and corresponds to the vapor pressure at 98.6°F. It is usually expressed as 47 millimeters of mercury partial pressure and in a standard atmosphere of 760 millimeters of mercury will be 47/760 or 6.2% of the total. This 6.2% of water vapor reduces the effective percentages of the gases breathed. Thus dry air contains about 79% nitrogen but after it enters the lungs it is reduced to about 79 over 106.2 x 100, or to about 74%. In the lungs the carbon dioxide which is being deposited by the blood is about 5.3%. As breathing proceeds fresh air is taken into the lungs and is mixed with the air in the lungs. Upon exhalation the mixture is released and this will contain somewhat less than 5.3% carbon dioxide. With each breath the carbon dioxide is washed out of the lungs so that the amount left is always about 40 mm partial pressure. Through automatic features in what is called the respiratory center through which the blood flows the depth of the breath and the number of breaths per minute are regulated so as to maintain the partial pressure of the $CO_2$ in the blood and the partial pressure in the lungs nearly constant.

Should the body be exposed to two atmospheres of external pressure, that is, one atmosphere excess, the partial pressure of both water vapor and carbon dioxide would remain the same but the actual percentage of the gas present would be halved. The importance of this fact may be seen when we consider breathing mixtures of gases which contain carbon dioxide. For instance, if air containing 4% $CO_2$ were breathed at atmospheric pressure it is easy to see that a great increase in lung ventilation is necessary in order to keep the $CO_2$ in the lungs at 5.3%. Also, if we breathe air containing more than 5% $CO_2$ we would soon find that no amount of ventilation would keep the lung $CO_2$ down to 5.3% and this would result in severe panting followed by collapse.

Likewise at two atmospheres absolute pressure if we breathe more than 3% $CO_2$ in air we would encounter distress. Thus if a man is breathing air in a confined space at one atmosphere and the $CO_2$ builds up to one or two per cent he may not

notice the change in breathing. If however, this space were suddenly compressed to several atmospheres as in the case of a submarine compartment when flooding for excape, or in a diving bell when lowering in the water, the $CO_2$ effect would increase in direct proportion to the increased pressure and the same percentage that was hardly noticeable before would now become intolerable.

To much emphasis cannot be placed upon the importance of *keeping the gases breathed free from $CO_2$ when working at* higher pressures.

Every one is familiar with the fact that we breathe air in order to obtain oxygen which in turn supports life. While oxygen is no exception to the gas laws, its action in the blood is somewhat different from the other gases. It does go into solution in the blood much the same as does nitrogen, but almost immediately thereafter it combines loosely with the blood haemoglobin in a chemical combination and leaves but a small amount remaining in physical solution. It is chemically combined oxygen which supplies the tissues and for all practical purposes we do not have to consider oxygen as a gas in solution, even though it does exert its influence upon the percentage of the other gases, that actually enter into solution in the lungs. In effect this action of the oxygen produces a partial pressure vacancy. This vacancy must be filled by the other gases present when going from higher pressure to a lower pressure before a state of super-saturation can exist.

For example, consider the body exposed to two atmospheres, pressure 66 feet absolute and the gas breathed to be air. Suppose the nitrogen partial pressure is 79% x 66 or 52 feet absolute. Neglecting the influence of the other gases which will be discussed later and considering only the partial pressure vacancy created by the oxygen action we should be able to drop the pressure to 52 feet absolute without incurring any super-saturation on the part of nitrogen. We know that in addition to the drop in pressure that we can tolerate a certain amount of drop by reason of super-saturation. The degree of super-saturation that the tissues in the body can stand has been determined experimentally and is expressed as the ratio of the partial pressure to the absolute pressure of the depth. This ratio is about 1.7 to 1.0. In the case discussed above if the body is saturated at two atmospheres and the partial pressure of the nitrogen is 52 feet the pressure may be dropped by reason of taking advantage of super-saturation to a point obtained by dividing 52 by 1.7 which is 30.5 feet absolute.

Since 33 feet absolute is atmospheric pressure it would be safe to surface after saturation at 2 atmospheres or 33 feet gauge. Again suppose a diver remains at 100 feet gauge long enough to become fully saturated. This would be 133 feet absolute and by the same calculations he would have a nitrogen partial pressure of 79 x 133 or 105 feet. The absolute depth of the point at which he would have to stop would be 105 feet absolute divided by 1.7 or 62 feet absolute which would be 62 minus 33 equals 29 feet gauge.

Haldane, in his studies of pressure problems, inferred that all parts of the body do not saturate at the same rate because of different rate of blood supply and because of differenct capacities of the different types of tissues. His conception of time tissues are classified in accordance with the time that it takes them to become fully saturated. The process of saturation, as explained earlier is one of continuous equalization between the blood stream and the tissues. The curve formed by plotting per cent saturation against time is exponential in form and the values have been computed and made up into a table for convenient use. Figure 1. The designation given to a tissue is that time, expressed in minutes which it takes the tissue to half saturate. Thus a 20 minute tissue is one which will become 50% saturated in 20 minutes, 75% saturated in 40 minutes, 87 1/2% saturated in 60 minutes and half of each remaining amount for each additional 20 minute period, or for each additional time unit.

Of course, there are a great number of different time tissues and the tissues belonging to each are widely scattered. For convenience Haldane selected certain times for classifying the tissues. These are 5,10,20,40 and 75 minute tissues.

The writer prefers to plot all tissues in a continuous curve so as to obtain a clearer view of the state of saturation at each stage of the exposure to pressure. Such a series of curves which represent the saturation and desaturation of the body is given in Figure 2. While this hypothesis has been satisfactory in its application to diving on air, the use of helium as a substitute for nitrogen as a diluent of oxygen in breathing mixtures, has led to the belief that diffusion from one tissue to another, especially in the faster tissues has considerable influence on gas elimination. Lieut. A. R. Behnke, Medical Corps, U. S. Navy, a member of the staff of the Experimental Diving Unit, Navy Yard, Washington, D.C. believes that diffusion plays an important part in the problem; so much that he prefers to consider that the body saturates and desaturates as a single unit rather than as separate time units.

There is experimental evidence to support both theories and it is quite likely that both theories play an equally important part when using a gas as highly diffusible as helium.

Earlier investigators of the use of helium in diving made fundamental errors in their methods of calculation. These errors led to discouragement and prevented advancement of the problem. For instance, it was believed that if a mixture of half nitrogen and half helium were used that each of the two gases would act independently toward bubbling and that decompression needed would be only half because of breathing this mixture. This error led the British to report unfavorably on the possible use of helium and led our experimenters into serious trouble resulting in many cases of bends.

There can be no doubt that the peculiar mental effect that is experienced when exposed to high air pressure is caused by the nitrogen. This effect becomes so serious when divers reach depths beyond about 200 feet that many of them are unable to perform even the simplest tasks. Some even become unconscious at depths around 300 feet. A number of writers have claimed that the effect was caused by excess oxygen "burning up the tissues", "oxygen jag", or "oxygen poisoning". That this is not the case has, fortunately, been clearly demonstrated by Behnke in his work at Harvard - and by repeated exposures to high oxygen pressures by men of the Experimental Diving Unit, Navy Yard, Washington, D.C.

The groggy feeling or sense of depth is not experienced when men are breathing helium mixtures even to pressures corresponding to 500 feet, 16 atmospheres. Some forty divers have breathed the helium oxygen mixtures at various depths and the concensus of opinion seems to be that they sense a depth of about 1/4 of the actual depth to which they are exposed. Since helium is about 1/6 the weight of air it was natural to conclude that the groggy effect of air was caused by the weight of the gas in solution in the blood and possibly certain tissues. In order to develop this theory, a quantity of argon gas was obtained. Argon having a molecular weight of about 40 as compared to nitrogen 28 and helium 4, should cause the divers to feel deeper than when breathing air.

All divers who breathed argon-oxygen mixtures reported that they felt about 50% deeper than their actual depth, each was given a different depth and the information as to the actual depth was withheld from them. At a depth of three hundred feet breathing was very difficult, vision was impaired and a feeling of extreme giddiness was experienced.

An interesting experiment was carried out using the yeoman attached to the unit, L. B. Poush as a subject. Being an expert typist, it was felt that he could best demonstrate the efficiency of continued mental and physical coordination. He was placed in the recompression chamber with his typewriter suitably arranged so that he could breathe through a mask and at the same time copy a standard typing exercise. The pressure being raised to a point corresponding to 200 feet depth, first breathing air and next breathing a helium oxygen mixture, Poush copied from the exercise book for five minute periods. Upon completion of the tests he stated that he felt that he had done better when breathing air. Actually he had made nearly three times as many errors, even to the point of skipping whole lines, while breathing air. Yet, his sense of well being sometimes described as intoxication, caused him to believe that he had done well while he was quite conscious of having made some errors while breathing helium-oxygen.

It thus appeared very convincing that the weight of the carrier gas has a decided influence upon the mental condition of the diver.

From the standpoint of mental effect alone it seems that divers should be able to go to a depth of one thousand feet and perform useful work while breathing helium-oxygen mixtures.

The question naturally arises as to why use helium, or nitrogen or any other gas than oxygen. If it were possible to use pure oxygen, it would certainly provide an ideal solution, for no decompression would be necessary, since the tissues would use up the oxygen as fast as the blood could deliver it. A man at rest uses about 250 cc of oxygen per minute and performing very hard work about 4 liters per minute. The blood stream can carry in a rough figure about 800 cc of oxygen. There seems to be a limiting figure on the amount of oxygen that the body can stand in physical solution. Within the safe ranges of oxygen pressures, the amount of oxygen held in physical solution is reduced by the action of the blood haemoglobin combining chemically with this oxygen. This action creates the partial pressure vacancy which in turn causes the carbon dioxide to enter into solution to be carried off from the tissues. It seems to follow that if this partial pressure vacancy is destroyed by the fact that the oxygen in solution becomes greater than the amount that the haemoglobin has lost and can absorb, that the elimination of $CO_2$ will be delayed with subsequent harmful effects.

When symptoms are produced by breathing excess oxygen they are almost immediately and completely removed by lowering the partial pressure of the oxygen breathed.

The effects appear as ringing in the ears, sudden drowsiness, twitching of the muscles or emotional feelings such as irritability. The symptoms may develop rapidly into serious convulsions. For this reason there should be no delay in removing the cause.

It is a distinct advantage to use as high an oxygen percentage as is safe so as to keep the partial pressure of the helium at as low a level as possible. For instance if two and one half atmospheres is safe to breathe and it is desired to dive at 100 foot depth we would use a mixture of 62.5% oxygen and 37.5% helium. This is obtained as follows: 100 feet is 3 atmospheres gauge or 4 atmospheres absolute, which divided into 21/2 atmospheres, the limit of oxygen desired, gives 62.5%. The helium partial pressure would be 37.5% of (100 plus 33) or 50 feet. Since the body may be saturated to 1.7 x 33 or 56 feet partial pressure without requiring decompression, it follows that the time that a person can remain at 100 feet gauge, without decompression, is unlimited if two and a half atmospheres of oxygen is used. On the other hand if a percentage mixture equivalent to air were used the partial pressure would be 80% of 133 feet or 106 feet and the diver would have to stop for decompression at 106/1.7 equals 62.5 minus 33 or 29.5 feet gauge. The length of this and subsequent stops would depend upon the length of the exposure on the bottom.

Thus the partial pressure vacancy created by oxygen is used to its maximum advantage. The principle is also used for decompression and pure oxygen is used for stages at and below sixty feet.

As previously stated the gas comes out of the tissues into the blood stream during decompression. The rate of elimination depends upon the difference in partial pressure between that of the tissues and that of the blood. Consequently, if the partial pressure of the helium in the blood is reduced to zero by breathing oxygen the maximum flow of the helium into the blood stream will be effected and decompression will take place in a minimum of time.

Following a helium dive, decompression may be given with helium, air or oxygen. The method of computing this decompression is the same in general for all cases. If the maximum partial pressure of oxygen is desired, the percent oxygen is obtained as previously stated, that is 2.5 divided by the depth expressed in atmospheres absolute.

The consensus of opinion of all writers on this subject seems to be that no matter what respirable gas is being breathed the carbon dioxide in the alveolar air of the lungs will be about 5.3% and the water vapor about 6.2%. These percentages will vary inversely with the pressure.

The alveolar oxygen percentage will be less than that breathed by the amount of the carbon dioxide and also by a proportional amount of the water vapor percentage for the pressure.

Thus at one atmosphere 20% oxygen will be reduced first to 20 minus 5.3 or 14.7% for the carbon dioxide and then to 14.7 over 106.2 times 100 or 13.9% by reason of the water vapor. Thus we should expect to find about 14% oxygen in the arterial blood.

In the venous blood it has been determined that there is about 5.3% oxygen after the haemoglobin has partially restored itself by taking up the excess in solution.

The carbon dioxide being about 5.3% in the alveolar air will also be that amount in the arterial blood, but will increase to something over 6% in the venous blood.

To summarize the blood will contain the following gases:

| | Arterial | Venous |
|---|---|---|
| Nitrogen | 74.5 | 74.5 |
| Water vapor | 6.2 | 6.2 |
| Carbon dioxide | 5.3 | 6.0 |
| Oxygen | 14.0 | 5.3 |
| TOTAL | 100.0 | 92.0 |

The difference between these two totals, 8% represents the partial pressure vacancy.

Similarly at two atmospheres the amounts will be as follows:

| | Arterial | Venous |
|---|---|---|
| Nitrogen | 76.8 | 76.8 |
| Water vapor | 3.1 | 3.1 |
| Oxygen | 17.4 | 3.7 |
| Carbon Dioxide | 2.7 | 3.0 |
| TOTAL | 100.0 | 86.6 |

The partial pressure vacancy will be 13.4%.

While the oxygen percentage does increase a small amount of this is the percentage of one atmosphere and at pressures in excess of one atmosphere the figure must be divided by the pressure expressed in atmospheres to obtain the true percentage of the total.

The following table shows the partial pressure vacancy for each atmosphere up to ten:

| Atmosphere | Partial Pressure Vacancy (percent) |
|---|---|
| 1 | 8.0 |
| 2 | 13.4 |
| 3 | 15.3 |
| 4 | 16.2 |
| 5 | 16.9 |
| 6 | 17.5 |
| 7 | 18.0 |
| 8 | 18.3 |
| 9 | 18.6 |
| 10 | 18.9 |

These values are for a mixture of gas containing 20% oxygen and they will vary for different mixtures.

It is convenient for plotting the curve of saturation to take time units in ten minute increments up to 60 minute tissues. The time units of each tissue are obtained by dividing the time of the exposure by each time unit. While it is not accurate, it is customary to include the time going to the bottom in the exposure. Actually only half of this time should be included. With the time units obtained, the per cents of saturation are obtained from the table given in Figure 1. These percentages are multiplied by the partial pressure of the gauge depth to give the increased partial pressure of each tissue. Since the body is in a state of full saturation for one atmosphere, each of the partial pressure increases must be added to 27 which is the partial pressure of 1 atmosphere. The next step is the very important one of determining the first stop for decompression. It has been stated previously that when the body is fully saturated the ratio of the partial pressure to the absolute depth to which a diver may ascend is as 1.7 is to 1. While at shallow depths for short exposures it seems that the faster tissues can stand a greater ratio than 1.7 to 1, it appears to be quite safe and is not very wasteful in time to consider this 1.7 to 1 ratio for all tissues and all conditions, for it seems that helium is released in the tissues faster than the blood stream can carry it off and that a substantial stop at a position calculated in this manner is necessary. The partial pressure of the five minute tissue is divided by 1.7 for a trial first stop. This figure is absolute depth and 33 feet must be subtracted from it to obtain the gauge depth. The partial pressure corresponding to this depth is then calculated and using this figure and the partial pressure on the bottom the average partial pressure in going to the first stop is obtained.

The time of ascent to this stop is taken from the table of Rates of Ascent. This time is then divided by 5 to obtain the time units. From the table Figure 1 the percentage is taken. This is the percentage of the differential pressure that the five minute tissue will lose. The difference in pressure is obtained by subtracting the average partial pressure coming to the stop from the partial pressure of that tissue on the bottom. By subtracting the amount lost from the amount on the bottom we get the partial pressure upon arrival at that stop. Again dividing by 1.7 a new first stop is obtained. This process may be repeated until the minimum first stop is obtained. It is advisable to work out the ten minute tissue as well for it sometimes happens that it controls the first stop. For sake of convenience stops are always made at even ten foot marks, and when the first stop is finally selected it should be the 10 foot mark next deeper than the calculated figure, unless this happens to come to a figure exactly divisible by 10.

The time at all first stops should be 7 minutes for it has been found by experience that this amount of time is required to eliminate the initial outrush of released helium. This time comes in handy for the diver to get on his stage or to enter the submersible decompression chamber.

The next step is to calculate the loss or gain of all of the other tissues in coming to the first stop. This is accomplished in the same manner as above. The gain or loss in all tissues for the stay at the first stop is next calculated. The partial pressure corresponding to the first stop is the percentage of all other gases times the absolute depth. The elgebraic sum of the partial pressure of the stop gives the differences in pressure. The signs are minus or plus as the tissues are losing or gaining. The time level minutes is divided by each time tissue giving the corresponding time units. From Table I, the corresponding percentages are obtained. These percentages are multiplied by their corresponding differences in pressure which gives the loss or gain in partial pressure during this part of the decompression. The next stop is determined by dividing the maximum partial pressure of the gases by the ratio 1.7 and subtracting 33. The partial pressure of this stop is obtained and the differences in pressure are determined. From this point, a little different procedure is followed. The absolute pressure of the next stop is multiplied by 1.7 in order to obtain the maximum allowable partial pressure for the next stop. This figure is subtracted from the partial pressure of the tissues which are greater in order to find the amount to lose. The amount to lose divided by the corresponding difference in pressure gives the percent to lose for each tissue. From Table I, the corresponding time units are obtained. These time units are multiplied by their tissue times. The results

give the times that it will take the various tissues to lose a sufficient amount to enable the diver to ascend to his next stop. The maximum time obtained from the various tissues is, of course, selected as the time of the stop. The amount that each tissue gains or loses is then calculated and applied.

This process is repeated until the diver is ready to surface. If oxygen is used after arrival at 60 feet the partial pressure of the stop is very much reduced and the stops may be figured the same as above except that it is not necessary to hurry the stops after 50 feet is reached because nearly maximum decompression will take place even though surfacing from the 50 foot stop. It has been found that when surfacing from 50 feet while breathing oxygen it is good safe practice to use the last five minutes of the time to come up to the surface at the rate of 10 feet per minute.

## RATE OF ASCENT

In computing the rate of ascent to the first stop we have attempted to prevent a state of super-saturation in the venous blood. Since the blood in the veins has a partial pressure vacancy which nearly corresponds to the oxygen percentage being breathed, the pressure may be reduced by that amount without creating a state of super saturation. During the ascent to the first stop, after an exposure to excess pressure, it is extremely important to avoid the starting of bubble formation in the blood stream, for if it is once started, gas diffuses into the bubbles and the size of the bubbles increases. The danger, like a snowball rolling downhill, increases as the pressure is lowered and it is very doubtful that a blockage of blood vessels can be avoided. Consequently the rate of ascent should be regulated upon the basis of per cent change in pressure as well as the per cent of oxygen being breathed. If we can assume that the venous blood clears itself through the lungs in forty seconds, the rate of ascent can be calculated. This assumption is probably correct for since using this method of ascending to the first stop, no cases of bends have been encountered that could be traced to this part of the decompression.

Further evidence of the correctness of this theory was reported by Lieutenant W. A. New, U.S. Navy, Officer in Charge of the Diving School. When breathing air and ascending to the first stop at the usual fifty feet per minute many of the divers developed pronounced itch on the surface of their bodies. He reduced the rate of ascent to 25 feet per minute and no further symptoms were encountered. It is well known that this itch is a form of bends and that it indicates that a dangerous border line is being approached in the decompression procedure.

As an example of calculation of the correct rate of ascent we will take two cases, one 20% oxygen, the other 15%. Owing to the influence of water vapor an $CO_2$ in the lungs the oxygen tension in the lungs for the first atmosphere is 20% minus 6% $CO_2$ over 1.062 for water vapor, or about 13.2%. For the second atmosphere it will be 20 plus 13.2 divided by 2 or about 16.6% etc.

The following table shows these approximate amounts:

| Atmospheres | Oxygen Per Cent (15) | Oxygen Per Cent (20) |
|---|---|---|
| 1 | 8.5 | 13.2 |
| 2 | 11.8 | 16.6 |
| 3 | 12.8 | 17.7 |
| 4 | 13.4 | 18.3 |
| 5 | 13.7 | 18.6 |
| 6 | 13.9 | 18.8 |
| 7 | 14.1 | 19.0 |

Consider coming up from 200 feet to 167 feet a rise of 33 feet. The per cent change in pressure is from 7 to 6 atmospheres or 14.3%. When breathing 20% oxygen, the actual per cent at 7 atmospheres taken from the table above is 19. The time of ascent should be 14.3/19 or .75 times the time interval which it takes for the blood to clear (.67 minutes) or .5 minutes. The rate per minute will be 33 over .5 equals 66 feet per minute. The change in going from 100 to 67 feet would be 25%. The time (25 divided by 18.3) x .67 equals 91 and the rate 33/.91 about 36 feet per minute. Likewise the rate when coming from 66 feet to 33 feet would be about 26 feet per minute and from 33 to the surface 17 feet per minute.

In view of the large number of cases where men have greatly exceeded these rates of ascent without apparent symptoms it would seem that they are greatly exaggerated. However, when the time involved is such time as would be otherwise used for decompression, it is felt that it would be an added comfort to be able to feel that the probability of starting bubbles in this manner is eliminated.

If 15% oxygen is breathed the rate of ascent from 200 to 167 feet would be 49 feet per minute.

The rates would compare as follows:

| Ascent | 20% Oxygen | 15% Oxygen |
|---|---|---|
| 200 to 167 | 66 ft. per min. | 49 ft. per min. |
| 167 to 133 | 56 ft. per min. | 41 ft. per min. |
| 133 to 100 | 46 ft. per min. | 34 ft. per min. |
| 100 to 67 | 36 ft. per min. | 27 ft. per min. |
| 67 to 33 | 26 ft. per min. | 19 ft. per min. |
| 33 to 0 | 17 ft. per min. | 12 ft. per min. |

It is recognized that there is a small amount of oxygen carried in the venous blood (5 to 13.5% of an atmosphere) and that this reduces the partial pressure vacancy. This has not been used in the above discussion but has been incorporated in the table of rates of ascent.

This has been applied by computing the oxygen percent or an atmosphere in the venous blood for each atmosphere of pressure. The oxygen varies from 5.3% when breathing 20% at one atmosphere or 1/5 of an atmosphere effective to 13.5% when breathing three atmospheres effective oxygen. The per cent of an atmosphere is then divided by the number of atmospheres of pressure to get the actual per cent for that pressure. This per cent is subtracted from the per cent of alveolar oxygen to obtain the true partial pressure vacancy in the venous blood.

It is evident from the following table of Rates of Ascent that as the oxygen percentages are reduced for the purpose of preventing high tensions of oxygen on deep dives, care must be taken to not exceed the proper rate of ascent.

TABLE OF RATES OF ASCENT FEET PER MINUTE

| Depth at Point ascent begins | OXYGEN PER CENT - DRY SAMPLE | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 55 | 60 | 54 | 70 |
| 600 | 56 | 132 | | | | | | | | | | | |
| 550 | 51 | 118 | 157 | | | | | | | | | | |
| 500 | 46 | 106 | 143 | | | | | | | | | | |
| 450 | 42 | 97 | 132 | | | | | | | | | | |
| 400 | 37 | 87 | 118 | 150 | | | | | | | | | |
| 350 | 32 | 76 | 103 | 135 | 159 | | | | | | | | |
| 300 | 27 | 65 | 89 | 114 | 137 | 161 | | | | | | | |
| 250 | 22 | 52 | 72 | 94 | 115 | 137 | 159 | | | | | | |
| 200 | 16 | 41 | 58 | 75 | 92 | 109 | 126 | 143 | 160 | | | | |
| 150 | 12 | 30 | 43 | 57 | 71 | 85 | 99 | 113 | 127 | 141 | 155 | | |
| 100 | 7 | 21 | 30 | 40 | 50 | 60 | 70 | 80 | 90 | 100 | 110 | 120 | 130 |
| 50 | 3 | 10 | 17 | 23 | 29 | 35 | 41 | 47 | 53 | 60 | 67 | 74 | 80 |

Since it is not practical to use such odd figures when bringing a diver up to his first stop this table will be rearranged. It is never practical to bring a diver up at a greater rate than 75 feet per minute.

TABLE OF RATES OF ASCENT FEET PER MINUTE

| Depth at Point ascent begins | OXYGEN PER CENT - DRY SAMPLE | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 55 | 60 |
| 600 | 50 | | | | | | | | | | |
| 550 | 50 | | | | | | | | | | |
| 500 | 40 | | ALL OTHERS + 75 FEET PER MINUTE | | | | | | | | |
| 450 | 40 | | | | | | | | | | |
| 400 | 30 | | | | | | | | | | |
| 350 | 30 | | | | | | | | | | |
| 300 | 20 | 50 | | | | | | | | | |
| 250 | 20 | 50 | | | | | | | | | |
| 200 | 10 | 40 | 50 | | | | | | | | |
| 150 | 10 | 30 | 40 | 50 | | | | | | | |
| 100 | 10 | 20 | 30 | 40 | 50 | | | | | | |
| 50 | 10 | 10 | 20 | 20 | 30 | 30 | 40 | 50 | | | |

(B) EXAMPLE OF COMPUTATION OF A DECOMPRESSION TABLE FOR USE WITH HELIUM-OXYGEN DIVING

This example differs from the actual computations as follows:

(a) The minimum tissue sued is 60 minute where as in the tables submitted the 70 minute tissue was used.

(b) The time of exposure was a "rest" time while the tables submitted are for "work" time, which is twice "rest" time.

(c) All tables are calculated considering the mixture used during decompression to be 16% oxygen in order to be on the safe side. In the example, 25% is used.

An example of computing a decompression table follows and the curves of this decompression are shown in Figure 2.

Suppose the depth selected is 300 feet, the time on the bottom 30 minutes, and that the gas breathed is helium and 25% oxygen.

Example of computation of Decompression Table:

Depth - 300 feet.
Time on bottom - 30 minutes.
Gas used - 25% oxygen - 75% helium.
Effective oxygen 25 minus 2 equals 23% (Allowing for a small amount of oxygen in venous blood and loss in helmet).
Absolute depth of dive is 300 plus 33 equals 333 feet
PP of all other gases 77 (100 - 23% 02) times 333 equals 256.4.
PP increase saturation effect 77 times 300 equals 231.
All calculations are made to the nearest foot

Tissue saturation is obtained as follows:

| 1 Tissue | 2 Time Units | 3 %Saturation | 4 PP increase | 5 Total |
|---|---|---|---|---|
| 5 | 6 | 98.5 | 228 | 255 |
| 10 | 3 | 87.5 | 202 | 229 |
| 20 | 1.5 | 64.6 | 149 | 176 |
| 30 | 1 | 50 | 116 | 143 |
| 40 | .75 | 40.5 | 94 | 121 |
| 50 | .6 | 34 | 79 | 106 |
| 60 | .5 | 29.3 | 68 | 95 |

1 - Tissues selected to plot curve.
2 - Time of exposure divided by tissue time.
3 - From Table I.
4 - Percentage (column 3) times 231.
5 - 27 feet plus increase (column 4).

Trial first stop 255 divided by 1.7 equals 150 feet, 117 feet gauge.

Using next higher 10 foot mark, the stop is 120 feet.

From the table of Rates of Ascent when using 23% oxygen, we may come from 300 feet to 250 feet at 104 feet per minute,
250 feet to 200 feet at 75 feet per minute,
200 feet to 150 feet at 63 feet per minute,
150 feet to 120 feet at 50 feet per minute.

For practical purposes the diver should not be brought up at a rate greater that 75 feet per minute. The time of ascent to 120 feet would be 3 minutes. Using the average partial pressure in coming to the first stop is accurate enough for determining the change of partial pressure in the various tissues and the figure is determined by adding the bottom pressure to the pressure of the stop and dividing by two: 256 plus (153 times 77) over 2 equals 187 feet.

Check first stop.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| Tissue | PP | Av.PP | DP | Time | TU | % | Loss | PP at 1st Stop | |
| 5 | 255 | 187 | 68 | 3M | .6 | 34 | 23 | 232 | 136 |
| 10 | 229 | 187 | 42 | 3M | .3 | 18.7 | 8 | 221 | |

Stop will be 136 - 33 equals 103 feet and 110 will be used.

1 - Tissues to be considered.
2 - From saturation and calculation.
3 - Calculated above.
4 - Column 2 less column 3.
5 - Time of ascent.
6 - Column 5 divided by column 1.
7 - Taken from Table 1.
8 - Column 4 times column 7.
9 - Column 2 less column 8.
10 - Maximum amount in column 9 divided by 1.7.

The average pp when coming to 110 feet gauge or 143 feet absolute will be 256 plus (143 times 77) over 2 or 183 feet.

There will be no change in the time of ascent.

The change in pp of all tissues when coming to 110 feet gauge is computed as follows:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|
| Tissue | PP | Av.PP | DP | TU | % | Gain or Loss | PP |
| 5 | 255 | 183 | -72 | .6 | 34 | -24 | 231 |
| 10 | 229 | 183 | -46 | .3 | 18.7 | - 9 | 220 |
| 20 | 176 | 183 | + 7 | .15 | 9.8 | + 1 | 177 |
| 30 | 143 | 183 | +40 | .1 | 6.6 | + 2 | 145 |
| 40 | 121 | 183 | +62 | .075 | 5.0 | + 3 | 124 |
| 50 | 106 | 183 | +77 | .06 | 4.0 | + 3 | 109 |
| 60 | 95 | 183 | +88 | .05 | 3.4 | + 3 | 98 |

1 - Tissues.
2 - pp saturation.
3 - Computed above.
4 - Column 3 minus column 2.
5 - Time units for 3 minutes; 3 divided by column 1.
6 - Percentages for TU in column 5, Table 1.
7 - Column 4 times column 6.
8 - Column 2 plus or minus column 7.

Change in partial pressure as a result of remaining at first stop for 7 minutes

| 1 Tissue | 2 PP | 3 PPofStop | 4 DP | 5 TU | 6 % | 7 Change | 8 PP |
|---|---|---|---|---|---|---|---|
| 5 | 231 | 110 | -121 | 1.4 | 62.1 | -75 | 156 |
| 10 | 220 | 110 | -110 | .7 | 38.4 | -42 | 178 |
| 20 | 177 | 110 | -67 | .35 | 21.5 | -14 | 163 |
| 30 | 145 | 110 | -35 | .233 | 14.9 | -5 | 140 |
| 40 | 124 | 110 | -14 | .175 | 11.4 | -2 | 122 |
| 50 | 109 | 110 | +1 | .14 | 9.2 | 0 | 109 |
| 60 | 98 | 110 | +12 | .12 | 8 | +1 | 99 |

1 - Tissues.
2 - pp at arrival at 110 feet.
3 - (110 plus 33) times 77 equals 110.
4 - Column 2 less column 3.
5 - 7 minutes divided by column 1.
6 - Table 1.
7 - Column 4 times column 6.
8 - Column 2 plus or minus column 7.

It will be noted that the highest point on the curve of saturation will be near the 10 minute tissue and the 10 minute tissue will be used for computing the next stop. 178 divided by 1.7 equals 105 minus 33 equals 72.

One minute should be allowed for bringing the diver to the next stop and the 10 minute tissue will lose about 5 feet in this time so the next stop will be 70 feet.

The average pp will be 110 plus (103 times 77 over 2 or 95.

The change during the ascent will be as follows:

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 5 | 156 | 95 | -61 | .2 | 12.9 | -8 | 148 |
| 10 | 178 | 95 | -83 | .1 | 6.6 | -5 | 172 |
| 20 | 163 | 95 | -68 | .05 | 3.4 | 2 | 161 |
| 30 | 140 | 95 | -45 | .033 | 2.2 | -1 | 139 |
| 40 | 122 | 95 | -27 | .025 | 1.7 | 0 | 122 |
| 50 | 109 | 95 | -14 | .02 | 1.3 | 0 | 109 |
| 60 | 99 | 95 | -4 | .017 | .9 | 0 | 99 |

At 70 feet it will be necessary to remain until the

maximum tissue reaches the absolute pressure of the next stop 60 feet times 1.7 or (60 plus 33) times 1.7 or 158.

The highest tissue, 10 minute, has 172 feet and must lose 172 minus 158 or 14 feet. The difference in pressure will be 178 minus pp of stop (103 times 77) or 99. 14 feet is 14/99 or 14.1% and from Table I this is .22 time units. The time that it will take the 10 minute tissue to lose 14 feet will be 10 times .22 or 2.2 minutes. Since it is more convenient to use even minute intervals the stop will be taken as 3 minutes.

The change will be as follows:

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 5 | 148 | 79 | 69 | .6 | 34 | -23 | 125 |
| 10 | 172 | 79 | 93 | .3 | 18.7 | -17 | 155 |
| 20 | 161 | 79 | 82 | .15 | 9.8 | -8 | 153 |
| 30 | 139 | 79 | 60 | .1 | 6.6 | -4 | 135 |
| 40 | 122 | 79 | 43 | .075 | 5.0 | -2 | 120 |
| 50 | 109 | 79 | 30 | .06 | 4.0 | -1 | 108 |
| 60 | 99 | 79 | 20 | .05 | 3.4 | -1 | 98 |

The decompression from this point may be effected by using pure oxygen or by continuing with the same mixture. Both methods will be computed for comparison. The time for ascending ten feet is not computed separately but is part of the time of the next stop. While the 10 minute tissue is actually highest, it will hose more than the 20 minute tissue and the 20 minute tissue will control.

The 20 minute tissue has 153 feet and has to be reduced to (50 plus 33) times 1.7 equals 141, before coming to 50 feet. It must, therefore, lose 12 feet.

The difference in pressure will be 153 minus 72 (93 times 77) equals 81. The per cent to lose will be 12/81 equals 14.8 and from Table I the TU will be .23. Time will be 20 times .23 or 4.6 minutes. The time will be taken as 5 minutes.

Change while at 60 feet will be as follows:

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 5 | 125 | 72 | 53 | 1 | 50 | -27 | 98 |
| 10 | 155 | 72 | 83 | .5 | 29.3 | -24 | 131 |
| 20 | 153 | 72 | 81 | .25 | 15.8 | -13 | 140 |
| 30 | 135 | 72 | 63 | .167 | 10.8 | - 7 | 128 |
| 40 | 120 | 72 | 48 | 125 | 8.3 | - 4 | 116 |
| 50 | 108 | 72 | 36 | 1 | 6.6 | - 2 | 106 |
| 60 | 98 | 72 | 26 | .083 | 5.5 | - 1 | 97 |

It is not necessary to continue the 5 and 10 minute tissues.

At 50 feet the 20 minute tissue must be reduced to 124 in order to proceed to the 42 foot level and must lose 16 feet. This is 16/76 or 21% which is .34 TU. Time is .34 times 20 equals 6.8 minutes. Time will be 7 minutes.

Change while at 50 feet:

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 20 | 140 | 64 | 76 | .35 | 21.5 | -16 | 124 |
| 30 | 1 8 | 64 | 64 | .233 | 14.9 | -10 | 118 |
| 40 | 116 | 64 | 52 | .175 | 11.4 | - 6 | 110 |
| 50 | 106 | 64 | 42 | .14 | 9.2 | 4 | 102 |
| 60 | 9 | 64 | 33 | .12 | 8 | -3 | 94 |

The 30 minute tissue will now control and at 40 feet it will have to be reduced to 63 times 1.7 equals 107 before it will be safe to come to 30 feet. It must lose 11 feet or 11/62 equal 1 .8%. This is 28 TU times 30 equals 8.4 min. and the stop will be 9 min.

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 30 | 118 | 56 | 62 | .3 | 18.7 | -12 | 106 |
| 40 | 110 | 56 | 54 | .225 | 14.4 | -8 | 102 |
| 50 | 102 | 56 | 46 | .18 | 11.7 | -5 | 97 |
| 60 | 94 | 56 | 38 | .15 | 9.8 | -4 | 90 |

The 40 minute tissue will now control and at 30 feet it will have to be reduced to 53 times 1.7 equals 90 before it will be safe to come to 20 feet. It must lose 12 feet or 12/53 or 22.6% equals 37 TU times 40 equals 14.8. The stop will be 15 minutes.

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 40 | 102 | 49 | 53 | 375 | 22.8 | -12 | 90 |
| 50 | 97 | 49 | 48 | .3 | 18.7 | -9 | 88 |
| 60 | 90 | 49 | 41 | .25 | 15.8 | -6 | 84 |

The 50 minute tissue now controls and at 10 feet it will have to be reduced to 43 times 1.7 equals 73 before it will be safe to come to 10 feet. It must lose 15 feet or 15/47 equals 31.9% or .55 TU. The time will be 50 times .55 or 27.5 minute. The stop will be 28 minutes.

| Tissue | PP | Av.PP | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 50 | 88 | 41 | 47 | .56 | 32.2 | -15 | 73 |
| 60 | 84 | 41 | 43 | .47 | 27.8 | -12 | 72 |

The 60 minute tissue now controls and at 10 feet it will have to be reduced to 33 times 1.7 or 56 feet before surfacing. It must lose 16 feet. The difference in pressure is 72 minus 33 equals 39. Per cent to lose equals 16/39 or 41%. TU equals .763. Time will be 60 times .763 equals 45.78 or 46. minutes.

Since it is safe to use oxygen at 60 feet for short periods a great saving of time will be accomplished by shifting to oxygen at that point.

When shifting to oxygen at 60 feet the suit is ventilated by admitting 18 cubic feet of oxygen into the helmet over a period of one minute. This gives about 80% oxygen mixture for breathing and the best conditions from the standpoint of gas expended and time saved, are obtained.

When using the submersible decompression chamber, pure oxygen can be breathed through a mask and the best decompression effected thereby. The following computations will be based upon 80% oxygen.

At 60 feet the pp on all other gases will be 93 times 20 or 19. The diver will be kept at 60 feet for 10 minutes. This is more than ample, but very little advantage is gained by dropping pressure. In fact better decompression is obtained at 50 feet than at 10 feet when breathing pure oxygen.

The change while at 60 feet for 10 minutes will be as follows: *

| Tissue | PP | PPStop | DP | TU | % | Change | PP |
|---|---|---|---|---|---|---|---|
| 5 | 98 | 19 | 79 | 2 | 75 | -59 | 39 |
| 10 | 131 | 19 | 112 | 1 | 50 | -56 | 75 |
| 20 | 140 | 19 | 121 | .5 | 29.3 | -35 | 105 |
| 30 | 128 | 19 | 109 | .33 | 20.6 | -22 | 106 |
| 40 | 116 | 19 | 97 | .25 | 15.8 | -15 | 101 |
| 50 | 106 | 19 | 87 | .2 | 12.9 | -11 | 95 |
| 60 | 97 | 19 | 78 | .167 | 10.8 | - 8 | 89 |

At 50 feet the pp will be 20% times 83 equals 17.
The 30 minute tissue controls.
The times to reduce all tissues to 56 will now be computed:

| Tissue | PP | PPStop | DP | PP to lose | % to lose | TU | Time |
|---|---|---|---|---|---|---|---|
| 30 | 106 | 17 | 89 | 50 | 56.2 | 1.19 | 35.7 |
| 40 | 101 | 17 | 84 | 45 | 53.5 | 1.11 | 44.4 |
| 50 | 95 | 17 | 78 | 39 | 50 | 1.0 | 50 |
| 60 | 89 | 17 | 72 | 33 | 45.8 | .885 | 53.1 |

PP to lose is found by subtracting 56 from the pp of the tissues. Percent to lose is found by dividing pp to lose by DP. Time is found by multiplying tissue by TU. The maximum time will be 53.1 or 54 minutes will be used.

*Note: It is more accurate to consider the first 3 minutes at this stop as breathing the Hilium Oxygen mixture - in order to allow for rinsing out the lungs with oxygen.

The two tables are shown for comparison.

| | On helium-oxygen mixtures | | Going on oxygen at 60 feet. |
|---|---|---|---|
| To stop | 110 | 3 minutes | 3 minutes |
| at | 110 | 7 minutes | 7 minutes |
| to | 70 | 1 minute | 1 minute |
| at | 79 | 3 minutes | 3 minutes |
| at | 60 | 5 minutes | 10 minutes |
| at | 50 | 7 minutes | 54 minutes |
| at | 40 | 9 minutes | |
| at | 30 | 15 minutes | |
| at | 20 | 28 minutes | |
| at | 10 | 46 minutes | |
| | TOTALS --- | 124 minutes | 78 minutes |

It must be recognized that in computing the foregoing tables, that if a lower percentage of oxygen were used and the same pp of AOG were used for the dive, the loss at each stop would be less because the pp of AOG is increased with the reduction in oxygen pp. This would result in a smaller difference in pressure and consequently less loss in pp at each stop.

The same exposure 256 feet pp, but with 10% oxygen has been computed to show this difference. The gauge depth would be only 250 feet, and the rate of ascent to the first stop would be less.

| Using 25% oxygen 300 feet gauge, 256 feet pp A.O.G. | | Using 10% oxygen 250 feet gauge; 256 feet pp A.O.G. | |
|---|---|---|---|
| to 110 feet | 3 min. | to 110 feet | 6 min. |
| at 110 feet | 7 min. | 110 feet | 7 min. |
| to 70 feet | 1 min. | 70 feet | 1 min. |
| at 70 feet | 3 min. | 70 feet | 3 min. |
| at 60 feet (Breathing) | 10 min. | 60 feet | 10 min. |
| at 50 feet (Oxygen ) | 54 min. | 50 feet | 60 min. |

Another point to be considered is that the partial pressure of (all other gases) AOG in the first atmosphere has a tendency to equalize toward the pp which would result from the percentage of oxygen breathed during the exposure.

If when calculating the table, it is considered that the pp of AOG in the first atmosphere is never reduced any errors introduced will be in the direction of safety.

Since it is not always convenient to mix the helium and oxygen in the exact proportions desired, decompression tables have been arranged in two parts. First, a table of partial pressures and depths for different oxygen percentages has been arranged. Having the depth of water and the oxygen percentage the partial pressure is picked out from the table. It is proper to interpolate to the nearest foot.

The probability of oxygen loss in the helmet due to respiration and the oxygen percentage in the venous blood which must be included in AOG have been included in determining the partial pressures of AOG in this table.

The second table shows decompression requirements for various partial pressures of AOG, and for various times of exposure, measured from the time that the diver starts down. In selecting the table interpolation is not allowed. If the time of exposure is not exactly given in the table the next higher time must be used. Likewise if the exact partial pressure is not found in the table the next higher partial pressure is used. These tables are computed upon the assumption that the diver is active while on the bottom.

FIGURE 1

PERCENTAGE FACTOR OF DESATURATION AS A FUNCTION OF THE TIME UNIT

| Time Unit | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 0.0 | --- | 0.5 | 1.3 | 2.0 | 2.7 | 3.4 | 4.0 | 4.7 | 5.3 | 6.0 |
| 0.1 | 6.6 | 7.3 | 8.0 | 8.6 | 9.2 | 9.8 | 10.4 | 11.0 | 11.7 | 12.3 |
| 0.2 | 12.9 | 13.5 | 14.1 | 14.7 | 15.3 | 15.8 | 16.4 | 17.0 | 17.6 | 18.2 |
| 0.3 | 18.7 | 19.3 | 19.8 | 20.4 | 21.0 | 21.5 | 22.0 | 22.5 | 23.1 | 23.7 |
| 0.4 | 24.2 | 24.7 | 25.3 | 25.7 | 26.3 | 26.8 | 27.3 | 27.8 | 28.3 | 28.8 |
| 0.5 | 29.3 | 29.7 | 30.2 | 30.7 | 31.2 | 31.7 | 32.2 | 32.6 | 33.0 | 33.5 |
| 0.6 | 34.0 | 34.4 | 34.9 | 35.3 | 35.8 | 36.2 | 36.7 | 37.1 | 37.5 | 38.0 |
| 0.7 | 38.4 | 38.8 | 39.3 | 39.7 | 40.1 | 40.5 | 40.9 | 41.3 | 41.7 | 42.2 |
| 0.8 | 42.5 | 42.9 | 43.3 | 43.7 | 44.1 | 44.5 | 44.9 | 45.3 | 45.6 | 46.0 |
| 0.9 | 46.3 | 46.7 | 47.1 | 47.5 | 47.8 | 48.2 | 48.5 | 48.9 | 49.3 | 49.6 |
| 1.0 | 50.0 | 50.3 | 50.6 | 51.0 | 51.3 | 51.6 | 52.0 | 52.3 | 52.6 | 52.9 |
| 1.1 | 53.3 | 53.6 | 53.9 | 54.3 | 54.5 | 54.8 | 55.2 | 55.5 | 55.8 | 56.1 |
| 1.2 | 56.4 | 56.7 | 57.0 | 57.3 | 57.6 | 57.9 | 58.2 | 58.5 | 58.8 | 59.1 |
| 1.3 | 59.3 | 59.6 | 59.8 | 60.2 | 60.5 | 60.7 | 61.0 | 61.3 | 61.5 | 61.8 |
| 1.4 | 62.1 | 62.3 | 62.6 | 62.8 | 63.1 | 63.3 | 63.6 | 63.8 | 64.1 | 64.3 |
| 1.5 | 64.6 | 64.8 | 65.0 | 65.3 | 65.5 | 65.7 | 66.0 | 66.3 | 66.5 | 66.7 |
| 1.6 | 66.9 | 67.2 | 67.4 | 67.6 | 67.9 | 68.1 | 68.3 | 68.5 | 68.7 | 68.9 |
| 1.7 | 69.2 | 69.4 | 69.6 | 69.8 | 70.0 | 70.2 | 70.4 | 70.6 | 70.8 | 71.0 |
| 1.8 | 71.2 | 71.4 | 71.6 | 71.8 | 72.0 | 72.2 | 72.4 | 72.6 | 72.8 | 72.9 |
| 1.9 | 73.2 | 73.3 | 73.6 | 73.7 | 73.9 | 74.1 | 74.3 | 74.5 | 74.6 | 74.8 |
| 2.0 | 75.0 | 75.2 | 75.3 | 75.5 | 75.6 | 75.8 | 76.0 | 76.2 | 76.4 | 76.5 |
| 2.1 | 76.6 | 76.8 | 76.9 | 77.1 | 77.3 | 77.4 | 77.6 | 77.8 | 77.9 | 78.0 |
| 2.2 | 78.2 | 78.4 | 78.5 | 78.6 | 78.8 | 79.0 | 79.2 | 79.4 | 79.5 | 79.6 |
| 2.3 | 79.7 | 79.9 | 80.0 | 80.1 | 80.3 | 80.4 | 80.5 | 80.6 | 80.8 | 80.9 |
| 2.4 | 81.1 | 81.3 | 81.4 | 81.5 | 81.6 | 81.7 | 81.8 | 82.0 | 82.1 | 82.3 |
| 2.5 | 82.4 | 82.5 | 82.6 | 82.7 | 82.8 | 83.0 | 83.1 | 83.2 | 83.3 | 83.4 |
| 2.6 | 83.5 | 83.6 | 83.7 | 83.9 | 84.0 | 84.1 | 84.3 | 84.4 | 84.5 | 84.6 |
| 2.7 | 84.7 | 84.8 | 84.9 | 85.0 | 85.1 | 85.2 | 85.3 | 85.4 | 85.5 | 85.6 |
| 2.8 | 85.7 | 85.8 | 85.9 | 86.0 | 86.1 | 86.2 | 86.3 | 86.4 | 86.5 | 86.6 |
| 2.9 | 86.6 | 86.7 | 86.8 | 86.9 | 87.0 | 87.1 | 87.2 | 87.3 | 87.4 | 87.5 |

| Time Unit | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 3.0 | 87.5 | 87.6 | 87.7 | 87.8 | 87.9 | 88.0 | 88.0 | 88.1 | 88.2 | 88.3 |
| 3.1 | 88.4 | 88.5 | 88.5 | 88.6 | 88.7 | 88.8 | 88.9 | 89.0 | 89.0 | 89.1 |
| 3.2 | 89.2 | 89.3 | 89.4 | 89.4 | 89.5 | 89.5 | 89.6 | 89.7 | 89.8 | 89.8 |
| 3.3 | 89.9 | 90.0 | 90.0 | 90.1 | 90.2 | 90.2 | 90.3 | 90.4 | 90.5 | 90.6 |
| 3.4 | 90.6 | 90.6 | 90.7 | 90.8 | 90.8 | 90.9 | 90.9 | 91.0 | 91.0 | 91.1 |
| 3.5 | 91.2 | 91.2 | 91.3 | 91.4 | 91.4 | 91.5 | 91.5 | 91.6 | 91.6 | 91.7 |
| 3.6 | 91.8 | 91.8 | 91.9 | 91.9 | 91.9 | 92.0 | 92.0 | 92.0 | 92.1 | 92.2 |
| 3.7 | 92.2 | 92.3 | 92.4 | 92.4 | 92.5 | 92.5 | 92.5 | 92.5 | 92.6 | 92.6 |
| 3.8 | 92.7 | 92.8 | 92.8 | 92.9 | 92.9 | 93.0 | 93.0 | 93.0 | 93.1 | 93.1 |
| 3.9 | 93.2 | 93.2 | 93.3 | 93.4 | 93.4 | 93.5 | 93.5 | 93.5 | 93.6 | 93.6 |
| 4.0 | 93.7 | 93.7 | 93.8 | 93.8 | 93.9 | 93.9 | 94.0 | 94.0 | 94.0 | 94.1 |
| 4.1 | 94.1 | 94.1 | 94.2 | 94.2 | 94.2 | 94.3 | 94.4 | 94.4 | 94.4 | 94.5 |
| 4.2 | 94.5 | 94.5 | 94.5 | 94.6 | 94.7 | 94.7 | 94.8 | 94.8 | 94.8 | 94.9 |
| 4.3 | 94.9 | 95.0 | 95.0 | 95.0 | 95.0 | 95.1 | 95.1 | 95.1 | 95.2 | 95.2 |
| 4.4 | 95.3 | 95.3 | 95.4 | 95.4 | 95.4 | 95.5 | 95.5 | 95.5 | 95.5 | 95.5 |
| 4.5 | 95.6 | 95.6 | 95.6 | 95.7 | 95.7 | 95.7 | 95.8 | 95.8 | 95.8 | 95.9 |
| 4.6 | 95.9 | 95.9 | 95.9 | 96.0 | 96.0 | 96.0 | 96.0 | 96.0 | 96.0 | 96.0 |
| 4.7 | 96.0 | 96.1 | 96.1 | 96.1 | 96.2 | 96.2 | 96.2 | 96.2 | 96.3 | 96.3 |
| 4.8 | 96.3 | 96.3 | 96.3 | 96.4 | 96.4 | 96.4 | 96.4 | 96.5 | 96.5 | 96.5 |
| 4.9 | 96.5 | 96.5 | 96.5 | 96.5 | 96.6 | 96.6 | 96.6 | 96.6 | 96.6 | 96.7 |
| 5.0 | 96.7 | 96.7 | 96.8 | 96.8 | 96.8 | 96.8 | 96.9 | 96.9 | 96.9 | 96.9 |
| 5.1 | 97.0 | 97.0 | 97.0 | 97.0 | 97.0 | 97.1 | 97.1 | 97.1 | 97.2 | 97.2 |
| 5.2 | 97.2 | 97.2 | 97.2 | 97.2 | 97.3 | 97.3 | 97.3 | 97.4 | 97.4 | 97.4 |
| 5.3 | 97.4 | 97.5 | 97.5 | 97.5 | 97.5 | 97.6 | 97.6 | 97.6 | 97.6 | 97.6 |
| 5.4 | 97.7 | 97.7 | 97.7 | 97.7 | 97.7 | 97.8 | 97.8 | 97.8 | 97.8 | 97.8 |
| 5.5 | 97.8 | 97.8 | 97.9 | 97.9 | 97.9 | 97.9 | 97.9 | 97.9 | 98.0 | 98.0 |
| 5.6 | 98.0 | 98.0 | 98.0 | 98.0 | 98.0 | 98.0 | 98.1 | 98.1 | 98.1 | 98.1 |
| 5.7 | 98.1 | 98.1 | 98.1 | 98.1 | 98.2 | 98.2 | 98.2 | 98.2 | 98.2 | 98.2 |
| 5.8 | 98.2 | 98.3 | 98.2 | 98.3 | 98.3 | 98.3 | 98.3 | 98.3 | 98.4 | 98.4 |
| 5.9 | 98.4 | 98.4 | 98.4 | 98.4 | 98.4 | 98.4 | 98.5 | 98.5 | 98.5 | 98.5 |
| 6.0 | 98.5 | 98.5 | 98.6 | 98.6 | 98.6 | 98.6 | 98.6 | 98.6 | 98.6 | 98.6 |

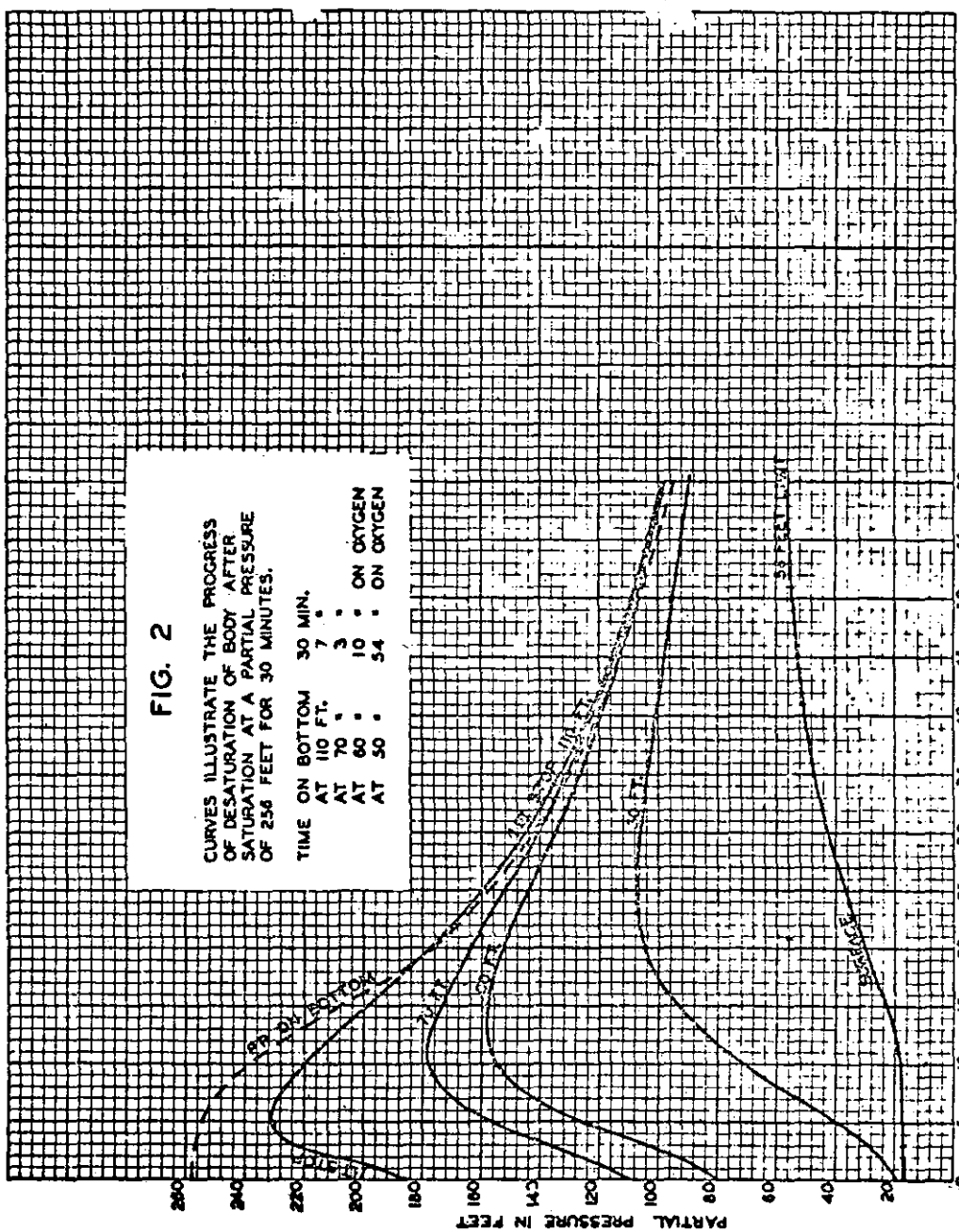


FIG. 2
CURVES ILLUSTRATE THE PROGRESS OF DESATURATION OF BODY AFTER SATURATION AT A PARTIAL PRESSURE OF 256 FEET FOR 30 MINUTES.
TIME ON BOTTOM 30 MIN.
AT 110 FT. 7 "
AT 70 " 3 "
AT 60 " 10 " ON OXYGEN
AT 50 " 54 " ON OXYGEN
PARTIAL PRESSURE IN FEET
TISSUES — MINUTES
256 FT. ON BOTTOM
110 FT.
70 FT.
60 FT.
50 FT.
30 FT.
SURFACE

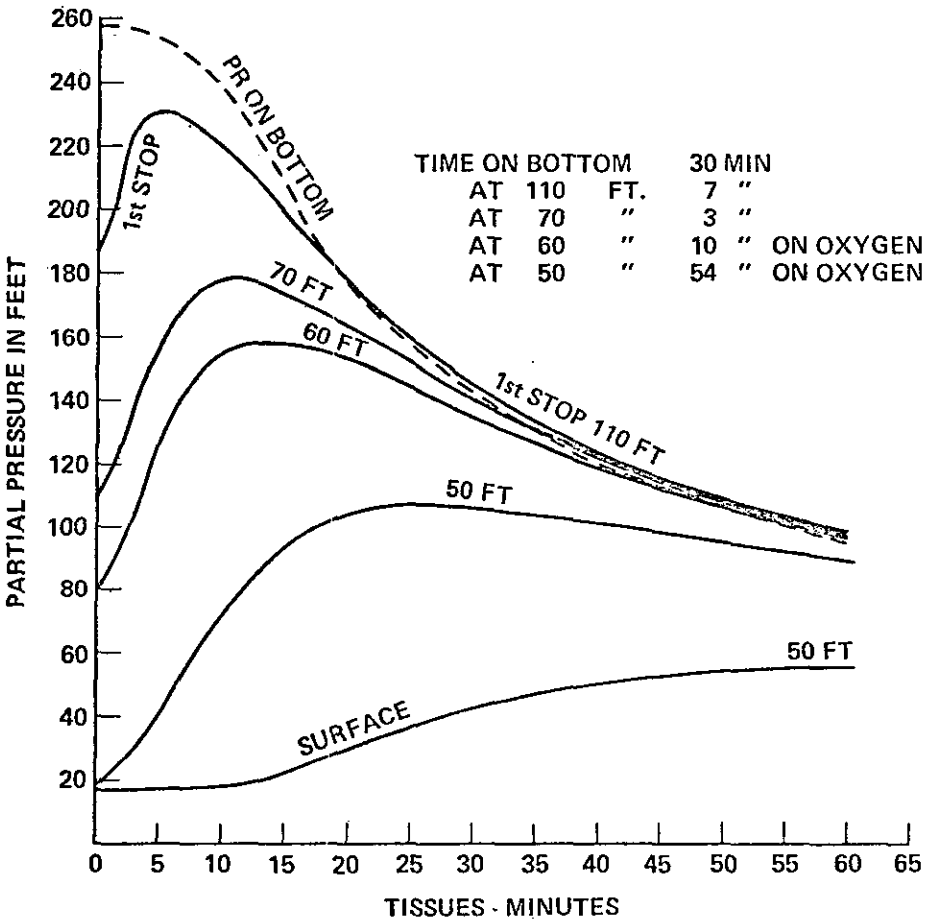



FIGURE 2.

CURVES ILLUSTRATE THE PROGRESS OF DESATURATION OF BODY AFTER SATURATION AT A PARTIAL PRESSURE OF 256 FEET FOR 30 MINUTES.

## (C) HELIUM DECOMPESSION TABLES UP TO 450 FEET

The following Decompression Tables are computed for all time and oxygen combinations and all depths up to 450 feet gauge.

While it may not be practical to dive for the longer periods, an emergency may arise where it will be necessary to have the tables.

All tables are computed with maxiumu safety factors and it is believed they are safe for all conditions to which a diver may be exposed.

Decompression on oxygen after arrival at 60 feet has been considered as standard.

Decompressions on Helium-Oxygen mixtures after arrival at 60 feet or on air from any depth will be considered emergencies and the tables provided herein are emergency tables, and are therefore for maximum exposures.

It is important to keep $CO_2$ below 2% effective.

These tables were computed by Lt. Comdr. C. B. Momsen, U. S. Navy, and Lieutenant (jg) K. R. Wheland, U. S. Navy, and it is requested that any apparent errors discovered be referred to either of them.

### DECOMPRESSION TABLES

### FOR USE WHEN DIVING IN SEA WATER WITH HELIUM-OXYGEN MIXTURES

Table for Depths up to 100 feet when decompression is not necessary for any exposure.

| DEPTH IN FEET | OXYGEN PERCENTAGE |
|---|---|
| 30 | 13 to 100 |
| 40 | 26 to 100 |
| 50 | 34 to 100 |
| 60 | 42 to 90 |
| 70 | 48 to 80 |
| 80 | 52 to 73 |
| 90 | 57 to 67 |
| 100 | 60 to 62 |
| No Decompression Necessary | |

HELIUM-OXYGEN

TABLE OF PARTIAL PRESSURES 10 FEET to 600 FEET

ENTER THIS TABLE - - - SELECT PARTIAL PRESSURES

| DEPTH | PERCENTAGE OF OXYGEN USED | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 13 | 15 | 17 | 19 | 21 | 23 | 25 | 30 | 35 | 40 | 45 | 50 | 55 | |
| 10 | | | | | | | | | | | | | | *ND to 100%O2 |
| 20 | | | | | | | | | | | | | | *ND to 100%O2 |
| 30 | | | | | | | | | | | | | | *ND to 100%O2 |
| 40 | 65 | 64 | 62 | 61 | 59 | 58 | 56 | | | | | | | *ND to 100%O2 |
| 50 | 74 | 72 | 71 | 69 | 68 | 66 | 64 | 60 | 56 | | | | | *ND to 100%O2 |
| 60 | 83 | 81 | 79 | 78 | 76 | 74 | 72 | 67 | 63 | 58 | 53 | | | *ND to 90% O2 |
| 70 | 92 | 90 | 88 | 86 | 84 | 82 | 80 | 75 | 69 | 64 | 59 | 54 | | *ND to 80% O2 |
| 80 | 101 | 99 | 96 | 94 | 92 | 90 | 87 | 82 | 76 | 71 | 65 | 59 | 53 | *ND to 73% O2 |
| 90 | 110 | 107 | 105 | 103 | 100 | 98 | 95 | 89 | 83 | 77 | 71 | 65 | 58 | *ND to 67% O2 |
| 100 | 119 | 116 | 113 | 111 | 108 | 105 | 103 | 96 | 90 | 83 | 76 | 70 | 63 | |
| 110 | 128 | 124 | 121 | 119 | 116 | 113 | 110 | 103 | 97 | 89 | 82 | 75 | 67 | |
| 120 | 136 | 133 | 130 | 127 | 124 | 121 | 118 | 110 | 103 | 95 | 87 | 80 | 72 | |
| 130 | 145 | 142 | 139 | 135 | 132 | 129 | 126 | 118 | 109 | 101 | 93 | 85 | | |
| 140 | 154 | 151 | 147 | 144 | 140 | 137 | 133 | 125 | 116 | 107 | 99 | | | |
| 150 | 165 | 159 | 156 | 152 | 148 | 145 | 141 | 132 | 123 | 114 | 104 | | | |
| 160 | 172 | 168 | 164 | 160 | 157 | 153 | 149 | 139 | 129 | 120 | | | | |
| 170 | 181 | 177 | 173 | 169 | 165 | 160 | 156 | 146 | 136 | 126 | | | | |
| 180 | 190 | 186 | 181 | 177 | 173 | 169 | 164 | 154 | 143 | | | | | |
| 190 | 199 | 194 | 190 | 185 | 181 | 176 | 172 | 161 | 150 | | | | | |
| 200 | 208 | 205 | 198 | 194 | 189 | 184 | 180 | 168 | 156 | | | | | |
| 210 | 216 | 212 | 207 | 202 | 197 | 192 | 187 | 175 | | | | | | |
| 220 | 225 | 220 | 215 | 210 | 205 | 200 | 195 | 183 | | | | | | |
| 230 | 234 | 229 | 224 | 219 | 213 | 208 | 203 | 190 | | | | | | |
| 240 | 243 | 238 | 232 | 227 | 222 | 216 | 211 | 197 | | | | | | |
| 250 | 252 | 247 | 241 | 235 | 230 | 224 | 218 | | | | | | | |
| 260 | 261 | 255 | 249 | 243 | 237 | 231 | 225 | | | | | | | |
| 270 | 270 | 264 | 258 | 252 | 246 | 240 | 233 | | | | | | | |
| 280 | 280 | 273 | 267 | 260 | 253 | 247 | 241 | | | | | | | |
| 290 | 288 | 281 | 275 | 268 | 262 | 255 | 249 | | | | | | | |
| 300 | 297 | 290 | 283 | 277 | 270 | 263 | 257 | | | | | | | |

*(ND) - No decompression

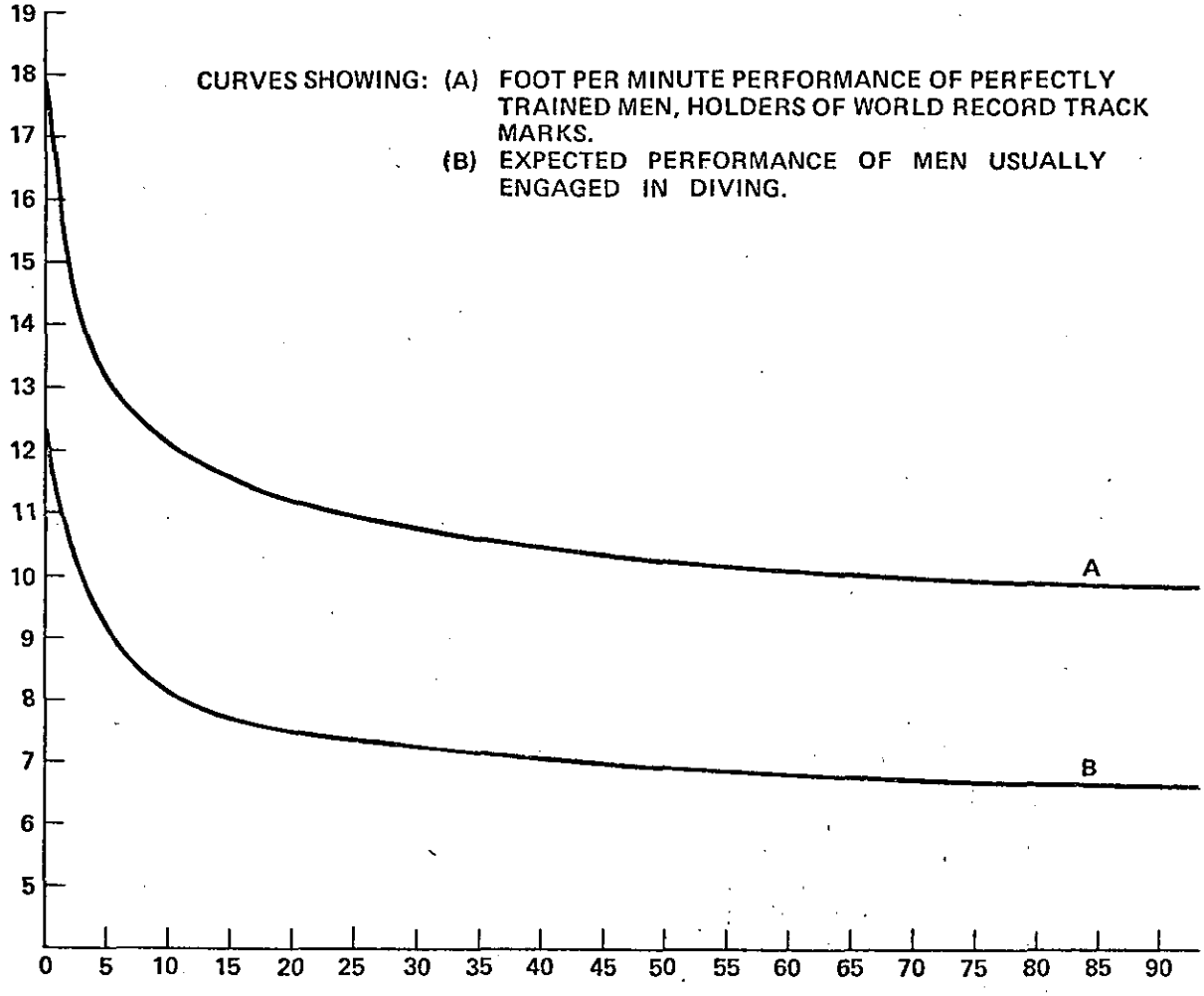



FIGURE 5.
TIME WORK CURVES

TABLE OF PARTIAL PRESSURES - 10 FEET to 600 FEET (Continued)

| | PERCENTAGE OF OXYGEN USED | | | | | |
|---|---|---|---|---|---|---|
| DEPTH | 13 | 15 | 17 | 19 | 21 | 23 |
| 310 | 306 | 299 | 292 | 285 | 278 | 271 |
| 320 | 314 | 307 | 300 | 293 | 286 | 279 |
| 330 | 323 | 316 | 309 | 302 | 294 | 287 |
| 340 | 332 | 325 | 317 | 310 | 303 | 295 |
| 350 | 341 | 334 | 326 | 318 | 311 | 303 |
| 360 | 350 | 343 | 335 | 327 | 319 | |
| 370 | 359 | 351 | 343 | 335 | 327 | |
| 380 | 368 | 359 | 351 | 343 | 334 | |
| 390 | 377 | 368 | 360 | 351 | | |
| 400 | 386 | 377 | 368 | 359 | | |
| 410 | 395 | 386 | 377 | 368 | | |
| 420 | 403 | 394 | 385 | 376 | | |
| 430 | 412 | 403 | 394 | 385 | | |
| 440 | 421 | 412 | 403 | | | |
| 450 | 430 | 420 | 410 | | | |
| 460 | 439 | 429 | 419 | | | |
| 470 | 448 | 438 | 428 | | | |
| 480 | 457 | 447 | 437 | | | |
| 490 | 466 | 456 | 446 | | | |
| 500 | 475 | 465 | | | | |
| 510 | 484 | 473 | | | | |
| 520 | 493 | 482 | | | | |
| 530 | 502 | 492 | | | | |
| 540 | 511 | 500 | | | | |
| 550 | 520 | 509 | | | | |
| 560 | 529 | 518 | | | | |
| 570 | 538 | 527 | | | | |
| 580 | 548 | | | | | |
| 590 | 557 | | | | | |
| 600 | 566 | | | | | |

## INSTRUCTIONS FOR USE OF OXYGEN DECOMPRESSION CURVES

Using depth of water and oxygen per cent to be breathed on the bottom, select parial pressure from "Table of Partial Pressures". Partial Pressure as used in these tables and the curve is obtained by the following formula:

100 - (02% - 2 x (D plus 33) D - is depth. 02% is per cent of oxygen in gas mixture used.

2. Use up to 141 feet partial pressure ONLY.

3. The limits of oxygen to be used are indicated in "Table of Partial Pressures".

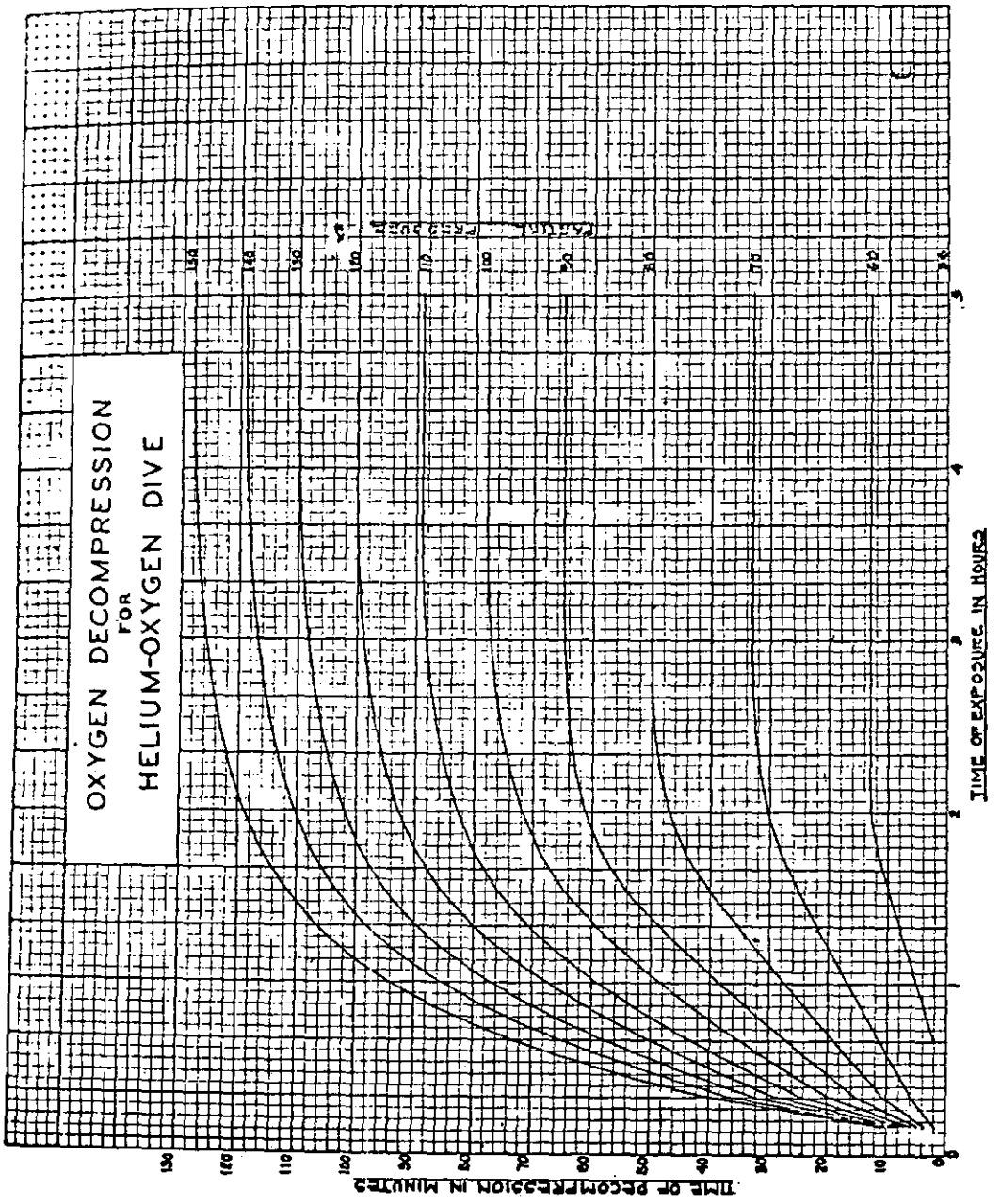
4. All stops are at 50 feet gauge.

5. Breathe oxygen at 50 feet and until reaching surface.

Ventilate 25 cu.ft. and circulate remaining period.

6. Rate of ascent:

| | |
|---|---|
| Up to 100 feet partial pressure | 1 minute. |
| Over 100 feet partial pressure | 2 minutes. |
| From 50 feet to surface | Last 5 mins. of dive. |


OXYGEN DECOMPRESSION
FOR
HELIUM-OXYGEN DIVE
TIME OF EXPOSURE IN HOURS
TIME OF DECOMPRESSION IN MINUTES

## OXYGEN DECOMPRESSION TABLES FOLLOWING HELIUM-OXYGEN DIVE

1. Using depth of water and oxygen per cent to be breath on the bottom, select partial pressure from "Table of Partial Pressures"

2. Using next higher partial pressure given in these tables and next higher "time of dive" including time of descent, select table of decompression.

3. The time of ascent unless indicated, will be included in the subsequent stop.

4. At 60 feet, ventilate 25 cu.ft. of oxygen and then circulate oxygen for the remaining period at 60 feet, and the entire time at 50 feet. If the first stop is at 50 feet, ventilate 25 cu.ft. of oxygen and then circulate oxygen for the remaining period. If using the submersible decompression chamber, oxygen is breathed through a mask at 60 feet and at 50 feet.

### PARTIAL PRESSURE 60

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 0 | 2 |
| 20 | 2 | 0 | 2 |
| 30 | 2 | 0 | 2 |
| 40 | 2 | 0 | 2 |
| 60 | 1 | 4 | 5 |
| 80 | 1 | 7 | 8 |
| 100 | 1 | 10 | 11 |
| 120 | 1 | 12 | 13 |

### PARTIAL PRESSURE 70

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 0 | 2 |
| 20 | 1 | 5 | 6 |
| 30 | 1 | 8 | 9 |
| 40 | 1 | 10 | 11 |
| 60 | 1 | 15 | 16 |
| 80 | 1 | 21 | 22 |
| 100 | 1 | 26 | 27 |
| 120 | 1 | 29 | 30 |
| 140 | 1 | 31 | 32 |
| 160 | 1 | 32 | 33 |

PARTIAL PRESSURE 80

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 1 | 4 | 5 |
| 20 | 1 | 9 | 10 |
| 30 | 1 | 14 | 15 |
| 40 | 1 | 18 | 19 |
| 60 | 1 | 26 | 27 |
| 80 | 1 | 34 | 35 |
| 100 | 1 | 42 | 43 |
| 120 | 1 | 46 | 47 |
| 140 | 1 | 48 | 49 |
| 160 | 1 | 49 | 50 |

PARTIAL PRESSURE 90

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 5 | 7 |
| 20 | 2 | 13 | 15 |
| 30 | 2 | 19 | 21 |
| 40 | 2 | 25 | 27 |
| 60 | 2 | 36 | 38 |
| 80 | 2 | 46 | 48 |
| 100 | 2 | 55 | 57 |
| 120 | 2 | 59 | 61 |
| 140 | 2 | 61 | 63 |
| 160 | 2 | 62 | 64 |
| 180 | 2 | 63 | 65 |

PARTIAL PRESSURE 100

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 6 | 8 |
| 20 | 2 | 17 | 19 |
| 30 | 2 | 26 | 28 |
| 40 | 2 | 33 | 35 |
| 60 | 2 | 46 | 48 |
| 80 | 2 | 57 | 59 |
| 100 | 2 | 65 | 67 |
| 120 | 2 | 70 | 72 |
| 140 | 2 | 73 | 75 |
| 160 | 2 | 74 | 76 |
| 180 | 2 | 75 | 77 |
| 200 | 2 | 76 | 78 |

PARTIAL PRESSURE 110

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 6 | 8 |
| 20 | 2 | 21 | 23 |
| 30 | 2 | 32 | 34 |
| 40 | 2 | 41 | 43 |
| 60 | 2 | 57 | 59 |
| 80 | 2 | 69 | 71 |
| 100 | 2 | 76 | 78 |
| 120 | 2 | 81 | 83 |
| 140 | 2 | 84 | 86 |
| 160 | 2 | 85 | 87 |
| 180 | 2 | 86 | 88 |
| 200 | 2 | 87 | 89 |

PARTIAL PRESSURE 120

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 8 | 10 |
| 20 | 2 | 27 | 29 |
| 30 | 2 | 38 | 40 |
| 40 | 2 | 48 | 50 |
| 60 | 2 | 65 | 67 |
| 80 | 2 | 78 | 80 |
| 100 | 2 | 86 | 88 |
| 120 | 2 | 91 | 93 |
| 140 | 2 | 94 | 96 |
| 160 | 2 | 95 | 97 |
| 180 | 2 | 97 | 99 |
| 200 | 2 | 98 | 100 |

PARTIAL PRESSURE 130

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 9 | 11 |
| 20 | 2 | 31 | 33 |
| 30 | 2 | 44 | 46 |
| 40 | 2 | 56 | 58 |
| 60 | 2 | 75 | 77 |
| 80 | 2 | 88 | 90 |
| 100 | 2 | 95 | 97 |
| 120 | 2 | 100 | 102 |
| 140 | 2 | 103 | 105 |
| 160 | 2 | 105 | 107 |
| 180 | 2 | 106 | 108 |
| 200 | 2 | 107 | 109 |
| 220 | 2 | 108 | 110 |

PARTIAL PRESSURE 140

| Time of Dive | To 1st Stop | Feet and Minutes 50 | Total Time |
|---|---|---|---|
| 10 | 2 | 10 | 12 |
| 20 | 2 | 34 | 36 |
| 30 | 2 | 50 | 52 |
| 40 | 2 | 63 | 65 |
| 60 | 2 | 83 | 85 |
| 80 | 2 | 96 | 98 |
| 100 | 2 | 104 | 108 |
| 120 | 2 | 109 | 111 |
| 140 | 2 | 111 | 113 |
| 160 | 2 | 113 | 115 |
| 180 | 2 | 115 | 117 |
| 200 | 2 | 116 | 118 |
| 220 | 2 | 117 | 119 |

PARTIAL PRESSURE 150

| Time of Dive | To 1st Stop | Feet 60 | and Minutes 50 | Total Time |
|---|---|---|---|---|
| 10 | 3 | 0 | 10 | 13 |
| 20 | 3 | 0 | 36 | 39 |
| 30 | 3 | 0 | 56 | 59 |
| 40 | 3 | 10 | 61 | 74 |
| 60 | 3 | 10 | 81 | 94 |
| 80 | 3 | 10 | 94 | 107 |
| 100 | 3 | 10 | 101 | 114 |
| 120 | 3 | 10 | 106 | 119 |
| 140 | 3 | 10 | 109 | 122 |
| 160 | 3 | 10 | 111 | 124 |
| 180 | 3 | 10 | 113 | 126 |
| 200 | 3 | 10 | 114 | 127 |
| 220 | 3 | 10 | 114 | 127 |
| 240 | 3 | 10 | 115 | 128 |

PARTIAL PRESSURE 160

| Time of Dive | To 1st Stop | Feet 60 | and Minutes 50 | Total Time |
|---|---|---|---|---|
| 10 | 3 | 0 | 21 | 24 |
| 20 | 3 | 10 | 34 | 42 |
| 30 | 3 | 10 | 54 | 67 |
| 40 | 3 | 10 | 69 | 82 |
| 60 | 3 | 10 | 91 | 104 |
| 80 | 3 | 10 | 102 | 115 |
| 100 | 3 | 10 | 108 | 121 |
| 120 | 3 | 10 | 113 | 126 |
| 140 | 3 | 10 | 115 | 128 |
| 160 | 3 | 10 | 116 | 129 |
| 180 | 3 | 10 | 117 | 130 |
| 200 | 3 | 12 | 117 | 132 |
| 220 | 3 | 14 | 117 | 134 |
| 240 | 3 | 15 | 117 | 135 |

PARTIAL PRESSURE 170

| Time of Dive | To 1st Stop | Feet 70 | and 60 | Minutes 50 | Total Time |
|---|---|---|---|---|---|
| 10 | 3 | 0 | 10 | 16 | 29 |
| 20 | 3 | 0 | 10 | 38 | 51 |
| 30 | 3 | 0 | 10 | 61 | 74 |
| 40 | 3 | 0 | 10 | 75 | 88 |
| 60 | 3 | 7 | 10 | 94 | 114 |
| 80 | 3 | 7 | 10 | 106 | 126 |
| 100 | 3 | 7 | 10 | 113 | 133 |
| 120 | 3 | 7 | 10 | 117 | 137 |
| 140 | 3 | 8 | 13 | 117 | 141 |
| 160 | 3 | 10 | 14 | 117 | 144 |
| 180 | 3 | 12 | 15 | 117 | 147 |
| 200 | 3 | 13 | 15 | 117 | 148 |
| 220 | 3 | 14 | 15 | 117 | 149 |
| 240 | 3 | 15 | 15 | 117 | 150 |

PARTIAL PRESSURE 180

| Time of Dive | To 1st Stop | Feet 80 | and 70 | Minutes 60 | 50 | Total Time |
|---|---|---|---|---|---|---|
| 10 | 3 | 0 | 7 | 10 | 19 | 39 |
| 20 | 3 | 0 | 7 | 10 | 43 | 63 |
| 30 | 3 | 0 | 7 | 10 | 64 | 84 |
| 40 | 3 | 0 | 7 | 10 | 80 | 100 |
| 60 | 3 | 0 | 7 | 10 | 101 | 121 |
| 80 | 3 | 0 | 9 | 10 | 110 | 132 |
| 100 | 3 | 7 | 5 | 12 | 117 | 144 |
| 120 | 3 | 7 | 9 | 13 | 117 | 149 |
| 140 | 3 | 7 | 11 | 14 | 117 | 152 |
| 160 | 3 | 7 | 14 | 15 | 117 | 156 |
| 180 | 3 | 7 | 17 | 15 | 117 | 159 |
| 200 | 3 | 7 | 19 | 15 | 117 | 161 |
| 220 | 3 | 7 | 21 | 15 | 117 | 163 |
| 240 | 3 | 7 | 23 | 15 | 117 | 165 |

PARTIAL PRESSURE 190

| Time of Dive | To 1st Stop | Feet and Minutes 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 7 | 10 | 21 | 42 |
| 20 | 4 | 0 | 7 | 10 | 49 | 70 |
| 30 | 4 | 0 | 7 | 10 | 70 | 91 |
| 40 | 4 | 7 | 0 | 10 | 87 | 108 |
| 60 | 4 | 7 | 5 | 10 | 103 | 129 |
| 80 | 4 | 7 | 9 | 10 | 115 | 145 |
| 100 | 4 | 7 | 13 | 11 | 117 | 152 |
| 120 | 4 | 7 | 17 | 13 | 117 | 158 |
| 140 | 4 | 9 | 19 | 14 | 117 | 163 |
| 160 | 4 | 11 | 20 | 15 | 117 | 167 |
| 180 | 4 | 13 | 21 | 15 | 117 | 170 |
| 200 | 4 | 14 | 22 | 15 | 117 | 172 |
| 220 | 4 | 15 | 23 | 15 | 117 | 174 |
| 240 | 4 | 16 | 23 | 15 | 117 | 175 |

PARTIAL PRESSURE 200

| Time of Dive | To 1st Stop | Feet and Minutes 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 0 | 7 | 10 | 24 | 45 |
| 20 | 4 | 0 | 7 | 0 | 10 | 55 | 76 |
| 30 | 4 | 0 | 7 | 0 | 10 | 74 | 95 |
| 40 | 4 | 0 | 7 | 4 | 10 | 91 | 116 |
| 60 | 4 | 0 | 7 | 9 | 10 | 109 | 139 |
| 80 | 4 | 7 | 3 | 13 | 12 | 115 | 154 |
| 100 | 4 | 7 | 6 | 16 | 14 | 117 | 164 |
| 120 | 4 | 7 | 8 | 20 | 15 | 117 | 171 |
| 140 | 4 | 7 | 11 | 21 | 15 | 117 | 175 |
| 160 | 4 | 7 | 15 | 23 | 15 | 117 | 181 |
| 180 | 4 | 7 | 17 | 23 | 15 | 117 | 183 |
| 200 | 4 | 7 | 18 | 23 | 15 | 117 | 184 |
| 220 | 4 | 7 | 20 | 23 | 15 | 117 | 186 |
| 240 | 4 | 8 | 20 | 23 | 15 | 117 | 187 |

PARTIAL PRESSURE 210

| Time of Dive | To 1st Stop | Feet and Minutes 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 7 | 0 | 10 | 27 | 48 |
| 20 | 4 | 0 | 7 | 0 | 10 | 57 | 78 |
| 30 | 4 | 7 | 0 | 3 | 10 | 79 | 103 |
| 40 | 4 | 7 | 0 | 7 | 10 | 94 | 122 |
| 60 | 4 | 7 | 4 | 10 | 10 | 110 | 145 |
| 80 | 4 | 7 | 8 | 14 | 12 | 117 | 162 |
| 100 | 4 | 7 | 12 | 17 | 14 | 117 | 171 |
| 120 | 4 | 8 | 15 | 21 | 15 | 117 | 180 |
| 140 | 4 | 10 | 17 | 21 | 15 | 117 | 184 |
| 160 | 4 | 12 | 17 | 22 | 15 | 117 | 187 |
| 180 | 4 | 14 | 18 | 22 | 15 | 117 | 190 |
| 200 | 4 | 16 | 18 | 23 | 15 | 117 | 192 |
| 220 | 4 | 17 | 19 | 23 | 15 | 117 | 194 |
| 240 | 4 | 18 | 20 | 23 | 15 | 117 | 196 |

PARTIAL PRESSURE 220

| Time of Dive | To 1st Stop | Feet and Minutes 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 0 | 7 | 0 | 10 | 29 | 50 |
| 20 | 4 | 0 | 7 | 0 | 1 | 10 | 62 | 84 |
| 30 | 4 | 0 | 7 | 0 | 6 | 10 | 84 | 111 |
| 40 | 4 | 0 | 7 | 3 | 9 | 10 | 98 | 131 |
| 60 | 4 | 7 | 0 | 9 | 11 | 11 | 113 | 155 |
| 80 | 4 | 7 | 3 | 11 | 15 | 13 | 117 | 170 |
| 100 | 4 | 7 | 6 | 14 | 17 | 15 | 117 | 180 |
| 120 | 4 | 7 | 8 | 18 | 23 | 15 | 117 | 192 |
| 140 | 4 | 7 | 11 | 18 | 23 | 15 | 117 | 195 |
| 160 | 4 | 7 | 14 | 19 | 23 | 15 | 117 | 199 |
| 180 | 4 | 7 | 15 | 20 | 23 | 15 | 117 | 201 |
| 200 | 4 | 7 | 16 | 20 | 23 | 15 | 117 | 202 |
| 220 | 4 | 8 | 17 | 20 | 23 | 15 | 117 | 204 |
| 240 | 4 | 9 | 19 | 20 | 23 | 15 | 117 | 207 |

## PARTIAL PRESSURE 230

| Time of Dive | To 1st Stop | Feet and Minutes 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 0 | 0 | 7 | 0 | 10 | 31 | 52 |
| 20 | 4 | 0 | 0 | 7 | 0 | 3 | 10 | 66 | 90 |
| 30 | 4 | 0 | 0 | 7 | 2 | 4 | 10 | 87 | 116 |
| 40 | 4 | 0 | 7 | 0 | 6 | 9 | 10 | 102 | 138 |
| 60 | 4 | 0 | 7 | 4 | 9 | 12 | 11 | 114 | 161 |
| 80 | 4 | 0 | 7 | 8 | 12 | 17 | 14 | 117 | 183 |
| 100 | 4 | 0 | 7 | 12 | 15 | 20 | 15 | 117 | 194 |
| 120 | 4 | 0 | 8 | 14 | 19 | 23 | 15 | 117 | 204 |
| 140 | 4 | 0 | 10 | 16 | 20 | 23 | 15 | 117 | 209 |
| 160 | 4 | 7 | 6 | 18 | 20 | 23 | 15 | 117 | 214 |
| 180 | 4 | 7 | 7 | 19 | 20 | 23 | 15 | 117 | 216 |
| 200 | 4 | 7 | 9 | 19 | 20 | 23 | 15 | 117 | 218 |
| 220 | 4 | 7 | 11 | 19 | 20 | 23 | 15 | 117 | 220 |
| 240 | 4 | 7 | 13 | 19 | 20 | 23 | 15 | 117 | 222 |

## PARTIAL PRESSURE 240

| Time of Dive | To 1st Stop | Feet and Minutes 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 0 | 7 | 0 | 0 | 10 | 35 | 56 |
| 20 | 4 | 0 | 7 | 0 | 1 | 4 | 10 | 71 | 97 |
| 30 | 4 | 0 | 7 | 0 | 5 | 7 | 10 | 90 | 123 |
| 40 | 4 | 7 | 0 | 3 | 7 | 9 | 10 | 103 | 143 |
| 60 | 4 | 7 | 0 | 8 | 10 | 14 | 11 | 115 | 169 |
| 80 | 4 | 7 | 3 | 10 | 14 | 18 | 14 | 117 | 187 |
| 100 | 4 | 7 | 6 | 12 | 17 | 23 | 15 | 117 | 201 |
| 120 | 4 | 7 | 7 | 16 | 19 | 23 | 15 | 117 | 208 |
| 140 | 4 | 7 | 11 | 16 | 20 | 23 | 15 | 117 | 213 |
| 160 | 4 | 7 | 13 | 19 | 20 | 23 | 15 | 117 | 218 |
| 180 | 4 | 8 | 15 | 19 | 20 | 23 | 15 | 117 | 221 |
| 200 | 4 | 8 | 17 | 19 | 20 | 23 | 15 | 117 | 223 |
| 220 | 4 | 9 | 17 | 19 | 20 | 23 | 15 | 117 | 224 |
| 240 | 4 | 11 | 17 | 19 | 20 | 23 | 15 | 117 | 226 |

## PARTIAL PRESSURE 250

| Time of Dive | To 1st Stop | Feet and Minutes 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 0 | 7 | 0 | 0 | 1 | 10 | 38 | 60 |
| 20 | 4 | 0 | 0 | 7 | 0 | 1 | 6 | 10 | 73 | 101 |
| 30 | 4 | 0 | 7 | 0 | 4 | 6 | 6 | 10 | 95 | 132 |
| 40 | 4 | 0 | 7 | 0 | 5 | 8 | 9 | 10 | 106 | 149 |
| 60 | 4 | 0 | 7 | 4 | 8 | 11 | 14 | 12 | 117 | 177 |
| 80 | 4 | 0 | 7 | 7 | 11 | 16 | 18 | 15 | 117 | 195 |
| 100 | 4 | 0 | 7 | 10 | 14 | 19 | 23 | 15 | 117 | 209 |
| 120 | 4 | 7 | 3 | 12 | 17 | 19 | 23 | 15 | 117 | 217 |
| 140 | 4 | 7 | 4 | 15 | 18 | 19 | 23 | 15 | 117 | 222 |
| 160 | 4 | 7 | 7 | 16 | 19 | 19 | 23 | 15 | 117 | 227 |
| 180 | 4 | 7 | 9 | 17 | 19 | 20 | 23 | 15 | 117 | 231 |
| 200 | 4 | 7 | 11 | 17 | 19 | 20 | 23 | 15 | 117 | 233 |
| 220 | 4 | 7 | 12 | 17 | 19 | 20 | 23 | 15 | 117 | 234 |
| 240 | 4 | 7 | 13 | 17 | 19 | 20 | 23 | 15 | 117 | 235 |

## PARTIAL PRESSURE 260

| Time of Dive | To 1st Stop | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|
| 10 | 4 | 0 | 0 | 7 | 0 | 0 | 2 | 10 | 41 | 64 |
| 20 | 4 | 0 | 7 | 0 | 0 | 3 | 7 | 10 | 77 | 105 |
| 30 | 4 | 0 | 7 | 0 | 4 | 6 | 8 | 10 | 97 | 136 |
| 40 | 4 | 0 | 7 | 2 | 5 | 9 | 9 | 10 | 109 | 155 |
| 60 | 4 | 7 | 0 | 7 | 9 | 12 | 16 | 13 | 116 | 184 |
| 80 | 4 | 7 | 3 | 9 | 13 | 15 | 21 | 15 | 117 | 204 |
| 100 | 4 | 7 | 6 | 11 | 14 | 19 | 23 | 15 | 117 | 216 |
| 120 | 4 | 7 | 8 | 13 | 19 | 20 | 23 | 15 | 117 | 226 |
| 140 | 4 | 7 | 11 | 15 | 19 | 20 | 23 | 15 | 117 | 231 |
| 160 | 4 | 8 | 13 | 17 | 19 | 20 | 23 | 15 | 117 | 236 |
| 180 | 4 | 9 | 14 | 17 | 19 | 20 | 23 | 15 | 117 | 238 |
| 200 | 4 | 10 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 241 |
| 220 | 4 | 11 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 242 |
| 240 | 4 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 244 |

PARTIAL PRESSURE 270

| Time of Dive | To 1st Stop | Feet and Minutes 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 4 | 0 | 0 | 7 | 0 | 0 | 0 | 4 | 10 | 44 | 70 |
| 20 | 4 | 0 | 0 | 7 | 0 | 2 | 4 | 6 | 10 | 80 | 113 |
| 30 | 4 | 0 | 7 | 0 | 2 | 5 | 6 | 9 | 10 | 100 | 143 |
| 40 | 4 | 0 | 7 | 0 | 3 | 8 | 9 | 10 | 10 | 110 | 161 |
| 60 | 4 | 0 | 7 | 3 | 7 | 10 | 14 | 16 | 13 | 117 | 191 |
| 80 | 4 | 0 | 7 | 6 | 10 | 13 | 17 | 23 | 15 | 117 | 212 |
| 100 | 4 | 7 | 2 | 9 | 13 | 16 | 20 | 23 | 15 | 117 | 226 |
| 120 | 4 | 7 | 4 | 11 | 14 | 19 | 20 | 23 | 15 | 117 | 234 |
| 140 | 4 | 7 | 5 | 14 | 15 | 19 | 20 | 23 | 15 | 117 | 239 |
| 160 | 4 | 7 | 7 | 15 | 17 | 19 | 20 | 23 | 15 | 117 | 244 |
| 180 | 4 | 7 | 9 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 247 |
| 200 | 4 | 7 | 11 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 249 |
| 220 | 4 | 7 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 251 |
| 240 | 4 | 7 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 253 |

*Take 1 extra minute from 1st stop to next stop.

PARTIAL PRESSURE 280

| Time of Dive | To 1st Stop | Feet and Minutes 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 4 | 0 | 0 | 7 | 0 | 0 | 1 | 3 | 10 | 47 | 73 |
| 20 | 4 | 0 | 7 | 0 | 0 | 2 | 6 | 6 | 10 | 84 | 119 |
| 30 | 4 | 0 | 7 | 0 | 3 | 6 | 6 | 9 | 10 | 104 | 149 |
| 40 | 4 | 7 | 0 | 2 | 5 | 8 | 8 | 12 | 11 | 113 | 170 |
| 60 | 4 | 7 | 0 | 6 | 8 | 10 | 14 | 18 | 14 | 116 | 197 |
| 80 | 4 | 7 | 3 | 8 | 11 | 14 | 17 | 23 | 15 | 117 | 219 |
| 100 | 4 | 7 | 5 | 11 | 13 | 16 | 20 | 23 | 15 | 117 | 231 |
| 120 | 4 | 7 | 8 | 12 | 16 | 19 | 20 | 23 | 15 | 117 | 241 |
| 140 | 4 | 7 | 10 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 248 |
| 160 | 4 | 8 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 252 |
| 180 | 4 | 9 | 14 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 254 |
| 200 | 4 | 10 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 256 |
| 220 | 4 | 12 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 258 |
| 240 | 4 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 260 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 290

| Time of Dive | To 1st Stop | 140 | 130 | 120 | Feet 110 | and 100 | Minutes 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 4 | 0 | 0 | 0 | 7 | 0 | 0 | 2 | 3 | 10 | 49 | 76 |
| 20 | 4 | 0 | 0 | 7 | 0 | 0 | 4 | 6 | 7 | 10 | 86 | 124 |
| 30 | 4 | 0 | 7 | 0 | 1 | 5 | 5 | 9 | 9 | 10 | 105 | 155 |
| 40 | 4 | 0 | 7 | 0 | 4 | 6 | 8 | 9 | 12 | 11 | 114 | 175 |
| 60 | 4 | 0 | 7 | 4 | 6 | 8 | 12 | 15 | 18 | 14 | 117 | 205 |
| 80 | 4 | 7 | 0 | 7 | 9 | 11 | 15 | 17 | 23 | 15 | 117 | 225 |
| 100 | 4 | 7 | 2 | 9 | 11 | 15 | 17 | 20 | 23 | 15 | 117 | 240 |
| 120 | 4 | 7 | 4 | 11 | 13 | 16 | 19 | 20 | 23 | 15 | 117 | 249 |
| 140 | 4 | 7 | 5 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 256 |
| 160 | 4 | 7 | 8 | 14 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 260 |
| 180 | 4 | 7 | 10 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 263 |
| 200 | 4 | 7 | 12 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 265 |
| 220 | 4 | 7 | 13 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 266 |
| 240 | 4 | 7 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 267 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 300

| Time of Dive | To 1st Stop | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 3 | 3 | 10 | 52 | 81 |
| *20 | 5 | 0 | 0 | 7 | 0 | 0 | 1 | 6 | 6 | 6 | 10 | 91 | 133 |
| 30 | 5 | 0 | 0 | 7 | 0 | 2 | 5 | 5 | 9 | 9 | 10 | 106 | 158 |
| 40 | 5 | 0 | 0 | 7 | 0 | 5 | 7 | 8 | 11 | 13 | 12 | 111 | 179 |
| 60 | 5 | 0 | 7 | 0 | 6 | 7 | 9 | 12 | 15 | 20 | 15 | 117 | 213 |
| 80 | 5 | 0 | 7 | 2 | 8 | 10 | 12 | 16 | 19 | 23 | 15 | 117 | 234 |
| 100 | 5 | 0 | 7 | 5 | 10 | 12 | 15 | 19 | 20 | 23 | 15 | 117 | 248 |
| 120 | 5 | 0 | 7 | 8 | 11 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 258 |
| 140 | 5 | 0 | 8 | 9 | 14 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 263 |
| 160 | 5 | 0 | 8 | 13 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 268 |
| 180 | 5 | 7 | 3 | 13 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 270 |
| 200 | 5 | 7 | 5 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 273 |
| 220 | 5 | 7 | 6 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 274 |
| 240 | 5 | 7 | 9 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 277 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESURE 310

| Time of Dive | To 1st Stop | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Feet and Minutes | | | | | | | | | | | | | |
| *10) | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 1 | 3 | 3 | 10 | 54 | 84 |
| 20 | 5 | 0 | 0 | 7 | 0 | 0 | 3 | 5 | 6 | 6 | 10 | 93 | 135 |
| 30 | 5 | 0 | 7 | 0 | 0 | 5 | 5 | 7 | 8 | 13 | 10 | 109 | 165 |
| 40 | 5 | 0 | 7 | 0 | 3 | 5 | 8 | 8 | 11 | 20 | 11 | 115 | 186 |
| 60 | 5 | 0 | 7 | 3 | 6 | 7 | 10 | 12 | 17 | 23 | 15 | 117 | 219 |
| 80 | 5 | 7 | 0 | 6 | 9 | 11 | 12 | 16 | 19 | 23 | 15 | 117 | 240 |
| 100 | 5 | 7 | 1 | 9 | 10 | 14 | 17 | 19 | 20 | 23 | 15 | 117 | 256 |
| 120 | 5 | 7 | 4 | 11 | 12 | 14 | 17 | 19 | 20 | 23 | 15 | 117 | 263 |
| 140 | 5 | 7 | 5 | 12 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 270 |
| 160 | 5 | 7 | 8 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 275 |
| 180 | 5 | 7 | 10 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 277 |
| 200 | 5 | 7 | 12 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 279 |
| 220 | 5 | 8 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 281 |
| 240 | 5 | 9 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 282 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 320

| Time of Dive | To 1st Stop | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Feet and Minutes | | | | | | | | | | | | | | |
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 2 | 3 | 3 | 10 | 57 | 88 |
| *20 | 5 | 0 | 0 | 7 | 0 | 0 | 1 | 4 | 5 | 6 | 7 | 10 | 94 | 140 |
| 30 | 5 | 0 | 0 | 7 | 0 | 2 | 4 | 5 | 7 | 8 | 11 | 10 | 110 | 169 |
| 40 | 5 | 0 | 7 | 0 | 1 | 4 | 6 | 7 | 8 | 12 | 15 | 12 | 117 | 194 |
| 60 | 5 | 0 | 7 | 0 | 5 | 6 | 9 | 11 | 13 | 17 | 20 | 15 | 117 | 225 |
| 80 | 5 | 0 | 7 | 3 | 7 | 9 | 11 | 13 | 17 | 20 | 23 | 15 | 117 | 247 |
| 100 | 5 | 0 | 7 | 5 | 9 | 11 | 13 | 17 | 19 | 20 | 23 | 15 | 117 | 261 |
| 120 | 5 | 0 | 7 | 7 | 12 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 271 |
| 140 | 5 | 7 | 2 | 9 | 12 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 277 |
| 160 | 5 | 7 | 3 | 11 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 282 |
| 180 | 5 | 7 | 5 | 11 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 284 |
| 200 | 5 | 7 | 6 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 287 |
| 220 | 5 | 7 | 7 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 288 |
| 240 | 5 | 7 | 9 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 290 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 330

| Time of Dive | To 1st Stop | Feet and Minutes 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 3 | 3 | 3 | 10 | 60 | 92 |
| 20 | 5 | 0 | 0 | 7 | 0 | 0 | 2 | 5 | 5 | 6 | 8 | 10 | 96 | 144 |
| 30 | 5 | 0 | 7 | 0 | 0 | 4 | 4 | 6 | 7 | 9 | 11 | 11 | 112 | 176 |
| 40 | 5 | 0 | 7 | 0 | 4 | 4 | 6 | 7 | 9 | 12 | 16 | 14 | 114 | 198 |
| 60 | 5 | 7 | 0 | 2 | 6 | 8 | 9 | 11 | 14 | 17 | 23 | 15 | 117 | 234 |
| 80 | 5 | 7 | 0 | 6 | 8 | 8 | 13 | 14 | 19 | 20 | 23 | 15 | 117 | 255 |
| 100 | 5 | 7 | 2 | 7 | 10 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 271 |
| 120 | 5 | 7 | 4 | 9 | 12 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 277 |
| 140 | 5 | 7 | 6 | 11 | 13 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 282 |
| 160 | 5 | 7 | 8 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 287 |
| 180 | 5 | 7 | 10 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 289 |
| 200 | 5 | 7 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 291 |
| 220 | 5 | 9 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 293 |
| 240 | 5 | 10 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 294 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 340

| Time of Dive | To 1st Stop | Feet and Minutes 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Tot Ti |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 3 | 3 | 4 | 10 | 64 | 98 |
| *20 | 5 | 0 | 0 | 7 | 0 | 0 | 1 | 3 | 4 | 6 | 5 | 10 | 10 | 98 | 15 |
| 30 | 5 | 0 | 0 | 7 | 0 | 1 | 4 | 5 | 6 | 8 | 8 | 13 | 11 | 113 | 18 |
| 40 | 5 | 0 | 7 | 0 | 1 | 4 | 5 | 7 | 7 | 10 | 12 | 17 | 13 | 117 | 20 |
| 60 | 5 | 0 | 7 | 0 | 5 | 6 | 8 | 9 | 11 | 15 | 19 | 23 | 15 | 117 | 24 |
| 80 | 5 | 0 | 7 | 2 | 7 | 8 | 10 | 13 | 15 | 19 | 20 | 23 | 15 | 117 | 26 |
| 100 | 5 | 0 | 7 | 5 | 9 | 9 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 27 |
| 120 | 5 | 7 | 1 | 7 | 10 | 13 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 28 |
| 140 | 5 | 7 | 2 | 9 | 12 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 29 |
| 160 | 5 | 7 | 4 | 10 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 29 |
| 180 | 5 | 7 | 5 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 29 |
| 200 | 5 | 7 | 6 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 29 |
| 220 | 5 | 7 | 8 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 30 |
| 240 | 5 | 7 | 10 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 30 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 350

| Time of Dive | To 1st Stop | Feet and Minutes 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 2 | 3 | 3 | 4 | 10 | 67 | 102 |
| *20 | 5 | 0 | 0 | 7 | 0 | 0 | 1 | 4 | 5 | 7 | 8 | 9 | 10 | 99 | 156 |
| 30 | 5 | 0 | 7 | 0 | 0 | 3 | 5 | 5 | 6 | 8 | 9 | 13 | 10 | 115 | 186 |
| 40 | 5 | 0 | 7 | 0 | 2 | 4 | 6 | 7 | 8 | 10 | 13 | 16 | 14 | 117 | 209 |
| 60 | 5 | 7 | 0 | 3 | 5 | 6 | 9 | 10 | 13 | 16 | 18 | 19 | 15 | 117 | 243 |
| 80 | 5 | 7 | 0 | 7 | 7 | 8 | 11 | 13 | 15 | 19 | 20 | 23 | 15 | 117 | 267 |
| 100 | 5 | 7 | 2 | 8 | 8 | 12 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 282 |
| 120 | 5 | 7 | 4 | 9 | 11 | 13 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 291 |
| 140 | 5 | 7 | 6 | 11 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 298 |
| 160 | 5 | 7 | 9 | 11 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 301 |
| 180 | 5 | 8 | 9 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 303 |
| 200 | 5 | 8 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 305 |
| 220 | 5 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 307 |
| 240 | 5 | 11 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 308 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 360

| Time of Dive | To 1st Stop | Feet and Minutes 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 2 | 3 | 3 | 5 | 10 | 69 | 106 |
| *20 | 5 | 0 | 0 | 7 | 0 | 0 | 0 | 3 | 4 | 5 | 5 | 7 | 9 | 10 | 102 | 158 |
| 30 | 5 | 0 | 0 | 7 | 0 | 1 | 4 | 4 | 5 | 7 | 8 | 11 | 13 | 11 | 114 | 190 |
| 40 | 5 | 0 | 7 | 0 | 1 | 3 | 5 | 6 | 7 | 8 | 11 | 14 | 17 | 15 | 117 | 216 |
| 60 | 5 | 0 | 7 | 0 | 5 | 5 | 8 | 8 | 11 | 12 | 16 | 19 | 23 | 15 | 117 | 251 |
| 80 | 5 | 0 | 7 | 2 | 7 | 7 | 10 | 11 | 13 | 17 | 19 | 20 | 23 | 15 | 117 | 273 |
| 100 | 5 | 7 | 0 | 6 | 8 | 9 | 11 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 288 |
| 120 | 5 | 7 | 1 | 7 | 9 | 12 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 297 |
| 140 | 5 | 7 | 3 | 9 | 11 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 304 |
| 160 | 5 | 7 | 4 | 10 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 307 |
| 180 | 5 | 7 | 5 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 309 |
| 200 | 5 | 7 | 7 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 311 |
| 220 | 5 | 7 | 9 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 313 |
| 240 | 5 | 7 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 314 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 370

| Time of Dive | To 1st Stop | Feet and Minutes 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | 5 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 2 | 2 | 3 | 7 | 10 | 69 | 106 |
| 20 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 1 | 3 | 4 | 5 | 5 | 8 | 10 | 10 | 104 | 162 |
| 30 | 5 | 0 | 0 | 7 | 0 | 0 | 3 | 3 | 5 | 6 | 7 | 8 | 11 | 12 | 14 | 117 | 198 |
| 40 | 5 | 0 | 0 | 7 | 0 | 2 | 4 | 5 | 7 | 7 | 9 | 10 | 14 | 19 | 15 | 117 | 221 |
| 60 | 5 | 0 | 0 | 7 | 2 | 5 | 6 | 7 | 9 | 11 | 14 | 16 | 19 | 23 | 15 | 117 | 256 |
| 80 | 5 | 0 | 7 | 0 | 6 | 6 | 8 | 11 | 12 | 14 | 16 | 19 | 20 | 23 | 15 | 117 | 279 |
| 00 | 5 | 0 | 7 | 2 | 7 | 8 | 11 | 13 | 13 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 293 |
| 20 | 5 | 0 | 7 | 4 | 8 | 10 | 12 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 302 |
| 40 | 5 | 7 | 0 | 7 | 9 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 309 |
| 60 | 5 | 7 | 0 | 9 | 10 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 312 |
| 80 | 5 | 7 | 2 | 9 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 315 |
| 00 | 5 | 7 | 3 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 317 |
| 20 | 5 | 7 | 5 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 319 |
| 40 | 5 | 7 | 7 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 321 |

-Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 380

| Time of Dive | To 1st Stop | Feet and Minutes 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *10 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 0 | 2 | 3 | 3 | 3 | 7 | 10 | 72 | 113 |
| *20 | 5 | 0 | 0 | 7 | 0 | 0 | 0 | 2 | 4 | 4 | 5 | 5 | 8 | 10 | 10 | 105 | 166 |
| *30 | 5 | 0 | 7 | 0 | 0 | 1 | 3 | 4 | 4 | 7 | 7 | 8 | 11 | 16 | 11 | 117 | 202 |
| 40 | 5 | 0 | 7 | 0 | 0 | 4 | 4 | 5 | 6 | 8 | 10 | 11 | 14 | 20 | 15 | 117 | 226 |
| 60 | 5 | 0 | 7 | 0 | 4 | 5 | 7 | 8 | 9 | 11 | 13 | 17 | 20 | 23 | 15 | 117 | 261 |
| 80 | 5 | 7 | 0 | 3 | 6 | 7 | 9 | 10 | 12 | 15 | 17 | 19 | 20 | 23 | 15 | 117 | 285 |
| 100 | 5 | 7 | 0 | 6 | 7 | 9 | 10 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 300 |
| 120 | 5 | 7 | 1 | 7 | 9 | 11 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 309 |
| 140 | 5 | 7 | 2 | 9 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 315 |
| 160 | 5 | 7 | 4 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 318 |
| 180 | 5 | 7 | 5 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 319 |
| 200 | 5 | 7 | 7 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 321 |
| 220 | 5 | 7 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 323 |
| 240 | 5 | 8 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 325 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 390

| Time of Dive | To 1st Stop | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Feet and Minutes | | | | | | | | | | |
| *10 | 5 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 0 | 2 | 3 | 3 | 4 | 7 | 10 | 74 | 116 |
| *20 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 1 | 2 | 4 | 5 | 5 | 5 | 9 | 9 | 10 | 109 | 172 |
| 30 | 5 | 0 | 0 | 7 | 0 | 0 | 2 | 4 | 5 | 6 | 7 | 8 | 10 | 12 | 12 | 12 | 116 | 206 |
| 40 | 5 | 0 | 0 | 7 | 0 | 2 | 3 | 5 | 6 | 6 | 8 | 9 | 13 | 14 | 21 | 15 | 117 | 231 |
| 60 | 5 | 0 | 7 | 0 | 2 | 5 | 5 | 8 | 8 | 9 | 11 | 15 | 17 | 20 | 23 | 15 | 117 | 268 |
| 80 | 5 | 0 | 7 | 0 | 5 | 7 | 8 | 9 | 11 | 12 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 292 |
| 100 | 5 | 0 | 7 | 2 | 7 | 8 | 9 | 11 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 307 |
| 120 | 5 | 0 | 7 | 5 | 8 | 9 | 11 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 316 |
| 140 | 5 | 7 | 0 | 7 | 10 | 10 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 322 |
| 160 | 5 | 7 | 1 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 325 |
| 180 | 5 | 7 | 3 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 327 |
| 200 | 5 | 7 | 5 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 329 |
| 220 | 5 | 7 | 7 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 331 |
| 240 | 5 | 7 | 8 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 332 |

*Take 1 extra minute from 1st stop to next stop.





## PARTIAL PRESSURE 400

| Time of Dive | To 1st Stop | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Feet and Minutes | | | | | | | | | | |
| *10 | 5 | 0 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 2 | 3 | 3 | 6 | 9 | 10 | 74 | 121 |
| *20 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 4 | 4 | 4 | 5 | 8 | 8 | 10 | 10 | 109 | 176 |
| *30 | 5 | 0 | 0 | 7 | 0 | 0 | 0 | 4 | 4 | 4 | 5 | 7 | 7 | 10 | 11 | 15 | 13 | 117 | 209 |
| 40 | 5 | 0 | 0 | 7 | 0 | 1 | 4 | 5 | 6 | 6 | 6 | 7 | 10 | 11 | 16 | 18 | 15 | 117 | 234 |
| 60 | 5 | 0 | 7 | 0 | 0 | 5 | 5 | 6 | 7 | 8 | 11 | 13 | 14 | 17 | 20 | 23 | 15 | 117 | 273 |
| 80 | 5 | 0 | 7 | 0 | 3 | 6 | 6 | 8 | 10 | 12 | 12 | 15 | 17 | 19 | 20 | 23 | 15 | 117 | 295 |
| 100 | 5 | 0 | 7 | 0 | 6 | 7 | 8 | 10 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 312 |
| 120 | 5 | 0 | 7 | 2 | 6 | 9 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 321 |
| 140 | 5 | 0 | 7 | 2 | 8 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 324 |
| 160 | 5 | 0 | 7 | 3 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 327 |
| 180 | 5 | 0 | 7 | 5 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 329 |
| 200 | 5 | 0 | 7 | 7 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 331 |
| 220 | 5 | 0 | 7 | 9 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 333 |
| 240 | 5 | 7 | 1 | 9 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 334 |

*Take 1 extra minute from 1st stop to next stop.

## PARTIAL PRESSURE 410

| Time of Dive | To 1st Stop | Feet and Minutes | | | | | | | | | | | | | | | | | Total Time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | |
| *10 | 5 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 0 | 2 | 2 | 3 | 3 | 6 | 9 | 10 | 78 | 126 |
| *20 | 5 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 2 | 4 | 4 | 4 | 5 | 7 | 9 | 11 | 10 | 110 | 179 |
| 30 | 5 | 0 | 0 | 7 | 0 | 0 | 2 | 3 | 4 | 4 | 5 | 7 | 8 | 12 | 15 | 15 | 12 | 117 | 216 |
| 40 | 5 | 0 | 0 | 7 | 0 | 2 | 3 | 4 | 6 | 6 | 6 | 9 | 11 | 13 | 16 | 20 | 15 | 117 | 240 |
| 60 | 5 | 0 | 7 | 0 | 2 | 5 | 5 | 6 | 7 | 10 | 10 | 13 | 15 | 19 | 20 | 23 | 15 | 117 | 279 |
| 80 | 5 | 0 | 7 | 0 | 5 | 6 | 8 | 8 | 9 | 12 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 302 |
| 100 | 5 | 0 | 7 | 3 | 6 | 7 | 8 | 11 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 316 |
| 120 | 5 | 7 | 0 | 5 | 7 | 10 | 10 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 325 |
| 140 | 5 | 7 | 0 | 7 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 330 |
| 160 | 5 | 7 | 2 | 8 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 334 |
| 180 | 5 | 7 | 3 | 9 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 336 |
| 200 | 5 | 7 | 5 | 9 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 338 |
| 220 | 5 | 7 | 7 | 9 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 340 |
| 240 | 5 | 7 | 8 | 9 | 10 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 19 | 20 | 23 | 15 | 117 | 341 |

*Take 1 extra minute from 1st stop to next stop.

## EMERGENCY TABLES FOR USING HELIUM-OXYGEN

### ONLY FOR DECOMPRESSION

In an emergency it may be that oxygen cannot be used for decompression, owing to failure of supply or possibly to oxygen symptoms due to excessive carbon dioxide. Either air or helium-oxygen may be used. Emergency tables for using helium-oxygen mixtures may be calculated for the particular dive being made. In order to have a table that may be immediately available, the decompression provided in regular tables should be given up to 60 feet and from that point on, this table should be used:

| 60 ft. | 50 ft. | 40 ft. | 30 ft. | 20 ft. | 10 ft. |
|---|---|---|---|---|---|
| 23 m. | 26 m. | 30 m. | 35 m. | 42 m. | 55 m. |

## EMERGENCY TABLES FOR USING AIR FOLLOWING HELIUM-OXYGEN DIVE

In emergencies when it is not possible to use Helium-Oxygen Mixtures or oxygen during decompression it may become necessary to use air. Decompression for each case can be calculated. However, since the emergency may occur at any point from the bottom to the last stop, it seems impracticable to attempt to cover all of the possibilities in tables. Therefore, a table for maximum saturation is provided and this table may be used for any emergency. When it is possible to do so, the first twenty minutes of these tables, the air should be administered through the circulator. Otherwise the diver may experience uncomfortable symptoms, dizziness, weakness, etc.

The tables are provided for each fifty feet and the table selected should be the one next higher than the actual depth, unless the depth is at an even fifty foot figure.

-:TREATMENT TABLE:-

| Depth | 230 | 220 | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 100 | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | 14: | 42: | 52: | 68: | 175 |
| 150 | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | : | 22: | 30: | 35: | 42: | 52: | 68: | 249 |
| 200 | : | : | : | : | : | : | : | : | : | : | : | : | : | : | 7: | 22: | 24: | 26: | 30: | 35: | 42: | 52: | 68: | 306 |
| 250 | : | : | : | : | : | : | : | : | : | : | : | : | 13: | 18: | 19: | 22: | 24: | 26: | 30: | 35: | 42: | 52: | 68: | 351 |
| 300 | : | : | : | : | : | : | : | : | : | 4: | 14: | 16: | 16: | 18: | 19: | 22: | 24: | 26: | 30: | 35: | 42: | 52: | 68: | 387 |
| 350 | : | : | : | : | : | : | : | 9: | 13: | 13: | 15: | 16: | 17: | 18: | 20: | 22: | 24: | 27: | 30: | 35: | 42: | 52: | 68: | 421 |
| 400 | : | : | : | : | 3: | 11: | 12: | 12: | 13: | 14: | 15: | 16: | 17: | 18: | 20: | 22: | 24: | 27: | 30: | 35: | 42: | 52: | 68: | 451 |
| 450 | : | : | 6: | 10: | 11: | 11: | 12: | 12: | 13: | 14: | 15: | 16: | 17: | 18: | 20: | 22: | 24: | 27: | 30: | 35: | 42: | 52: | 68: | 475 |
| 500 | : | 9: | 9: | 10: | 10: | 11: | 11: | 12: | 12: | 13: | 14: | 15: | 16: | 17: | 18: | 20: | 22: | 24: | 27: | 30: | 35: | 42: | 52: | 68: | 497 |

(D)

INSTRUCTIONS FOR MIXING HELIUM AND OXYGEN FOR USE IN DIVING

Helium gas is kept in storage at the Naval Air Station, Lakehurst, N. J. It is obtained through the Bureau of Aeronautics. Requests are submitted to the Bureau of Construction and Repair for the number of cylinders required. Cylinders are charged to about 1800 pounds per square inch and they contain about 180 cubic feet of the gas at one atmosphere pressure. Whenever the term "cubic feet of gas used" appears it means the amount is at one atmosphere pressure. Precautions are taken to see that the helium cylinders and the gas are kept oil free because of the danger of explosion when oxygen is added if oil is present.

Helium fittings are made up with a left hand thread and special fittings must be made when using the cylinders.

Because of the high pressure in the cylinders when helium is received, an empty cylinder is attached to a full cylinder and the gas is allowed to equalize in the two cylinders. This step requires a fitting with two helium threaded nuts.

In order to add oxygen to the helium, a cylinder with pressure reduced as above is connected to an oxygen cylinder which contains gas at a pressure higher than that in the helium cylinder. This requires a fitting with one oxygen nut and one helium nut.

Both of the above fittings can be combined by using a cross shaped fitting having the four outlets, provided with two helium nuts, one oxygen nut and one pressure gauge (0-2000 pounds).

The percentage of oxygen to be added to the helium is obtained by determining the amount of increase of the pressure in the helium cylinder by the application of Boyle's Law. It requires some practice on the part of the gas mixer to be able to judge the temperature factors. Experience has shown that if the oxygen is allowed to enter the helium flask rapidly more accurate results are obtained. A fairly accurate thumb rule for mixing is to take the percentage of oxygen desired, add eleven, then multiply this percentage by the pressure in the helium cylinder which gives the amount of pressure to be added to the helium.

Gas should be mixed several days before it is to be used because the mixing of the gases is slow. Samples for analysis should not be drawn from the mixed cylinders until about 36 hours after mixing.

From Part I of the decompression tables it can be seen that there is considerable range of oxygen percentages for each depth. The greater the percentage, however, up to the limit for that depth, the less will be the decompression time required.

Therefore, extreme accuracy in the percentages obtained when mixing is not essential.

The analysis must be accurate to within one per cent and may be made by any standard gas analysis apparatus suitable for shipboard use.

Samples are obtained from the mixed cylinder by using a fitting of 1/4" high pressure tubing with a male helium thread and one end and a short section rubber tube on the other end. A "Hoke Needle Valve" is placed in the metal tube for controlling the amount of the sample. The threaded end is fitted to the cross fitting which is fitted to the cylinder. The rubber tube can then be fitted to a glass sample tube. Samples should be taken over mercury.

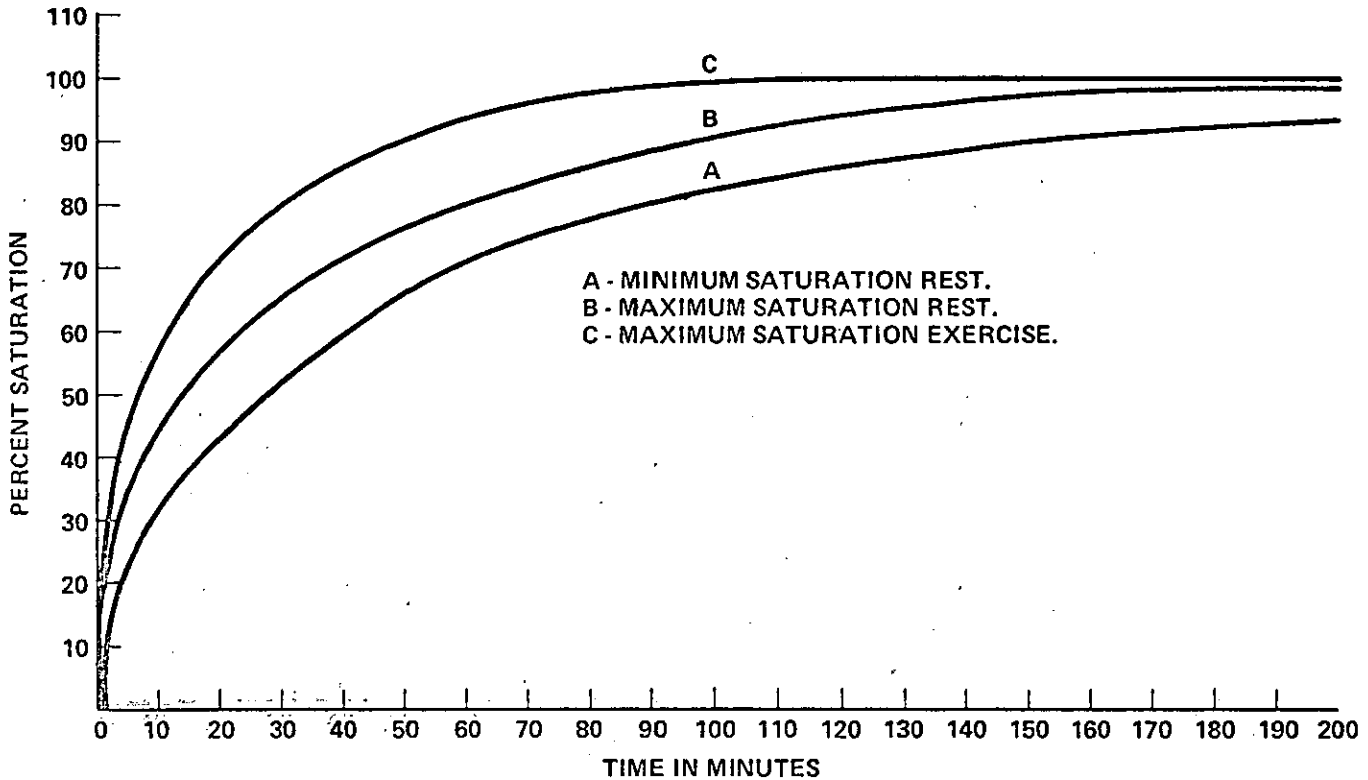
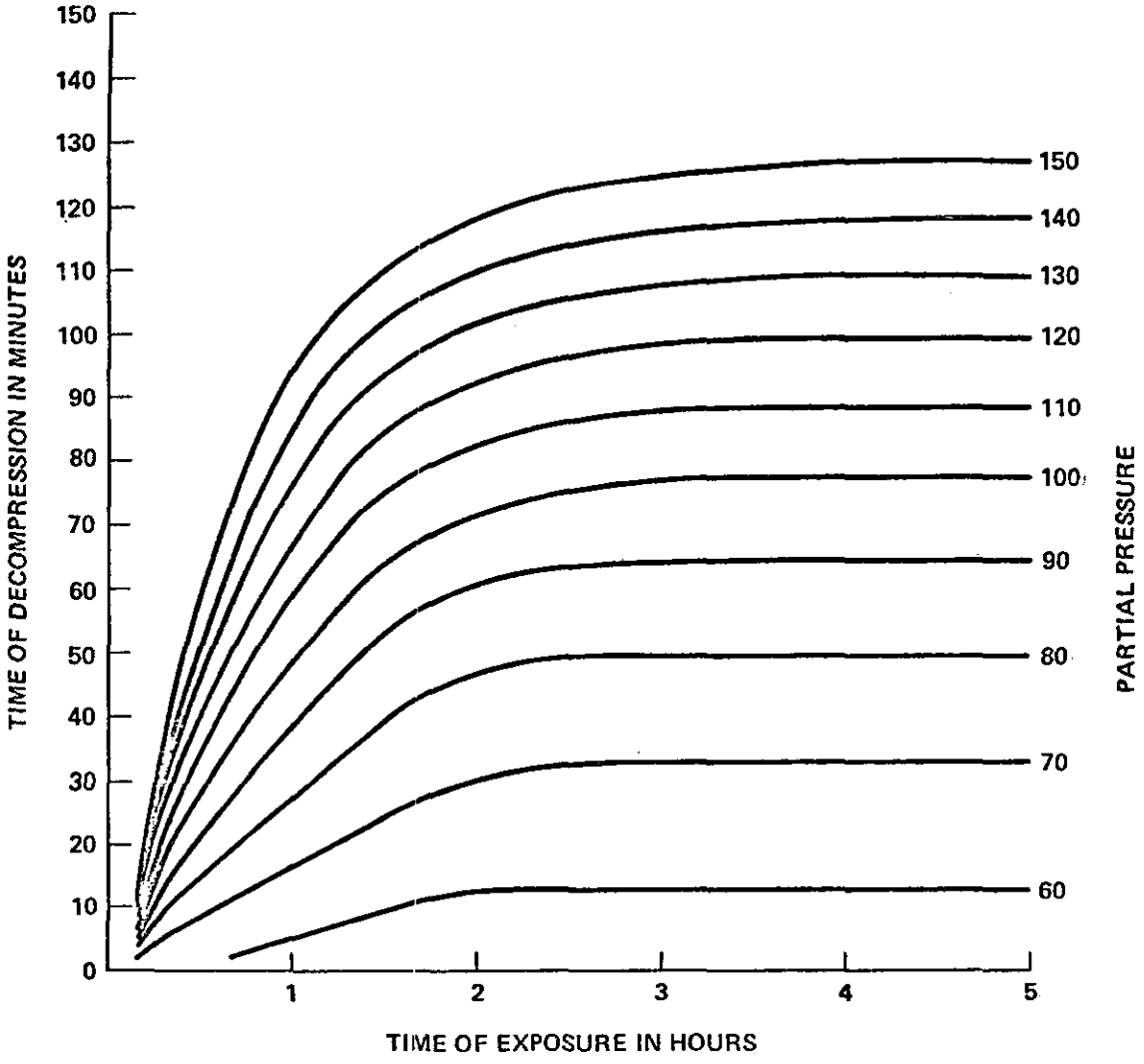



FIGURE 4.

HELIUM ELIMINATION BAND




OXYGEN DECOMPRESSION
FOR
HELIUM - OXYGEN DIVE

## INSTRUCTIONS FOR USING HELIUM-OXYGEN GAS MIXTURES FOR DIVING
***REVISED***

The oxygen tension should not exceed 2.5 atmospheres. While it has been extablished that under ideal conditions a tension in excess of this can be breathed, the influence of $CO_2$ reduces the safe limit and it has been determimed that 2.5 atmospheres is safe under working conditions. Symptoms of excess oxygen may take the form of drowsiness, ringing of the ears, irritability and other emotional upsets, and should be reported promptly so that immediate steps can be taken to correct it. The reduction of the tension will give relief and may be accomplished by:

(a) Reducing the depth.
(b) Reducing the percentage of oxygen breathed.
(c) Reducing the $CO_2$ in the helmet by ventilating.

The maximum percentage permissable may be obtained as follows:

$$P = \frac{82.5}{D + 33}$$

where D is actual depth of water.

Cylinders of mixed gas, in banks of five cylinders each, the oxygen percentages of which is within 2 per cent of each other, are attached to a manifold in such a way that each may be used for the divers' supply. A volume tank of about three (3) cubic feet capacity is attached to the manifold to take care of a sudden surge of demand and the divers' supply is taken from the volume tank.

The gas pressure is always kept at 50 pounds more than the pressure at the position of the diver. (over bottom pressure).

At the helmet the gas is admitted through an aspirator, the action of which is to partially circulate the gas in the helmet through a canister containing a carbon dioxide absorbent, Shell Natron. The gas supply, more than 3 cu.ft. per minute at 300 feet, is the driving force in the circulating system and also provide make up oxygen to the divers.

This gas supply is taken off the usual hose ahead of the control valve. It has a separate valve so that it can be closed off.

The control valve can be used at any time to ventilate the suit or to build up the pressure, for instance when decending.

The exhaust valve is kept closed when using the aspirator and the diver may have to operate the chin valve from time to time to keep from getting light.

In returning to the surface the gas is administered in the same manner as above during the decompression stages up to 60 feet. At this point pure oxygen is used. By ventilating twenty five (25) cubic feet of oxygen through the helmet, using the control valve, the helium oxygen gas is about eighty (80) per cent replaced by oxygen. The arrangement for using oxygen is similar to that described for helium-oxygen mixture.

When using the submersible decompression chamber, the suit is removed from the diver and either helium oxygen or oxygen is breathed through a mask.

## SURFACE DECOMPRESSION PROCEDURE

The following surface decompression has been tried and proven satisfactory:

(a) In tables where first stop is 50 feet, allow diver to remain on oxygen for 10 minutes then surface diver and return him to 50 feet in the chamber as fast as possible and put him back on oxygen for the time as shown in the tables. EXAMPLE: Page 42, PP 110. Time of dive 20 mins. Bring diver to 50 feet in 2 minutes. Ventilate 25 cu.ft. of oxygen after arrival at 50 feet. Keep diver at 50 feet for 10 minutes. Bring diver to the surface and return him to 50 feet in the chamber and have him use an oxygen mask for 21 minutes at this depth.

(b) Where first stop is other than 50 feet, give decompression as listed until he arrives at the 50 foot stop then give him the same time at 50 feet as he has had at 60 feet. Surface him and return him to 50 feet in the chamber, giving him the time in the chamber as shown by the tables for his 50 foot stop. EXAMPLE: Page 50 PP 270. Time of dive 40 minutes. Give the diver the following decompression - 4 mins. to 120 feet, 7 minutes at 120 feet, 3 minutes at 100 ft., 8 minutes at 90 ft., 9 mins. at 80 ft., 10 mins. at 70 ft. Arrival at 60 feet shift to oxygen, ventilating for 25 cu.ft. and allow diver to remain there for 10 minutes as shown. Stop at 50 feet for 10 minutes. Bring diver to the surface and return him to 50 feet in the chamber and on oxygen for 110 minutes.

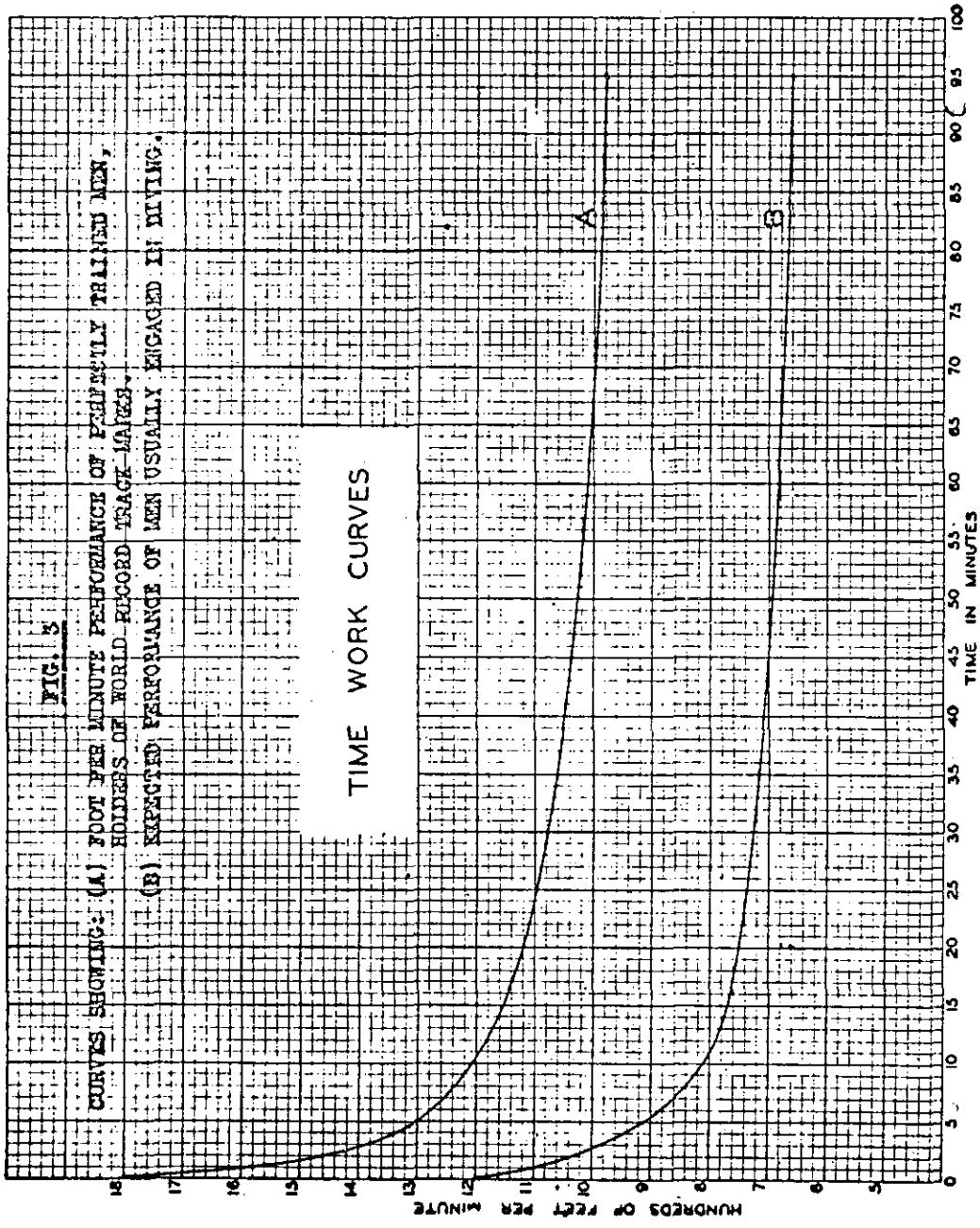



FIG. 3

CURVES SHOWING: (A) FOOT PER MINUTE PERFORMANCE OF PROPERLY TRAINED MEN, HOLDERS OF WORLD RECORD TRACK MARKS.

(B) EXPECTED PERFORMANCE OF MEN USUALLY ENGAGED IN DIVING.

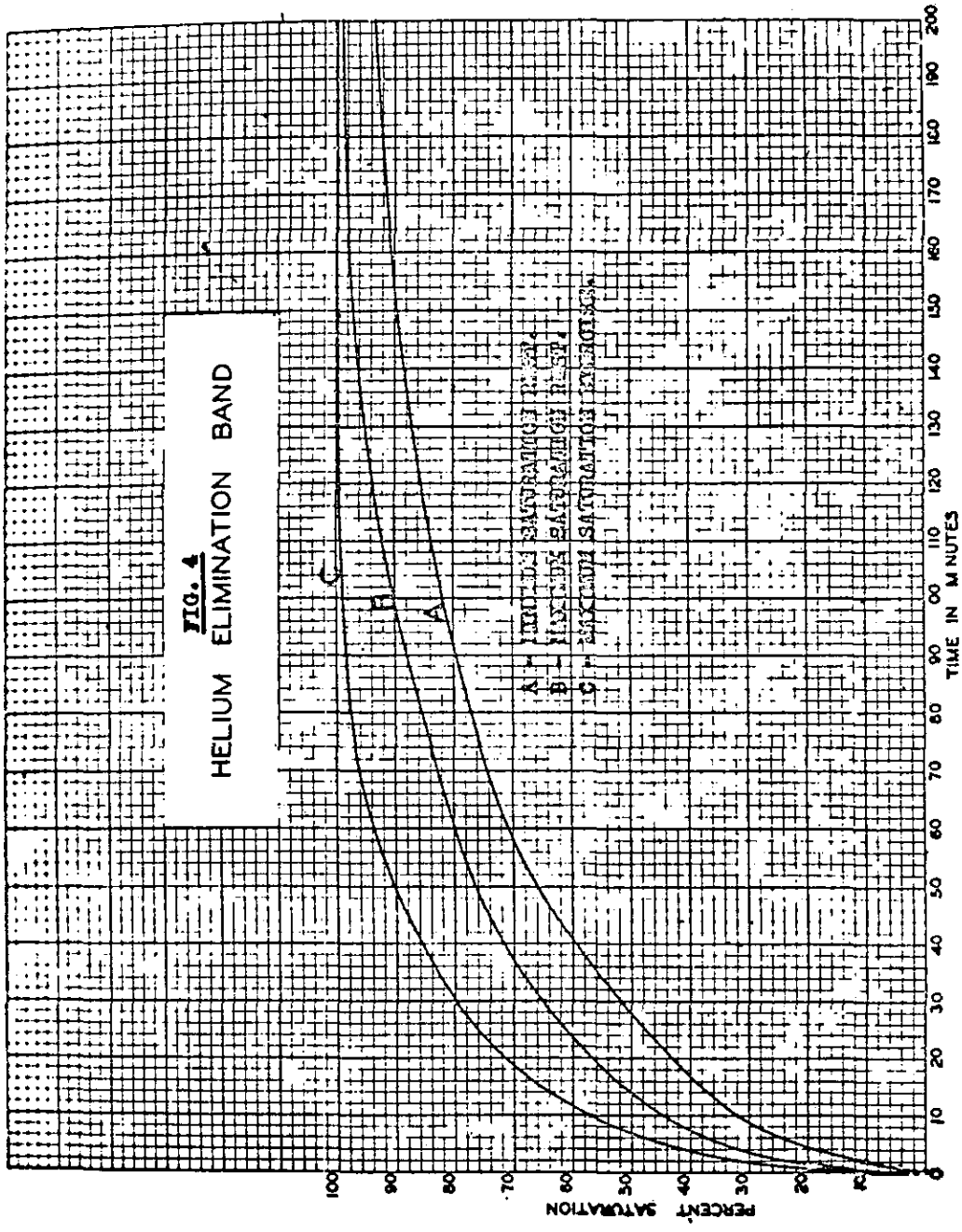


FIG. 4
HELIUM ELIMINATION BAND
A
B
C
PERCENT SATURATION
TIME IN MINUTES

## (F) INFLUENCE OF EXERCISE ON DECOMPRESSION REQUIREMENTS

It is a well known fact that an increase in the circulatory rate of the blood stream will cause the body to absorb an increased amount of gas in a given time, when the body is exposed to a pressure greater than atmospheric. It is also well known that certain things produce an increase of circulatory rate in the body. Those things which might increase the rate in the diver's body are exercise, excitement, fear, breathing carbon dioxide etc. The amount of work etc. that a man can stand per minute decreases as the time factor increases.

For the purpose of determining the relation between work per minute and time, the world's record track times for all distances were plotted on cross section paper using feet per minute against time. This performance was considered to be the point of perfection for the perfectly trained human body.

The oxygen consumed by the body is in direct proportion to the foot pounds of work done during a given period.

By comparing the oxygen consumption of some of the world's greatest athletes while performing at their best, with the amounts consumed by Navy divers when working to a point just short of exhaustion it has been determined that the best that can be expected of the divers will be about 67 per cent of that of the perfect performance.

It followed that a curve, Figure 3, drawn parallel to the curve of perfect performance using 67 per cent of the feet per minute values, would represent amounts of work which might be expected from the Navy divers.

Using this curve as a basis, tasks were performed on an exercise bicycle while the men were breathing helium-oxygen mixtures. The amount of gas absored by the body was measured and checked against the amount absorbed when the men were at rest.

The percentages of increased saturation were obtained for various periods of work and it was found that the body absorbs, in any unit of time during which work to exhaustion is performed, an amount of gas approximately equal to the amount that would have been absorbed in two units of time, but at rest. This has been shown in Figure 4.

No one is able to judge what increase in circulation rate of the blood a diver experiences when he is in the water and for that reason the only safe decompression that can be provided is that which is based upon his having absorbed the maximum amount of gas during his period of exposure.

Therefore decompression tables that have been calculated for helium-oxygen diving are based upon the assumption that the diver has worked to exhaustion.

While it is admitted that under certain favorable conditions the decompression times may be reduced, to do so would cause the matter of complete decompression to enter a zone of probability.

It may be justified to take risks when the working conditions are such that excessive delays in operations are caused by having men in the water undergoing long periods of decompression, but when by using the submersible decompression chamber the divers can be removed from the water promptly, it appears that sound practice should dictate the use of tables that are safe beyond a doubt.

Report No. 2870
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REPORTS OF INVESTIGATIONS

DEPARTMENT OF THE INTERIOR--BUREAU OF MINES

# POSSIBILITIES IN THE USE OF HELIUM-OXYGEN MIXTURES AS A MITIGATION OF CAISSON DISEASE.

By R. R. Sayers[1], W. P. Yant[2], and J. H. Hildebrand[3].

## SUMMARY STATEMENT

The Bureau of Mines, in conducting investigations of atmospheres in mines and tunnels for the purposes of determining and combating hazards to the health and safety of workers, has from time to time closely cooperated with municipal, State and Federal agencies in safety work in engineering and ventilating problems.

Recently the writers have conducted experiments with animals and men breathing helium-oxygen mixtures under pressure. The object of this work was to determine whether helium-oxygen atmospheres can be utilized to advantage in place of normal air for caisson and diving work. In such work the permissible pressures and times of compression and decompression are limited by the physiological effects on man. The major effect is that the nitrogen, which is the inert constituent of normal air and is absorbed by the body tissues and fluids in abnormal amounts when under pressure, tends to form bubbles in the tissues on too rapid decompression from high pressures.

The Bureau of Mines is interested in this problem on account of the possibilities of mitigating caisson illness in tunnel construction and other engineering operations requiring men to work in compressed air. In addition, the Navy Department is interested on account of the possibilities for extending the range of salvaging and marine engineering operations. The results of the experiments conducted by the writers lead to the following conclusions:

Helium is without odor or taste and has physical properties which promise to be of interest physiologically and which have been found to have possibilities of great practical use, especially in making a synthetic atmosphere that will reduce the hazard of caisson disease. The substitution of helium for the nitrogen ordinarily present in the air we breathe has been found to result in an atmosphere which is as respirable as that provided by nature. The results obtained indicate that helium not only has the advantage of being less soluble than nitrogen, but

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[1] Chief Surgeon, Bureau of Mines, Department of the Interior, Surgeon U. S. Public Health Service.

[2] Associate Chemist, Pittsburgh Experiment Station, Bureau of Mines, Department of the Interior.

[3] Professor of Chemistry, University of California, Consulting Chemist, Bureau of Mines, Department of Interior.

also has the advantage of diffusing more rapidly in the body fluids and tissues which results in rapid elimination of the gas from the tissues during decompression. Along with mitigating the hazard of caisson illness, helium should markedly increase the scope of other kinds of engineering work in compressed air.

The tests conducted by the writers indicated that through the use of helium and oxygen mixtures as a substitute for air in diving work, the time of decompression can be materially reduced. In a series of experiments on animals, after similar exposures decompression could be made from the helium-oxygen mixtures in as low as one-sixth the time necessary for air or nitrogen-oxygen mixtures. In a few preliminary experiments on men, decompression was made in one-fourth to one-eighth the time ordinarily recommended for air. These man tests will not be described in this report as they are too few to justify conclusions regarding the final factor of advantage. The U. S. Navy Department and the Department of the Interior, Bureau of Mines are at present carrying out cooperatively an extensive program of experiments with men.

FUNDAMENTAL PRINCIPLES AND LIMITATIONS OF COMPRESSED AIR WORK.

In late years little progress has been made towards materially reducing the hazards and extending the limits of operations where men are required to work under excessive pressure, except that the nature of the dangers encountered are perhaps more thoroughly understood, and the technique for avoiding them has been improved. Thus in caisson and tunnel work, dangers from air pressures of 25 to 30 pounds have been practically eliminated through improvement in technique and the development of proper decompression tables.[4] However, if the working pressure is increased to approximately 50 pounds, there is a marked increase in the number of cases of caisson illness[5], even though considerably longer decompression periods and extra precautions are used. Should it be necessary to carry on tunnel or caisson work at pressures markedly in excess of 50 pounds, it will be seen that the seemingly unavoidable increase in caisson sickness and in the length of period required for decompression, are serious problems.

In diving work, the apparatus most commonly used is the regulation diving equipment consisting of a metal helmet and rubber suit, and the well-known diving bell. In both of these it is necessary to subject the diver to an air pressure equal to that of the water at the depth of operations. At a depth of 200 feet of water (which has been regarded as about the limit for diving work of any great extent), a diver is subjected to a pressure of approximately 100 pounds per square inch. This seems enormous when it is remembered that the average body has 2,300 square inches of surface and, therefore, at 200 feet the total pressure on the body would be 230,000 pounds. However, the human system adjusts itself to take care of the pressure, by building up within, chiefly through the respiratory and circulatory system, a pressure in equilibruim to that of the air in the diving apparatus, caisson, or tunnel. Consequently, the man is able to work without marked discomfort or physiological harm.

The speed of compression or going under pressure seems to be governed by the effect on the man's ears. The middle ear is an air compartment separated from the exterior air by a thin membrane known as the ear drum. This membrane, by virtue of its function in promoting the sense of hearing, is very sensitive to inequality of pressures between the interior of the compartment and the exterior air. In order to maintain equality of pressure the drum is provided with a small opening known as the Eustachian tube, which connects to the back of the throat and through which air may pass in or out. Comparatively small differences in pressure cause the drum to be forced in or out, accompanied by a roaring in the ears; greater differences will cause pain and possibly rupture the membrane.

With experienced workers, ear trouble presents no great difficulty and they are able to go under pressure at rates of 15 to 20 pounds or 30 to 40 feet depth per minute. It is always desired to go under pressure as rapidly as possible, because (as described later) this indirectly reduces the time of decompression after a given period at the working pressure, that is, reduces the time

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[4] Levy, Edward. Compressed-air illness and its engineering importance. Department of the Interior, Bureau of Mines Technical Paper 285, 1922, p. 34.

[5] Report of the New York State Bridge and Tunnel Commission, Legislative Document No. 86, 1924, 36 pp.

of exposure, which in part governs the time of decompression.

The chief difficulty, as already mentioned, in safely extending the limits of work conducted in compressed air arises from the fact that during compression and at the working pressure, the body fluids and tissues absorb a large volume of air in accordance with the physical law governing the solubility of gases in liquids. The amount of gas in solution at equilibrium increases directly with the pressure. If it be assumed for analogy that the body fluids are perfect liquids, they would at equilibrium have in solution ten times as much gas at a pressure of ten atmospheres as at one atmosphere.

The absorption of this abnormal volume of gas while going under pressure seems to cause no trouble. The difficulty arises during decompression or return to the surface. As the pressure decreases, the tissues and fluids tend to give up the excess gas that they have in solution. However, there is what might be termed a "lag" in maintaining equilibrium between the tissues and the exterior, due to the time required for diffusion and removal of the gas.

If the decrease in pressure is not carefully controlled, and sufficient time is not permitted for the gas to escape quietly into the blood and thence from the lungs, bubbles will form in the tissues and blood vessels. This bubbling action is very similar to that of a carbonated beverage when the bottle is opened, except that the gas which causes the liquid to effervesce is carbon dioxide, whereas in caisson sickness the bubbles are mostly nitrogen. The bubbles are most dangerous if formed in the spinal cord and brain, causing paralysis or death. If bubbles form, an additional danger is their tendency to increase in size on further lowering of pressure. There is also the possibility that a number of small bubbles may aggregate to form large ones. Control of the decompression to prevent the formation of bubbles is the most difficult problem of caisson and diving work.

The length of time required for safe decompression is governed by the air pressure to which the man is exposed, and the percentage of saturation of the body fluids with inert gases at the given pressure. The percentage of saturation attained is dependent upon the length of time of exposure at a given pressure. According to the United States Navy tables[6], it seems that at a pressure greater than 200 feet of water a condition is reached where, except for comparatively short exposures, the minimum time of ascent or decompression becomes too long when compared with the useful work period. While it would require only five or ten minutes to descend to that depth, it would require two hours to safely bring a diver back to the surface after a 45-minute stay at the bottom. For the same reason, caisson work above certain pressures is prohibitive. Additional hazards in diving which limit the time required for ascent, are that a sudden storm, mechanical trouble with apparatus, or physical condition of the diver may necessitate that he be brought to the surface almost immediately. Moreover, during long periods of decompression, the mental strain on the diver of keeping his apparatus working perfectly and avoiding accidents becomes too fatiguing. The conservation of endurance and physical fitness of divers is of paramount importance in view of the exceedingly limited personnel available for work at great depths.

[6] U.S. Navy Department (revised). Reprint of Chapter 36 of the Manual of the Bureau of Construction and Repair, 1924.

## EXPERIMENTS WITH HELIUM-OXYGEN MIXTURES.

As shown in the previous paragraphs, it has been confirmed by experiment and practical diving that the greater physiological danger in diving and compressed air work is not during compression, but during decompression. Further, as has been stated, it is the nitrogen in the air breathed that is fundamentally responsible for bubbles forming in the fluids and tissues during ascent or decompression.[7] Any gas that would tend to reduce the danger of caisson disease, as well as reduce the period of decompression for a given condition of exposure, must have a lower coefficient of solubility and a greater diffusivity than nitrogen. In addition, the gas must be inert like nitrogen as regards physiological effects. That no investigation had been carried out along the lines of substituting a more suitable inert gas for nitrogen is perhaps due to the fact that a gas (helium) having the properties of a suitable substitute, has only recently become available in sufficient quantities. Since helium is chemically inert similar to nitrogen and has a lower solubility coefficient (0.008175 in water at 30° C. as compared with 0.0134 for nitrogen), it was thought that helium might be used to good advantage for work in compressed air.

SOLUBILITY OF HELIUM AND NITROGEN.

| Gas | Formula | 0° | 2° | 10° | 25° | 30° | Authority |
|---|---|---|---|---|---|---|---|
| Helium | He | --- | 0.00937 | 0.008955 | 0.008635 | 0.008175 | Cady, Elsey & Berger 1922[a] |
| Nitrogen | $N_2$ | 0.0239 | | 0.018600 | 0.014300 | 0.013400 | Bohr and Bock, 1921[b] |

In addition to the advantage of lower solubility, it appeared to the authors that the greater diffusivity of helium would be an additional advantage, resulting in more rapid and easier escape from the tissues and body fluids during

[7] The work of Bert, Hoppe-Seyler, Sir Thomas Oliver, Heller, Nager, and von Schrotter. Described by Leonard Hill in Caisson sickness and the physiology of work in compressed air, London, 1912, 255 pp.

[a] Cady, H. P., Elsey, H. M., Berger, E. V. The solubility of helium in water. Journal of the American Chemical Society, Vol. XLIV, July-Dec., 1922, pp. 1456-1461.

[b] Bohr, Christian, and Bock, Johannes. Determination de l'absorption de quelques gaz dans l'eau à des températures comprises entre 0 et 100°. Oversigt over det Konglige Danske Videnskabernes Selskabs, Forhandlinger, Kjøbenhavn, 1891, pp. 84-115; also, Annalen der Physik und Chemie, 44, 1891, 318-343.

decompression. Theoretically, the molecular weight of the two gases would affect their rates of diffusion, and helium, being the lighter of the two, would diffuse through and come out of the tissues and body fluids more readily than nitrogen. The weight of the helium molecule is less than that of nitrogen in the ratio of 4 to 28, and travels at a higher velocity, hence it should escape more easily. Accordingly the writers, who had for some time been considering the diving problem, conducted the investigation herein described.

Scope of present investigation:

Tests were conducted on white rats and later on guinea pigs. Comparative experiments with both helium and nitrogen were conducted on the same species, the results of which gave relative data that can be applied to men with a fair degree of accuracy.

For the preliminary work conducted on white rats, an arbitrary decompression schedule was chosen. In succeeding tests on guinea pigs, the schedules given in Table 1 were used; these were arranged from the Admiralty Tables given by Davis[B] in his Diving Manual.

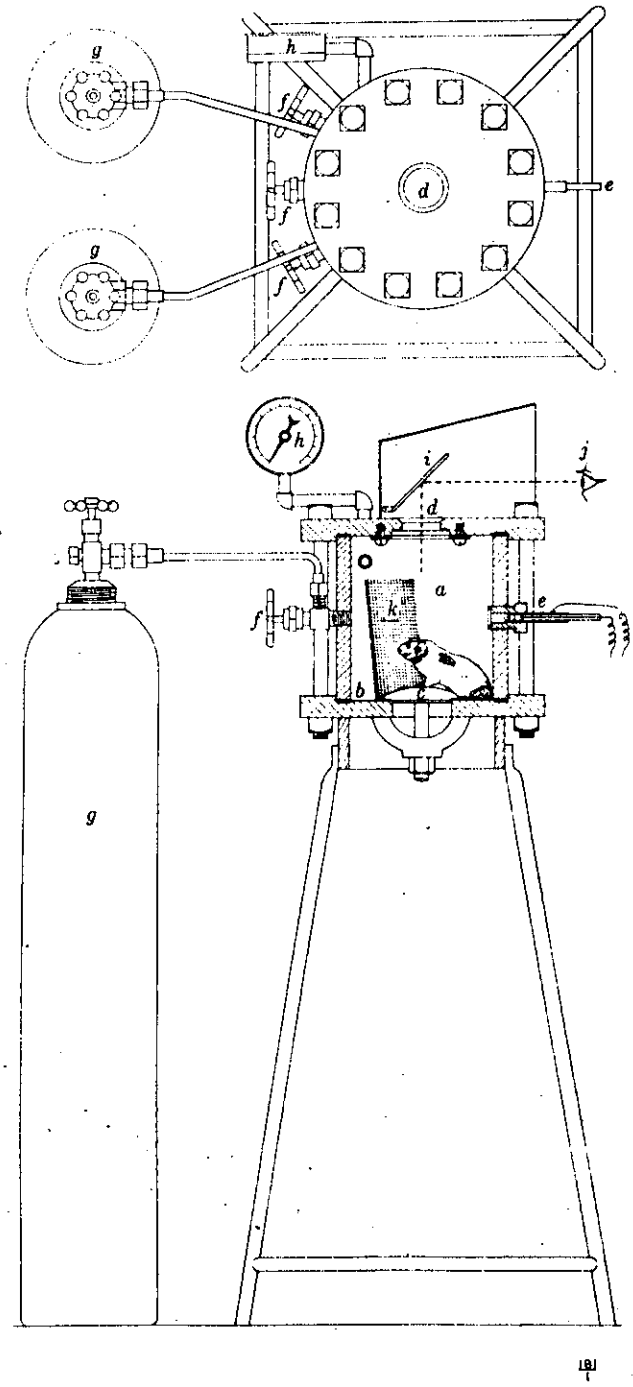
The tables given in that publication cover ranges up to approximately two hours' exposure and slightly more than 50 pounds pressure. In the Bureau of Mines tests 150 pounds was the minimum pressure used, consequently the schedules in Table 1 contain extrapolations for the higher pressures. Also the period for each stage of decompression was reduced proportionately (as 1/5, 1/7, 1/9, etc.) in order to eliminate both the safety factor included in the Admiralty Tables and the factor due to difference in size between men and the small animals. Small animals have been found to withstand more rapid decompression than man. These stage periods were then further decreased to cover a range from those having no apparent effect, as observed both from symptoms and gross pathology, to those causing death.

The periods of exposure were varied from 1 to 5 hours, in order to ascertain the effects of time of exposure on time of decompression, as well as to observe any inherent effects of the inert gas. For the purpose of developing and exaggerating any deleterious effects, the same animals were subjected to repeated exposures. Some of these were then killed for pathological examination, and the remainder observed for several weeks for the development of untoward symptoms.

Apparatus for animal tests.

The tests were conducted in a specially constructed pressure chamber in which the effect on the subject is the same as in a diving suit under water. The animal chamber is shown in Figure 1. The chamber a was constructed from a short piece of 8-inch "double extra heavy" wrought-iron pipe. This was closed at each end by an "extra heavy" steel flange having a circular, 1/4-inch recess into which the end of the pipe fitted, and the whole was held together by twenty 3/4-inch bolts. Thin lead gaskets b were used. An elliptical opening was made in the lower flange for the admission of the animals. This was closed with a standard boiler hand-hold plate arrangement c. The upper flange was fitted with a 1-1/2-inch circular window, d, covered with a 3/4-inch plate glass. This glass was

[B] Davis, R. H., Diving Manual. Published by Siebe Gorman & Co., Ltd., 187 Westminster Bridge Road, London, 87 pp.




Apparatus for exposing small animals to pressure.

carefully fitted into a milled recess, which was tapered a few thousandths of an inch from the edge so that the greatest pressure on the rubber gasket would be at the rim of the hole, thus reducing the possibility of the gasket blowing out. Into the side of the chamber was fitted a brass plug or light well e, also closed at the end with a plate-glass window. This light well contained a small electric light for illuminating the chamber. The gas was introduced and released from the chamber through needle valves, f. Two of these were connected by thick-walled copper tubing to cylinders of gas, g, and the other was open to the air for release. A gage, h, indicated the pressures. In order to guard against serious injury to the observers through possible fracture and blowing out of the observation window when working at high pressures, a mirror device, i, was used which reflected the light coming through the window, so that the animal on test could be observed from the side j. Inside the chamber was placed a carbon dioxide absorbent consisting of a piece of ordinary blotting paper wet with 5 per cent NaOH solution and inclosed in a screen envelope k. With the exception of the gas cylinders, the entire apparatus was mounted on a stand having a skeleton top which permitted accessibility to the opening for introducing the animals.

Procedure for animal tests.

The procedure used in making tests was to introduce an animal through the hand hole in the bottom, close the latter, and purge the chamber by permitting some of the gas to pass slowly through it. The release valve was then closed, and the pressure permitted to build up to the desired test condition, after which the supply valve was closed and the exposure continued for a definite time. At intervals during the exposure, the atmosphere was changed by opening the inlet and outlet valve simultaneously, and regulating them so that a stream of gas passing through the chamber maintained the pressure at the test condition. With the exception of a preliminary series of tests on rats (Table 2), decompression was effected according to the stage schedules (Table 1).

The data obtained from animal tests are given in Tables 2 to 6. Table 2 represents a series of tests made on white rats exposed to 20 atmospheres' pressure for one hour, and decompressed according to the arbitrary schedule given. This work was preliminary to the succeeding tests on guinea pigs. Tables 3, 4, and 5 represent series of tests on guinea pigs exposed to 10 atmospheres' pressure for periods ranging from 1 to 5 hours, and decompressed as noted according to the schedules given in Table 1. Table 6 gives the results of pathological examination made after exposure to 10 atmospheres' pressure for one hour and decompressed according to the various schedules given.

Discussion of results of animal tests.

From a comparative examination of all data, as regards the decompression periods, and the symptomatic and pathological findings, it is very evident that with similar exposures and decompression periods the condition of the animals exposed to helium-oxygen mixtures is far better than that of those exposed to nitrogen-oxygen mixtures. It is further shown by varying the decompression time that the periods producing equal symptoms and pathological effects are somewhere in the order of 1 to 5 or 4 for helium and nitrogen, respectively.

TABLE 1:-DECOMPRESSION SCHEDULES: 1 to 5 HOURS EXPOSURE TO 10 ATMOSPHERES, (after Davis).

| Schedule. | Continuous pressure drop, first stage, and time, minutes. | Pressure in atmospheres at various stages of decompression* | | | | | | | | | | | Total decompression time. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 3-2/3 | 3-1/3 | 3 | 2-2/3 | 2 | 1-2/3 | 1-1/3 | 1 | 2/3 | 1/3 | 0 | |
| | Atm. Min. | Time in minutes at above stages. | | | | | | | | | | | Min. |
| I | 10-4 in 5 | 2 | 2 | 2 | 2 | 3 | 3 | 4 | 4 | 4 | 5 | 5 | 45 |
| II | 10-4 " 5 | 1-1/2 | 1-1/2 | 1-1/2 | 1-1/2 | 2 | 2 | 2-1/3 | 3 | 3 | 4 | 4 | 34-1/2 |
| III | 10-4 " 5 | 1-1/2 | 1 | 1 | 1 | 1-1/2 | 2 | 2 | 2 | 2-1/2 | 3 | 3 | 26 |
| IV | 10-4 " 4 | 1 | 1-1/2 | -- | - | 1 | 1-1/2 | 1-1/2 | 1-1/2 | 1-1/2 | 1-1/2 | 1-1/2 | 18 |
| V | 10-4 " 4 | 1/3 | 1/3 | 1/2 | 1/2 | 3/4 | 1 | 1 | 1-1/2 | 1-1/2 | 1-1/2 | 3/4 | 15 |
| VI | 10-4 " 3 | 1/3 | 1/3 | 1/3 | 1/2 | 3/4 | 3/4 | 3/4 | 1 | 2/3 | 1-1/2 | 1-1/2 | 12-1/3 |
| VII | 10-4 " 3 | 1/3 | 1/3 | 1/3 | 1/3 | 1/3 | 3/4 | 3/4 | 3/4 | 3/4 | 1 | 1 | 9-3/4 |
| VIII | 10-4 " 3 | 1/2 | 1/2 | -- | 1/2 | -- | 1/2 | 1/2 | 1/2 | 1/2 | 3/4 | 3/4 | 7-1/2 |
| IX | 10-3 " 2½ | -- | 1/2 | -- | 1/2 | 1/2 | 1/2 | -- | -- | -- | 1/2 | -- | 4-1/2 |

Atmosphere indicated on gage used was equal to 14.7 lb.

* Note: Above time periods include both time required to lower pressure and that at stages. Rate of lowering pressure after first stage was approximately 1/3 atmosphere per 10 seconds, or 2 atmospheres per minute.

TABLE 2: EXPOSURE OF 7/4 DAY WHITE RATS TO 20 ATMOSPHERES PRESSURE FOR 1 HOUR.

| Test No. | Decompression schedule | Condition of animal after decompression. | Remarks and symptoms during decompression (Pressures in atmospheres) at corresponding pressures. |
|---|---|---|---|
| | | HELIUM-OXYGEN MIXTURE (1.5 per cent oxygen). | |
| 1 | Decompression schedule used for all tests in this table was as follows: | Normal, runs around. | Breathing a little rapid before decompression. Active during decompression. Scratches self and rubs nose a good deal. Stand up in chamber. Walks around. Few signs of uneasiness. |
| 2 | | Normal, drinks water, runs around. | Little dyspnoea before decompression. Symptoms during decompression practically same as test 1. |
| 3 | | Both animals normal and active. | Two rats used; both breathing a little rapid before decompression. Symptoms during decompression similar to test 1. |
| 4 | Time in pressure<br>min. atm<br>2 18<br>4 16<br>8 11<br>11 9<br>16 7<br>23 5<br>27 3-1/2<br>28 2-1/2<br>29 2<br>34 0<br>Total time for all periods, 34 min. | Both animals normal and active | Two rats used. Breathing rapid before decompression. Symptoms during decompression similar to test 1. |

TABLE 2 (Contd.)

| Test No. | Decompression schedule | Condition of animal after decompression. | Remarks and symptoms during decompression (Pressures in atmospheres) at corresponding pressures. |
|---|---|---|---|
| | | NITROGEN-OXYGEN MIXTURE (2.7 per cent Oxygen). | |
| 1 | | Dead | Moves rear legs awkardly, with suggestion of slight paralysis before decompression. Little dyspnoes. Symptoms during decompression 11 atm., lying still as if helpless; 8-1/2 same; 7 licks feet; 2-1/2 stands on hind feet; 1 jerky convulsion followed by death. |
| 2 | Same decompression schedule used as for helium-oxygen mixture. | Paralysis in hind legs. | Apparent inability to use hind legs during latter period of exposure more pronounced, little better just before decompression. Symptoms during decompression 16-1/2 distressed, mild convulsions; 11 more signs of distress; 5 spins around dizzily on hind legs; 2-1/2 stands up uneasy, seems to itch; 1-1/2 cramps and convulsions relieved by raising pressure to 2; lowered to 1-1/2 cramps; up to 2 relieved; down to 1-1/2 cramps; up to 4 relieved, down to 1 cramps; up to 1-1/2 relieved; 1 and slowly to 0, rat seemingly paralyzed in rear legs; drags them around. |
| 3 | | Both animals dead. | Two rats used. Condition during exposure similar to tests 1 and 2 (nitrogen). Paralysis noted. Symptoms during decompression, scratches self and rubs nose a good deal. Active most of time but often quiet. Convulsions at 1 atm. and both died. |
| 4 | | Both animals dead. | Two rats used. Condition during exposure similar to tests 1,2, and 3, (nitrogen), with respect to paralysis. Move about with difficulty in rear legs. Apparently O.K. in fore legs. Decompression symptoms similar to tests 1 and 3. At 1-atm. one rat prostrate, the other having convulsions. at 1/2 atm. both dead. |

Note: Two rats were used in tests 3 and 4 for both gases. Oxygen pressure reduced to avoid oxygen poisoning. In test procedure chamber was filled with normal air at start. In decompression, 1 atmosphere of pure oxygen was added to the chamber at stage 5 atm. pressure to prevent effects of low oxygen in low-pressure air.

TABLE 3: EXPOSURE OF GUINEA PIGS TO 10 ATMOSPHERES PRESSURE FOR PERIOD OF 1 HOUR.

| Test No. | Decompression schedule. | Total time of decompression, min. | Condition after decompression. | Symptoms during decompression at corresponding pressure. (Pressures in atmospheres.) |
|---|---|---|---|---|
| | HELIUM-OXIGEN MIXTURE, 14.4 to 15.7 per cent Oxygen. | | | |
| 1 | Down to 5 atm. in 5 min., and 1 atm. per 5 min. | 30 | Normal, strong. | 10-5 active, scratches self, respiration a little increased; 5-0 fairly quiet. |
| 2 | Down to 4 in 2 min. 4-0 in 2 min. | 4 | " | Good condition before decompression; 10-4 active; 4-0 active; few signs of distress. |
| 3 | Down to 4 atm. 3 min. 4-0 in 6 min. | 9 | " | Good condition before decompression; active throughout decompression. |
| 4 | Down to 4 in 1 min.; 4-1 in 2 min., 1-0 in 1 min. | 4 | Dead. | Good condition before decompression. Symptoms 10-4 active but O.K. 4-2 few signs of distress. 2-1 more signs, 1 mild convulsions terminating in unconsciousness. |
| 5 | Down to 4 atm. in 2 min. from 4-0 in 5 min. | 7 | Normal, strong. | Good condition before decompression. Active through decompression. Out O.K. Killed 5 min. later for autopsy. |
| 6 | See schedule V, Table 1. | 15 | Apparently normal. | Good condition before decompression. Symptoms active no marked symptoms of distress. Killed immediately after decompression for autopsy. |
| 7 | See schedule VI. Table 1. | 12-1/2 | " | Good condition before decompression. Symptoms same, Test 6, Helium. Killed immediately after decompression for autopsy. |
| 8 | See schedule VII, Table I. | 8 | " | Good condition before decompression. Symptoms during decompression same as Test 6, Helium. Killed immediately after decompression for autopsy. |

TABLE 3 (Contd.)

| Test No. | Decompression schedule. | Total time decom-pression, min. | Condition after decom-pression. | Symptoms during decompression at corresponding pressure. (Pressures in atmospheres.) |
|---|---|---|---|---|
| | | NITROGEN-OXYGEN MIXTURE, 14.1 per cent Oxygen. | | |
| 1 | See schedule II, Table I. | 34-1/2 | Normal strong. | Good condition before decompression. Symptoms 10-2 quiet; 2-0 few signs of uneasiness. |
| 2 | See schedule II, Table II. | 34-1/2 | Little weak, O.K. next day. | Good condition before decompression; Symptoms 10-3 quiet; 3-2 active and uneasy; Out in fair shape. |
| 3 | See schedule III, Table I. | 26 | Dead. | Good condition before decompression; Symptoms fairly quiet 10-3 uneasiness; 3-1/3 convulsion; worse 2/3 gasping 1/3; dead 0; autopsy. |
| 4 | See schedule III, | 26 | Dead. | Good condition before decompression. Symptoms 10-3 quiet; 3-2 uneasy and scratches and bites legs and neck; 2-1 signs of cramps; 1 convulsion; Dead. Autopsy. |
| 5 | 1 atm. per min. to 5 atm. Then 1 atm. each 3. | 30 | Dead | Condition before decompression; Jerky respiration, otherwise O.K. Walks around. Symptoms 10-6 quiet; 6-4 scratches and walks around; 4-2 same; at 2 gets excited; scratches self vigorously, 1 starts into cramps; convulsion 0; dead. |
| 6 | Same as Test 1, Helium. | 33 | Apparently normal, strong | Breathing rapidly before decompression; Symptoms 10-3 quiet; 3-2 nervous; 2-1 more excited; out O.K. |
| 7 | See schedule 1, Table I. | 45 | Apparently normal. | Good condition before decompression. Quiet during first stages and active from 2 to 0 atm; no signs of distress. Killed immediately after decompression for autopsy. |
| 8 | See schedule III, Table I. | 26 | Fair shape, weak. | Good condition before decompression; Symptoms similar to Test 7; Nitrogen only signs of oncoming convulsions at 1-0 atm. No developments; Killed immediately after decompression for autopsy. |
| 9 | See schedule II, Table I. | 34-1/2 | Apparently normal. | Good condition before decompression. Symptoms similar to Test 7, Nitrogen. Signs of distress during 3-0 atm. Killed immediately after decompression for autopsy. |

TABLE 4: EXPOSURE OF GUINEA PIGS TO 10 ATMOSPHERES PRESSURE FOR PERIODS OF TWO HOURS.

| Test No. | Decompression schedule (refer to Table 1). | Total time of decompression, minutes. | Condition after decompression. | Symptoms during decompression at corresponding pressure-Remarks (Pressure in atmospheres). |
|---|---|---|---|---|
| | | | HELIUM-OXYGEN MIXTURE (14.4 per cent oxygen). | |
| 3 | I | 45 | Normal, strong. | 10-0 active at times, scratches self, no signs of distress. |
| 4 | II | 34-1/2 | " " | 10-0 active at times, scratches self, no signs of distress. |
| 5 | III | 26 | " " | Breathing a little heavy before decompression; 10-9-8-7-6 active, 4-3-2-1-0 less active, scratches self. |
| 6 | IV | 18 | " " | Breathing a little heavy before decompression, symptoms similar to Test 5, Helium, above. |
| 7 | V | 15 | " " | Breathing heavy before start of decompression, symptoms 10-6 very active almost distressed. |
| 8 | VI | 12-1/3 | " " | Breathing little heavy at end of 60 min. exposure. Air changes, animal better. Symptoms 10-5 same as test 6, Helium. 5-0 same. |
| 9 | VII, less 1-3/4 mins. | 8 | " " | Good shape before decompression, active but no distressed symptoms. East 2 min. after decompression. |
| 10 | IX | 4 | " " | Good condition before decompression. No symptoms except activity. |
| 11 | IX | 4 | " " | No symptoms. Eats in 2 mins. after decompression. |
| | | | NITROGEN-OXYGEN MIXTURE (15.1 per cent oxygen). | |
| 1 | II | 34-1/2 | Paralyzed in hind legs, died 4 days later. | Animal in good shape before decompression; 10-4 quiet and normal; 4-2 scratches self considerably and shows signs of convulsions at 2 atm. More signs during 2-1-0. Paralyzed in hind legs. Died 4 days later. |
| 2 | II | 34-1/2 | Paralyzed in hind legs. Recovered in 24 hours. | Breathing a little heavy before decompression. Symptoms 9-2 quiet, respiration normal, 2-1 active at times 1-0 distressed. Paralyzed in hind legs. Seemingly recovered in 24 hours. |
| 3 | III | 26 | Paralyzed in hind legs. Died next day. | Decompression symptoms similar to Test 2, Nitrogen; Badly paralyzed in hind legs. Died next day. |
| 4 | III | 26 | Dead. | Breathing a little hard before start of decompression. 10-2 little more active than Tests 2-3, Nitrogen; 1-2/3 uneasy; 1 very uneasy; 1/3 goes into cramp; dies. |
| 5 | II | 34-1/2 | Dead. | In good condition before decompression. 10-3 quiet; 3-1/3 excited during blow down. 1-1/3 start of cramps; 2/3 convulsions, death. |

TABLE 5: EXPOSURE OF GUINEA PIGS TO 10 ATMOSPHERES PRESSURE FOR PERIODS OF 3 HOURS OR LONGER.

| Test No. | Duration of exposure. | Oxygen, per cent. | Decompression schedule. | Total time of decompression. | Condition after decompression. | Symptoms during decompression at corresponding pressure; Remarks. (Pressure in atmospheres) |
|---|---|---|---|---|---|---|
| | | | HELIUM-OXYGEN MIXTURE. | | | |
| 1 | 180 | 14.4 | 6 atm. in 5 min. 4 atm. in 5 min. 1/3 atm. stages | 10 | Apparently normal, strong. | Breathing a little heavy before decompression. Symptoms active as if excited. |
| 2 | 240 | 14.4 | 1 atm. per min. 1/3 atm. stages | 10 | Normal | Symptoms and condition same as Test 1, Helium. |
| 3 | 300 | 9.7 | Accidental rate and time not known except that it was less than 20 min. | X | Normal, strong. | Chamber valve not closed, allowing gas escape. Animal was in good shape when found. |
| 4 | 240 | 9.7 | Down by stage method in 8 min. | 8 | " | Symptoms same as Test 1 and 2, Helium. Animal O. K. Eats immediately after decompression. |
| | | | NITROGEN-OXYGEN MIXTURE. | | | |
| 1 | 240 | 15.1 | Schedule II plus 2 minutes. | 36-1/2 | Dead. | In good condition before decompression. 9-2 1/3 quiet and normal; 2-1/3 uneasy; 1-2/3 quiet with jerky spells; 1 signs of convulsions 2/3 convulsions; 1/3 dying. |
| 2 | 240 | 15.1 | Schedule I. | 45 | Apparently normal, strong. | Good condition before decompression. 9-3 2/3 quiet and normal; 3-2/3 scratches legs uneasily. This continued to 2/3 when animal was uneasy. |
| 3 | 210 | 15.1 | Schedule II. | 34-1/2 | Dead. | In good condition before decompression. 10-4 quiet; 4-2 moves around; 2-1 excited; 1 convulsions and death. |

TABLE 5: GROSS PATHOLOGICAL EXAMINATION.
Guinea Pigs Exposed to 10 Atmospheres for 60 Minutes.

| Test reference (see note). | Decompression Schedule, atmospheres. | Total time of decompression. | Condition after decompression. | Pathological Finding and Remarks: | Total time from start of decompression until animal was killed |
|---|---|---|---|---|---|
| | | | HELIUM-OXYGEN MIXTURE. | | |
| 5 | Down to 4 atm. in 2 min. 4 to 0 in 5 min. | 7 | Apparently normal, strong. | Killed 5 minutes after decompression by injection of 5 c.c. $MgSO_4$ solution into heart. No bubbles noted anywhere. Fatty degeneration of kidney also some of liver. Intestines normal. | 12 |
| 3 | Down to 4 atm. in 3 min, 4-0 in 6 min. | 9 | " | Killed 2 minutes after decompression by blow on head. Heart beating when opened 2 minutes later. Bubbles in venous system, especially in small vessels. Few in heart; none in fatty tissue; other organs normal. | 11 |
| 7 | Schedule VI | 12-1/2 | " | Killed 1-1/2 minutes after decompression by blow on head. Bubbles in veins and a few in heart; none in fatty tissue; other organs normal; heart beating when opened 3 min. after decompression. | 14 |
| 8 | " V | 15 | " | Killed 1-1/2 minutes after decompression by blow on head. No signs of bubbles, organs normal. Heart beating when opened 3 min. later. | 16-1/2 |
| | | | NITROGEN-OXYGEN MIXTURE. | | |
| 7 | Schedule I | 45 | " | Killed 2 minutes after decompression by blow on head. Heart beating when opened 5 minutes later. No bubbles in heart, large veins or fatty tissue. Few bubbles in small veins along abdominal walls. Other organs normal. | 47 |
| 9 | " II | 34-1/2 | Apparently normal | Killed 1-1/2 minutes after decompression by blow on head. Heart beating when opened 3 min. later. Bubbles in fatty tissue and large veins. None visible in heart. Other organs normal. | 36 |
| 8 | " III | 26 | Fair shape, weak. | Killed 1 min. after decompression; opened 4 mins. later. Heart beating bubbles in heart and venous system. Other organs normal. | 27 |
| 3 | " III | 26 | Dead. | Bubbles in blood veins of mesentery. Fatty tissue near small of back; blood vessels around stomach. Lungs filled with foam. Heart fills with foam. | 26 |
| 4 | " III | 26 | Dead. | Blood vessels and heart filled with bubbles. | |

For symptoms, see corresponding [illegible] under Table 3.

Although the equivalent periods of decompression for the two gases are in the ratio of 1 to 3 or 4 in these tests, it seems possible that with larger animals and men requiring longer periods, even greater differences might be found. It is reasonable to believe that there is a maximum decompression rate which can not be exceeded, regardless of lower solubility or more rapid diffusion, because the circulatory system would be unable to carry the gas away as rapidly as it is diffused into the blood, thereby allowing bubbles to form. With guinea pigs it might be possible that this condition is approached if the decompression period is less than 10 minutes. Even if this possibility be disregarded, and it is assumed that the comparative relation obtained with small animals will hold in a fair degree for men, it can be concluded that the use of helium-oxygen mixtures will greatly decrease the safe period of decompression, and will thus permit men to work for longer periods. What is more important, it opens the possibility of working at depths beyond the practical limits with compressed air. The ratio of relative decompression periods (1 to 3 or 4) is greater than can be explained from the solubility coefficients of the two gases, and the difference is apparently due to the greater diffusivity of helium.

This is substantiated by a study of the symptomatic data. After exposure to helium, the animals are active throughout the period of decompression. If the decompression is very rapid, they show a tendency to irritation or distress from the very beginning, thus indicating the gas to be coming out rapidly from the start. With nitrogen, the symptoms are quite different. The animals are quiet and apparently normal throughout practically the first 60 to 75 per cent of the decreasing pressure range, but in the lower stages they experience distress and must be decompressed very slowly. This latter indicates a "lag" or tendency toward retention of the nitrogen in the tissues until the lower pressures are reached, when there exists a condition of excessive gas, or what might be termed supersaturation.

When the decompression tables have been tested out, it may be found that the time of decompression may be decreased even to less than 1/3 or 1/4 that for air, for it is reasonable to believe that the different properties of helium and nitrogen would also be manifested in the optimum schedules for each. This is evidenced by the symptomatic data given above, namely, that with helium the animals showed signs of distress in the higher stages, thus indicating that the rates shown in the ordinary tables for the higher stages are too fast and promote injury.

While the property of helium to diffuse more readily than nitrogen is an advantage in decompression, it was thought that this same property might cause a greater saturation of the body fluids during a given period of exposure, which might offset to some extent the advantage of lower solubility. While this may be true for very short exposures, no disadvantageous effect was observed for exposures of 1 to 5 hours. It has been shown that the relation of comparable decompression periods for the two gases is 1 to 3 or 4 throughout the varying lengths of exposure. Also, a study of the decompression periods of each individual gas for exposure periods of 1 to 5 hours, shows that complete saturation is practically attained with either gas in about two hours. Thus, it follows that in periods of sufficient duration for practical diving and caisson work, the greater diffusibility of helium during compression and exposure is not significant.

Since, as far as could be learned, the investigation described herein is the first in which helium-oxygen mixtures have been used as a substitute for normal air, a few experiments were conducted to verify the physiological inertness of the gas and its freedom from causing deleterious effect to the body tissues. The same animals were used for two to four exposures of 1 to 3 hours to a pressure of 10 atmospheres within a period of 3 to 7 days. They were then killed for pathological examination (Table 6). One case showed degeneration of one kidney and spots on the liver, findings not uncommon in guinea pigs. With the exception of bubbles in certain other cases the remainder were found to be apparently normal. Also four guinea pigs were exposed on 8 consecutive days to a helium-oxygen mixture at 10 atmospheres' pressure for one hour and decompressed in 25 minutes. These guinea pigs were observed for four weeks with no apparent effects or symptoms.

In order to ascertain whether any discomfort would be caused from breathing helium, the gas was inhaled by several of the investigators for periods up to 2 hours. There was no noticeable effect, except a temporary rise in the pitch of the voice. The gas was found to be as agreeable and pleasant as normal air.

The advantages which helium has been found to possess may be employed either through supplying the men with the synthetic air throughout the diving period or during a shorter period at the end including the decompression. It also might be used as a wash gas during decompression only or as a treatment if compressed air illness has occurred with ordinary air, the benefits being due to the removal of the partial pressures of nitrogen in the medium that is removing the gas.

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OFFSHORE TECHNOLOGY CONFERENCE
6200 North Central Expressway
Dallas, Texas 75206

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# Neon: An Attractive New Commercial Diving Gas

By

Heinz R. Schreiner, Robert W. Hamilton, Jr., and Theodore D. Langley,
Ocean Systems, Inc.



## INTRODUCTION: CONSTRAINTS OF COMMERCIAL DIVING

Like other areas of technological development, the history of commercial diving shows us again that problems, as they arise, are overcome by new technology. The plague of decompression sickness from all but the shallowest of air dives was reduced if not eliminated by the introduction of stage decompression by Haldane in the early 1900's. This extended diving to the limit imposed by nitrogen narcosis, until the use of helium eliminated this restriction after the 1920's. A vast increase in efficiency of some types of underwater work was brought about by the adoption of saturation diving techniques, so aptly demonstrated by Edwin A. Link in 1962 and again in 1964 and by the Conshelf experiments of Cousteau and the Sealab projects of the U.S. Navy.

References and Illustrations at end of paper.

As requirements for deeper and deeper dives come up, the current techniques using helium are fast becoming inadequate. This paper presents a new approach toward solution of some of the problems involved in the type of deep commercial diving on which the offshore oil industry relies. Our proposition is that mixtures containing neon as the main inert ingredient offer a cost-effective way to improve underwater operations at continental shelf depths.

As the title indicates, this paper is concerned with an assessment of the merits and drawbacks of using neon in commercial diving. The constraints imposed by this approach are the following:

A. Depth: 200 to 700 fsw*

Continental shelf diving covers

* feet of sea water

depths up to perhaps 700 fsw. Dives to 150-200 fsw are normally made with air, so the range under serious consideration here is that between 200 and 700 fsw.

B. Duration: Less than one hour

Commercial dives, certainly those in service of the offshore oil industry, are virtually all scheduled to perform jobs that can be done in less than three quarters of an hour, more generally in less than one-half hour. This means that rapid compression and straightforward, immediate decompression are usually the methods of choice.

C. Cost/effectiveness

The entire diving "system" must be economically competitive from a cost/effectiveness point of view. (The Navy is cost conscious, but has a mission responsibility that often overrides this consideration; in commercial diving, on the other hand, if the cost is too great, the job just simply will not be done employing diving systems.)

A major part of total cost/effectiveness is the capital investment necessary. Further, sophisticated equipment and instrumentation which may improve capability but at the same time greatly increases the cost and complexity of the operation, may not be desirable.

D. Safety

In a well-managed diving company, diving safety is a concern of primary importance. Passage of the 1970 Occupational Health and Safety Act will extend adherence to sound safety principles to all commercial diving firms.

E. Logistics

Many jobs are in remote locations, often thousands of miles from the U.S. mainland, which complicates logistics. On the other hand, there is usually a reasonable lead time for planning and preparation.

## PROBLEMS OF DEEP HELIUM DIVING

The biochemical toxicity of oxygen at high pressures makes it necessary to use an inert gas in the mixture breathed by a diver. Air of course is a suitable mixture based on nitrogen as the inert gas. Nitrogen is the inert gas of choice for all dives to depths of less than about 150-200 fsw in fact, nitrogen can be used safely and effectively even at depths somewhat greater than that under the proper circumstances. But even at 150 fsw, when breathing air most divers feel the effects of nitrogen narcosis and helium is preferred by most for dives beyond this depth. For the depth range immediately beyond air diving (e.g. 150-250 fsw) helium is well suited: it does not cause narcosis at this pressure or for that matter at any pressure to at least 37 atm. (1200 fsw); it is relatively inexpensive; and for U.S. operators it is readily available. Helium has a low density and is, therefore, easy to breathe at high pressures.*

But there are problems for the diver breathing helium, problems that are seriously amplified as diving depths approach those of the outer continental shelves and beyond.

A. Communication

First there is the problem of communication. The destructive effect that breathing helium has on the normal human voice is well known if not well understood. Due principally, it is believed, to changes in the speed of sound in the gas medium, this effect is a sensitive function of depth. Helium speech at sea level is distorted in a way that seems funny both to the listener and the speaker, but it is completely intelligible. At 200 fsw helium speech is still reasonably intelligible; under usual diving conditions the limitation is likely to be as much the fault of the electronics as that of the gas. Most communication systems are built to optimize the frequencies which encompass the greater part of the information content of normal speech; they may not handle adequately the frequencies associated with helium speech. As depths increase to the range between 400 and 600 fsw the situation becomes more serious, and to the manager trying to get a job done the sound of helium speech is no longer considered funny. Speech in this range is totally lost on an untrained ear, though anticipated statements can be

* This paper is concerned with inert gases; we may and generally do refer to the breathing of helium or neon, with no reference to oxygen. Whether mentioned or not, oxygen must always be present in breathing gas.

understood by a listener familiar with the voice and the situation. So often, however, a sudden change in the topic of conversation throws everyone off, and it is necessary for the diver to speak slowly, repeat himself and to try to say things in a different way. It can be done but it is slow and consequently expensive.

There are available today electronic helium voice unscramblers whose purpose is to convert helium speech to intelligible if not normal speech. They actually do this, and reasonably well, but such devices are not yet in general use in commercial diving, probably because of initial cost, added complexity, and the fact that diving operators are concerned about their reliability and seaworthiness.

B. Cold

Another problem of deep diving that is particularly accentuated by the use of helium is that of cold. Even in equatorial waters, ocean temperatures in the helium diving range are likely to be cold enough to limit diving times. Standard air diving gear, even the simple neoprene wet suit of the SCUBA diver is adequate for dives in water as cold as ocean water ever gets, for durations of up to perhaps an hour, provided the depth is not too great. But when the depth is beyond about 200 fsw the situation changes. Insulation, most of which depends on dead air space for its effectiveness, is compressed and becomes virtually ineffective.

The thermal conductivity of helium is roughly six times greater than that of nitrogen. Consequently, the rate of heat loss into a helium-based gaseous environment is considerably greater than into air. It is hardly necessary to discuss the limitations to effective human performance imposed by cold. A chilled diver takes much longer to do a given job, is less likely to respond properly to emergencies and probably is more difficult to decompress.

As in the case of speech unscramblers, there are available several types of heated diving suits which offer a solution to the heat loss problem. Hot water furnished to a "wet" type suit and vented in an open circuit fashion is probably the most economical method of effective diver heating presently in use, despite the difficulties of supplying water at the proper temperature and through a long hose. The effectiveness of this approach dwindles, however, as the distance between the diver and the heat source increases. Electrically heated suits are expensive and not well accepted by divers, and, along with the more sophisticated closed circuit water-heated suits, are expensive and not readily available to the commercial diver.

Even if the diver can be kept warm long enough to finish his work, a bone-chilling sojourn awaits him when he returns to the heliox-filled diving bell. This is considered by most divers to be more stressful and unpleasant than working in cold water.

C. Availability

There is no problem in obtaining helium in the United States and Canada, the only significant producers of helium in the free world. But it is worth noting that many tons of iron must be shipped in order to move a few pounds of helium to a diving location. The fact that helium is not universally available on a world-wide basis is revealed by the high level of interest, particularly in European laboratories, in the use of hydrogen as a diving gas. Hydrogen, lighter than helium, is worse than helium in chilling the diver and distorting his voice, not to mention the potential explosion hazard. Nevertheless, work is in progress in several laboratories investigating the use of hydrogen in diving as a means of eliminating dependence on helium.(1) The fact that this work takes place at all is ample evidence of the need for a helium substitute.

D. Tremor

Rapid compression--such as might be used to minimize bottom time and hence decompression from very deep dives--causes both human laboratory subjects and experimental animals to exhibit hyperexcitability of the nervous system, a condition known as "helium tremors" or the High Pressure Nervous Syndrome. Current thinking holds that this is not really caused by helium itself, but by the rapid rate of compression. In any case it represents a special problem which may restrict deep diving to some extent.

E. Decompression

Decompression is not a special problem with helium--it is a problem associated with all deep dives. Although saturation techniques make the continental shelves accessible to all operators who command the requisite resources, this kind of diving is neither easy nor necessarily economical. In the commercial diving situation, where the working time in most cases need be only a few minutes or a fraction of an hour, efficient and safe decompression procedures are essential. Under certain conditions the low solubility and high diffusivity of helium, (properties which together determine the rate of transport of inert gases in the human body), make helium the gas of choice, from a decompression point of view. But in a deep, relatively short dive involving hard work on the bottom where there is a desire for the fastest possible safe decompression, these same transport properties make helium probably the worst possible gas. Too little is really known about the biophysics of decompression and decompression sickness to make this a worthwhile point to belabor--it is sufficient to say that no matter what gas is breathed decompression is a difficult and slow process, and is probably the most serious problem facing the deep diving operator.

## THE CASE FOR NEON

Given the special constraints of commercial diving--short, deep dives involving efficient decompression at the lowest possible cost--and the special problems invoked by the use of helium as an inert breathing gas in such diving--voice distortion, chilling of the diver, logistics and decompression--we here propose for the first time a new dimension in diving technology, the use of neon as a major component in divers' breathing gas. Neon is a chemically inert noble gas like helium and has an atomic weight of 20, or five times that of helium. The possible utility of neon as a diving gas has been mentioned for years, but its frightful expense in the forms in which it is routinely available has prevented the testing of neon in diving, and in fact has considerably restricted its use even in the laboratory. This report contains research data and records of experience with the use of neon which show, first, its physiological safety to both animals and man; second, its utility in the particular environment of commercial diving; and third, progress in the development of neon as a diving gas, including its promising potential with regard to decompression.

## SUMMARY OF NEON PROPERTIES

There exists a gas mixture of helium and neon, which is available in sufficient quantities for diving and can be obtained at a price which makes it competitive with pure helium, all things considered. Wherever atmospheric air is condensed and distilled for the purpose of obtaining oxygen or nitrogen, an uncondensed fraction remains of which neon is the major constituent. This gas fraction is known as "crude neon"; it contains neon and helium in approximately the proportions in which they are found in atmospheric air--about 75% neon, 25% helium. (2) Table I compares the physical properties of neon with those of nitrogen and helium. Because of its physical properties (related primarily to its greater density) neon causes far less voice distortion and heat loss than helium, and there is good reason to believe that it will permit more rapid decompression from a deep working dive than is possible with helium. Crude neon is potentially available anywhere in the world where there is extensive industrial development.

Recently a major supplier of industrial gases contracted to supply to the National Accelerator Laboratory more than a million cubic feet of neon at a price which works out to less than 20 cents per cubic foot of the crude mixture. (3) Even lower prices for bulk crude neon may reasonably be expected in the future.

Because it is a larger molecule than helium, neon might be expected to have narcotic properties; further, one might expect restrictions in its use at high pressures, since it is more difficult to breathe than helium.

Neon is indeed more difficult to breathe than helium, but it has been clearly demonstrated experimentally that despite its density, moderate work can be carried out while breathing crude neon at pressures as great as 1200 fsw. In these and other experiments it has also been convincingly demonstrated that neon

does not cause narcosis to a degree sufficient to reduce diver performance. Subjective impressions also suggest that there is less tremor when neon is used, than with helium.

Another physical property of neon which might under certain conditions make it the gas of choice is the high heat of vaporization of the liquid phase. Neon is the easiest gas to store and handle as a liquid, and has the highest liquid-to-gas ratio. In circumstances where logistics become a greater problem than cost, it might be best to store and ship diving gases in liquid form.

Exactly what role the physical properties of gases play in their individual decompression characteristics is not well understood, but it seems reasonable that low solubility would be advantageous, and that in the case of short dives a low diffusion coefficient would be best. In this regard neon seems to combine the better aspects of both nitrogen and helium, having both a low solubility and a low diffusion coefficient. (cf. Table I)

## RESEARCH WITH NEON

Although neon is being introduced at this time into commercial diving as new technology, it is not without considerable animal and human laboratory experience that this is being done. Most animal experiments have been concerned with the safety of living in a neon-enriched environment, while the human experiments have been concerned with whether or not neon had narcotic properties, with man's ability to breathe this gas at great depths, with speech and with decompression. A summary of all major neon experiments and their findings is given below:

### A. Physiological Compatibility: Laboratory exposures

First it is pertinent to mention the animal experiments which established the innocuous nature of neon-oxygen mixtures as a breathing medium. A number of experiments have been done which involved the exposure of animals to neon, and the universal finding is that the effects of neon are either not remarkable or are in their proper place in reference to other atmospheric gases. Table II summarizes the findings of principal neon experiments.

### 1. Ocean Systems' 650 fsw saturation experiment, 1965(4).

This experiment represented the first exposure of man to saturation diving conditions at continental shelf depths. Two subjects, while saturated with a mixture of 95% helium, 4% nitrogen and about 1 1/2% oxygen breathed a neon-oxygen mixture by mask while carrying out two different performance tests and making speech recordings. Figure 1 shows results of one of these tests. Psychomotor performance, demonstrated with a standard pursuit rotor, showed no detectable difficulty during neon breathing, and in fact slight improvement was noted; this may well have been a consequence of the superior motivation of our subjects that stemmed from the unique nature of the experiment. Voice recordings made on the neon mixture showed far greater intelligibility than similar recordings made on a helium-oxygen mixture.

### 2. Royal Naval Physiological Laboratory neon performance, 1966(5).

Using multiplication and a simple test of muscular coordination involving picking up ball bearings with tweezers, Bennett tested ten divers breathing both neon-helium-oxygen (65.6%,16.4%, 18%) at 7 atmospheres (200 fsw) and on air at 5.8 atm. (152 fsw), depths chosen to provide equal partial pressures of the inert gases. His subjects felt no narcosis on neon, but were quite affected by breathing air at that pressure. Test results corroborated these impressions, with an appreciable (12-15%) decrement being noted in air, while subjects in neon showed a 3% lower arithmetic score and did just as well if not better on the ball bearing test.

### 3. Experimental Diving Unit, pulmonary function, 1968(6).

During the laboratory preparation state of the Sealab III operation saturation experiments were conducted at the U.S. Navy Experimental Diving Unit involving exposures to 600 and 825 fsw pressure equivalent. As part of these experiments crude neon-oxygen mixtures were breathed by four subjects during a study of pulmonary function. At 825 feet (26 atmospheres) the density of the breathing mixture was 15 times that of sea level air, or the equivalent to the density of a helium-oxygen mixture at a depth of over 2500 fsw.

Under these conditions the subjects were able to move 40-50 liters of gas per minute, in and out of their lungs, enough to do moderate work with some reserve.

4. Duke University, EEG and reaction time with neon, 1970(7).

In a saturation experiment primarily devoted to a study of cardiorespiratory parameters, recordings of EEG, reaction time and alpha blocking were made under identical experimental conditions using neon, helium and nitrogen at a pressure equivalent to 200 fsw. No statistically significant differences between neon and helium were seen, but nitrogen caused an increase in reaction time. All measurements were made under normoxic conditions. The neon mixture was presumably made with crude neon. A graph of the reaction time results is shown in Figure 2.

5. University of Pennsylvania, 1200 fsw saturation experiment, 1971.

During the summer of 1971 the Institute for Environmental Medicine at the University of Pennsylvania, in collaboration with the U.S. Navy's Bureau of Medicine and Surgery and Ocean Systems, Inc., and with the experimental cooperation of several other laboratories, conducted what is probably the most ambitious and extensive laboratory diving experiment yet completed. Four subjects spent 24 days at pressure during the main saturation and many days on short and shallower preliminary tests. The general concept of the experiment, conceived and managed by Dr. C. J. Lambertsen, was to take a "dose-response" look at a wide variety of physiological parameters as they might be affected by a dozen or more pressures between one and 37 atmospheres, and in gas mixtures having different density, viscosity and narcotic potency. The main experimental use of neon was to provide a dense gas devoid of narcotic properties. In the process neon was tested under conditions suitable for diving at 400, 700, 900 and 1200 fsw. While at 1200 fsw, the subjects breathed neon mixtures of a density equal to that which would be encountered on helium-oxygen in a dive to 5000 fsw. Under these conditions they were able to perform physical work at a rate of approximately 70% of their normal maximum at sea level. The limitation was one of gas density, not narcosis and not oxygen transport. At 900 fsw the subjects were able to complete work loads estimated to be 80% of the maximum they could attain at sea level.

To test the condition of the central nervous system of the subjects and to assess their cognitive ability, two subjects took a "paced" arithmetic test at several depths. This test presents simple one-by-two digit multiplication problems at a predetermined rate, so that subjects can be graded on their accuracy independently of speed, which eliminates the problem of trying to decide whether "number attempted" or "number correct" is most significant. Results of these tests are given in Figure 3. Although we see the anticipated variability found in this type of test, it is evident that neon causes no loss of mental ability, even at pressure equivalent to 1200 fsw.

B. Operational compatibility: Commercial diving situation

The preceeding section has dealt with the innocuous nature of neon as far as breathing it and living in it are concerned; this section deals with neon under the special environmental conditions imposed by commercial diving. We have shown that neon is safe and reasonably easy to breathe to depths far deeper than the world's continental shelves, and that at lower pressures no ill effects have been detected even after extended exposures. But these have all been situations in which the pressure has been changed slowly if at all; we now discuss a series of experiments which tested neon under the particular conditions of a commercial dive--rapid pressurization to the working depth, followed by a short period of intense activity and a decompression accomplished as quickly and efficiently as possible. In 1970 and 1971 Ocean Systems conducted, in cooperation with the U.S. Navy, a parametric comparison of the performance aspects of neon, nitrogen and helium in the mode of the short working dive.(8)

This was the first experiment designed to test neon in a side-by-side comparison with nitrogen and helium over a range of depths and under non-saturation conditions. In a series of 32 short (about 30 minutes) individual exposures to these three gases in the depth range of 200 to 600 fsw, comparisons were made in various types

of human performance, in tremor and in decompression, under test conditions as nearly identical as we could provide. Crude neon was used as the primary diving gas in 12 cases. Equivalent sets of tests were performed with helium, while nitrogen was not used beyond 400 fsw. In dives to 200, 300 and 400 fsw the oxygen level was 10%, while in dives to 500 and 600 fsw we used 7% oxygen. The oxygen partial pressures were, therefore, in the range between 0.7 and 1.3 atm.; this is typical of the working dive situation, where high oxygen levels are used to facilitate decompression.

The divers breathed directly from the chamber atmosphere without the aid of breathing equipment. A variety of tests showed no detectable narcotic effect of neon in comparison to helium, while such measurements revealed clearly the detrimental effects of nitrogen at all depths tested. A representative test, one designed to measure mechanical dexterity, is shown in Figure 4. This "nut and bolt" test showed no real difference between neon and helium, but a substantial effect of nitrogen. Results presented in Figure 4 are typical of the results we obtained with tests of coordination, vigilance, reaction time and mental ability. Steadiness, measured by movement of a magnetic stylus held over a fixed target, showed a slightly reduced degree of tremor in those subjects compressed with neon as compared to helium.

In another type of test we determined the depression of evoked brain responses. When a stimulus (such as a click or light flash) is given to an individual it is possible to record changes in the electrical activity of his brain which reflect the brain's response to that stimulus. This response, measured as a voltage detected on the scalp, represents the end result of several neurological events. Not all investigators agree on the interpretation of the changes which various factors have on these evoked potentials. (9,10) However, in Figure 5 it can be seen that the depression of the $N_1$-$P_2$ interval is greater in nitrogen, known to be narcotic, than in either helium or neon, and further that there is no real difference between these two gases.

C. Decompression

Because of the relative insensitivity of standard performance testing methods it has not been possible to show any differences between neon and helium in terms of the effects of these gases on psychomotor or mental function. This gives neon a clean bill of health as far as the safety of its use is concerned, but we have yet to show advantages to the use of neon that would justify its slight extra cost. There are three areas--in addition to its worldwide availability--where the biophysical properties of neon may give it real advantages over helium in diving. Having a lower thermal conductivity, neon may reduce the chilling effects of diving in deep water where insulation is ineffective and it is always cold. Further, neon is not as likely to distort the voice as is helium. These are marked problems, and any relief from them is worth investigating. But there is another area where neon may offer an even greater economic and operational advantage: decompression.

In shallow air diving an offshore rig must shut down any time a diver is working or "hanging off" during decompression. With a more modern system using a bell and deck chamber this is usually not required. However, when unusual problems develop--such as the need for several successive dives--a rig may need to remain idle while waiting for a diver to decompress. These shutdowns are costly, and measures which save a few minutes to a few hours of this time may be extremely valuable. From the limited data which is presently available it looks as if the use of neon may make possible a reduction in decompression time or an equivalent increase in decompression safety, or perhaps both.

If one accepts the theoretical calculations of Roth (11) based on the physical properties of inert gases and his assumptions about the circumstances taking place in the body relative to bubble formation and growth, then under the conditions of short, deep dives such as those we are considering, neon holds a theoretical advantage over helium. We cannot make a strong case for neon on theoretical calculations which themselves are based on assumed models, so it is probably not worthwhile to go into the mathematical details here. Intuitively, however, the possible advantages of neon can be described in a qualitative way. Considering the comparison between just those two gases, crude neon and helium, the

neon mix shows an advantage in three ways. The main difference in the properties of neon and helium is diffusivity, since both have about the same solubility in both water and fat. To the extent that this property may affect the uptake of gas, neon should be taken up more slowly than helium.

The same property may of course affect the rate at which the gas is eliminated from the body; consequently any potential advantage must depend on the depth and bottom time. For example, under equivalent conditions in the 200 fsw range, the U.S. Navy diving tables call for shorter decompression times with nitrogen than with helium up to a bottom time of about one-half hour, while for longer times the advantage swings to helium. A similar situation may prevail in comparing helium and neon, and the advantage for a short dive (such as is usually required) would rest with more slowly diffusing neon.

Further, neon shows an advantage in Roth's calculations in the case of diffusion into a bubble which has already begun to form. Here the slower diffusion of neon causes slower bubble growth, a factor which should result in easier decompression with neon. Roth's "bubble factors" for in situ intravascular bubble growth in adipose tissue are Ne 0.34, He 0.64, $N_2$ 1.0, and Ar 1.9, with the higher value indicating greater risk.

In still another way the crude neon mixture we are considering may have a slight advantage over helium alone, inasmuch as that in a mixture of two inert gases neither will exert as high a partial pressure (or degree of supersaturation) as will a single gas alone. This will reduce the probability of bubble formation in the first place.

Much modern decompression theory is based on the concept that the limiting factor in gas transport within the body is not diffusion but rather perfusion, of the tissues by blood. With reference to gas dissolved in tissue, the higher the ratio of dissolved inert gas pressure to total pressure the greater the probability of bubble formation. This ratio is known as the Haldane ratio, or surfacing ratio when applied to the conditions on arrival at sea level pressure. Calculations in our laboratory (12) have shown that neon offers a theoretical advantage in the circumstance where slowly perfused tissues are limiting the rate of ascent; here the surfacing ratio is lower for neon than for helium.

Animal experiments have supported the theoretical advantages of neon in most cases where direct comparisons have been made. Animal studies in our laboratory by Doebbler et al., (13) produced evidence (Table III) which supports Roth's relative ranking of these gases; however, the distinction between neon and helium was not marked. In these experiments, rats were decompressed from depth (168 fsw) by stages to altitude (10,000 feet equiv. or 510 mm Hg). Bennett and Hayward (14) observed a relative decompression advantage for neon and a neon-helium mixture over nitrogen for rats decompressed from 290 fsw (Table IV). Again a possible advantage of neon over helium was indicated.

Table V summarizes some of our unpublished data on neon compared to helium and nitrogen for rats decompressed by continuous ascent at 67 fsw/min. from 265 fsw after various times of exposure at depth. The limited data again support the possibility of an advantage for neon.

Heavy (500-650 gm) male rats saturated with various inert gas-oxygen mixtures at 900 mm Hg for 24 hours before decompression to 100 mm Hg in pure oxygen have been studied by Doebbler and Hamilton (15). Results are summarized in Table VI. Of special interest is the apparent decompression advantage of crude neon (73/27 vol. mix. of neon and helium) over neon alone, and in terms of asymptomatic animals, over helium (21% vs 10%).

Van Liew and Passke (16) have observed in subcutaneous gas pockets in rats that neon and nitrogen are absorbed at about the same rates. This would agree with Roth's assumptions based on diffusivity. Neon bubbles or bubbles into which neon was diffusing would grow more slowly than helium bubbles; this increases the probability that a clinically insignificant neon bubble could be re-dissolved in the course of decompression without having caused tissue injury.

All of the above animal experiments were carried out with very small animals, and it would be risky to place

too much credence into the direct applicability of this data. In one additional series of experiments we have conducted comparative decompressions of animals saturated with various inert gases; in this case we used as an experimental animal the miniature pig. (17). Pigs have a physiological and biochemical resemblance to man that makes these experiments far more relevant than those performed on rats. These were also altitude decompression, similar in format to others mentioned above. Pigs were scored on the seriousness of signs of decompression sickness, on an arbitrary scale ranging from 1 to 4 and covering signs ranging from mild difficulty in walking to total collapse and paralysis. Figure 6 shows how the gases arrayed themselves in the results of 26 experiments on three animals. It can be seen clearly that the responses are quite consistent for all three pigs, with the possible exception of the one named Kitty; in her case crude neon would rank higher than pure neon. In all cases the advantage of neon over helium seems apparent. These are experiments designed to simulate the space-flight situation and as such may not be completely applicable to diving, but they are the best comparative decompression data available today on large experimental animals.

The neon performance experiments mentioned in section B above were accomplished on a short-dive format which required decompression at the end of the work period. These were decompression dives, and as such were man's first experience in the use of neon in decompression. Conditions of decompression were not uniform enough in the different runs to allow a strict comparison between helium and neon, but some general conclusions are evident. In a total of 12 dives made on crude neon and an equivalent number in helium, the degree of uneventful decompression was strikingly better in neon. This is illustrated in Table VII. Decompressions were made from bottom times 30 or 35 minutes in length and from depths of 200, 300, 400, 500 and 600 fsw. Using tables which resulted in approximately the same decompression time (for the same bottom time) for either helium or neon, there were three cases of decompression sickness on helium-oxygen and only one on neon-oxygen. A confounding factor here is the fact that in all cases an abrupt shift to air was made at 150 fsw during decompression for operational reasons. This prevents a completely valid comparison of the efficiencies available with neon and helium, since in those cases where decompression sickness occurred, nitrogen may have been involved in bubble formation in addition to the inert gases under study. In any case, the overall decompression experience in this experimental series clearly favors neon.

## DEVELOPMENT OF NEON AS A DIVING GAS

The laboratory results presented here have convinced us that there is enough to be gained from the use of neon as our primary diving gas that Ocean Systems has moved with this gas from the research into the development phase. We are now engaged in solving the practical problems of changing our procedures in small ways to make possible the use of neon where its use is indicated. At the same time we are continuing to learn more about the basic properties of this gas.

Our development efforts are centered in three areas. We have carried out tests in the laboratory to determine in a quantitative way the effects of neon on voice communications, we have developed decompression procedures for short working dives to 680 fsw, and we are conducting field trials with neon.

Our voice experiments were designed to compare the effect of gas composition at 300 fsw, and in the presence of 2% oxygen, on intelligibility across the compositional spectrum from pure helium-oxygen through three in-between mixtures to pure neon-oxygen. Word lists and vowel sounds were recorded in air and five experimental gas mixtures. As well as it could be controlled neither the investigators nor the subjects knew the mixture being breathed. Quantitative results of the intelligibility tests are not yet available, but to the crew there appeared to be two mixtures which had greater intelligibility than the others; there was not much difference between these two and no appreciable difference between the other three. The mixtures which were easier to understand were neon-oxygen and the crude-neon-oxygen mixture (74% neon, 24% helium and 2% oxygen). The divers had about the same subjective impressions as the topside crew.

Preliminary spectrograms have been run on the vowel sounds. These were examined by a speech psychologist who did not know the gas mixtures, and his division of the spectrograms into two groups was identical to our subjective groupings of the experimental voice recordings. In one group there was the typical loss of energy in the domain of the second formant frequencies--1-3 KHz--and in the other group this loss was appreciably less. (18) The samples taken in mixtures containing 49% helium or more were distorted, the others (74% and 98% neon) were essentially normal.

Word from the field trials backs up the laboratory conclusions. In shallow dives, where helium distortion is not so great as to prevent communication but enough to make it difficult, the feeling is that neon is more comfortable to use because no effort is needed for the diver to be understood. Our operational groups appreciate the facts revealed here. Not only does it mean that it may not be necessary to get helium voice unscramblers so soon, but also that existing communications equipment may not need to be replaced. Part of the problem of understanding divers is the loss in the system of the higher frequencies of speech--the part which contains most of the information when the diver is breathing helium. Neon, especially crude neon, will not entirely eliminate this problem, but it now seems clear that it will reduce it greatly.

There have not yet been any laboratory tests to measure the effect of switching to neon on the heat loss problem. Our only data in this area is the subjective feelings of Ocean Systems divers who have used neon in cold water.

They like it. It feels warm from the moment they begin to breathe by mask, throughout the work period and especially when they return to the bell. One experienced diver in re-entering a neon-filled bell at 220 feet described it as "like coming back into a toasty oven. There wasn't any of the fogging and cold, cloudy effect inside the bell that you have with helium. It stayed dry. It was really warm and really felt good coming back." He said further that "neon has to help decompression" because of warmth in the bell. Divers in the field as well as those in the laboratory say that there is no appreciable difference during the compression phase between the two gases--both feel warm.

Possibly the most significant of all our neon experiments was the recent series of four laboratory dives to 680 feet, conducted to provide the information needed to develop operational capability to that depth. These were 30-minute dives, two divers each time, with a provision for exercise on the bottom by both divers. The exercising diver wore a standard Kirby-Morgan KMB-8 band mask. Breathing gas was crude neon containing 5% nitrogen and 5% oxygen.

Bends were expected and mild ones were encountered--this is routine in an experimental series such as this. But by the time the four dives were complete we had reduced the bends probability to an acceptable level and at the same time were left with acceptable decompression efficiency.

We did encounter a problem which should be mentioned--but assuredly not as a physiological problem but rather a mechanical one. To provide breathing gas for the diver while he rode the bicycle ergometer inside our high pressure chamber, we connected the appropriate neon mixture to our existing chamber breathing line. This line comprised several feet of 1/4 inch tubing feeding a first stage regulator, located several feet from the chamber wall, which dropped the supply pressure to 500 psi; the balance of the tubing was 3/8 inch in diameter. This system had worked well during many decompressions for the administration of oxygen, but this occurred necessarily always at low pressures. When the diver began to demand more gas from his breathing regulator as his exercise progressed (our schedule called for 100 watts for six minutes) he soon found himself unable to draw enough gas to satisfy his respiratory needs. Both divers quit before they finished the required work during the first dive, and also on the second dive--the modifications we made were not sufficient. The inadequacies of the system were obvious, as supply regulators showed sharp pressure drops each time the diver took a breath. With further modifications--5/8 inch lines to the chamber wall bypassing the first stage regulator and a larger second state regulator--as well as more thorough briefings of the divers who had not used this type of equipment before, we were able to

finish the series successfully.

This discussion of a routine engineering problem which properly should not have been allowed to happen is included here to point up the fact that neon can be used with existing helium diving equipment, but that at this depth it cannot be done without careful elimination of system faults and the use of proper procedures. Given proper equipment a confident diver who paces his work, breathes deliberately and uses free flow judiciously will not experience difficulties with the use of neon-based breathing mixtures.

## CONCLUSIONS

This paper consolidates most of the available data that relates to the use of neon in diving. Much of the experimental data comes from our own laboratory and in presenting it, we run the risk of leaning on this data in such a way as to support our conclusions. Some of our observations are subjective and need very much to be repeated in other laboratories. But in all our experiments we have seen nothing that might dampen our enthusiasm for neon as an attractive new commercial diving gas.

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TABLE I - PHYSICAL PROPERTIES OF HELIUM, NEON AND NITROGEN

| Property and Units | Helium | Neon | Nitrogen |
|---|---|---|---|
| Mol. Wt. | 4.003 | 20.183 | 28.016 |
| Density, gm. $l^{-1}$ (0°C) | 0.1785 | 0.8999 | 1.2506 |
| Viscosity, $\mu$ poise (30°C) | 200.78 | 320.78 | 178.1 (27.4°C) |
| Thermal Conductivity, cal. $cm^{-1}sec^{-1}$ $°C^{-1}$ x $10^5$ (30°C) | 36.25 | 11.82 | 5.95 (15.5°C) |
| $\gamma \left[ {}^{cp}/_{cv} \right]$ (0-20°C) | 1.63 | 1.642 | 1.404 |
| Velocity of Sound, $m\text{-}sec^{-1}$, 1 atm 0°C | 970 | 435 | 337 |
| Solubility, water (Bunsen Coeff., 37°C) | 0.0087 | 0.0097 | 0.0125 |
| olive oil " " | 0.0148 | 0.0193 | 0.0609 |
| human fat " " | | 0.0197 | 0.0617 |
| Diffusion Coefficient, 37°C, $cm^2sec^{-1}$ x $10^6$, | | | |
| water | 63.2 | 34.8 | 30.1 |
| olive oil | 18.6 | 8.34 | 7.04 |
| Vol. gas/vol. liquid | 700 | 1445 | 696 |
| Boiling point of liquid, °C | -268.9 | -246.1 | -195.8 |
| Heat of vaporization at boiling point, | | | |
| cal./liter | 610 | 24,800 | 38,200 |
| cal./g-mol | 19.5 | 415 | 1322 |
| Specific heat, cal. $g^{-1}$, °C | 1.242 | 0.246 | 0.248 |

TABLE II - CELL AND ANIMAL EXPOSURES TO NEON

| Biological System | Exposure | Findings | Reference |
|---|---|---|---|
| Neurospora Crassa | 35 atm | Neon falls between helium and nitrogen on inhibition scale | Schreiner et al. 19 |
| N. Crassa | 120 atm | No greater inhibition than 50%; dose response curve flat above 35 atm. | Buckheit et al. 20 |
| HeLa cells in tissue culture | - | Neon inhibits growth as a function of pressure less than $N_2$ or He. | Robinson et al. 21 |
| Frog gastrocnemius muscle | 15 atm | No effect of neon | Gottlieb et al. 22 |
| Newts, mice | 125 atm | No detectable narcotic effects | Smith 23<br>Miller et al. 24 |
| Rats, rabbits | 1 atm; 1 week | No effect attributable to neon | Hamilton et al. 27 |
| Mice | 1 atm; weeks | No effect attributable to neon | Aldrete 25 |
| Mice | 1 atm; weeks | No effect attributable to neon | Weiss 26 |

TABLE III - COMPARATIVE DECOMPRESSION SICKNESS IN RATS

| Gas Comp. | Number of rats | % of Max. Decomp. Sickness Score | % of Animals with Paralysis or Death |
|---|---|---|---|
| 20/80 $O_2$-He | 16 | 22 | 19 |
| 20/80 $O_2$-Ne | 15 | 14 | 13 |
| 20/80 $O_2$-$N_2$ | 24 | 93 | 96 |

Stage decompression to 510 mm Hg following 2 hour exposure at 168 fsw.

(Doebbler et al., 1967)

TABLE IV - COMPARATIVE DECOMPRESSION SICKNESS IN RATS

| Gas Comp. | Number of rats | % of Animals with Symptoms: Paralysis | % of Animals with Symptoms: Death |
|---|---|---|---|
| 20/80 $O_2$-He | 60 | 33 | 12 |
| 20/80 $O_2$-Ne | 40 | 28 | 23 |
| 20/80 $O_2$-$N_2$ | 40 | 10 | 48 |
| 20/40/40 $O_2$-Ne-He | 20 | 25 | 15 |

Decompression at 0.9 atm. (30 fsw.) per minute after 60 minute exposure to 9.7 atm. at 290 fsw.

(Bennett and Hayward, 1968)

TABLE V - DECOMPRESSION SICKNESS IN RATS AFTER CONTINUOUS ASCENT (67f/m) FROM 265 FSW. DEPTH USING NITROGEN, NEON, OR HELIUM-OXYGEN FOR VARIOUS TIMES AT DEPTH

| Inert Gas | Time At Depth Mins. | Number of Animals Exhibiting Symptoms: None | Walking Difficulty | Paralysis | Death | Total |
|---|---|---|---|---|---|---|
| He | 30 | 0 | 1 | 2 | 5 | 8 |
| Ne | 30 | 1 | 5 | 1 | 1 | 8 |
| $N_2$ | 30 | 0 | 2 | 1 | 5 | 8 |
| He | 60 | 1 | 1 | 0 | 2 | 4 |
| Ne | 60 | 1 | 1 | 1 | 1 | 4 |
| $N_2$ | 60 | 1 | 0 | 1 | 6 | 8 |

TABLE VI - DECOMPRESSION SICKNESS IN RATS DECOMPRESSED TO ALTITUDE (100 mm Hg) AFTER SATURATION IN VARIOUS INERT GAS ENVIRONMENTS

| Inert Gas | % of Animals Exhibiting Symptoms*: None | Walking Difficulty | Paralysis | Death |
|---|---|---|---|---|
| Nitrogen | 2 | 42 | 23 | 33 |
| Neon | 21 | 58 | 4 | 17 |
| Neon-Helium | 21 | 71 | 8 | 0 |
| Helium | 10 | 85 | 4 | 0 |

* 24 animals each in Ne and Ne-He; 48 animals each in He and $N_2$. See text for details.

(Data from Doebbler and Hamilton, 1970)

TABLE VII - SUMMARY OF NEON PERFORMANCE SERIES (DEC. 1, 1970 - JUNE 2, 1971)

| Depth (fsw) | Bottom Time (min.) | Total Decom. Time (min) | Bottom Gas Sample % $O_2$ | % He | % $N_2$ | % Ne | Diver | Description of Decompression Sickness |
|---|---|---|---|---|---|---|---|---|
| | | | HELIUM-OXYGEN DIVES | | | | | |
| 200 | 30 | 67 | 10.25 | 86.2 | 3.42 | .14 | A | None |
| | | | | | | | B | None |
| 200 | 30 | 67 | 10.77 | 85.0 | 4.29 | - | A | None |
| | | | | | | | B | None |
| 300 | 30 | 169.3 | 10.60 | 86.95 | 2.2 | .15 | A | None |
| | | | 12.0 | 78.36 | 9.4 | .13 | B | Pain only in left knee 10 min. after surfacing; treated on short $O_2$ table, Table 5 U. S. Navy Diving Manual. |
| 400 | 30 | 544.6 | 10.4 | 85.6 | 4.0 | - | A | None |
| | | | 10.5 | 85.5 | 4.0 | - | B | None |
| 500 | 34.7 | 2837 | 7.3 | 89.8 | 2.9 | - | A | Inner ear hit at 140 fsw and 160 decompression time; treated by recompression to 200 fsw and breathing 37% oxygen in helium mixed gas. Decompressed from 200 fsw on saturation profile. |
| | | | 7.2 | 90.2 | 2.6 | - | B | None |
| 600 | 33.1 | 1540 | 7.1 | 89.4 | 3.5 | - | A | Bilateral hip pain at 40 fsw and 600 decompression time; treated by recompression to 60 fsw and $O_2$ breathing. Decompression rates were reduced to 1 ft/min. |
| | | | 7.1 | 89.5 | 3.4 | - | B | Sinus squeeze at 70 fsw and 423 decompression time; treated with Tyzine nasal drops and actifed. |
| | | | CRUDE NEON-OXYGEN DIVES | | | | | |
| 200 | 30 | 67 | 11.3 | 21.23 | 5.6 | 61.8 | A | None |
| | | | 11.3 | 21.05 | 5.3 | 62.2 | B | None |
| 200 | 34.0 | 84.4 | 11.4 | 19.25 | 2.9 | 66.3 | A | None |
| | | | 11.5 | 18.84 | 3.3 | 66.2 | B | None |
| 300 | 30.0 | 170.0 | 11.0 | 18.13 | 3.9 | 66.9 | A | None |
| | | | 11.1 | 17.51 | 3.6 | 67.7 | B | None |
| 400 | 30.0 | 544.7 | 10.7 | 17.63 | 3.1 | 68.5 | A | None |
| | | | 10.5 | 18.74 | 2.9 | 67.8 | B | None |
| 500 | 31.7 | 1101 | 8.3 | 19.9 | 5.2 | 66.6 | A | None |
| | | | 8.3 | 20.6 | 4.7 | 66.4 | B | None |
| 600 | 35 | 2140 | (Sample cylinder leaked) | | | | A | Pain only in right knee at 40 fsw and 623 decompression time; treated by recompression to 70 fsw; decompression saturation profile. |
| | | | | | | | B | None |

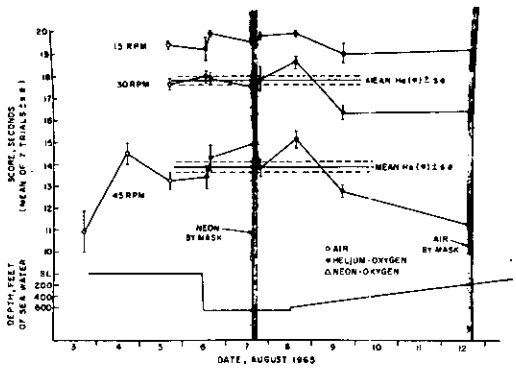


Fig. 1 - Results of pursuit rotor test, Dive 58, Christensen.

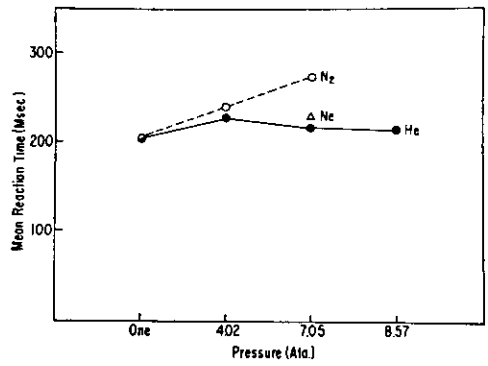


Fig. 2 - Reaction time.

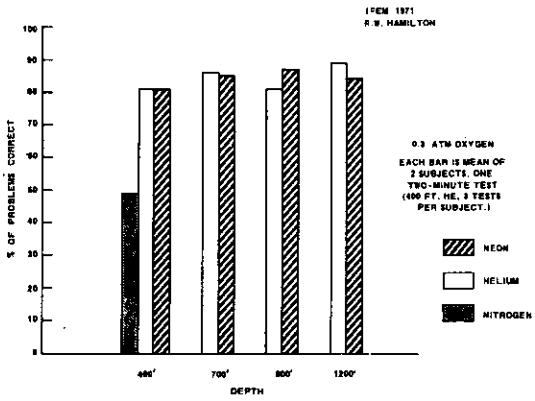


Fig. 3 - Paced arithmetic test.

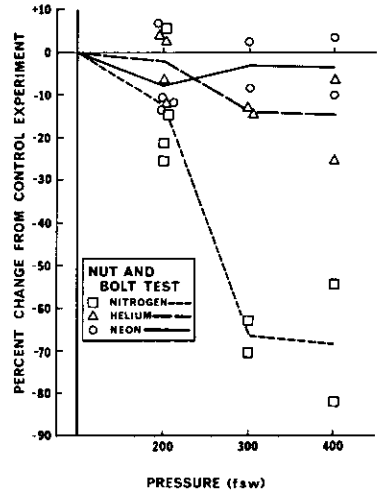


Fig. 4 - Sea level control experiment.

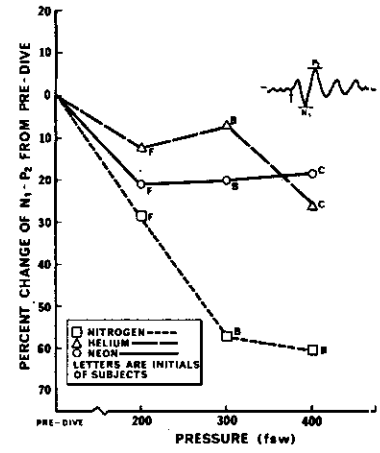


Fig. 5 - Auditory evoked response during arithmetic test.

| ANIMAL | INERT GAS | Decompression Sickness Category increasing severity → 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| DONALD | Ne | ● | | | |
| | Crude Ne | | ●● | | |
| | He | | | ●● | |
| | $N_2$ | | | ●● | |
| | Ar | | | | ● |
| LUCY | Ne | ● | | | |
| | Crude Ne | ● | ●● | | |
| | He | | ● | ● | ● |
| | $N_2$ | | | | ● |
| | Ar | | | | ● |
| KITTY | Ne | | ● | | |
| | Crude Ne | ● | ●● | | |
| | He | | | ●●● | |
| | $N_2$ | | | ● | |
| | Ar | | | | |

Fig. 6 - Distribution of decompression sickness severity according to animal and inert gas.

# PROCEEDINGS

# OF THE

# UNDERWATER PHYSIOLOGY

# SYMPOSIUM

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1955

## 3.5 SOME THEORETICAL ASPECTS OF THE USE OF MULTIPLE-GAS MIXTURES FOR DEEP-SEA DIVING

A. P. Webster
Commander, Medical Corps, USN (Ret)
U. S. Naval Air Development Center

The theoretical aspects of the use of multiple-gas mixtures for diving are somewhat in conflict with the practical aspects. On theoretical grounds, when the deformation pressure, D, surrounding a bubble exceeds some threshold value, D', nerve fibers or endings are stimulated by the mechanical deformation of the tissues and symptoms result. On theoretical grounds, then, the deformation pressure does not depend on what kind of gases are present, but rather on the sum of the partial pressures of all the gases present, see Figure 3.5-1.

Note that the deformation pressure, D, is large when any of the respective partial pressures are large, and in the words of Nims[70] "Decompression sickness would appear irrespective of which gas had the largest partial pressure; and it is only an accident of nature that nitrogen is the gas which is the chief factor

$$P_{N_2} + P_{CO_2} + P_{O_2} + P_{He} + P_{H_{20}} - H = D + \left(\frac{2\gamma}{r}\right)$$

where

$P_{N_2}$, $P_{CO_2}$, etc. = partial pressures of the respective gases within the bubble

H = hydrostatic pressure

O = *deformation pressure*

$\gamma$ = gas-water interfacial tension of the fluid surrounding the bubble

r = radius of the bubble

Figure 3.5-1 Pressure Conditions within a Bubble

in decompression sickness....." in air. It has been stated that symptoms occur whenever the gaseous pressure of the bubble exceeds the hydrostatic pressure of the tissues by a significantly large amount, that it does not matter what the particular gases in the bubble are, or how the hydrostatic pressure in the vicinity of the bubble is altered. If the deformation pressure, D, is greater than a given critical value, pain results.

Assuming the foregoing remarks to be substantially correct, there are two other main events taking place simultaneously which must be considered: The diffusion of gases from the tissues into the bubble and the desaturation of the tissue gases via the lungs. Both of these phenomena are considered to be exponential with specific time constants. The important point, however, is that the rate at which a specific gas, e.g., nitrogen or helium, enters a bubble may be different for different gases, whereas the time (or diffusion) constant governing the exchange of gas between the tissues and the alveolar air is generally considered to be, for all practical purposes, the same for various gases. And, in fact, this constant has been shown by Jones[71] to be proportional to blood flow through the tissue, and the time constants for the elimination of helium, nitrogen, krypton, argon, and xenon have been shown to be substantially the same.

The rate of entry of gas into the bubble may, however, be largely controlled by the size of the molecule and hence tend to follow Graham's Law, in which the diffusion is proportional to the reciprocal of the square root of the molecular weight. If this is the case, helium would tend to enter a bubble at a faster rate than would nitrogen, and high helium concentrations in the respired gas would tend to prolong the decompression time since rapid entry of gas into the bubble would cause an early approach to the critical deformation pressure, D'.

Figure 3.5-2 shows the advantages and disadvantages of the three gases, $O_2$, $N_2$, and $H_e$.

| | | ADVANTAGES | DISADVANTAGES |
|---|---|---|---|
| HIGH CONCENTRATIONS OF | $O_2$ | Survival<br>Prolong Dive | Toxicity |
| | $N_2$ | Rapid Decompression at Shallow Depths for Short Times | Narcosis |
| | He | Physiologically Inert | Slow Decompression Requires $O_2$ |

Figure 3.5-2 Advantages and Disadvantages of Oxygen, Nitrogen, and Helium

One of the questions before us is what is the advantage of a multiple-gas mixture over a single-gas-plus-oxygen mixture. Further, what would be the advantage in using a mixture composed of nitrogen, helium, krypton, argon, and oxygen. Since we do have established decompression tables for air and helium-oxygen mixtures, I have confined the following calculations to helium-nitrogen-oxygen mixtures, as illustrated in Figure 3.5-3.

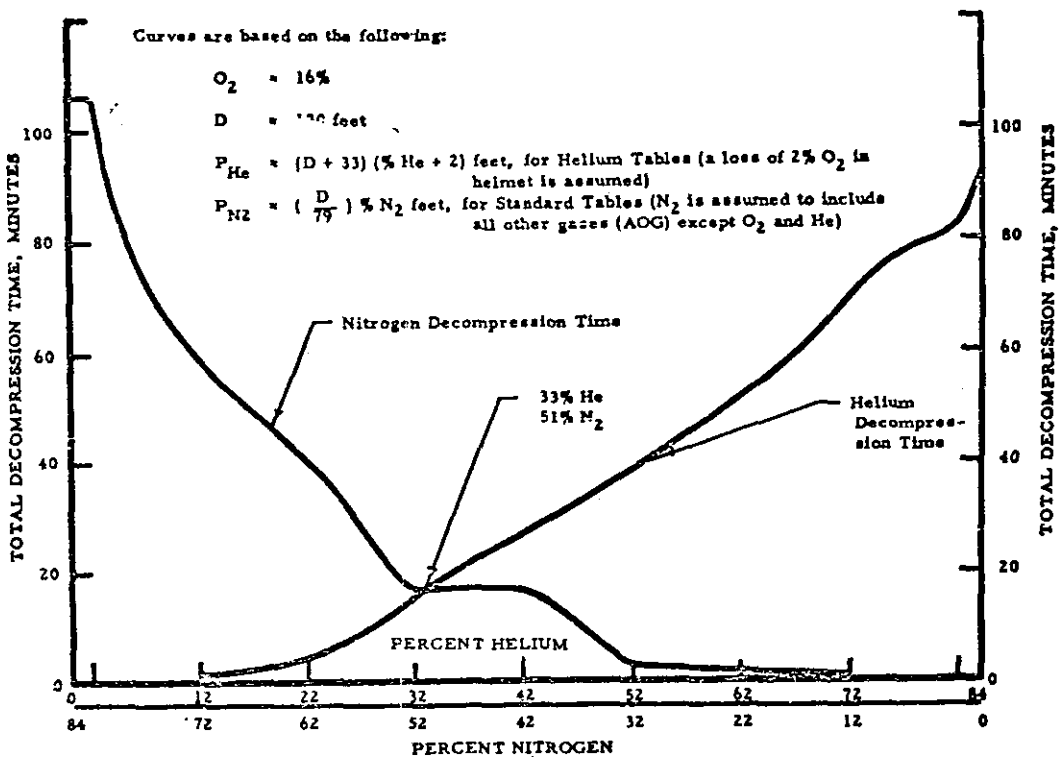
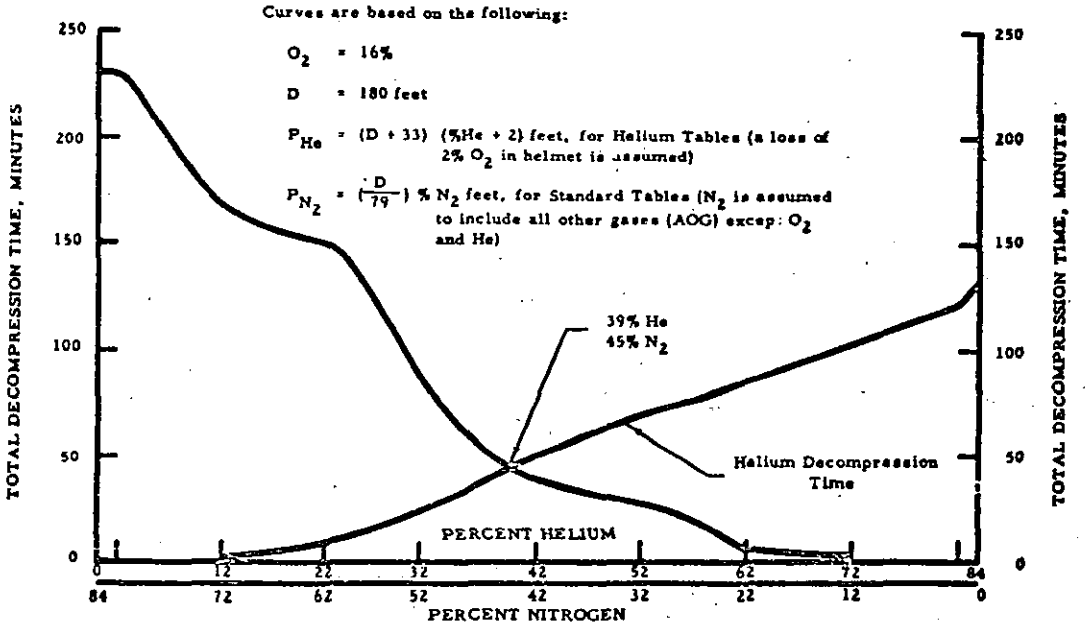



Figure 3.5-3 Theoretical Decompression Times for Dive to 180 Feet for 30 Minutes

These curves were prepared by assuming that a dive is to be made at a given depth, for a given time, and with a given oxygen percentage. For various percentage mixtures of the two gases, helium and nitrogen, the partial pressures of these two gases in the mixture were calculated in feet. Entering the Helium Tables and the Standard Tables,[72] the total decompression time for each gas separately was obtained and plotted.

In order to fit the practical calculations based on the Helium Tables and the Standard Tables into the theoretical framework, one may assume that for both the helium and nitrogen decompression curves, when a mixture of both is used, the critical deformation pressure is just reached at each point along each curve. For the combined gases the deformation pressure is 2D' or twice the critical pressure to produce pain, Figure 3.5-4.




Figures 3.5-4 Theoretical Decompression Times for Dive to 180 Feet for 60 Minutes

Note that the intersection of the two curves for this 60-minute dive is at about the same place as the 30-minute dive.

Figure 3.5-5, an 80-foot dive for 50 minutes, shows that the intersection of the two curves is about where it was for the deeper dive. Note that the intersection of the two curves is at approximately the same percentages of helium and nitrogen.

It is not easy to predict whether any advantage is to be gained using a multiple-gas mixture. If one accepts the thesis that the inert gas helium has its primary advantage in preventing necrosis, and that the gas nitrogen has its primary advantage in requiring shorter decompression times at the shallower depths (or lower partial pressure equivalents), then it is possible to conceive that a mixture of the two may yield some of the advantages of both.

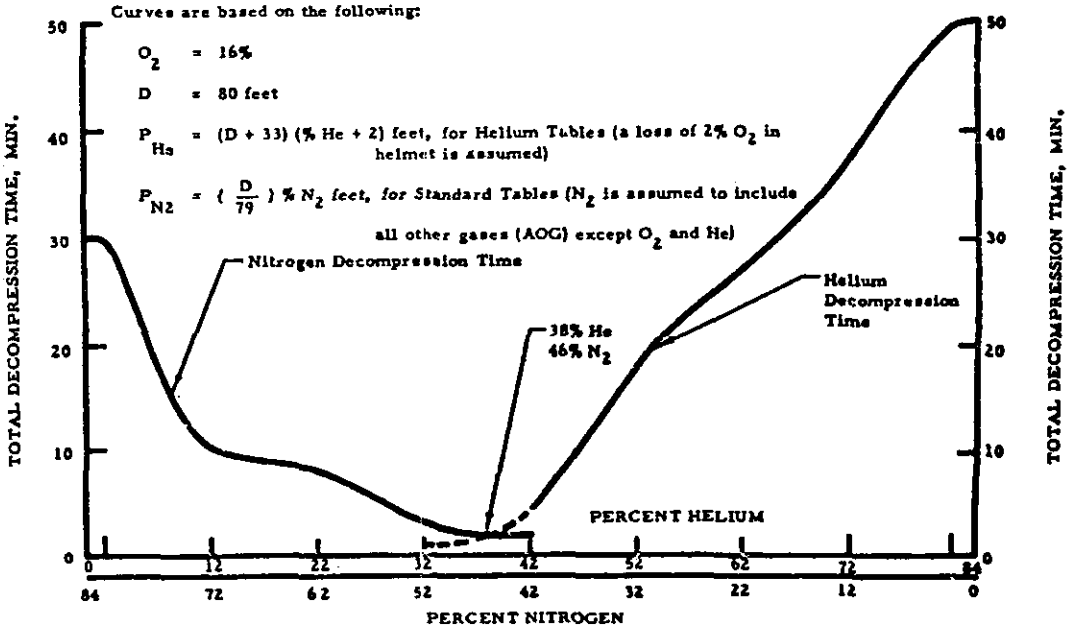



Figure 3.5-5 Theoretical Decompression Times for Dive to 80 Feet for 50 Minutes

# DIVING MEDICINE: THE HIGH PRESSURE NEUROLOGIC SYNDROME

Articles selected by Ralph W. Brauer, Ph.D.
Institute of Marine Biomedical Research
Wilmington, North Carolina

# 6

# DIVING MEDICINE: THE HIGH PRESSURE NEUROLOGIC SYNDROME

RALPH W. BRAUER

Recognition of the effects of hydrostatic pressure as a limiting factor in diving physiology has a curious history, characterized in part by reluctance of the scientific community to recognize pressure as an environmental factor. In marine environments, it has an importance second only to that of temperature. Regnard's (1885) paper, based on work beginning in the 1880's, seems to be the first record of excitement, disturbed locomotion, and eventual paralysis in marine (albeit invertebrate) animals exposed to high hydrostatic pressures. For more than 30 years after Regnard's original publication, studies of effects of high pressure on excitable tissues progressed slowly. It was only during the 1920's that a series of publications began to appear dealing with effects of high hydrostatic pressures on a variety of excitable tissues. Among these, and almost completely overlooked by subsequent workers, was the first report of effects in a vertebrate which we should now recognize as manifestations of the high pressure neurologic syndrome (Ebbecke, 1936).

Since most of the effects observed by these early workers occurred only at pressures well over 100 atm, it is not surprising that when, during the 1960's, investigators first came across manifestations of what we now recognize to be HPNS in man, the possibility that these effects might reflect the influence of hydrostatic pressure did not at once come to mind. Thus, the first observations of tremors and performance impairment in men rapidly compressed to depths of the order of 1000 ft of sea water were attributed to helium narcosis (Zaltsman, 1968), or to histotoxic effects, possibly of oxygen or helium (Bennett, 1967). Tremors and convulsions in mammals compressed in heliox or hydrox atmosphere were first recognized by Brauer and coworkers as the result of the action of hydrostatic pressure, rather than of pharmacologic or respiratory effects of respired gases, based upon studies comparing effects of the two gas mixtures in both monkeys and mice (Brauer et al., 1967). Subsequent work by this group led to description of the tremor and convulsion stages of HPNS, to demonstration that these phenomena occur in all vertebrate orders, and to description of the antagonisms of inert gas anesthetics against these manifestatons (Brauer et al., 1971; Brauer et al., 1968).

Meanwhile Oxford investigators, pursuing the problem of pressure reversal of anesthesia, observed HPNS effects in the mouse and extended the description of the syndrome by inclusion of high pressure death. In addition, experiments showing similar effects in newts compressed hydraulically led these investigators to infer that "the loss of activity in all cases resulted from the effects of high pressure alone" (Miller et al., 1967). Further development of their observations led Miller and colleagues to formulate a more general hypothesis to account for both pressure reversal of inert gas narcosis and HPNS in terms of their "critical volume hypothesis" (Miller, 1974). Attribution of these effects to hydrostatic pressure as such was further supported by experiments showing that tremors and convulsions could be induced in liquid-breathing mice in the absence of helium during hydraulic compressions (Kylstra et al., 1967).

With these observations in mind, a Franco-American research team conducted a series of deep chamber dives which confirmed the occurrence of similar symptoms (short of convulsions) in man and led to description of the essential features of what was now first identified as the High Pressure Neurological Syndrome (HPNS) as it occurs in divers (Brauer et al., 1969).

Acceptance of this interpretation was by no means instantaneous. A number of workers continued to feel that these effects should be attributed to impairment of respiratory gas exchange by the dense high pressure atmospheres employed (Chouteau, 1971). This view was disproved by animal experiments showing normal $O_2$ and $CO_2$ contents in the blood of squirrel monkeys subjected to HPNS convulsions, as well as by HPNS convulsions in mice occurring at the same total pressures in isonarcotic gas mixtures of widely varying density (Brauer et al., 1974). It was not laid to rest fully, however, until workers at the University of Pennsylvania demonstrated that gas exchange of men breathing high density atmospheres remained adequate even at gas densities far exceeding those producing HPNS symptoms (Peterson et al., 1976).

Attempts to minimize deleterious effects of HPNS upon divers followed two main routes. Early work on the antagonisms of HPNS symptoms by inert gas anesthetics had led to formulation of a "hydrogen equivalent" ternary gas mixture consisting of helium, nitrogen, and oxygen (Brauer et al., 1968; Brauer et al., 1974) to demonstrate its beneficial effects in increasing HPNS tremor and convulsion threshold pressures in animal experiments. Lever at al. (1971), comparing several anesthetics, likewise reported that addition of nitrogen to heliox breathing mixtures caused a substantial increase in the pressure at which high pressure death occurred in mice, that nitrous oxide and argon possibly caused similar effects, and that remarkably effective protection was afforded by pretreating animals with sodium pentobarbital. They suggested that "addition of some $N_2$ to $O_2$-He mixtures at high pressures may prove beneficial." Bennett and coworkers subsequently applied such mixtures in human diving experiments and confirmed the protective effect of this "trimix" against HPNS manifestations in man (Bennett et al., 1974).

Suggestions that low onset pressures for HPNS manifestations in the British, Russian, and Franco-American experiments were related to the relatively rapid compressions employed led to successful experiments proving the effectiveness of slow compression in postponing onset and perhaps in reducing severity of HPNS manifestations in divers (Bennett and Towse, 1971). This line of thought was developed further by Fructus and colleagues, who sought to optimize compression schedules (Fructus et al., 1973). They used animal experiments to define quantitative relations between the time course of compression and onset of HPNS manifestations, further revealing the complex nature of HPNS. During saturation dives, it became clear that, in man, at least some of the HPNS symptoms continue to manifest themselves even after sojourn at depth for periods of at least 1 week (Rostain and Lemaire, 1973).

Thus, by the end of 1974, the general outlines of both the clinical appearance and etiology of HPNS had become fairly well established. It had also become clear that as the result of action of high hydrostatic pressures upon the CNS of man (and indeed of all vertebrates tested), substantial and reversible changes in performance and locomotor behavior could be induced, and that further exploration of these effects promised considerable rewards not only from the point of view of improving the deep diving capabilities of man, but also in terms of improved understanding of CNS function, and indeed, of behavior of excitable tissues in very general terms.

# DIVING MEDICINE: THE HIGH PRESSURE NEUROLOGIC SYNDROME

R. W. BRAUER

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Bennett P. B.: *Psychometric impairment in men breathing oxygen-helium at increased pressures*. Med Res Council RNPRC Rept UPS 251. Great Britain. Abstract and summary only. 1965.

Bennett P. B.: Performance impairment in deep diving due to nitrogen, helium, neon, and oxygen, in Lambertsen C. J. (ed): *Underwater Physiology III*. Baltimore, Williams & Wilkins, 1967, pp. 327–340. Copyright 1967, Williams and Wilkins Co.

Bennett P. B., Blenkarn G. D., Roby J., Youngblood D.: Suppression of the high pressure nervous syndrome in human deep dives by He-$N_2$-$O_2$. *Undersea Biomed Res* 1974; 1:221–237. Copyright 1974, Undersea Med Soc Inc.

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Rostain J. C., Lemaire C.: Évolution du tremblement au repos et pendant l'effort au cours de plongées profondes en atmosphère hélium-oxygène. *Rev EEG Neurophysiol* 1973; 3:203–206. Copyright 1973, Masson et Cie, Editeurs.

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## ABSTRACT

BENNETT, P.B.

Psychometric impairment in men breathing oxygen-helium at increased pressures.

Roy. Nav. Personnel Res. Comm. Rep. NSTIC/08342/66, 12 p. Sept. 1965.

(1) Opportunity was taken during recent deep diving experiments seeking safe decompression procedures from 600 feet and 800 feet in men breathing 5%/95% oxygen/helium to examine their psychometric performance. (2) Six men at 600 feet and 4 at 800 feet were required to carry out an arithmetic test (ab x c) and a test of neuromuscular control. In addition, at 600 feet a 5 choice reaction time test was used. (3) During the first hour of exposure to 600 feet there was an 18% fall in the number of sums correct and a 25% loss of efficiency of the neuromuscular test. This increased to a 42% fall and 53% loss respectively at 800 feet. (4) The loss of efficiency was accompanied by dizziness, nausea and tremor of the hands, arms and even the whole body. (5) With increasing time at pressure these signs and symptoms of physiological and psychological impairment became less marked until after 2-1/2 hours the men appeared normal. (Author's summary)

## SUMMARY

1. Opportunity was taken during recent deep diving experiments seeking safe decompression procedures from 600 feet and 800 feet in men breathing 5%/95% oxygen/helium to examine their psychometric performance.

2. Six men at 600 feet and 4 at 800 feet were required to carry out an arithmetic test (ab x c) and a test of neuromuscular control. In addition, at 600 feet a 5 choice reaction time test was used.

3. During the first hour of exposure to 600 feet there was an 18% fall in the number of sums correct and a 25% loss of efficiency of the neuromuscular test. This increased to a 42% fall and 53% loss respectively at 800 feet.

4. The loss of efficiency was accompanied by dizziness, nausea and tremor of the hands, arms and even the whole body.

5. With increasing time at pressure these signs and symptoms of physiological and psychological impairment became less marked until after 2 1/2 hours the men appeared normal.

# *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


The Williams & Wilkins Company
*Baltimore • 1967*

27 | PETER B. BENNETT

# Performance Impairment in Deep Diving Due to Nitrogen, Helium, Neon and Oxygen

Among the major factors likely to cause performance impairment at depths in excess of 300 feet are inert gas narcosis (17) and oxygen toxicity (16). An associated factor is carbon dioxide retention as a result of hypoventilation and the increased oxygen partial pressure (11, 13–15, 30, 38).

In any deep dive all of these factors are present to varying degrees and the resulting impairment is usually a function of all three. This paper will consider the extent of this mutual involvement and the effect of these factors on the efficiency of the diver at depths down to 800 feet.

## Compressed Air Intoxication

The problem of compressed air intoxication has already been considered in some detail in my recenty published monograph (17). It is however clear that the cause of the narcosis is the increased tension of nitrogen, associated causes being the density and oxygen partial pressure of the respired mixture. These may cause an increased carbon dioxide tension which synergistically potentiates the narcosis (11–14, 17, 25, 26).

During deep diving to depths in excess of 300 feet, Adolfson and Muren (2, 3) have studied compressed air intoxication on 30 subjects at 400 feet. In an arithmetic test the number of sums correct was reduced by 61.6%

with 25% more errors. Subjectively the narcosis was severe, being more similar to that found with hallucinogenic drugs such as LSD 25, rather than with alcohol.

Barnard, Hempleman and Trotter (8) and Albano (4) have compared the narcotic effect of air at 300 feet with mixtures of 95% $N_2$-5% $O_2$ or 96% $N_2$-4% $O_2$ respectively. In the former experiments, whereas air breathed at 300 feet caused an impairment of 44.4% in arithmetical efficiency, the mixture induced a 60.7% decrement. In the experiments by Albano (4), the mean impairment with air at 300 feet was 40.6% compared with 50.6% in men breathing 96% $N_2$-4% $O_2$. Decreasing the oxygen partial pressure and thereby increasing the nitrogen therefore potentiates the narcosis. Conversely, increasing the oxygen partial pressure at a constant nitrogen pressure may also potentiate the narcosis due to the associated increase in carbon dioxide tension and its synergistic action (13, 14, 17, 25, 26).

It should be remembered that the levels of narcosis described were derived from pressure chamber experiments with men usually at rest. The narcosis is likely to be greater in men wearing breathing equipment, swimming and working underwater due to the presence of exogenous or endogenous carbon dioxide. Frequent exposure will however result in some acclimatisation. It is also possible to dive for brief periods to 500 feet or perhaps even deeper with little or no narcosis, provided compression is extremely rapid (18).

### Rate of Compression

It is generally believed that rapid compression enhances narcosis due to carbon dioxide retention as a result of compressional inflow of gases into the lungs (1, 5, 9, 22). However, if insufficient time is permitted for the nitrogen tension in the brain to reach the critical molar concentration necessary to induce narcosis, the carbon dioxide factor is less important.

Men have been compressed to 400 and 500 feet in 20 seconds and their performance examined until decompression at 5–6 ft./sec. 40 seconds later (18). As the time at depth was only 40 seconds, two choice reaction time was used to test for narcosis. No tests could however be made during the 20 second compression, as the men were far too busy ensuring that their eardrums remained intact. At 400 feet the expected value of reaction time due to learning factors in 10 subjects was not significantly different from control values, but at 500 feet there was a significant 14–15% decrement in reaction time accompanied by euphoria (Table 44).

This level of impairment compares with a decrease of some 20% in two choice reaction time reported by Kiessling and Maag (29) in 10 subjects breathing air at 100 feet and a 10% decrease in 14 subjects at 150 feet of

TABLE 44

*Effect of Very Rapid Compression with Air to 400 Ft. and 500 Ft. on Two-choice Reaction Time (1/100th sec) (18)*

| | 400 Ft. | 500 Ft. |
|---|---|---|
| Atmospheric pressure | 40.1 ± 6.8 | 30.7 ± 4.4 |
| Expected result (learning) | 37.8 ± 5.8 | 29.9 ± 3.7* |
| Actual result at diving depth | 37.2 ± 4.8 | 34.2 ± 4.0* |
| Difference expected-actual | +0.06 ± 2.3 | +4.4 ± 2.2 |
| Return to atmospheric pressure | 36.1 ± 5.8 | 30.0 ± 3.8 |

* $p = 0.02$.

TABLE 45

*Oil Solubilities and Other Physical Constants of the Inert Gases (27, 28, 31)*

| Gas | Molecular Weight | Sol. in Olive Oil | Temp (° C) | Oil-Water Sol. Ratio |
|---|---|---|---|---|
| He | 4 | 0.015 | 37 | 1.7 |
| Ne | 20 | 0.019 | 37.6 | 2.07 |
| $N_2$ | 28 | 0.067 | 37 | 5.2 |
| Ar | 40 | 0.14 | 37 | 5.3 |
| Kr | 83.7 | 0.43 | 37 | 9.6 |
| Xe | 131.3 | 1.7 | 37 | 20.0 |

air reported by Shilling and Willgrube (37). The narcosis at 500 feet was therefore minimal but there can be no doubt that a slow compression rate such as 100 ft./min. would have resulted in the men being incapacitated on reaching depth.

### The Narcotic Potency of Neon

For more prolonged diving to great depths however other less potent inert gases must be used instead of nitrogen. The narcotic potency of inert gases has been related with varying success to most of their physical characteristics such as partition coefficient and molecular weight (10), adsorption coefficients (22), thermodynamic activity (20, 24) and clathrate formation (34, 35). The best relationship is found with oil solubility (10, 27, 28, 31) (Table 45).

On this basis neon is 3.5 times less potent than nitrogen and helium 4.5 times less potent. The latter has therefore been the choice for deep diving but neon could be a useful alternative. Marshall (33) seems to have been the first worker to have studied the narcotic potency of neon. She found the pressure required to produce reversible inhibition of reflex activity in the tibial nerve of frogs was 10 atmospheres of argon, 17 at-

TABLE 46

*Comparative Effect on Performance of Exposing 10 Men to a Partial Pressure of 4.6 Atm. Abs. (152 Feet) of Nitrogen or Neon (17)*

| | Nitrogen (air 190 ft.abs.) | Neon (65.6% Ne-16.4% He-18% $O_2$ 233 ft.abs.) |
|---|---|---|
| Sums correct | −12* | −3.3† |
| Sums attempted | −12* | −1.7‡ |
| No. of ball bearings | −15.6* | +2.7** |

* $P < 0.001$.
** $P < 0.05$.
† $P < 0.01$.
‡ Not significant.

mospheres of nitrogen, 54 atmospheres of neon and no effect even with 82 atmospheres of helium.

We have exposed ten men to 200 feet breathing a mixture of crude neon (80% neon and 20% helium) and oxygen giving an absolute neon partial pressure of 152 feet. This was compared with a similar partial pressure of nitrogen by exposing men to compressed air at 190 feet absolute.

The tests for narcosis were simple two figure by one figure multiplication, the score being the number of sums attempted and correct in two minutes and a test of manual dexterity and neuromuscular coordination, in which, in 40 seconds, as many ball bearings as possible were picked up one at a time with a pair of smooth ended tweezers and dropped into a tube whose diameter was just sufficient to permit entry of a ball bearing.

The results indicated that neon caused little or no narcosis at this partial pressure (Table 46).

Similar experiments in 2 subjects at 300 feet with a neon partial pressure equivalent to 212 feet add emphasis to its low narcotic potency. The mean number of sums correct improved from 8 on the surface to 11.5 at 300 feet and the sums attempted improved from 10 to 12. The number of ball bearings in the tube also improved from 11.5 to 13 with no subjective sensation of narcosis. Many more experiments are required with this gas as it does seem to be of low narcotic potency. However at present British neon is twice the cost of helium and some reduction will be required if neon is to be used more extensively.

At present we are therefore left with oxygen-helium as the mixture of choice for deep diving. Using this mixture what is the potential hazard of such a mixture as regards oxygen toxicity?

### The Effects of Inert Gases on Oxygen Toxicity

In 1961 Linaweaver (32) carried out experiments at depths down to 130 feet which suggested that breathing oxygen-helium rather than air, the depth-time oxygen limits could be exceeded. Lanphier (30) showed that this was because air at 100 feet causes hypoventilation which, with factors such as the increased oxygen partial pressure and the increased respiratory work due to the breathing apparatus, produces a serious carbon dioxide retention.

At shallow depths most of these problems can be overcome by breathing helium-oxygen and using more efficient breathing equipment. Lanphier however predicted that with the advent of very deep diving these problems would occur even breathing helium-oxygen. Wood (38) added emphasis to this prediction by reporting a marked reduction of maximum breathing capacity in men breathing helium-oxygen at 15 atm. abs.

The time to oxygen convulsions was therefore compared in Wistar rats exposed either to 5.3 atm. abs. oxygen or a 90% He-10% $O_2$ mixture at 53.3 atm. abs. In the presence of helium there was a dramatic reduction in the time to convulsions (Table 47).

It seems probable that the reduction is due to hypoventilation as a result of the increased density of the mixture causing carbon dioxide retention which synergistically potentiates the toxicity. Support is given by studies of the comparative influence of argon, nitrogen and helium on oxygen toxicity in rats at a pressure of 18.6 atm. abs. It was observed that the

TABLE 47

*Effect of 48 Atm. Abs. Helium on the Time to Convulsions in Rats Exposed to 5.3 Atm. Abs. Oxygen*

| Gas Mixture | 5.3 Atm. Abs. Oxygen | 48 Atm. Abs. Helium 5.3 Atm. Abs. Oxygen |
|---|---|---|
| Time in minutes from start of compression to a convulsion | 22 | 6 |
| | 17 | 6 |
| | 18 | 7 |
| | 15 | 6 |
| | 23 | 7.5 |
| | 22 | 6.5 |
| | 21 | 5.5 |
| | 25 | 6 |
| | 16 | 7 |
| | 24 | 5.5 |
| Mean time | 20.3 ± 3.52 | 6.3 ± 0.67 |

TABLE 48

*Effect of 13.3 Atm. Abs. Helium, Nitrogen or Argon on the Time to Convulsions in Rats Exposed to 5.3 Atm. Abs. Oxygen (16)*

| Gas Mixture | 5.3 Atm. Abs. $O_2$ | 5.3 Atm. Abs. $O_2$ 13.3 Atm. Abs. He | 5.3 Atm. Abs. $O_2$ 13.3 Atm. Abs. $N_2$ | 5.3 Atm. Abs. $O_2$ 13.3 Atm. Abs. A |
|---|---|---|---|---|
| Time in minutes from start of compression to a convulsion | 26 | 25 | 20 | 16 |
| | 25 | 24 | 17 | 19 |
| | 20 | 20 | 24 | 18 |
| | 19 | 20 | 20 | 18 |
| | 21 | 23 | 18 | 16 |
| | 27 | 27 | 20 | 15 |
| | 24 | 22 | 20 | 16 |
| | 25 | 19 | 24 | 17 |
| | 27 | 25 | 21 | 20 |
| Mean time | 23.8 ± 3.03*† | 22.8 ± 2.74 | 20.4 ± 2.36* | 17.2 ± 1.64† |

* $P < 0.001$.
† $P < 0.001$.

TABLE 49

*Changes in Cortical Oxygen and Carbon Dioxide Tension in Chloralosed Cats at 8.67 Atm. Abs. Helium, Nitrogen or Argon and 2.34 Atm. Abs. Oxygen (13)*

| | $aO_2$* (mm Hg) | $P_{CO_2}$ (mm Hg) |
|---|---|---|
| 8.67 atm. abs. He-2.34 atm. abs. $O_2$..... | +297.9 ± 69.6 | +5.1 ± 2.18 |
| 8.67 atm. abs. $N_2$-2.34 atm. abs. $O_2$..... | +121 ± 52.7 | +12.1 ± 3.55 |
| 8.67 atm. abs. $A_2$-2.34 atm. abs. $O_2$..... | +91 ± 62.4 | +20.5 ± 5.29 |

* $aO_2$ denotes cortical available oxygen.

greater the density of the mixture the shorter the time to convulsions (Table 48).

Further support is given by measurements of cortical carbon dioxide and oxygen in chloralosed cats (13, 16). The greatest increase in carbon dioxide tension, in cats exposed to 11 atm. abs. of either argon-oxygen, nitrogen-oxygen or helium-oxygen, is found with the argon mixture and the least with the helium mixture. Conversely, the greatest increase in cortical oxygen is found with the helium mixture and the least with the argon (Table 49).

In addition to this problem of potentiation of oxygen toxicity by helium and other inert gases is the question whether, even with a gas of low narcotic potency such as helium, men will be able to perform efficiently at very great depths.

### Performance Impairment due to Helium-Oxygen

Based on fat solubility, narcosis equivalent to air at 100 feet should be present with helium-oxygen at some 450 feet and that equivalent to air at 300 feet would be expected at about 1,350 feet. When factors such as carbon dioxide retention due to the density, viscosity and increased oxygen partial pressure are also included, the limits as regards performance efficiency are likely to be only about 1,000 feet.

During the deep diving experiments carried out recently at the Royal Naval Physiological Laboratory we have measured the performance efficiency of divers in between periods of hard work on a rowing machine at depths between 300 and 800 feet for periods up to 4 hours. Earlier studies have already shown that there is no significant narcosis in men breathing helium at depths down to 200 feet (6, 19).

In the present studies the tests used included the arithmetic and ball bearing tests described previously and a maze tracking test, devised by Albano, which is a sensitive tracking task involving drawing with a pencil a line between two other lines $\frac{1}{12}''$ apart; the score being the number of times the pencil touches the sides and the distance travelled during 1½ minutes. The maze and ball bearing tests were chosen to quantify hand, limb or even whole body tremor reported by some of the divers during previous deep helium-oxygen dives. The tests were carried out on the surface and so far as possible at regular intervals during the 1 or 4 hour exposure at depth and again on return to the surface.

In 4 men at 300 feet breathing 90 % He-10 % $O_2$ tremor was present as shown by a decrement in both the ball bearing and maze tests. The arithmetic test was little affected. The deterioration in performance was at its worst during the initial 30 minutes of exposure and gradually improved over the 1 hour at depth (Fig. 97).

A very similar result was found in 4 men breathing 90 % He-10 % $O_2$ at 400 feet. Again the deterioration was at its worst initially and was followed by a gradual improvement. There was considerable individual variation in sensitivity and tremor was the prime cause of the performance impairment, arithmetic being little affected (Fig. 98).

At 500 feet, 2 subjects were tested over 1 hour breathing 95 % He-10 % $O_2$ and 2 on a mixture of 92.5 % He-7.5 % $O_2$. With the mixture of 7.5 % $O_2$ tremor was again marked, with little or no impairment of the arithmetic test. This suggests that the tremor is not a function of helium narcosis but is due to other factors (Fig. 99).

With only 5 % oxygen at 500 feet however the ball bearing test showed an improvement rather than decrement and the maze test was less affected. This result infers that the cause of the tremor is probably associated with the increased oxygen partial pressure (Fig. 100).

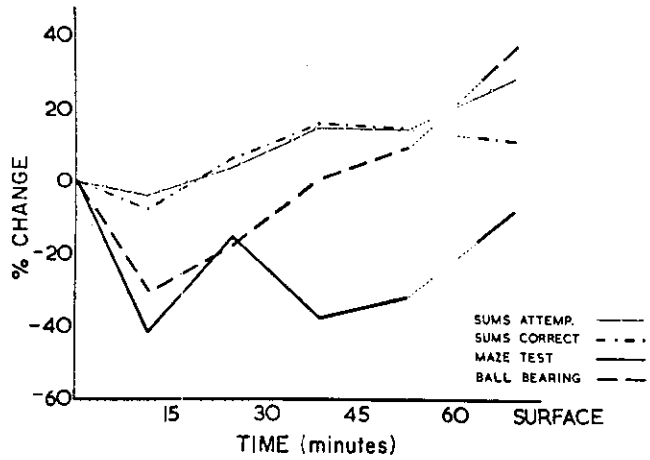


FIG. 97. Mean percentage change in performance in 4 subjects breathing 10% oxygen-90% helium at 300 feet for 1 hour.

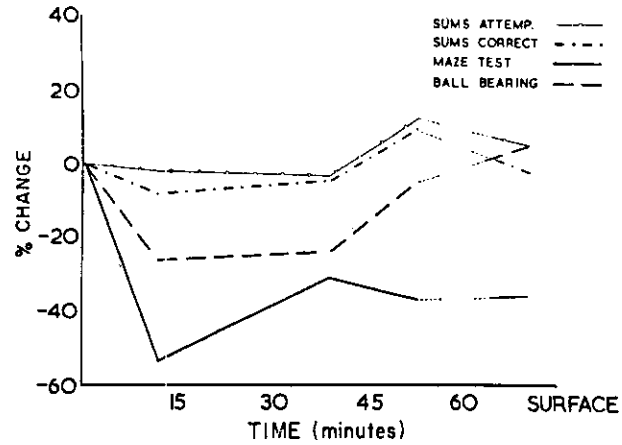


FIG. 98. Mean percentage change in performance in 6 subjects breathing 10% oxygen-90% helium at 400 feet for 1 hour.

At 600 feet, 6 subjects breathing 95% He-5% $O_2$ were tested over 4 hours with arithmetic, the ball bearing test and five choice reaction time (15). At this depth, in addition to the tremor, there was evidence of an impairment in mental performance as shown by a significant decrease in the number of arithmetic sums correct. However after 1 hour performance was little difference to that on the surface before compression (Fig. 101).

The performance impairment was sometimes accompanied by dizziness and nausea and very occasionally by vomiting during the latter part of the

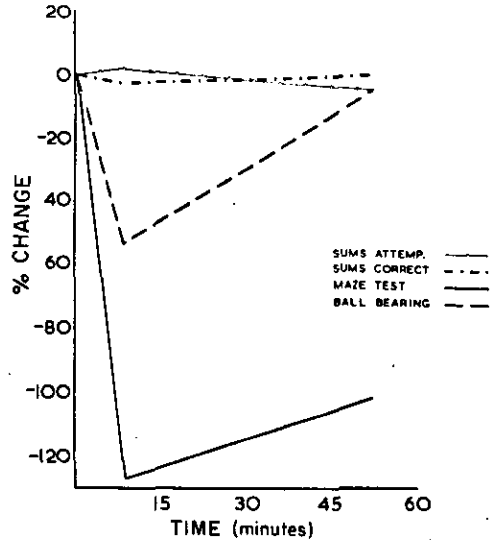


FIG. 99. Mean percentage change in performance in 2 subjects breathing 7.5% oxygen-92.5% helium at 500 feet for 1 hour.

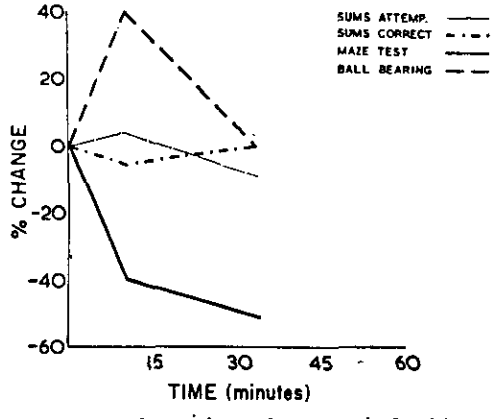


FIG. 100. Mean percentage change in performance in 2 subjects breathing 5% oxygen-95% helium at 500 feet for 1 hour.

exposure or at the initial stops during decompression. There was considerable inter-individual sensitivity. Two subjects who showed little quantitative impairment did report dizziness but were apparently able to exert enough self control to prevent any performance decrement. Whereas another showed a 60% decrement in the ball bearing test and another a 50% decrement in the number of sums correct.

Comparison of the mean deterioration during the initial time at depth

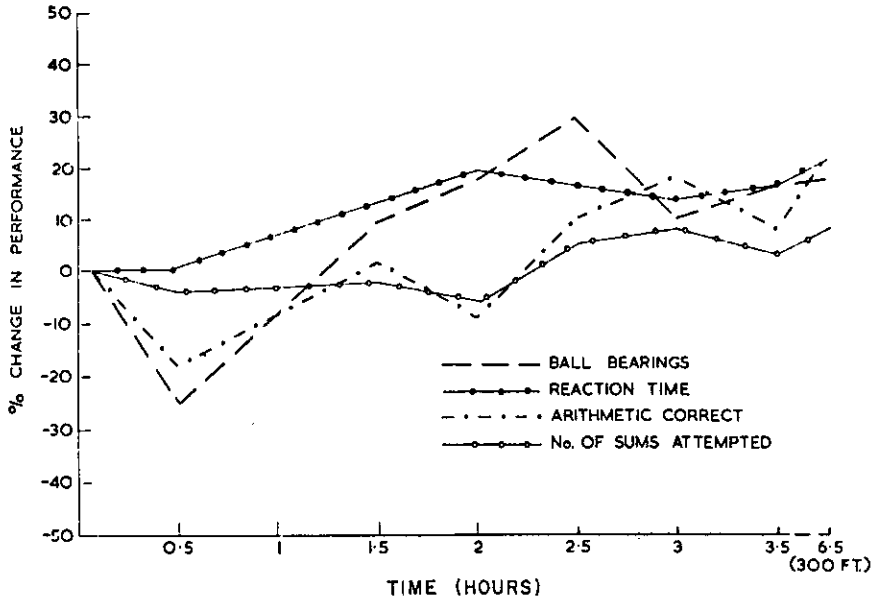


FIG. 101. Mean percentage change in performance in 6 subjects breathing 5% oxygen-95% helium at 600 feet for 4 hours (15).

TABLE 50

*Comparative Performance of 6 Subjects at 600 Feet and 4 Subjects at 800 Feet Breathing 5% Helium-95% Oxygen during the First 20 Minutes at Pressure (15)*

| | 600 FT. | 800 FT. |
|---|---|---|
| Sums correct | −18% | −42% |
| Sums attempted | −4% | −6% |
| No. of ball bearings | −25% | −53% |

in 6 men at 600 feet and 4 at 800 feet indicates that at 800 feet the performance decrement is 100% worse than at 600 feet. Both tremor and narcosis are severe. In fact both the quantitative measurements and subjective sensations are similar to those found in men breathing air at 300 feet (Table 50).

It is therefore evident that men exposed a further 200 feet to 1,000 feet on a 95% He-5% $O_2$ mixture can expect to be very severely affected indeed.

### The Cause of Oxygen-Helium Tremble and Its Prevention

Although the deterioration in arithmetical performance at 600 feet and 800 feet may be due to helium narcosis neither the tremor, nausea and occasional vomiting nor the improvement after time at depth are similar

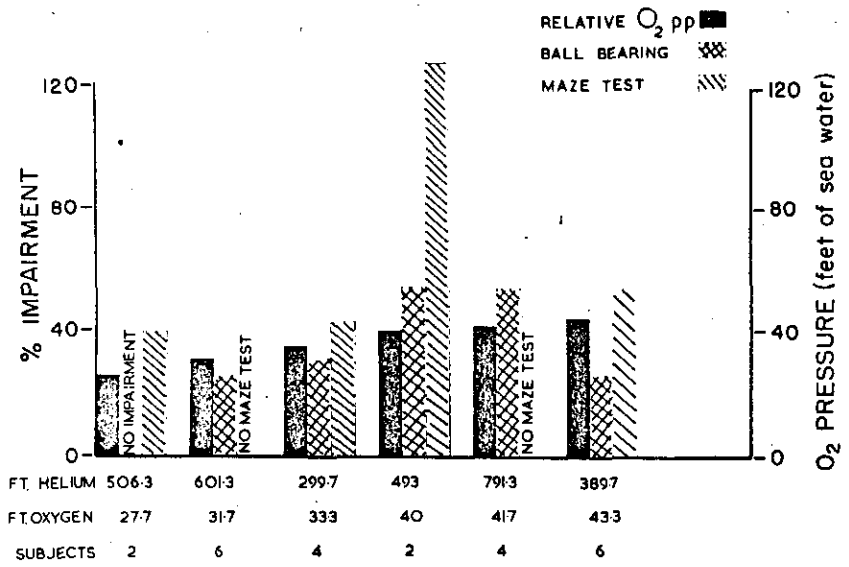


FIG. 102. Histogram of the mean impairment in the ball bearing and maze performance tests related to the oxygen partial pressure at depth.

to inert gas narcosis. The rate of compression does not seem to be the direct cause, for at 800 feet the mean compression time was 8 minutes 48 seconds, at 600 feet, 14 minutes 33 seconds and at 500 feet, 8 minutes 48 seconds.

The most likely cause would seem to be a hypercapnia due to too high an oxygen partial pressure accompanied by hypoventilation as a result of density and viscosity factors (21, 30, 38). That a significant 54.4% decrease in maximum breathing capacity occurs when breathing 95% He-5% $O_2$ at 500 feet was reported by Wood (38) at the last Symposium. Experiments by Lanphier (30), as discussed earlier in this paper and also by Seusing et al (36), point to the significance of an increased oxygen partial pressure and density in causing retention of carbon dioxide.

Although the results at 400 feet are anomalous, a histogram of the percentage impairment in the ball bearing and maze tests relative to the oxygen partial pressure suggests oxygen may indeed be one of the agents responsible (Fig. 102).

Barlow, McIntosh and Donald (7, 23) while investigating "shallow water blackout" in men using closed circuit oxygen sets at 20 feet reported exactly similar signs and symptoms as we have found in deep oxygen/helium diving. Are we now experiencing the initial stages of "deep water blackout"?

Rebreathing 50 litres of oxygen without absorbing carbon dioxide produces carbon dioxide intoxication with no signs of distress. Barlow and

co-workers noted a considerable variation of sensitivity in different subjects which was related to their rate of ventilation. Among the signs and symptoms which occurred were dizziness, tingling of the limbs and visual disturbances. Haziness, euphoria or sleepiness were common in sensitive subjects, without any change in the ventilation rate. Flushing of the face, dilatation of the pupils and sweating were present and muscular trembling was reported in some men, mainly in the arm, shoulder and neck muscles. Although hardly detectable in some subjects, in others they were coarse and violent and spread to all parts of the body. As the carbon dioxide intoxication became severe, the men worked at a feverishly increased rate, ignoring instructions, until they reached a stuporous condition and consciousness was lost. During recovery, consciousness was regained in less than a minute but many experienced an "off effect", with frontal headache, nausea or vomiting and a general fatigue and malaise.

These signs and symptoms of carbon dioxide intoxication in the presence of high oxygen tensions have been purposely described in detail as they are remarkedly similar to those found in our deep diving experiments, especially where 30–40 feet absolute oxygen was present. It is the use of helium in combination with a high oxygen partial pressure which appears to permit hypercapnia to occur. As indicated by the cortical $P_{CO_2}$ and $P_{O_2}$ measurements in cats described earlier, helium/oxygen will encourage increased carbon dioxide tensions in conjunction with high oxygen tensions so that a compensatory increased ventilation does not occur.

The solution may be to markedly reduce the oxygen partial pressure to probably as low as ½ atm. abs. (15 feet) at depths in excess of 400 feet. This will also help to reduce any synergistic potentiation of helium narcosis. Unfortunately, as a result decompression may be more prolonged. If, as a result of this measure, the density and viscosity is such that hypercapnia still results, a warning should then be given by an increased rate of ventilation. Further solutions may be to add a percentage of a higher density gas such as neon to the breathing mixture or to use some form of assisted ventilation.

Clearly many variables can affect performance efficiency in such very deep diving. It is however most important that every future opportunity should be taken to quantify them, for here may be a far more formidable barrier to the future of very deep diving than decompression sickness.

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# UNDERSEA BIOMEDICAL RESEARCH

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# Suppression of the high pressure nervous syndrome in human deep dives by He-$N_2$-$O_2$

P. B. BENNETT, G. D. BLENKARN, J. ROBY, and D. YOUNGBLOOD

*Department of Anesthesiology and Biomedical Engineering, Duke Medical Center, North Carolina; Harbor Branch Foundation, Florida*

Bennett, P. B., G. D. Blenkarn, J. Roby, and D. Youngblood. 1974. Suppression of the high pressure nervous syndrome in human deep divers by He-$N_2$-$O_2$. Undersea Biomed. Res. 1(3):221-237.–Four subjects were compressed to 720 fsw (23 ATA) in 20 min for 1 hour breathing 5.6 $N_2$-16.9 He ATA with 0.5 ATA $O_2$ (i.e. $N_2$ = 25%) and the result compared with exposures to 22.5 He-0.5 $O_2$ ATA or 7 ATA (200 fsw) compressed air (5.6 ATA $N_2$). Measurements were made of EEG, tremor, psychomotor and intellectual performance, subjective appreciation, and pulmonary function. Decompression using 0.8 ATA $O_2$ required 3 days. The same men were also compressed in 33 min to 1000 fsw (31 ATA) breathing $N_2$-He-$O_2$ (5.6 ATA $N_2$ = 18%) or He-$O_2$ or air at 200 fsw (7 ATA). Decompression took 4 days. At both depths with the trimix, $N_2$ suppressed completely the tremors noted when diving with He-$O_2$ alone. Psychomotor tests improved markedly and the nausea and dizziness associated with HPNS did not occur. Some decrement in intellectual function remained. The EEG results showed little change. Subjectively two subjects were HPNS-sensitive and preferred He-$N_2$-$O_2$; the other two found that nitrogen narcosis reduced their efficiency. Symptoms of pulmonary oxygen toxicity occurred during the first 24 hours of decompression but disappeared 24 hours later. There was a mean -4.62% reduction in forced vital capacity and +7.4 torr alveolar-arterial gradient post 1000 fsw dive. It is concluded that nitrogen will suppress HPNS but the present partial pressure was too high, causing narcosis and, therefore, needs to be reduced.

| | | |
|---|---|---|
| HPNS | performance | oxygen toxicity |
| helium | trimix | deep diving |
| hydrostatic pressure | nitrogen narcosis | tremor |
| | anesthesia mechanisms | |

When man is exposed to pressures greater than some 16 atmospheres absolute (ATA), such as when breathing oxygen-helium at 500 fsw (16 ATA) and deeper, signs and symptoms of the high pressure nervous syndrome (HPNS) start to appear. These become progressively more severe with increasing depth, particularly as compression rate increases, and are primarily characterized by disorientation, nausea, dizziness, tremors of the hands and arms, an increase in slow wave electrical activity (4-6 Hz) of the brain, and depression of other EEG activity. In man these lead to lapses of consciousness termed microsleep and in animals, convulsions. The etiology of this syndrome has been reviewed recently elsewhere (Bachrach and Bennett 1973; Hunter and Bennett 1974).

In 1961, Zaltsman (1968) noted that these effects with helium at high pressures were considerably different from the narcotic effects of nitrogen and the noble gas series (Bennett 1966; 1969) and, in the course of a protracted series of investigations, seems to be the first

to have studied physiological function in men exposed to He-$N_2$-$O_2$ mixtures to depths as great as 400 fsw (13 ATA). The characteristic trembling was not observed at shallower depths and only briefly sensed by the subjects starting at a helium partial pressure of 11 ATA. The helium, it was noted, did not intensify the narcotic effects of nitrogen. Experiments continued with air and helium with a maximum nitrogen partial pressure of 4.5 ATA. Under such conditions, at 527 fsw (17 ATA), heavy work between 221-580 kg · m/min was possible with little or no tremors and no thermal-balance or voice-distortion problems.

More recently Brauer and his colleagues (Brauer, Way, Jordan, and Parrish 1971; Brauer 1972; Brauer, Goldman, Beaver, and Sheehan 1974) reported that narcotic gases added to the breathing mixture of animals significantly raises the convulsion-threshold pressure, although they are less effective in regard to the tremor threshold, which seems only half as susceptible to such protection.

The early work of Zaltsman to reduce the narcotic effects of nitrogen by addition of helium was further extended by Smolin, Rappoport, and Kuchuk (1968) who exposed 4 men to mixtures of nitrogen, argon, and helium. Psychological tests and electroencephalogram (EEG) measurements were made with an exposure time of 30-40 min at maximum depth. With an argon-helium mixture (argon 3.5 atm) at 16 atm (530 fsw) difficulty was experienced with the tests due to narcosis but tremors were not observed. The same effect was found at 17.5 atm with an air-helium (nitrogen 5 atm) mixture and this corresponded only to the narcotic action of the 5 atm nitrogen present.

In preliminary studies Vigreux (1970) examined a mixture of 18% $O_2$, 42% $N_2$, 40% He, but, although the mixture was useful, it was found to cause respiratory embarrassment during moderate work at about 400 fsw (13 ATA). Accordingly, modifications were made so that at 400 fsw (13 ATA) the mixture was composed of 12% $O_2$, 12% $N_2$, and 76% He. This was satisfactory with effective pulmonary ventilation under moderate work and no narcosis.

Unfortunately, these and many of the previous studies give little or no quantitative data. Further, at 400 fsw (13 ATA) HPNS, if present, is only of a very mild nature indeed. At depths greater than 600 fsw (19 ATA) HPNS is more severe and at 800 fsw (25 ATA) and deeper (Bennett 1967; Hunter and Bennett 1974) it can become a serious hazard to the safety of divers operating from oil-drilling rigs or escaping from submarines where fast rates of compression are required so as not to court long decompression procedures.

There are good basic reasons why a narcotic may negate the effects of hydrostatic pressure (HPNS). Bennett, Papahadjopoulos, and Bangham (1967) have shown that increased pressures of nitrogen, oxygen, argon, and carbon dioxide are adsorped by a monolayer of egg-phospholipid. The resulting decrease in surface tension indicates, by application of Regular Solution Theory (Bennett, Simon, and Katz 1974), that a synonomous increase occurs in the membrane volume. Conversely, helium at increased pressures does not adsorp but causes an increase in surface tension and thus a decrease in the volume of the membrane. This is in keeping with contemporary concepts of anesthesia mechanisms (Clements and Wilson 1962; Bangham, Standish, and Miller 1965; Bennett and Hayward 1967; Sears and Fuller 1968; Bennett and Dossett 1970; Miller 1972; Miller, Paton, Smith, and Smith 1973; Bennett, Simon, and Katz 1974). If such theories are correct, then the right amounts of helium (hydrostatic pressure) and nitrogen should result in no change in surface tension or membrane volume and thus neither narcosis nor HPNS.

Pressure reversal of anesthesia has been known for sometime—since the early work with tadpoles of Johnson and Flagler (1950); it has been shown by a number of others in the

isolated nerve (Spyropoulos 1957) and in newts and mice (Miller et al. 1973).

In the present study the amount of narcotic, namely nitrogen, to be added to the helium-oxygen was calculated on the basis of the surface-tension measurements described earlier. This suggested that the correct partial pressure of nitrogen required was 5.6 ATA.

The present investigations were made, therefore, to study the protective effects of a narcotic additive such as nitrogen to men breathing oxygen-helium to depths as great as 1000 fsw (31 ATA) and with rapid rates of compression. Further, the experiments were planned to provide a direct comparison of the same subjects both with and without the narcotic additive while a quantitative investigation was made of the signs and symptoms of HPNS.

## METHODS

Four young men carried out all of the simulated dives. One (D.Y.) was one of the two clinicians who was responsible for the health and safety of the subjects while they were under pressure. He and the other two Harbor Branch subjects (C.S.; J.P.), had not previously dived greater than 200 fsw. The fourth subject (E.G.) was an experienced commercial diver of Oceaneering Inc., well used to deep oxygen-helium diving as deep as 500-600 fsw (16-19 ATA).

A 20-min test battery was evolved which would detect changes in intellectual function due to narcosis (arithmetic and visual analogy) or psychomotor performance due to HPNS (ball bearing and Purdue Pegboard), together with other measurements of tremor and electroencephalogram (EEG) activity. The subjects were tested extensively prior to the dives so that performance was stable and they were on their learning plateaux.

### TEST BATTERY

*Tests compatible with earlier work during deep dives to study HPNS* (Bennett and Towse 1971a; 1971b) and inert gas narcosis (Bennett 1966) were selected. Thus the arithmetic and visual analogy tests, as indicators of short-term memory and intellectual function, would be likely to be more sensitive to nitrogen narcosis than HPNS. Conversely, due to the hand tremors, psychomotor tests such as the ball bearing and Purdue Pegboard would likely be more sensitive to HPNS rather than nitrogen narcosis.

### PERFORMANCE TESTS

1. *Arithmetic.* The subjects were presented a sheet of 40 multiplication problems (e.g. 68 X 9 = ) and required to answer correctly as many as possible in 1 min (Bennett and Towse 1971a).

2. *Visual Analogy* (Wechsler Bellevue Digit Symbol Test). The subjects were required to relate symbols to a set of numbers from 1 to 9 given in a key. The score was the number correct in 1 min (Bennett and Towse 1971a).

3. *Ball-Bearing Test.* A subject was required to pick up ball bearings with tweezers and place them, one at a time, in a tube of almost the same diameter. Time for the test was 1 min and the score, the number of balls in the tube (Bennett and Towse 1971a).

4. *Purdue Pegboard.* In 1 minute as many pegs and washers as possible must be assembled correctly on a board. Score was the number of parts assembled, there being 4 parts to each unit (i.e. 1 peg, a flat washer, a thick washer (¼ inch), and another flat washer).

## TREMOR

1. *Postural Tremor.* A Grass SPA Tremor Transducer was attached to the middle finger of a subject by a rubber band. The output of this accelerometer was fed to a Grass 6-channel EEG and displayed. In addition it was recorded on tape with a Narco Physiotape recorder No. CDR411 for subsequent further power spectrum analysis.

2. *Intention Tremor.* An instrument constructed at the U.S. Naval Medical Research Institute, Behavioral Sciences Department, was utilized. This requires the subject to hold his finger against a transducer and exert a load of 500 g, guided by red and green lights as to whether too much load or too little is being exerted. The output of the transducer was fed to a tape recorder for subsequent frequency analysis.

## ELECTROENCEPHALOGRAM

### *Spontaneous EEG*

Electrodes were attached to the head by collodion after the scalp had been shaved and cleaned with alcohol. They were attached at the vertex and left occipital areas with a ground behind the ear. The output from the electrodes was fed to a Brush 6-channel polygraph and also to an Ampex ½-inch tape recorder. Further, the electrode output was fed to a Nihon Kohden EEG Frequency Analyzer MAF 5 and the analyzed output displayed on the polygraph recording on-line in the activity bands, delta (2-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta 1 (13-20 Hz), and beta 2 (20-30 Hz). Measurements were made for 1 min with eyes open and 1 min with eyes closed.

### *Visual evoked potentials*

Flash stimuli were applied to the darkened pressure chamber through a port by means of a Grass Photostimulator. The resulting evoked cortical potentials from 120 stimuli were averaged and displayed on a Technical Instruments CAT 1000 computer and recorded on an x-y plotter.

During the test battery, all the divers answered a questionnaire developed by Weybrew and Parker (1968) and kept a personal log of their signs and symptoms including the time of onset and site of any arthralgias.

The battery required 20 min to execute and was performed by the subjects immediately on arrival at depth and again 40 min after arrival, immediately prior to the start of decompression. A further control test was made, when possible, immediately on reaching the surface after decompression. During the trimix exposure to 1000 fsw (31 ATA), further tests were given on the change to oxygen-helium at 850 fsw (26.6 ATA) during the decompression.

## DIVE PROFILES

### *Air controls*

The subjects were compressed with air at 60 ft/min to 200 fsw (7 ATA) giving a nitrogen absolute partial pressure of 187 fsw (5.6 ATA); time at maximum depth was 30 min and decompression was by modified USN Tables. An air dive of this kind, during which the subjects completed one full test battery for comparison with predive controls, was made prior to each of the 720-fsw (23 ATA) and 1000-fsw (31 ATA) dives of this study.

*720 fsw (23 ATA).*

Two dives were made to 720 fsw with 60 min at maximum depth. In both cases compression was achieved in 17 min plus a 1-min stop at 50 fsw, 240 fsw, and 600 fsw (2.5, 8, and 19 ATA).

*Trimix*—In the first dive the subjects were compressed with trimix to give 0.5 ATA oxygen, 5.6 ATA nitrogen (25%), and 16.9 ATA helium. They were transferred, during decompression, into a chamber containing only He-$O_2$ with an $O_2$ of 0.8 ATA and decompressed over 77 hours using a modified Bühlmann et al. (1970) schedule with air from 60 fsw (2.8 ATA).

*Helium-oxygen*—In the second dive, 1 week later, the same subjects were compressed as previously to 720 fsw (23 ATA) breathing 0.5 ATA oxygen and helium throughout, with the decompression as before.

*1000 fsw (31 ATA)*

Two dives were made to 1000 fsw with 60 min at maximum depth. Compression in both cases was in 27 min plus 1-min stops at 50 fsw and 240 fsw (2.5 and 8 ATA) and 2-min stops at 600 fsw and 720 fsw (19 and 23 ATA).

*Trimix*—In this first exposure, the four subjects were compressed to give a mixture of 0.5 ATA oxygen and 5.6 ATA nitrogen (18%) and the remainder helium. They were decompressed using a modified Bühlmann et al. (1970) schedule in 97 hours. The subjects were decompressed to 850 fsw (26.6 ATA) breathing the trimix and then transferred to a larger chamber containing only helium-oxygen with the latter at 0.8 ATA. A change to air was made at 60 fsw (2.8 ATA).

*Helium-oxygen*—One week later the same subjects carried out a dive with only helium and oxygen (0.5 ATA) using the same compression and decompression profile as previously.

### PULMONARY FUNCTION TESTS

Due to the high oxygen partial pressures during the decompression, full pulmonary function tests were made and arterial blood samples taken pre- and post- the 1000-fsw dives. Measurements included forced vital capacity, functional residual capacity, total lung capacity, 1-sec forced expiratory volume, maximal mid-expiratory flow rate, $Pa_{CO_2}$, $Pa_{O_2}$.

## RESULTS

### SUBJECTIVE SIGNS AND SYMPTOMS

Subjective signs and symptoms checked by the subjects on the forms supplied and described in their personal logs were analyzed and these are summarized in Fig. 1 on a shaded histogram scale of 0 to 4 as follows:

0 - no symptoms
1 - barely perceptible or minimal
2 - definitely present but mild
3 - moderately severe
4 - very severe and incapacitating

It may be seen that there was considerably more tremor, dizziness, and nausea in the pure helium-oxygen exposure and except for the most sensitive subject, C.S., none of these were

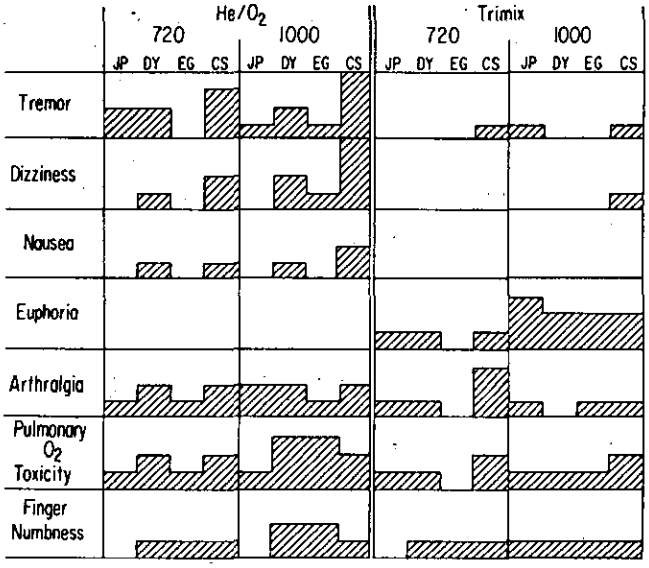


Fig. 1. Subjective experiences of the four subjects during exposure to $He\text{-}O_2$ or $He\text{-}N_2\text{-}O_2$ at 720 fsw (23 ATA) and 1000 fsw (31 ATA). At 720 fsw the $N_2$ was 25% and at 1000 fsw, 18%.

present with the trimix. On the other hand euphoria, a common symptom of compressed air narcosis, was not present with the helium-oxygen but was reported in subjects breathing trimix containing the narcotic nitrogen and in association with a sensation of "shimmering lights."

During otherwise uneventful decompressions, arthralgias and *popping* joints were slightly less with trimix as were symptoms of oxygen toxicity such as substernal pain on deep inspiration and numbness of the fingers.

The subjective signs and symptoms for trimix at 1000 fsw (31 ATA) compared with helium-oxygen exposure are similar to those at 720 fsw (23 ATA) (Fig. 1) except that the HPNS signs and symptoms were more severe at 1000 fsw (31 ATA) helium-oxygen. Two of the subjects (D.Y., C.S.) felt very nauseated and dizzy so that the dive was aborted 10 min prior to the 60 min planned. Indeed, it was only through considerable will power and cooperation of these two subjects that the dive was prolonged sufficiently to acquire the necessary data. With the 18% nitrogen in the trimix these two subjects felt no nausea and were able to tolerate the exposure comfortably. However, the other two men (J.P. and E.G.) remarked that the euphoria and narcosis from the nitrogen was subjectively higher than that experienced at 200 fsw (7 ATA) with some difference in sensations too. Time for each test seemed much prolonged. As with the 720 fsw (23 ATA) trimix, visual hallucinations of shimmering lights and halos around the chamber light bulbs were reported by J.P. and E.G. The general view was that there was less increase in efficiency with the trimix at 1000 fsw (31 ATA) compared to that noted with the 720 fsw (23 ATA), chiefly due to a more narcotic effect with the 1000 fsw (31 ATA) trimix.

Nevertheless, the divers stated that in spite of the narcosis problem, after such a fast compression they would only have been prepared to work underwater in a real situation outside a submersible chamber if the gas breathed was trimix.

When the change back to He-$O_2$ was made at 850 fsw (26.6 ATA) during the decompression from the trimix at 1000 fsw (31 ATA), the divers noted dizziness and tremors as the nitrogen came out of their bodies, leaving only helium-oxygen.

## PERFORMANCE TESTS

The comparative results for the three subjects who carried out the performance tests are shown in Figs. 2 and 3 for subject C.S., Figs. 3 and 4 for subject J.P., and Figs. 6 and 7 for subject E.G. The odd-numbered figures refer to the dives during which only helium-oxygen was breathed and the even-numbered ones refer to dives where nitrogen was present. The presence of the nitrogen partial pressure in the trimix effectively reduced the marked psychomotor decrement and tremors of the hands found with helium-oxygen alone, as shown by the ball-bearing and pegboard tests. The associated reduction in tremors is discussed in more detail later and further emphasizes the relationship between decrement in tremors and reduction in efficiency with psychomotor tests such as the ball-bearing test.

The math test in general also showed a decrement, although with more variation of the test results. Subject C.S. (Fig. 2) showed a decrement during the breathing of trimix synonomous with that produced by the same partial of nitrogen at 200 fsw (7 ATA) of compressed air. Much the same decrement also was found with the pure helium-oxygen (Fig. 3). This was probably due to the marked HPNS with nausea and dizziness in C.S., who was the most sensitive of the four divers to this syndrome. Thus, for this subject, although the nitrogen did ameliorate the psychomotor decrement of HPNS as shown by the ball-bearing and pegboard tests, there was no similar improvement in intellectual function.

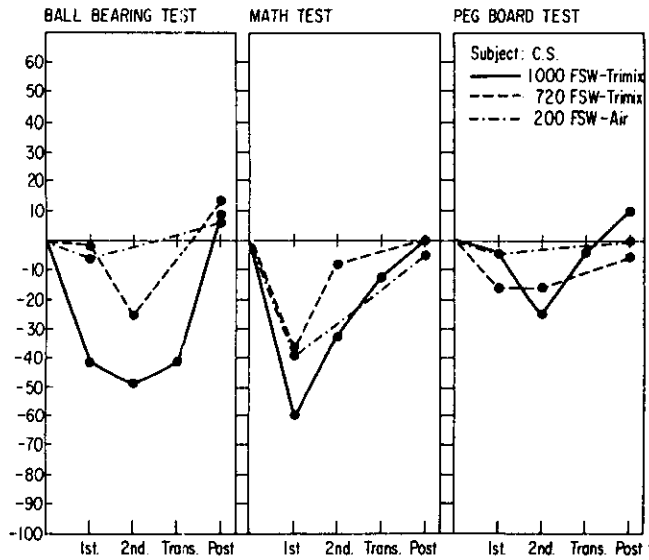


Fig. 2. Percentage changes in test performance of subject C.S. against predive controls during exposure to either air or trimix at 720 fsw (23 ATA) and 1000 fsw (31 ATA); 5.6 ATA $N_2$ was present in all experiments. The first measurements are on arrival at depth; the second, for the trimix dives only, is after 40 min at depth; and the third point, during the 1000 fsw exposure, is the result of transfer from trimix to helium-oxygen at 850 fsw. The final point is on return to the surface.

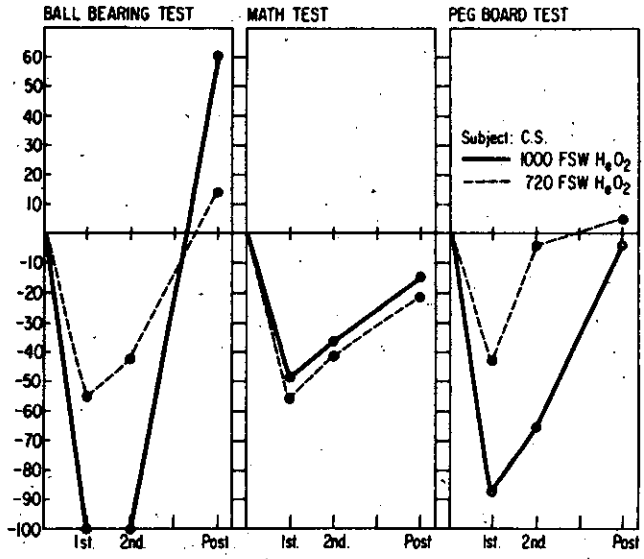


Fig. 3. Percentage change in test performance of subject C.S. during exposure to 720 fsw (23 ATA) and 1000 fsw (31 ATA) while breathing oxygen-helium. The first point is on arrival at depth, the second after 40 min at depth, and the final point on return to atmospheric pressure.

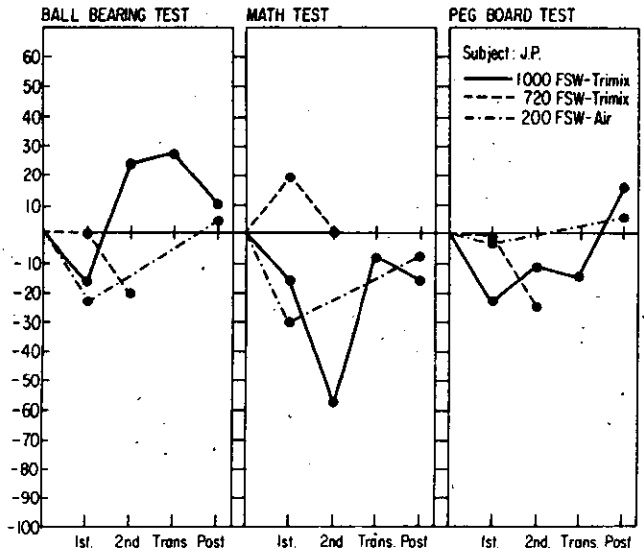


Fig. 4. Percentage change in performance as for Fig. 2 but in subject J.P.

The second subject, J.P., showed a similar result but to a lesser degree (Figs. 4 and 5). This individual showed more decrement in psychomotor performance during his exposure to helium-oxygen at 720 fsw (23 ATA) than at 1000 fsw (31 ATA), which was probably the result of apprehension to his first very deep dive beyond 200 fsw (7 ATA). With trimix, this decrement was reduced, especially in the sensitive ball-bearing test. The math test also

reflected the variability of the results of this individual. At 720 fsw (23 ATA) the test was not affected by breathing trimix but at the deeper level of 1000 fsw (31 ATA) the nitrogen presence caused a much greater decrement compared to helium-oxygen alone.

Subject E.G., an experienced commercial deep diver (Figs. 6 and 7), was little affected by the rapid helium-oxygen compression (Fig. 7). He showed only small changes in the tests, except with the most sensitive, the ball-bearing test, on arrival at depth. This is a good example, as perhaps are the results discussed previously for subject J.P., of the value of

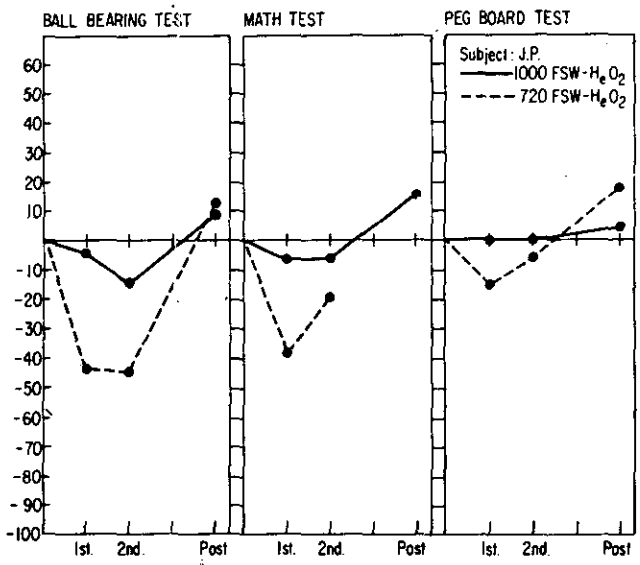


Fig. 5. Percentage change in performance as for Fig. 3 but in subject J.P.

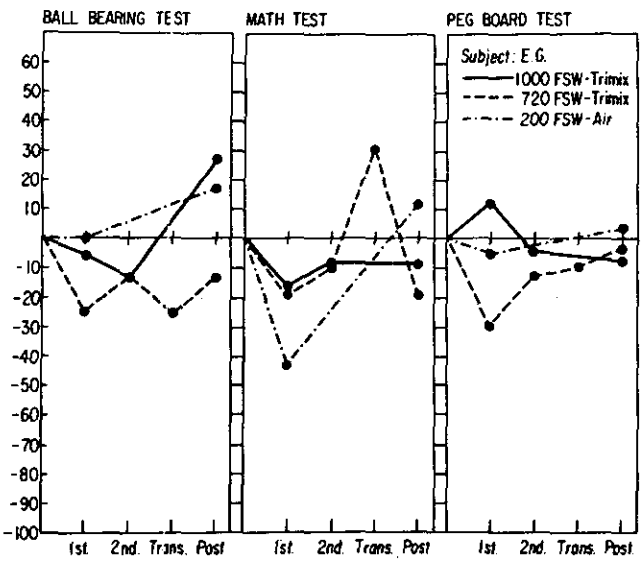


Fig. 6. Percentage change in performance as for Figs. 2 and 4 but for subject E.G.

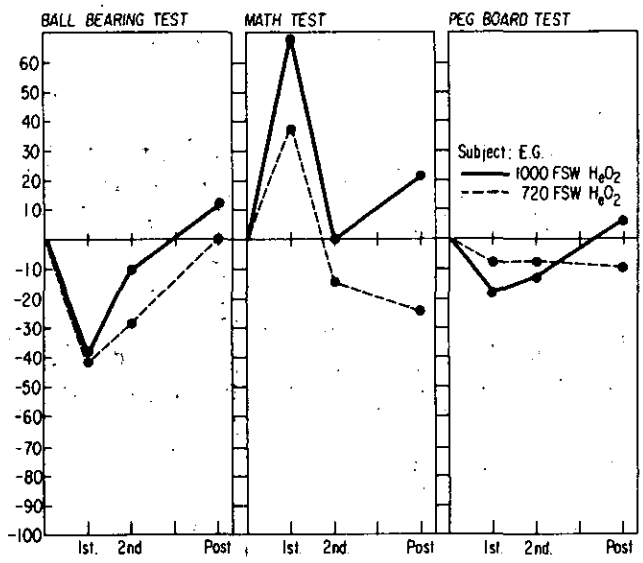


Fig. 7. Percentage change in performance as for Figs. 3 and 5 but for subject E.G.

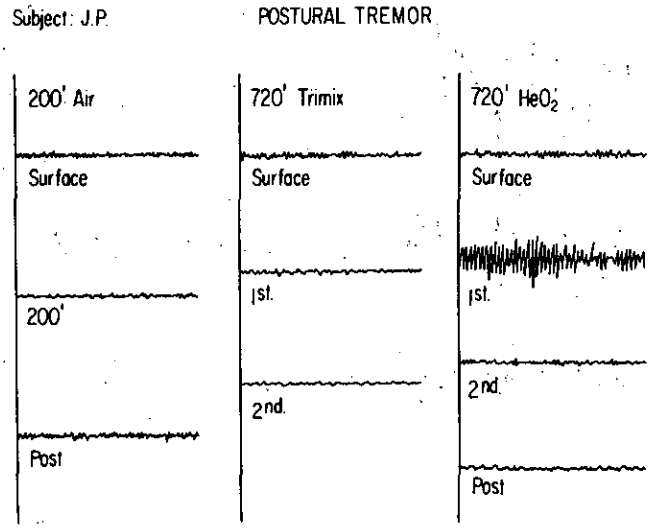


Fig. 8. Measurements of postural tremor in subject J.P. from a transducer attached to the middle finger with the hand outstretched and elbow rested. There is some suppression of normal resting tremor by air at 200 fsw. With He-$O_2$ at 720 fsw the increase in tremor is seen on arrival at depth with a return to normal during the 20 min before decompression at the end of 60 min at depth. With 25% $N_2$ (trimix) the increase in tremor is suppressed.

frequency of exposure in causing some adaptation to the signs and symptoms of HPNS.

When there was nitrogen in the breathing mixture subject E.G. showed a decrement on the math test, although this was not quite as severe as with air at 200 fsw (Fig. 6) and there was a minor improvement in the psychomotor tests. Thus, the nitrogen was of little value to

this individual and in fact served to make his performance worse by virtue of introduction of nitrogen narcosis.

The visual analogy test indicated only minor variations from controls under the various experimental conditions.

In general the performance tests and subjective sensations indicated amelioration of HPNS psychomotor decrement by the presence of nitrogen but narcosis resulting from the latter resulted in decrement of intellectual function and euphoria.

## POSTURAL TREMOR

The results of the output of the tremor transducer at 720 fsw (23 ATA) are illustrated in Fig. 8 for subject J.P., who was between the least affected (E.G.) and the most affected (C.S.) by tremors during the helium-oxygen compression. The characteristic tremor of the

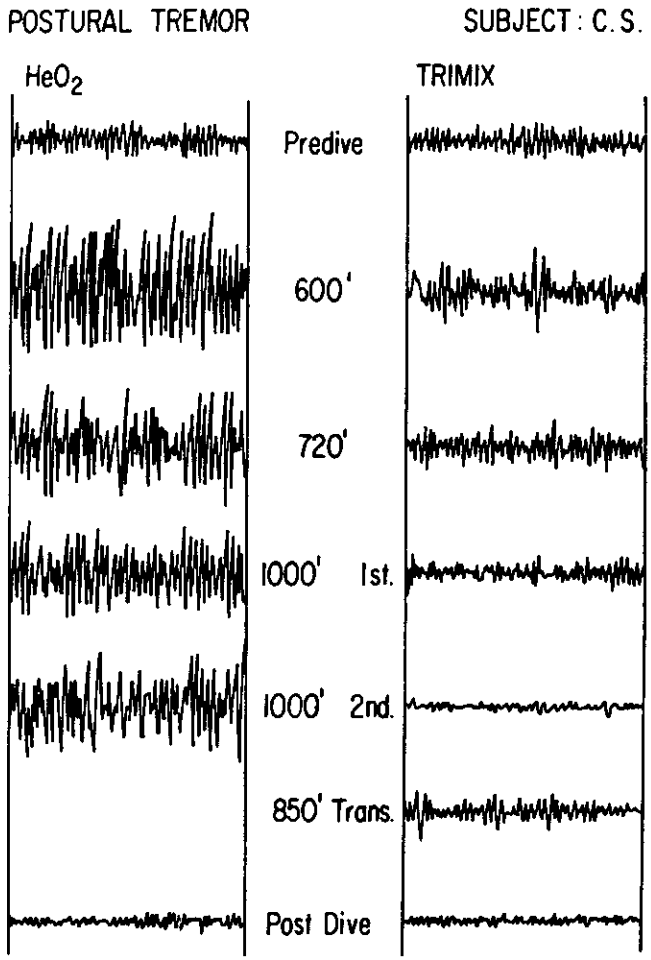


Fig. 9. Postural tremor measurements in subject C.S. during compression with oxygen-helium (He-$O_2$ or trimix [18% $N_2$]). Addition of nitrogen for the trimix was begun at 600 fsw. The comparative reduction of tremor is clearly seen. On return from trimix to oxygen-helium at 850 fsw, the tremor returns.

hands due to fast compression is illustrated as is the well-known adaptation during the 30-min break between measurements 1 and 2. Compressed air at 200 fsw (7 ATA) suppresses even the slight resting tremor and the 25% nitrogen in the trimix is very effective at suppression of the tremors elicited by compression to 720 fsw (23 ATA).

The comparative results of the changes in postural tremor during exposure to either helium-oxygen or trimix at 1000 fsw (31 ATA) are illustrated in Fig. 9 in subject C.S. With helium-oxygen there was a large increase in postural tremor as compression proceeded up to 600 fsw (19 ATA) and then was generally no worse from there to 1000 fsw (31 ATA). With trimix and the presence of 18% nitrogen the tremors were markedly suppressed, although there was still evidence of adaptation effects during periods 1 and 2 at 1000 fsw. During decompression on transfer from trimix to helium-oxygen at 850 fsw (26.6 ATA) the tremors returned. The other two subjects were not as severely affected but illustrated similar changes to varying degrees as next described for the intention tremor results.

## INTENTION TREMOR

The intention-tremor spectra results are illustrated in Fig. 10 for the same subject, J.P., described in Fig. 8. Although variation can be seen over time, the surface sample taken just before compression and the data collected at 200 fsw (7 ATA) showed suppression of the peak around 11 Hz. In the trimix dive to 720 fsw (23 ATA) little change was seen in comparing the spectra at the surface and at depth. The helium-oxygen exposure to 720 fsw (23 ATA) showed a sharp increase in both the low frequency 1-2 Hz and in the 11-Hz range.

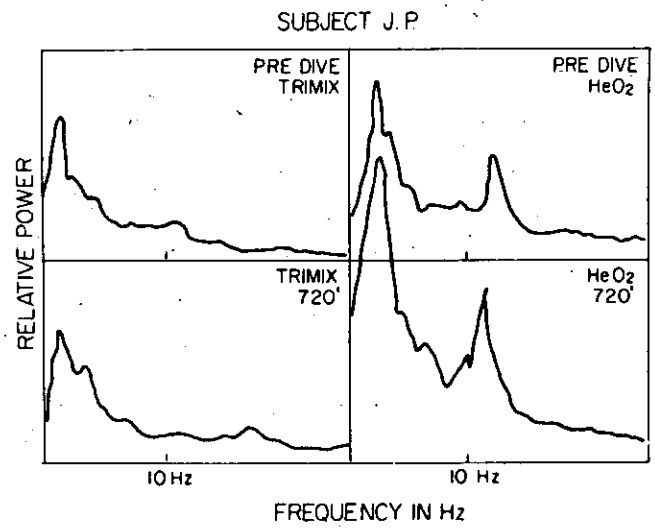


Fig. 10. Intention tremor measurements in subject J.P. predive and at 720 fsw (23 ATA) during exposure to He-$O_2$ or He-$N_2$-$O_2$ ($N_2$ = 25%).

The results of the 1000-fsw trimix and helium-oxygen dives showed results (Fig. 11) similar to the 720-fsw dives and compatible with the postural tremor results above. Subject E.G. exhibited little change on either dive. C.S.'s plots showed increases in tremor on both trimix and He-$O_2$ but a greater increase was seen with He-$O_2$. No changes were seen on subject J.P.'s spectra during the trimix dive, but increases in the 9-11 Hz area while on the He-$O_2$ dive were exhibited.

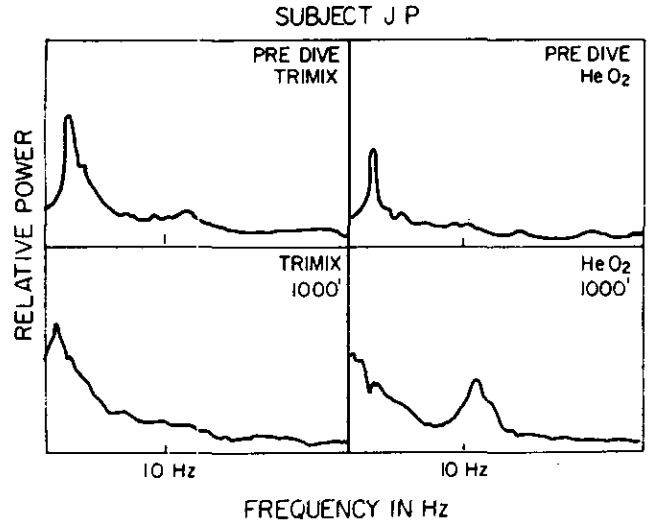


Fig. 11. Intention tremor measurements in subject J.P. predive and while breathing either trimix (18% $N_2$) or oxygen-helium at 1000 fsw.

## ELECTROENCEPHALOGRAM

The EEG analysis showed little variation from normal with either He-$O_2$ or trimix at 720 fsw (23 ATA). In general the mean activity showed a slight rise, which is in keeping with earlier studies reported in man at 450 fsw and 600 fsw (14.5 and 19 ATA) (Bennett and Towse 1971b). The two deep dives often indicated different effects, however, from the air exposure to 200 fsw (7 ATA). With delta (2-4 Hz) and theta (4-8 Hz) activity, the air dive showed a rise of some 20% with eyes open whereas there was little change with the deep dives. Theta showed a similar rise with the trimix but not with the helium-oxygen. With alpha (8-13 Hz) and beta (13-20 Hz) activities, however, there was generally a rise in activity which was not seen with air at 200 fsw (7 ATA).

Visual evoked potentials were not affected in any significant manner during exposure to these pressures and there was not sufficient difference between the compressed air and results with trimix to enable any firm statements to be made.

With eyes open, the helium-oxygen at 1000 fsw (31 ATA) resulted in an average increase of 25% in all activities. This was less pronounced with trimix for the delta (2-4 Hz) and beta (13-30 Hz) activities and only alpha (8-13 Hz) and theta (4-8 Hz) showed such a rise.

With eyes closed, there was no significant change with trimix but with helium-oxygen there was a rise in alpha and beta activity and a depression of theta.

## OXYGEN TOXICITY AND PULMONARY FUNCTION

During the first day of decompression with 0.8 ATA oxygen, the subjects experienced symptoms of oxygen toxicity such as substernal pain on deep inspiration and numbness of fingers and/or toes. However, the substernal pain was not of sufficient severity to concern

the subjects unduly. By the second day the signs and symptoms were markedly ameliorated and graudally became less or nonexistent throughout the remainder of the 4 days of decompression.

TABLE 1

Pulmonary function test data prior to and immediately after the two 1000-fsw dives

| Subject | Control FVC (L) | Post FVC (L) | % change | Control FEV (L) | Post FEV (L) | % change | Control MMEFR L/sec | Post MMEFR L/sec | % change |
|---|---|---|---|---|---|---|---|---|---|
| DY | 4.97 | 4.70 | -5.43 | 4.05 | 3.41 | -15.8 | 4.44 | 2.47 | -44.3 |
| EG | 6.95 | 6.71 | -3.45 | 4.22 | 4.91 | +16.4 | 4.04 | 4.66 | +15.4 |
| JP | 5.31 | 5.13 | -3.39 | 4.01 | 3.71 | - 7.5 | 3.69 | 2.95 | -20.1 |
| CS | 6.43 | 6.03 | -6.22 | 3.68 | 3.81 | + 3.4 | 2.90 | 4.50 | +55.2 |
| Mean | | | -4.62% | | | -0.87% | | | + 1.6% |

| Subject | Control FRC (L) | Post FRC (L) | % change | Control TLC (L) | Post TLC (L) | % change | Control A-a torr | Post A-a torr |
|---|---|---|---|---|---|---|---|---|
| DY | 3.12 | 2.78 | -10.9 | 6.13 | 5.73 | -6.53 | 20.0 | 32.0 |
| EG | 4.10 | 3.98 | -4.9 | 9.32 | 8.34 | -10.5 | 25.5 | 36.0 |
| JP | 2.90 | 2.30 | -20.7 | 6.77 | 6.34 | -6.35 | 37.5 | 44.5 |
| CS | 3.97 | 3.80 | -4.3 | 8.06 | 7.32 | -9.19 | 29.5 | 29.5 |
| Mean | | | -10.2% | | | -8.14% | 28.1 | 35.5 |

The pulmonary function data are shown in Table 1. All subjects manifested small restrictive-type defects as supported by reductions in the forced vital capacity (4.62%), functional residual capacity (10.2%), and total lung capacity (8.14%). In addition to this evidence of restrictive defects, two subjects had evidence of small airway obstruction to expiration as supported by reductions in the 1-sec forced expiratory volumes (15.8% and 7.5%) and the maximal mid-expiratory flow rates (44.3% and 20.1%). The other two subjects evidenced less obstruction to air flow than in the control in predive measurements. Subject C.S. had mild bronchitis at the time of the initial pulmonary function tests. The existence of this condition at this time might explain why he had no increase in his alveolar-arterial (A-a) oxygen gradient following the 1000-fsw (31 ATA) dives. There was a significant and meaningful increase in the A-a gradient in the other three subjects relative to their control values.

## DISCUSSION

It is clear from these results that trimix is effective in ameliorating signs and symptoms of HPNS as deep as 1000 fsw (31 ATA) although, in the present investigations, there is evidence that the inspired nitrogen partial pressure of 5.6 ATA in both trimix dives was too high and resulted in signs and symptoms of inert gas narcosis. These results are similar to those of an earlier study by Smolin et al. (1968) described in the introduction. Further, there was a significant interindividual variation in susceptibility to HPNS as has been reported during earlier studies (Bennett and Towse 1971b). Of the four subjects, two (E.G.

and J.P.) were not very sensitive to the high hydrostatic pressure and fast rates of compression with helium-oxygen and experienced only very mild HPNS signs and symptoms. These two subjects would have been capable of performing work at 1000 fsw (31 ATA) after only a surprisingly short compression compared with U.S. Navy practice and earlier deep dives summarized in the reviews by Bachrach and Bennett (1973) and Hunter and Bennett (1974). When breathing trimix, however, these two subjects appeared more sensitive to the nitrogen narcosis than the other two subjects.

Conversely, the other two men (C.S. and D.Y.) were highly sensitive to the HPNS, feeling dizzy, nauseated, and on the verge of vomiting. They were very pleased to have the ameliorating effects of the nitrogen in spite of the narcosis, especially as the compressed air narcosis was in general slightly less than that expected for compressed air at 200 fsw (7 ATA).

Recently, application of Regular Solution Theory to anesthesia mechanisms (Bennet et al. 1974) has emphasized that the *cohesive energy* of the anesthetic site $\delta a$ is equal to 4.3 $(cal/cm^3)^2$. This is much more compatible with olive oil as a model system rather than egg phospholipid. If olive oil is used as the substrate, then it can be calculated that the correct proportion of nitrogen to helium should be 1:10 if there is to be no change in volume of the substrate. On this basis, it is not surprising that nitrogen narcosis occurred when the nitrogen percentage was 18% at 1000 fsw (31 ATA) and further experiments with only 10% nitrogen are likely to be more successful.

The expected antagonism of the narcosis by hydrostatic pressure also occurred only to a minor extent of that implied in the earlier work of Zaltsman (1968). That such pressure reversal of narcosis may well be possible in man is indicated, however, in experiments by Proctor, Carey, Lee, Schaefer, and van der Ende (1972). During decompression from a 1000-fsw (31 ATA) dive, the divers breathed 3.5 atm nitrogen, 1-1.5 atm oxygen, and the remainder helium for 10 min at 600 fsw, 400 fsw, 240 fsw and 200 fsw (19, 13, 11, and 7 ATA). At 19 ATA there were no signs or symptoms of narcosis but at pressures less than that nitrogen narcosis occurred. Perhaps at 19 ATA the pressure was sufficient to antagonize the action of the narcotic nitrogen but not at the lower pressures.

The evidence of this present study is that although there was some indication of pressure antagonism of the narcosis it was very little and much higher pressures are required to negate the narcosis due to 7-ATA compressed air.

The subjective phenomena of induced tolerance to high inspired tensions of oxygen after 24 to 36 hours of exposure is surprising. However, the early symptoms of pulmonary oxygen toxicity originate from the large airways and their abatement does not necessarily imply that tolerance and a reversal of known pathological change is occurring peripherally in noninervated lung units. It also is somewhat disconcerting to see small but significant and consistent impairment in pulmonary function and alveolar-arterial oxygen gradients at a time when all the subjects reported freedom from all respiratory symptoms.

In this respect it is interesting to note that subject J.P. emphatically denied the development of respiratory symptoms at any time during the last 1000-fsw helium control dive, yet he had the largest arterial-oxygen gradient postdive (arterial $PO_2$ was the lowest at 52 mmHg). He was also the only diver who complained of postdive chest tightness. Is this further evidence of the dissociation between symptoms and what is actually going on in the lung pathologically, or does it represent interindividual variability of pathophysiologic responses that were observed in the other phenomena such as HPNS and narcosis? This merely underlines the need for more studies and for the development and use of better ways

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# THE HIGH PRESSURE NERVOUS SYNDROME DURING A SIMULATED OXYGEN–HELIUM DIVE TO 1500 FT

P. B. BENNETT AND E. J. TOWSE

*RN Physiological Laboratory, Fort Road, Alverstoke, Hants. (Great Britain)*

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Compressed air induces signs and symptoms of narcosis resulting in a decrement in mental and manual performance, EEG changes similar to anaesthesia by volatile anaesthetics and, at depths greater than 400 ft, loss of consciousness (Bennett and Elliott 1969). The inert gas helium, when substituted for the nitrogen of air, permits diving to such depths without narcosis and the limits to which it is possible to breathe helium have yet to be established. In 1965, experiments at 600 ft and 800 ft for durations of 4 h resulted in a decrement in mental efficiency and a marked tremor of the hands, arms and even whole body known as "helium tremors", which caused a deterioration in manual dexterity (Bennett 1965). Other experiments showed that, unlike nitrogen narcosis, recovery occurred in 1–2 h (Bennett 1967; Bennett and Dossett 1967) and that by using very slow compressions of some 40 ft/h, depths of 1000 ft could be attained without such problems (Overfield *et al.* 1969; Salzano *et al.* 1970).

At Marseille in June 1968, two subjects, breathing oxygen–helium, were exposed to a simulated depth of 1189 ft. However, after a 2 h compression and only 4 min at 1189 ft, the exposure was terminated due to the onset at depths greater than 1000 ft of a marked increase in theta activity (4–8 c/sec) in the EEG, helium tremors and "microsleep", which involved an imperceptible transition between brief periods of somnolence and wakefulness, with left–right disorientation and difficulty in reading instrument dials (Brauer 1968), the so called "High Pressure Nervous Syndrome" (HPNS). Earlier experiments had reported convulsions in monkeys breathing oxygen–helium at depths 35% greater than for the onset of tremors (Brauer *et al.* 1966) and it was proposed that the HPNS might possibly constitute a "Helium Barrier", preventing the extension of human deep diving beyond 1200 ft.

In a further human experiment in 1969 a simulated depth of 1000 ft was attained in 1 h. During the 3 days spent at 1000 ft, several excursions were made for 2 h to 1150 ft, using the same compression rate (Buhlmann *et al.* 1970). The many scientific measurements made established no changes of note in the EEG, no "microsleep" and only mild helium tremors. The existence of severe neurophysiological changes at only 50 ft deeper seemed unlikely when using this form of exposure.

Now Zaltsman (1968) and his colleagues noted that during compression, increases of temperature of as much as 7–15°C intensified the incidence of helium tremors and EEG changes and resulted in general convulsions in animals. Slowing the compression and thereby reducing the temperature increase, however, permitted rats and mice to reach simulated depths of over 4000 ft without convulsions (MacInnis *et al.* 1967; Dossett and Hempleman 1970). In order to probe the so-called "Helium Barrier" and to determine further the aetiology of the HPNS the present experiment was designed to expose two men to a simulated depth of 1500 ft with a dive profile involving slow compression, a temperature rise of no more than 5°C, and 3 stages of 24 h at interim depths in order to facilitate thorough physiological, psychological and medical investigation, particular emphasis being given to changes in theta activity in the EEG and the incidence of tremors and "microsleep". As it

happened, the introduction of these stages also significantly contributed to the successful attainment of 1500 ft.

## METHODS

The pressure chamber was 16 ft long by 5 ft 6 in diameter and consisted of 2 compartments, the larger and main living area having a capacity of 225 cu. ft. with a small 1 cu. ft. hand lock for the transmission of food or small equipment. Thirty-one partially or fully screened electrical connections were used to transmit the EEG and other data. The chamber was heated by electrical tapes around it and covered, except for the doors, with 50 mm of fiberglass insulation.

The chamber atmosphere was carefully monitored by means of gas chromatographs and paramagnetic and polarographic oxygen analysers and controlled by air driven impellers sucking the chamber gas through standard size soda lime canisters and silica gel to give the values shown in Table I.

A battery of psychological, neurophysiological and biochemical tests was devised and used throughout the 15.5 days of the experiment and during preliminary dives to 40, 100, 300 and 450 ft. This paper, however, is restricted primarily to the EEG findings during the very deep dive to 1500 ft. The remainder of the data are available elsewhere (Bennett 1970a, b).

### *The electroencephalogram*

During the preliminary experiments methods were perfected for attachment of EEG stick-on electrodes so that they would neither become detached nor give noise and artefact during periods of as much as 2 weeks continuous recording. Noise-free EEG records were obtained throughout the duration of the 1500 ft dive, lasting 15.5 days. Electrodes were attached at the vertex and left occipital areas with an earth behind the left ear. The hair was clipped and the scalp shaved to give a clear skin area of some 5 cm in diameter which was degreased by wiping with ethyl alcohol. Onto the clean surface was stuck a disc of 3 M brand Double Coated Plastic Medical Tape No 1522 with a hole cut in the middle. A Beckman stick-on electrode was held to the clear area of scalp while an additional disc of 3 M tape was used to secure the electrode. This had a small hole in the centre through which Aquasonic electrode jelly was squeezed under the electrode. Additional strips of surgical tape were stuck over the whole assembly and further electrode jelly was added at regular intervals throughout the experiment.

By the twelfth day of the 1500 ft dive the hair had grown to such an extent that the electrode resistance was over 5 kΩ. To reduce the possibility of "noise", the electrodes were removed, the scalp reshaved and the electrodes reattached by the subjects while in the pressure chamber.

The output of the EEG electrodes was fed through a single cable together with other physiological electrical data such as the electrocardiogram, to a Galileo E8A electroencephalograph. In addition to the EEG, on-line analyses of the EEG activities in five bands, delta (2–4 c/sec), theta (4–8 c/sec), alpha (8–13 c/sec), beta 1 (13–20 c/sec) and beta 2 (20–30 c/sec), derived from an integrated circuit Nihon Kohden EEG Frequency Analyser MAF 5, were displayed on-line with the EEG (Fig. 1). With this instrument, the original EEG signal wave form is integrated over 10 sec or 5 sec epochs with centre frequencies of 2.82, 5.65, 10.2, 16.1 and 24.5 c/sec in the bands delta, theta, alpha, beta 1 and beta 2, respectively, and displayed as relative amplitudes. The 10 sec mode was used in this experiment which permitted alternate display of the analysis of a 10 sec epoch for each subject (Fig. 1). The EEG and activity analyses were recorded continuously during compression and for fixed periods of 1 min with eyes open (Fig. 3 and 5, A to W at depth, A to I decompression) and 1 min with eyes shut (Fig. 4 and 6, A to W at depth and A to I decompression) during each application of the 1 h psycho-physiological test battery.

In analysis, 4 consecutive 10 sec epochs were

TABLE I

The environment inside the pressure chamber

| | |
|---|---|
| Oxygen | 0.45 ats. abs. |
| Carbon dioxide | less than 0.5% equivalent of 1 ats. |
| Nitrogen | less than 2.0% equivalent of 1 ats. |
| Helium | remainder |
| Relative humidity | 70–90% |
| Temperature | 30°C; on compression max. 35°C |

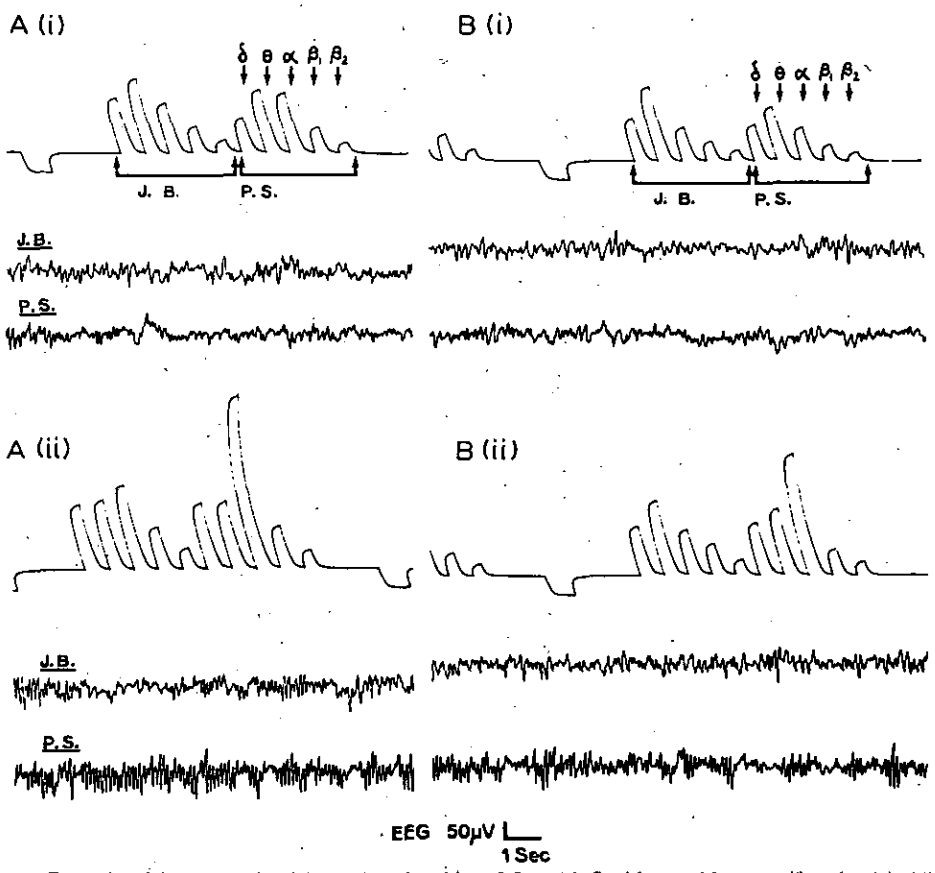


Fig. 1. Examples of the EEG and activity analyses in subjects J. B. and P. S. with eyes either open (*i*) or shut (*ii*) while breathing oxygen–helium at simulated depths of 50 ft (*A*) and 1500 ft (*B*). Frequency bands in c/sec: delta, 2–4 theta, 4–8; alpha, 8–13; beta 1, 13–20; beta 2, 20–30.

selected from each minute of the activity measurements. The datum levels and activity band peak heights for each epoch were measured to the nearest 0.1 mm and translated onto 8 hole punched tape by means of a D-Mac model 1A Digitizer and associated Westrex 1017 medium speed paper-punch. A LINC 8 computer was used to average the peak amplitudes of the individual activity bands over the 4 epochs and to calculate the percentage difference of these averaged activities from the control values obtained from the subjects at 50 ft, using the formula

$$\text{Percentage difference} = \left(\frac{E_{AV}}{C_{AV}} \times 100\right) - 100$$

where $E_{AV}$ is the average of one activity band in 4 epochs and $C_{AV}$ is the average of one activity band in 4 control epochs.

*Auditory evoked response*

Click stimuli were supplied through binaural earphones from a Devices Digitimer at 64 clicks in 1 min 36 sec (*i.e.*, a click each 1.5 sec). The resulting auditory evoked responses (AERs), after amplification by the Galileo E8A, were averaged by a Data Lab. Biomac 1000 computer. The AER potential was then displayed on a Bryans 22000 XY plotter. Percentage changes in the $N_1P_2$ spike height of the AER were measured, as this has been shown to be effective as a quantitative measurement of impairment of brain function

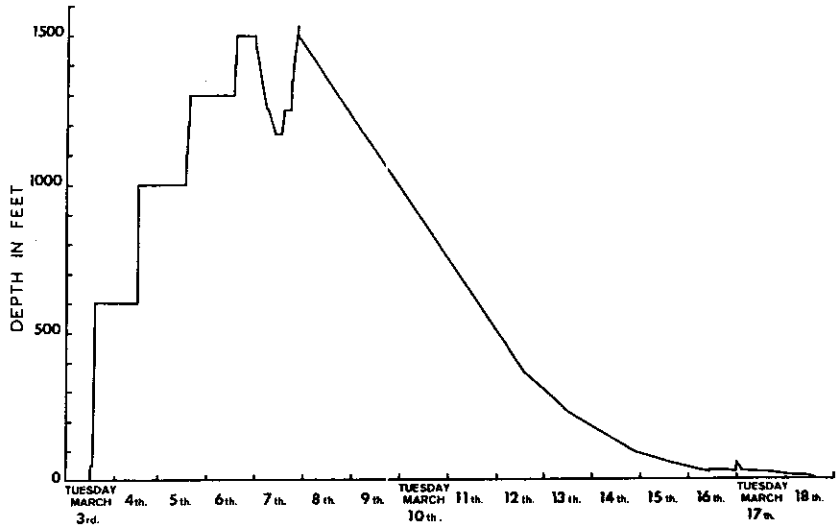


Fig. 2. The simulated dive profile during the 15 days of the experiment, showing the compression phase with the three 24 h stages, the recompression during the seventh and eighth days due to vestibular decompression sickness in P.S. and the small recompression at 30 ft due to pain in the right leg of J. B.

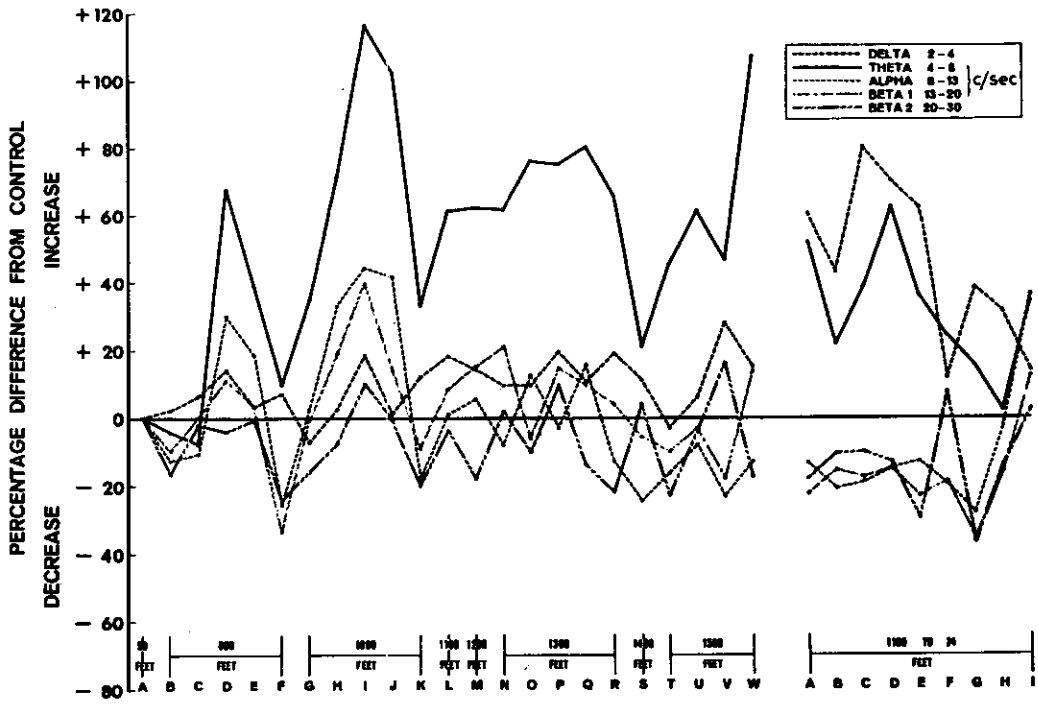


Fig. 3. Subject P. S. eyes open; analysis of percentage change in the delta, theta, alpha, beta 1 and beta 2 activities at various stable stages of the dive, as compared to control measurement at 50 ft.

due to inert gas narcosis (Bennett *et al.* 1969). All the EEG data were recorded also on a Philips Analog 7 FM instrumentation tape recorder.

## RESULTS

*The dive profile* (Fig. 2)

After control studies at 50 ft, the two subjects J.B. and P.S. were compressed at 6 min/100 ft to 600 ft where, during a total time of almost 24 h at this depth, EEG measurements were made on arrival (Fig. 3–7, B) and at 2 h (C), 4 h (D), 9.5 (E) and 19.5 h (F) after arrival. During a further 24 h at 1000 ft measurements were made on arrival (Fig. 3–7, G) and at 2 h (H), 6 h (I), 10 h (J) and 21 h (K) later. Measurements were recorded during 1 h at 1100 ft (L) and 1200 ft (M), followed by compression to 1300 feet for a further 5 recordings on arrival (Fig. 3–7, N) and at 2 h (O), 3 h (P), 8 (Q) and 18 h (R) afterwards. After an hour at 1400 ft (S) the two subjects were compressed to 1500 ft where measurements were made on arrival (Fig. 3–7, T) and at 2 h (U), 5 h (V) and 7 h (W) after.

During decompression at 40 ft/h, subject P.S. developed vestibular decompression sickness, resulting in vertigo, nausea, vomiting and photophobia. Therapeutic recompression to 1535 ft failed to produce an immediate improvement and at this depth subject J.B. reported that only by keeping himself busy and concentrating on keeping alert was he able to maintain consciousness, a condition similar to the "microsleep" reported by Brauer (1968). On decompression this impending loss of consciousness disappeared and decompression continued with a slow improvement in subject P.S. At 625 ft, during decompression (Fig. 3–7, D), subject J.B. complained of an ache in his right leg which became more severe on the 10the day of decompression but did not respond to therapeutic recompression.

*Control electroencephalograms at 50 ft*

Samples of the EEG and activity analyses of the two subjects at 50 ft were used as controls, examples of which are given in Fig. 1. Subject J.B. showed an irregular EEG with much slow wave activity and a minimal alpha blocking response whereas subject P.S. showed a well developed alpha activity responding well to opening of the eyes and with less slow activity than J.B.

*Compression electroencephalograms*

During compression the amount of fast activities in the alpha, beta 1 and beta 2 ranges, recorded with the eyes open, decreased while the theta and delta activities increased. This was seen initially during the compression from 600 ft to 1000 ft with theta activity especially, slowly increasing in amount during the 24 min compression. The subjects differed in that P.S. showed an increase of both delta and theta activity, whereas with J.B. the delta activity did not increase until compression from 1200 ft to 1300 ft.

However, the subject J.B. already had higher theta and delta activity with eyes open (Fig. 1) than P.S. and changes in these frequency bands therefore might be expected to be less. It should be noted, for example, that the total amount of theta activity in J.B. always exceeded that of P.S. throughout the experiment.

On compression from 1400 ft to 1500 ft depression of the fast activities was much more marked in both subjects and was accompanied by a reduction in theta and delta activity, suggesting an over-all reduction in the electrical activity of the central nervous system.

*Electroencephalograms at stable pressure*

On reaching stable pressure, EEG measurements during application of the test battery showed a continuation of the changes initiated by compression. Thus with eyes either open or shut on arrival at 600 ft in subject P.S., theta activity, and to a lesser extent delta activity, continued to increase for 6 h after arrival (Fig. 3 and 4). These changes were seen most readily with the eyes open. After reaching this peak, the theta activity slowly returned to control levels during an additional 12 h. Further compression to 1000 ft initiated a similar 18 h cycle but the theta activity was increased more markedly than at 600 ft.

The compressions to 1100 ft and 1200 ft initiated similar increases but, as the time spent at these depths was so short, the theta activity did not decrease. Only during the 24 h stage at 1300 ft was the necessary 18 h available for the

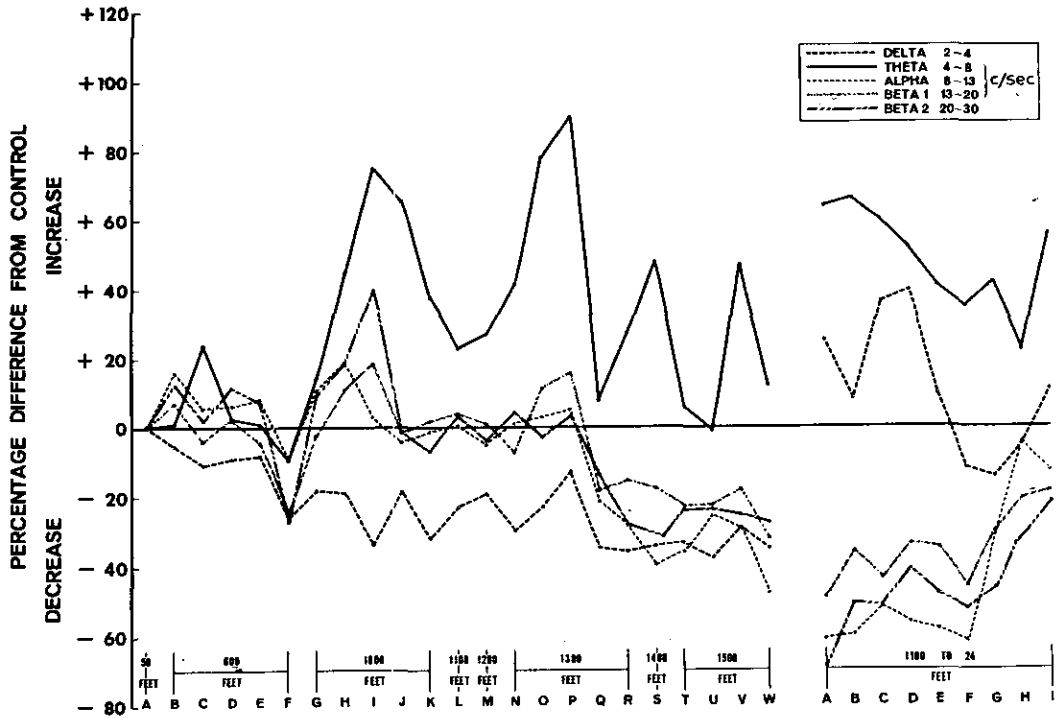


Fig. 4. Subject P. S. eyes shut; analysis of the percentage change in the spontaneous EEG activity bands as in Fig. 3.

theta activity to return to control levels (Fig. 3). At 1500 ft the same results were found but in addition, with eyes closed, between 1300 ft and 1500 ft, subject P.S. showed a reduction of all other activities by 30%. It is likely that this over-all reduction of activity is reflected also in the reduction in theta activity at these depths.

In subject J.B. marked changes in slow activity were not so clear, probably due to the large amounts of delta and theta activity seen in the controls (Fig. 4 and 5). This assessment was also made more difficult by an over-all reduction in all activities other than theta, as occurred between 1300 and 1500 ft with eyes closed in subject P.S. (Fig. 4). It should be remembered, however, that although the percentage increase in theta activity with J.B. was not nearly as great as in subject P.S. the actual theta activity was greater in the former than in the latter (Fig. 1).

*Decompression electroencephalograms*

As a result of the vestibular decompression sickness in subject P.S., few EEG measurements could be taken during the initial phase of decompression prior to 1100 ft. However, on the morning of Saturday, 7 March (Fig. 2) when pressure was held at 1170 ft to try to permit recovery, the EEG of P.S. with eyes closed showed severe reduction of all fast frequencies, including his normally predominant alpha activity. This was accompanied by a marked increase in both delta and theta activity, suggesting a serious interference with cerebral function. Recompression to 1535 ft produced no improvement in symptoms and resulted in a fall in theta activity from some 50% in excess of control levels at 1170 ft to 25% below at 1500 ft, and of delta activity from some 100% in excess of controls also to 25% below, suggesting the development of a marked depression of cerebral electrical activity. This depression had not improved greatly at 1220 ft a day later. However, at 1100 ft the theta and delta activities were again in excess of control levels, with a continued marked depression of other activities. Eyes open records were not started again until this depth due to the

manual dexterity and other changes, such as in urine electrolytes (Bennett 1970a, b), suggest physiological impairment by helium of cerebral and other functions, such changes seem restricted mostly to the compression phase. The lack of "microsleep" or helium narcosis similar to that with other inert gases at high pressures (Bennett 1970b) suggests that once adaptation has occurred man may survive for long periods at very great depths without undue functional or physiological impairment.

*The electroencephalogram*

Although changes in the EEG were noted from depths of 450 ft onward, involving depression of alpha and beta activities and increases in theta, and to a lesser extent delta activity, this was primarily made possible by a frequency analyser. The changes were almost undetectable by visual appraisal of the EEG records themselves. This is very different from the French/American dive, in which a frequency analyser was not used, but in which the records clearly showed large amounts of slow wave activity which certainly merited the concern shown in stopping the dive after only 4 min at 1189 ft.

The use of the analyser in the present dive permitted an increased understanding of these EEG changes. They are primarily a function of compression and are initiated by compression from the surface to relatively shallow depths well within the range of the Continental Shelf, as shown by similar changes at 450 and 600 ft (Bennett 1970a, b). However, it is a hopeful sign for future extension of man's diving limits that the percentage increase of theta activity between 1000 and 1500 ft was no more than that found previously at 450 ft, at which theta increases of 100% were noted (Bennett 1970b).

Conversely, the depression of the AERs and the over-all depression of cortical activity apparent in J.B. from 1000 ft and P.S. from 1300 ft suggest that some of the changes in the EEG may not be only the result of compression, and some caution is required in further extension of depth limits, which should only be made in conjunction with EEG measurements.

The increase of theta activity during compression conformed to a similar pattern on each occasion, with the increase of theta activity, once initiated, continuing over some 6 h, even when compression had stopped. At the end of the 6 h the theta activity returned over some 12 h to near control levels. Thus a full cycle of some 18–20 h was required after the initial increase of theta activity by compression, before a peak was reached and the EEG returned to normal. Brauer (1968) also found in his dive that, even during decompression, after 4 min at 1189 ft, the EEG did not return to normal until 12 h later.

In another series of experiments by Zaltsman (1968), with oxygen–helium at a compression rate of 30–60 ft/min and a partial pressure of oxygen of 1.4–2.0 ats. abs., subjects were exposed to depths between 200 and 630 ft and the results compared with exposure to nitrogen (70–360 ft) and argon (30–200 ft). The EEG changes consisted in a lessening of amplitude and increase in frequency of the alpha activity. With nitrogen and argon this was followed by intensification of fast activity on a background of suppressed alpha rhythm until the latter disappeared and was replaced by theta activity. The more pronounced changes of brain electrical activity could be correlated with behavioural effects, but no slow activity was seen with helium at 630 ft in spite of other signs such as impairment of mental efficiency, memory, motor reflexes and dimensions of writing (18–38%), similar to those reported by Bennett (1965, 1967).

In studies on dogs (Zaltsman 1968) exposed to nitrogen, argon and helium, with an oxygen partial pressure of 0.2–0.8 ats. abs., the first changes in the EEG with helium were at 500 ft. Definite differences were found between argon and nitrogen on the one hand and helium on the other. With inert gas narcosis due to the former gases there were 3 stages. First, depression of cortical activity; second, dominance of subcortical theta activity, and third, at 35–40 ats., generalized delta activity. These changes were regarded as due to a selective action on the thalamus and brain-stem and agree with earlier EEG work on humans exposed to 300 ft in air (Bennett and Glass 1961) and with comparative studies on the brain-stem and cortex of cats exposed to high pressures of inert gases (Bennett 1964). With helium, however, Zaltsman (1968) reported an initial slight increase in frequency in the non-specific structures of the brain-stem

and thalamus and later in the subcortical regions and sporadically in the cortex. The striate system remained activated while elsewhere the slow activity became generalized.

The EEG measurements made during the present experiments support those reported by Zaltsman (1968). Thus, in the 450 ft preliminary experiment there was an increase in alpha and fast beta activities associated with some theta activity. This was also seen at 600 ft in the present study. However, these faster activities were then depressed as part of cortical depression, as was shown also by the AER results. That the cortical depression was not an artefact due to electrode failure is supported by fast activities not being depressed while the eyes were open (P.S.) but being depressed with eyes closed. Unlike Zaltsman's (1968) results, the behavioural changes only reflected motor impairment due to the helium tremors and there was no decrement in mental performance. However, this was due probably to the very fast rate of compression in the Russian experiments compared with the much slower rate of the present 1500 ft experiment. In the earlier studies by Bennett (1965, 1967), using faster rates of compression, mental impairment did occur.

In connection with the marked EEG changes associated with the vestibular lesion in P.S. during the initial stage of decompression, it is pertinent to consider the EEG study of one hundred and seven caisson workers by Roth and Rozsahegyi (1966). In twelve subjects with no decompression sickness there was no significant change of EEG as a result of caisson work. However, of six men who suffered the labyrinthine form of decompression sickness, 50% showed abnormal EEG tracings, which compared with 66.7% of fifty-seven subjects who suffered from a central nervous system form of decompression sickness. Although the numbers of labyrinthine cases are too small to permit firm conclusions, it is relevant also that Engel *et al.* (1944) reported slowing of the alpha rhythm and increased slow wave activity in altitude-induced decompression sickness. Such changes were manifest in the eyes closed record of P.S. during his labyrinthine syndrome and in J.B. during test period D of the decompression at 625 ft (Fig. 6), when he first complained of an ache in the right leg which later developed into decompression sickness. Post-decompression EEGs were, however, normal and no permanent damage resulted from the present experiment.

SUMMARY

Previous simulated very deep diving experiments in which subjects have been exposed to high pressures of oxygen and helium have led to the suggestion of a "Helium Barrier" at 1200 ft due to the presence of a High Pressure Nervous Syndrome (HPNS), characterized by helium tremors, a marked increase in theta (4–8 c/sec) activity and "microsleep" involving periods of somnolence.

In the present 15 day experiment two subjects were compressed to 1500 ft in an oxygen–helium environment, where they spent 10 h. During the compression, 24 h were spent at 600, 1000 and 1300 ft. and 1 h at 1100, 1200 and 1400 ft. A thorough study was made of any physiological, psychological or medical changes, with particular note being made of changes in the EEG frequencies and auditory evoked response in order to determine the aetiology of the HPNS.

During each compression phase the theta activity markedly increased while the faster alpha, beta 1 and beta 2 activities decreased. These shifts continued for 6 h, even after compression had stopped, and during a further 12 h returned to much lower values. Auditory evoked potentials showed progressive depression at 1500 ft. These changes were accompanied by "helium tremors" or trembling of the hands and, in one phase of the experiment in one of the subjects, evidence of "microsleep".

It is concluded that the HPNS exists but that it may be ameliorated by slow compression, with stages of at least 24 h at interim depths to permit adaptation.

RESUME

SYNDROME NERVEUX D'HYPERPRESSION

Des expériences antérieures de simulation de plongées en grande profondeur au cours desquelles les sujets ont été exposés à de hautes pressions d'oxygène et d'hélium, nous ont conduits à l'hypothèse d'une barrière hélium à 1200 pieds, en raison de la présence d'un syndrome

nerveux d'hyperpression (SNHP), caractérisé par des tremblements, une augmentation massive de l'activité thêta (4 à 8 c/sec) et des séquences de "micro-sommeil" comportant des périodes de somnolence.

Au cours d'une expérience actuelle de 15 jours, deux sujets ont été amenés à une pression de 1500 pieds dans un environnement oxygène–hélium dans lequel ils ont passé 10 h. Pendant la compression ils ont passé 24 h à 600, 1000 et 1300 pieds, et 1 h à 1100, 1200 et 1400 pieds. Une étude soigneuse a été faite de toute modification physiologique, psychologique ou médicale, tenant tout particulièrement compte des changements de fréquences EEG et des réponses évoquées auditives, afin de déterminer l'étiologie du SNHP.

Au cours de chaque phase de compression, l'activité thêta augmente de façon marquée alors que les activités plus rapides alpha, bêta 1 et bêta 2 diminuent. Ces variations se poursuivent pendant 6 h, même après que la compression ait été arrêtée, puis, au cours des 12 h consécutives, reviennent à des valeurs nettement moindres. Les potentiels évoqués auditifs montrent une dépression progressive à 1500 pieds. Ces modifications s'accompagnent par les "tremblements à l'hélium" ou tremblements des mains, et, chez un sujet à une phase de l'expérience, de "micro-sommeil".

Les auteurs concluent que le SNHP existe réellement, mais qu'il peut être amélioré par une compression lente, avec des arrêts d'au moins 24 h à des profondeurs intermédiaires pour permettre l'adaptation.

Grateful appreciation is extended to Mr. J. Bevan and Mr. P. Sharphouse, the subjects of this pioneering exposure to 1500 ft, to Mr. A. N. Dossett and Miss B. Andrews for their technical assistance and to the pressure chamber control teams under the direction of Mr. J. Eaton and the Medical Safety Officers under the direction of Surgeon Commander E. E. P. Barnard, RN, without whom it would not have been possible to carry out the long and complex saturation diving experiment described in this paper.

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# SOCIÉTÉ D'ÉLECTROENCÉPHALOGRAPHIE ET DE NEUROPHYSIOLOGIE CLINIQUE DE LANGUE FRANÇAISE

*Séance du 5 mars 1969*

## Syndrome neurologique et électrographique des hautes pressions *,

par MM. **R. W. Brauer, S. Dimov, X.** et **P. Fructus, A. Gosset** et **R. Naquet**
(Marseille).

Dans le domaine *physiologique*, la plongée profonde aux mélanges gazeux jusqu'à 240 m ne pose plus de sérieux problèmes. Il n'en est pas de même des incursions à des profondeurs, et donc à des pressions, plus importantes, incursions que nous appellerons « plongées profondes ou à hautes pressions ».

Six expériences de plongées en caisson ont été réalisées entre le 24 mars et le 27 juin 1968, expériences au cours desquelles chaque fois deux plongeurs ont fait des descentes correspondant à des valeurs s'échelonnant entre 270 et 365 m ; la durée de la descente a en général varié entre 110 et 120 minutes. Au cours de chacune de ces expériences, des E.E.G. étaient enregistrés simultanément sur les deux plongeurs. Le mélange gazeux utilisé comprenait de l'oxygène et de l'hélium.

Dans nos conditions expérimentales, les plongées aux grandes profondeurs ont entraîné des signes nerveux et des modifications de l'*E.E.G.*

*Du point de vue neurologique*, apparaît aux environs de 21 ATA, un tremblement statique d'attitude des extrémités qui peut parfois persister dans l'acte. A partir de 33 ATA, apparaissent des troubles cinétiques (gestes saccadés, dysmétrie). Une baisse du niveau de vigilance s'installe en général à partir de 30 ATA et est parfois précédée par l'apparition de bâillements. Jusqu'à 35 ATA, elle est facilement vaincue par des stimuli extérieurs, la compréhension d'ordres simples est immédiate. A partir de 36 ATA, les sujets se désintéressent de plus en plus du monde extérieur, leur compréhension des ordres est ralentie, leur facies figé, la somnolence devient continue, sans s'approfondir, dès que le sujet est laissé quelques secondes au repos.

* *Ce travail a été réalisé en collaboration par : le Centre Expérimental Hyperbare de Marseille ; Wrightsville Marine Bio-Medical Laboratory (Wilmington) ; le Département de Neurophysiologie appliquée de l'Institut de Neurophysiologie et de Psychophysiologie du C.N.R.S. Marseille, et subventionné en partie par la Direction des Recherches et Moyens d'Essais (convention 68 34 501 00 480 75 01).*

*Du point de vue électroencéphalographique,* des anomalies peuvent apparaître dès 25 ATA ; elles sont de trois types : apparition d'une activité thêta survenant en bouffées, mêlée à l'activité alpha et occupant le territoire temporo-occipital ; apparition d'ondes thêta en bouffées à 6 c/s occupant les régions antérieures et moyennes des deux hémisphères ; transformation du tracé de veille en un tracé de sommeil de stade I et éventuellement II ; toutes ces activités réagissent parfaitement à l'ouverture des yeux et le tracé redevient analogue à un tracé de veille dès que l'on fait faire un travail dirigé aux plongeurs. Entre 35 et 36,5 ATA, les ondes thêta temporo-occipitales et rolando-vertex ne sont plus bloquées par l'ouverture des yeux ou par un travail imposé. Dès que le sujet est au repos, apparaît instantanément une activité de sommeil.

A la décompression, le tremblement disparaît rapidement, la somnolence domine pendant les premières heures et les sujets la perçoivent davantage. Les anomalies E.E.G. focalisées disparaissent entre 25 et 23 ATA.

Les causes de ces modifications neurologiques et électroencéphalographiques sont envisagées et la pathogénie en est discutée.

# UNDERSEA BIOMEDICAL RESEARCH

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*Undersea Biomedical Research, Vol. 1, No. 1, March 1974*

# $N_2$, $H_2$, and $N_2O$ antagonism of high pressure neurological syndrome in mice

R. W. BRAUER, S. M. GOLDMAN, R. W. BEAVER, and M. E. SHEEHAN

*Institute of Marine Biomedical Research, 7205 Wrightsville Avenue, Wilmington, North Carolina 28401*

Brauer, R. W., S. M. Goldman, R. W. Beaver, and M. E. Sheehan. 1974. Nitrogen, hydrogen, and nitrogen-oxygen antagonism of high pressure neurological syndrome in mice. Undersea Biomed. Res. 1(1): 59-72.–The addition of $N_2$, $H_2$, or $N_2O$ to heliox atmospheres significantly raises the onset of both convulsion and tremor phases of the high pressure neurological syndrome (HPNS) in two strains of mice. The antitremor effect is only about one-half as great as the anticonvulsant effect. The potencies of the several gases in both respects are directly proportional to their relative narcotic potencies. The antiHPNS effects of $N_2O$ are as great at a compression rate of 600 atm/hr as at 40 atm/hr. Gas density is not related to the onset of HPNS effects; thus, tremor and convulsion thresholds were the same in isonarcotic atmospheres of density 18 g/l in He-$H_2$ and 63 g/l in He-$N_2$ respectively. Significant protection against HPNS can be obtained at levels of inert gas narcosis well below those equivalent to 10 atm of nitrogen.

| | | |
|---|---|---|
| convulsions | hydrogen | animal (laboratory) |
| nitrogen | HPNS | tremor |
| oxygen | narcosis | breathing mixtures |

The first recognition of pressure-induced convulsions in a mammal, the rhesus monkey (*Macaca mulatta*), also brought forth evidence suggesting that the phenomenon could be elicited at lower pressures in helium-oxygen than in hydrogen-oxygen atmospheres (Brauer et al. 1966). Three alternative views have been expressed with regard to the etiology of the high pressure neurologic syndrome (HPNS). Zaltsman (1968) interpreted changes in the EEG of heliox-exposed dogs as due to an early stage of helium narcosis. Brauer and colleagues (1966; 1971) interpreted the convulsions seen in their monkeys and mice as "possibly due to the effects of hydrostatic pressure upon the central nervous system"; they suggested that the differences they observed between helium and hydrogen atmospheres might reflect antagonism of these hydrostatic pressure effects by the postulated narcotic effects of hydrogen and went on to measure the relative narcotic potencies of helium and hydrogen (Brauer and Way 1970) in support of this thesis. Chouteau and Lambert (1971) felt that the entire phenomenon reflected merely impaired respiratory gas exchange in the dense atmospheres at high pressures and suggested that differences in gas density between helium and the lighter hydrogen should account for any differences in the development of HPNS in the two types of atmosphere. While the observation that HPNS convulsions can be observed in liquid breathing mammals (Kylstra et al. 1967) and amphibians (Miller et al. 1967) pretty well disposed of the first and third of these hypotheses as far as the basic etiology of HPNS is concerned, the basis for the difference between He and $H_2$ atmospheres could be accounted

for by either of the remaining hypotheses. To discriminate between these possibilities it seemed necessary to study the onset of HPNS in isonarcotic gas mixtures of different densities, utilizing the concept of linear additivity of narcotic effects in binary inert gas mixtures, already tested and confirmed (Brauer and Way 1970).

Concurrently, Miller and his associates (1967) embarked upon a study of the reversal of anesthesia by high pressures, further strengthening the view that high hydrostatic pressures raises the level of excitability of the central nervous system. This work culminated in the promulgation of a *critical volume hypothesis* to bring together their observations in this field (Miller et al. 1973). This line of inquiry invites quantitation of the potency of several inert gases in suppressing the convulsant effects of high pressures in the hope of further linking the several sets of observations regarding central nervous system effects of high pressures.

Finally, from a practical point of view, it had been suggested as early as 1970 (Brauer et al. 1972) that the suppression of HPNS by suitably compounded inert gas mixtures with narcotic powers intermediate between those of helium and nitrogen might provide a potent tool to permit effective diving operations at depths where HPNS would otherwise prove a limiting factor. Recent interest in submarine escape (Barnard 1971) has focused attention on the marked lowering of HPNS thresholds at very rapid compression rates, and on the desirability of evaluating the extent to which inert gas narcotics could be used to mitigate HPNS severity under conditions of rapid compression.

These three problems, then, underlie the series of experiments to be reported in the present communication.

## METHODS

### ANIMAL SUBJECTS

Two strains of mice were utilized: the noninbred CD-1 mouse—a rugged, well standardized stock used for routine work at this laboratory; and the inbred AJ strain, supplied by Jackson Memorial Laboratory and chosen because of its high degree of susceptibility to HPNS convulsions (Brauer et al. 1971). Adult female animals were used throughout. Body weight ranges were 25 to 33 g for CD-1, and 19 to 23 g for AJ mice.

### COMPRESSION PROCEDURES

To avoid possible fluctuations in HPNS susceptibility due to diurnal rhythm effects, all experiments were started between noon and 2 p.m. Mice were exposed in flat multicompartment metal trays with perforated bottoms, sides, and tops. Each compartment held 1 mouse and 10 marked animals were used for each run. Adequacy of gas circulation through this assembly in the pressure chamber was verified using a smoke generator. The experiments were so designed that a single shipment of mice provided all animals for the comparative studies covering a given inert gas additive (e.g. $N_2$), and the experiments covering each such group were completed within 1 week. All but the rapid compression rate experiments were performed in a vertical 40-cm diameter, 60-cm deep steel chamber equipped with a conical observation window, internal lighting, and recirculator-$CO_2$ scrubber system that assured rapid mixing of chamber gases and maintained $CO_2$ tension below 0.001 atm throughout. The step compression schedule was the same as described in Brauer and Way (1970), providing a compression rate of 40 atm/hr in the pressure zone where convulsions were observed. At the start of each experiment the chamber was flushed with the appropriate inert gas mixture and oxygen was added to bring $P_{O_2}$ to 0.4-0.5 atm. The

appropriate gas mixture for compression was premixed in a cascade battery and the composition of each lot verified by gas chromatography using a thermal-conductivity detector (Carle Mark 8000). The column system consisted of a 3-ft. silica gel column and a 12-ft. Linde molecular sieve in series. Peak areas were compared to those of appropriate standard samples of known composition. The gases utilized were High Purity grade, with a guaranteed purity of 99.995 for He, 99.997 for $N_2$, 99.999 for $H_2$, and 98.5 for $N_2O$. Compression was carried out by successive additions of inert gas to the chamber via a venturi inlet, assuring mixing of each volume of new gas with chamber gas in the approximate proportions of 1:5. Oxygen as required to maintain $P_{O_2}$ within the set limits (0.4-0.5 atm) was added by the same route.

In the case of helium-hydrogen mixtures, a slightly different procedure was followed. The initial compression to 10 atm was carried out using He alone. $H_2$ was then added via the venturi until the desired He-$H_2$ ration was attained (using a Heise Company precision gauge to guide the procedure) and allowing $P_{O_2}$ to drop to 0.3 atm in some cases. Make-up $O_2$ was delivered in the form of premixed He:$H_2$:$O_2$ containing 2% $O_2$ and the appropriate He-$H_2$ blend. Further compression utilized He-$H_2$ premix in the same fashion as described above. Final atmosphere-compositions in all experiments were verified by sampling at 50 atm and at the end of each experiment, and by gas chromatographic analysis. The data indicate that gas mixing times are quite short relative to the intervals between successive gas additions and that chamber inert gas composition can confidently be equated to that derived from analysis of the sample taken at the time of convulsion.

$O_2$ and $CO_2$ concentrations were monitored continuously, utilizing a paramagnetic oxygen meter (Beckman Model E2) and an infrared $CO_2$ detector (Beckman 215-A) respectively. Mean chamber temperatures were held between 30 and 33°C with transient excursions due to adiabatic heating that amounted to less than 2°C and lasted less than 3 minutes after each compression step. Experiments to be reported elsewhere indicate that convulsion and tremor thresholds in mice are not affected by temperature fluctuations between 29 and 35°C.

For the rapid compressions (600 atm/hr) a smaller horizontal chamber (15-cm diameter, 30-cm deep) was utilized to avoid excessive adiabatic heating. This allowed exposure of only four mice per run, but was otherwise equipped and controlled in the same fashion as described above.

## BIOLOGICAL ENDPOINTS

The biological endpoints of these experiments were determined visually, a single observer being responsible for all animal observations on each strain to assure uniformity throughout the series, while actual compression, and observation and recording of gauges was performed by a second experimenter. Two endpoints were noted, tremor and convulsion.

*Tremor*, a term designating change in the motor behavior of the animals, is usually first noted in face and head movements, but very swiftly becomes evident in action of the forelimbs. Typically, tremors and modification of the normally smooth movements of the mice to somewhat jerky ones reminiscent of *rachet movements* mark the onset of this phase. Pressure at the onset of tremor, designated $P_T$, can be reproduced by a given observer under similar conditions to within ±5 atm.

*Convulsion*, corresponding here to the convulsion threshold pressure ($P_C$), is the pressure at which the first generalized motor siezure of such severity as to cause loss of normal posture of the animal occurs. Score was kept on each animal individually and exposure was

*continued until all animals in a given chamber population had undergone their first convulsive seizure.*

These endpoints appear to be well reproducible. Thus, comparing a series of experiments concerning strain differences performed in 1969 by one observer, with the present series completed largely in 1970, and with a recent series involving yet another observer in 1973, the values for $P_C$ were 100, 94, 98 atm, and for $P_T$, 50, 42, 49 atm.

## DATA REDUCTION

*In the case of the CD-1 mice on the standard compression schedule, means and variance* statistics were calculated for each gas mixture. The composition giving a convulsion pressure of 115 atm was determined graphically.

Data for AJ mice, and for the CD-1 mice on the fast-compression schedule, were treated on the assumption of a linear relation between concentration of additive gas and convulsion or tremor threshold (cf. Figs. 5 to 7) to derive linear regression coefficients for $P_C$ or $P_T$ on gas composition; origin, confidence limits for the regression coefficients; and correlation coefficients.

Partial pressure of the nonheliox gas component required to produce a standard elevation in convulsion threshold (the value used to estimate relative anticonvulsant potencies for the CD-1 mice on a standard compression regime) yields values which are proportional to the slope of the corresponding $P_C$ vs. concentration curves. These were used to analyze the remainder of the data. This permits direct comparison of all results obtained.

# RESULTS

## COMPARISON OF CD-1 MICE AND AJ MICE

Based on 110 CD-1 and 46 AJ mice the convulsion thresholds under standard compression conditions ($\dot{P}$ = 40 atm/hr, T = 30-33°C, $P_{O_2}$ = 0.4-0.5 atm) are:

for CD-1 mice—94.4 ± 3.4 atm,

for AJ mice—75.4 ± 1.2 atm.

Corresponding mean tremor thresholds are:

for CD-1 mice—41.8 ± 1.2 atm,

for AJ mice—49.5 ± 1.0 atm.

## INERT GAS ADDITIVES AND HPNS IN CD-1 MICE

Since the chamber which had to be used for most of this work has a rated limit of 130 atm, it is evident that only limited data on anticonvulsant effectiveness of inert gas additives could be expected. Figures 1 to 3 show that each of the three gases tested, $H_2$, $N_2$, and $N_2O$ is capable, when present in adequate concentration, of raising the HPNS convulsion threshold. Thus, comparing the mean convulsion threshold in helium-oxygen with that in the gas mixture giving a $P_C$ 20 or more atm greater, and applying the standard $t$ test, we find:

$$P < 0.001 \text{ for } 30\% H_2, P < 0.001 \text{ for } 10\% N_2, \text{ and } P < 0.001 \text{ for } 0.3\% N_2.$$

The parameter chosen for quantitative comparison of the potencies of these gases is the partial pressure at which the expected mean convulsion threshold was raised from 94 to 115

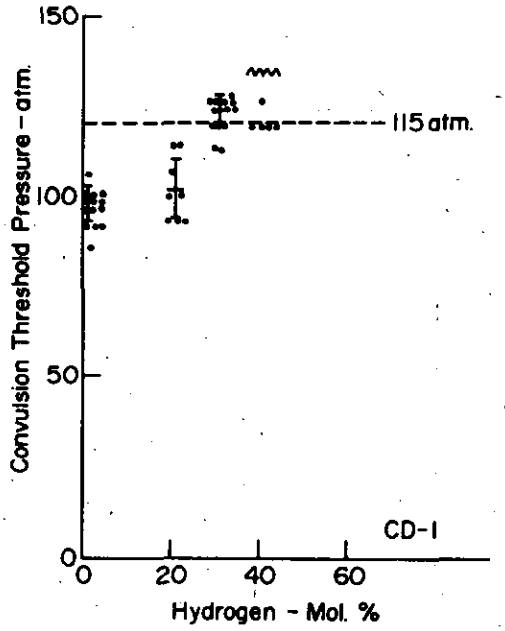


Fig. 1. Elevation of HPNS convulsion thresholds of CD-1 mice by partial substitution of hydrogen for helium in the compression atmosphere. Compression rate 40 atm/hr. (Animals indicated by ∧ failed to convulse at the highest pressure attained.)

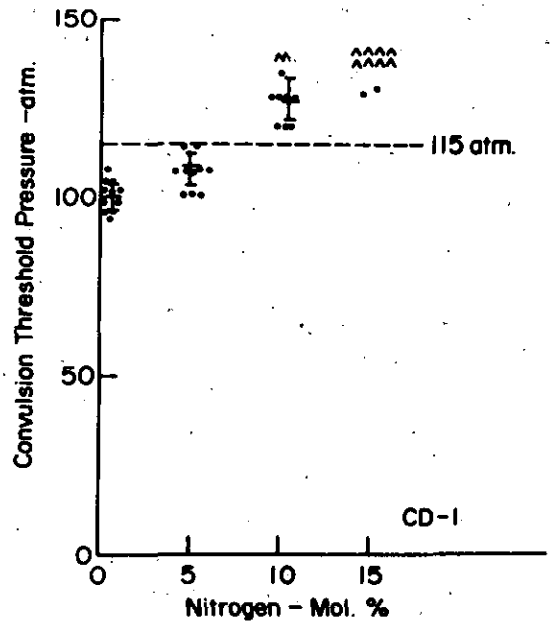


Fig. 2. Elevation of HPNS convulsion thresholds of CD-1 mice by partial substitution of nitrogen for helium in the compression atmosphere. Compression rate 40 atm/hr. (Animals indicated by ∧ failed to convulse at the highest pressure attained.)

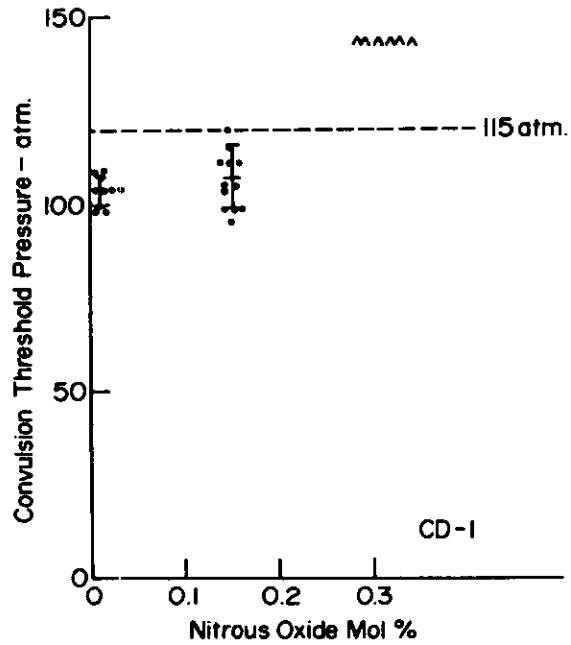


Fig. 3. Elevation of HPNS convulsion thresholds of CD-1 mice by partial substitution of nitrous oxide for helium in the compression atmosphere. Compression rate 40 atm/hr. (Animals indicated by $\wedge$ failed to convulse at the highest pressure attained.)

atm, graphically interpolated from the values of Figs. 1 to 3. The uncertainty of these derived values is estimated as approximately ±20%; more sophisticated statistical treatment of the interpolation, in the opinion of the authors, is not warranted by the data. The resulting values, and the relative potencies derived therefrom by multiplying $1/\bar{P}_x{}^{115}$ by $\bar{P}_{N_2}{}^{115}$ are shown in Columns 2 and 3 of Table 1.

TABLE 1

Estimation of relative antiHPNS convulsant potency of inert gases in CD-1 mice

| Inert gas added to heliox | Partial pressure-raising convulsion threshold to 115 atm ($\bar{P}_x{}^{115}$ atm) | Relative potency $\frac{1}{\bar{P}_x{}^{115}} \div \frac{1}{\bar{P}_{N_2}{}^{115}}$ |
|---|---|---|
| $H_2$ | 29 ± 6 | 0.3 ± 0.06 |
| $N_2$ | 10 ± 2 | 1 ± 0.2 |
| $N_2O$ | 0.25 ± 0.05 | 40 ± 8 |

## $N_2O$ EFFECT IN MICE DURING FAST COMPRESSION

A far more favorable test situation for studies of convulsion thresholds results if compression of CD-1 mice is performed rapidly with a consequent marked decrease in basic convulsion threshold. Thus, for CD-1 mice in helium-oxygen at a compression rate of 40 atm/hr,

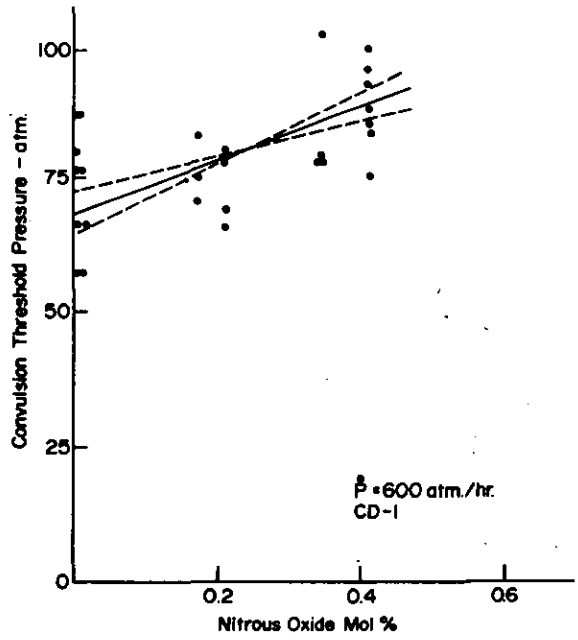


Fig. 4. Elevation of HPNS convulsion thresholds of CD-1 mice by partial substitution of nitrous oxide for helium in the compression atmosphere. Compression rate 600 atm/hr. The solid line is the least square regression line for $\bar{P}_C$ on $[N_2O]$. Dashed lines illustrate variance of regression coefficient.

the current mean convulsion threshold is 99.0 ± 2.5 atm; at a compression rate of 600 atm/hr, the corresponding value has dropped to 71 ± 4 atm. Figure 4 shows that under these circumstances, too, $N_2O$ additions produce a marked increase of the convulsion threshold, and that the relation between $N_2O$ concentration in the mixed gas and the convulsion pressure is adequately represented by an equation of the form

$$\bar{P}_C = \bar{P}_C{}^0 + a \cdot [N_2O] \tag{1}$$

where $\bar{P}_C$ = the mean convulsion pressure, $\bar{P}_C{}^0$ = the computed mean convulsion pressure in the absence of $N_2O$, $a$ = the regression coefficient, $[N_2O]$ = the concentration of the nitrous oxide in the chamber atmosphere. Using as units atmospheres for P, and volume (or mol) percent for $[N_2O]$, the regression analysis yields $\bar{P}_C{}^0 = 69$ atm, and $a = 45 \pm 9$ atm/mol. It is interesting to note that if the data for the slow compression rate (Fig. 1) are entered upon Fig. 4, they suggest a slope very similar to that calculated for the rapid compression. Thus, to increase $\bar{P}_C$ of CD-1 mice by 17 atm at the rapid compression rate of 600 atm/hr calls for a $N_2O$ concentration of about 0.33 or a partial pressure of 0.28 atm, compared to the value of 0.28 atm which, as estimated in Table 1, would produce a similar increase at a compression rate of 40 atm/hr.

## AJ MICE ON STANDARD COMPRESSION SCHEDULE

The low convulsion threshold of AJ mice in heliox promised a more satisfactory range of test values for precise quantitative evaluation of relative antiHPNS potencies. For each gas, a single batch of AJ mice of nearly the same age was used, and each series was completed

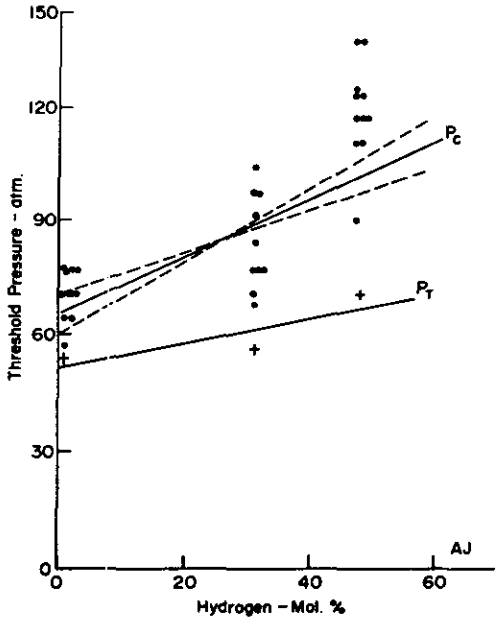


Fig. 5. Elevation of HPNS convulsion ($P_C$) and tremor ($P_T$) thresholds of AJ mice by partial substitution of hydrogen for helium in compression atmosphere. Compression rate 40 atm/hr. The solid line is the least square regression line for $P_C$ on $[H_2]$. Dashed lines indicate variance of regression coefficient.

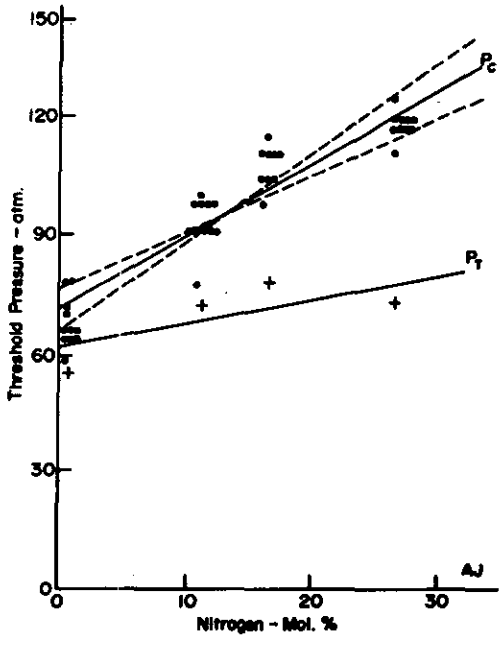


Fig. 6. Elevation of HPNS convulsion ($P_C$) and tremor ($P_T$) thresholds of AJ mice by partial substitution of helium by nitrogen in compression atmosphere. Compression rate 40 atm/hr. The solid line is the least square regression line for $P_C$ on $[N_2]$. Dashed lines indicate variance of regression coefficient.

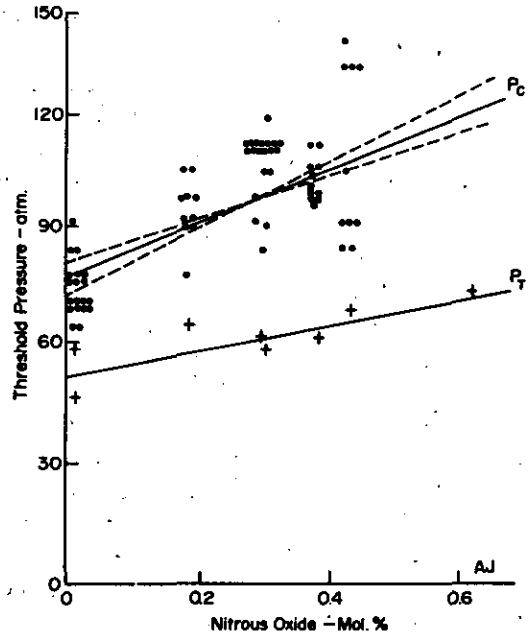


Fig. 7. Elevation of HPNS convulsion ($P_C$) and tremor ($P_T$) thresholds of AJ mice by partial substitution of helium by nitrous oxide in compression atmosphere. Compression rate 40 atm/hr. The solid line is the least square regression line for $P_C$ on $[N_2O]$. Dashed lines indicate variance of regression coefficient.

within 1 week after the first experiment of a set had been started. The results are shown in Figs. 5 to 7. Again, each of the gases tested is capable, when present in adequate concentrations, of raising the HPNS convulsion pressures. Thus, for $\bar{P}_C$ in heliox versus $\bar{P}_C$ in mixed gas, the following values result from application of the $t$ test:

$$P < 0.001 \text{ for } 47\% H_2; P < 0.001 \text{ for } 10\% N_2; 0.005 > P > 0.001 \text{ for } 0.3\% N_2O.$$

Linear regression analyses are justified by the trend of the data and the results are shown in Table 2.

TABLE 2

Estimation of relative antiHPNS potencies of inert gas in AJ mice

| Inert gas added | Convulsion threshold | | Tremor threshold | |
|---|---|---|---|---|
| | Regression coefficient $a_x^C$ atm/mol% | Relative potency $\frac{a_x^C}{a_{N_2}^C}$ | Regression coefficient $a_x^T$ atm/mol% | Relative potency $\frac{a_x^T}{a_{N_2}^C}$ |
| $H_2$ | 0.8 ± 0.2 | 0.4 ± 0.1 | 0.3 ± 0.15 | 0.17 ± 0.08 |
| $N_2$ | 1.8 ± 0.3 | 1.0 ± 0.2 | 0.7 ± 0.2 | 0.4 ± 0.1 |
| $N_2O$ | 71 ± 12 | 40 ± 7 | 33 ± 9 | 18 ± 5 |

The salient findings include *a.* confirmation of the rank order of the three gases with respect to their anticonvulsant effects, as suggested by the data for CD-1 mice (Table 1); *b.* the indication that antitremor potency for each gas is only one-half to one-third the corresponding anticonvulsant potency but that the rank order of the gases appears to be the same for both endpoints; and, finally, *c.* the demonstration for $N_2O$ that the regression coefficient is somewhat greater for the AJ mice compressed at 40 atm/hr than for the CD-1 mice compressed at 600 atm/hr (71 as against 45 atm/mol%).

## DISCUSSION

The data presented establish beyond all doubt that inert gas anesthetics raise the convulsion threshold of animals when exposed to high hydrostatic pressures. Application of the *t* test to the difference in mean convulsion thresholds for mice exposed in heliox and in helium-nitrogen, etc., mixtures establishes that in each case, once concentrations of the added gas have reached values where $P_C$ is increased by 20 atm or more relative to heliox, the probability of accidental occurrence of such differences between pairs of values is 0.005 or less. This is not the case for the change in tremor threshold where a significant effect of the added gases can only be established by utilizing statistics based upon all the data available for each gas additive. The *F* test applied to the linear regression model confirms that in all cases the regression coefficient is different from O, with $P < 0.05$. The potencies of the several gases are sufficiently distinct so that a probable error of 20% in the slopes of the regression lines—or the estimated gas composition yielding a specified $P_C$—does not seriously interfere with the estimation of relative anticonvulsant potencies. Columns 2 and 3 of Table 3 show that there is satisfactory agreement between the two strains tested, not only with respect to the rank order, but also with respect to the actual numerical values. Clearly, hydrogen is the least potent, and nitrous oxide by far the most potent HPNS anticonvulsant gas tested.

TABLE 3

Comparison of HPNS anticonvulsant and narcotic potencies of inert gases

| Inert gas added to heliox | Estimated relative anticonvulsant potency | | Relative narcotic potency (from Brauer and Way 1970) |
|---|---|---|---|
| | CD-1 Mice | AJ Mice | |
| $H_2$ | 0.3 ± 0.06 | 0.4 ± 0.1 | 0.28 |
| $N_2$ | 1.0 ± 0.2 | 1.0 ± 0.2 | 1.0 |
| $N_2O$ | 40 ± 8 | 40 ± 7 | 28 |

With regard to the question of the relation of gas density to the development of HPNS, the data of Figs. 5, 6, and 7 can be replotted showing convulsion threshold pressure as a function of gas density at that pressure for each of the mixed gas series (Fig. 8). Gas density ranged from just over 15 g/l to 63 g/l. The convulsion threshold evidently is not a function of gas density: Convulsions occur at substantially the same pressure of 120 atm, in $He\text{-}H_2$ at a density of 18 g/l, and in $He\text{-}N_2$ at a density of 63 g/l. Thus, neither high gas density, nor the excessive work of breathing, nor impaired respiratory exchange resulting therefrom, are

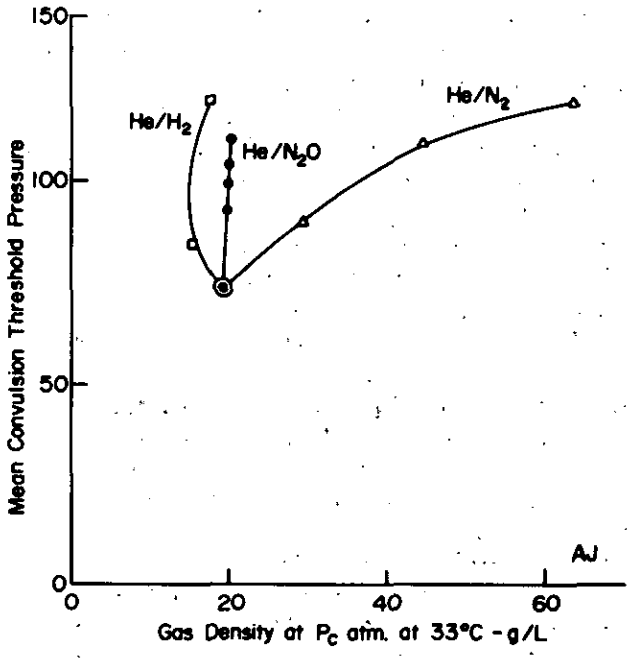


Fig. 8. Relation between density of chamber atmosphere at the time of convulsion to mean HPNS convulsion thresholds for AJ mice in helium-hydrogen, helium-nitrogen, or helium-nitrous oxide atmospheres. Data of Figs. 4-7.

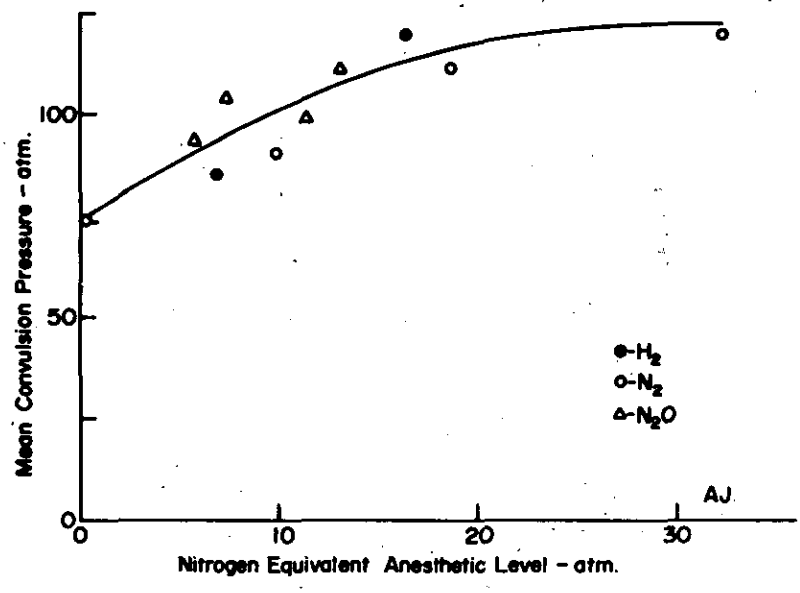


Fig. 9. Relation between calculated nitrogen-equivalent anesthetic effectiveness of chamber gas at the time of convulsion and mean HPNS convulsion thresholds for helium-hydrogen, helium-nitrogen and helium-nitrous oxide mixtures. Data from Figs. 4-7 and Brauer and Way (1970).

closely associated with development of the convulsions of the high pressure neurological syndrome. This is in line with observations concerning respiratory exchange in men breathing $He:N_2:O_2$ atmospheres of densities up to 21.5 g/l (Lambertsen *in press*).

To test for correlation of anesthetic effectiveness of the several gas mixtures at the convulsion threshold with the respective convulsion threshold pressures, the product of partial pressure of the narcotically effective component at $P_C$ and the relative narcotic potency of the admixture based upon $N_2$ as unity (Brauer and Way 1970), is used to compute narcotically equivalent nitrogen partial pressures for the several experimental conditions. A plot of these values against the corresponding convulsion threshold pressures demonstrated that the increase in $\tilde{P}_C$ is closely related to the narcotic effectiveness of the gas mixture employed (Fig. 9). Such a graph shows that powerful antiHPNS effects can be expected in mice from gas mixtures having narcotic effects which are at most equivalent to 10 atm of $N_2$, and which, as a result of pressure reversal of anesthesia at the pressures giving rise to HPNS (Miller et al. 1967), are probably a good deal less marked. Figure 9 suggests that the effectiveness of inert gas narcotics in combatting HPNS is limited and ceases to be linearly related to nonhelium inert gas partial pressure or concentration before the heliox convulsion threshold has been doubled.

To evaluate the relation between narcotic and HPNS anticonvulsant potencies of the three gases tested, Fig. 10 shows a plot of the logarithms of the relative antiHPNS potencies from Table 3 against the logarithms of the corresponding relative narcotic potencies from Brauer and Way (1970). Fig. 10 shows that the several sets of data tested (including anticonvulsant effects for the two strains and antitremor effects for the AJ mice) conform to the general relation

$$\Pi_C = K\Pi_a^{\,l} \tag{2}$$

where $\Pi_a$ and $\Pi_C$ are relative anesthetic and antiHPNS potencies, the exponent $l$ is equal to

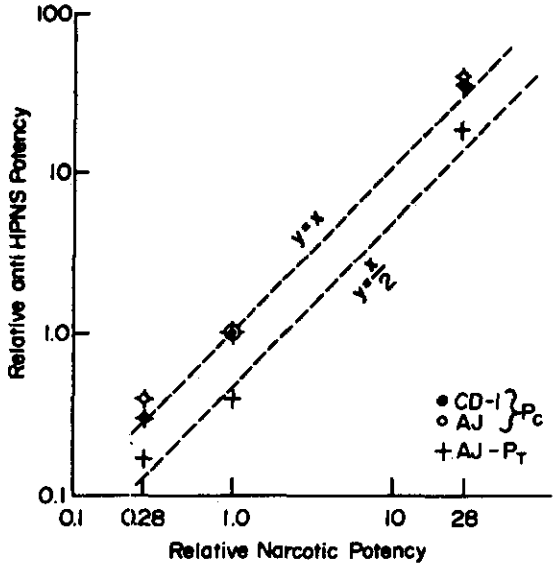


Fig. 10. Relation between relative antiHPNS convulsant tremor potencies and relative narcotic potencies of hydrogen, nitrogen, and nitrous oxide in CD-1 and AJ mice. Data from Figs. 1-3, 4-7, and Brauer and Way (1970). (log-log plot, with lines for $y = x$ and $y = x/2$ indicated.)

1.0, and the constant of proportionality $K$ is approximately twice as large for the anticonvulsant as for the antitremor potency. Thus, the antiHPNS potencies are seen to be directly proportional to the narcotic potencies of these three gases, though HPNS tremors—like many other types of tremors—appear considerably more refractory to pharmacologic treatment than HPNS convulsions.

In the above analysis helium has been treated as a physiologically inert gas. Studies comparing the narcotic potencies of helium and other metabolically inert light gases have led to the conclusion that "the narcotic power of helium is either nil, or in any event not greater than 3% that of $N_2$" (Brauer and Way 1970). With respect to the interaction with the effects of hydrostatic pressure, this conclusion seems to be in satisfactory accord with experiments comparing the effects of hydraulic and helium compression in animals capable of breathing liquid as well as gaseous media (Miller et al. 1967; Kylstra et al. 1967). Recent results obtained by Dr. Alister Macdonald at this laboratory (November, 1973) using another test system (cell division in *Tetrahymena pyriformis*) suggest that the effect of helium may be measurable, but that its magnitude under those conditions, too, is quite small, even when compared to that of hydrogen.

The rank order as well as the general numerical relations observed here are in good general agreement with corresponding figures derived by Miller and his associates for arousal by pressure from anesthesia (Miller et al. 1973), indicating that in a general way the phenomena of pressure reversal of anesthesia and of the antagonism of high pressure-induced convulsions are closely related. Nonetheless, the present authors are inclined to consider HPNS a far more complex entity than is likely to be accounted for by any simple physical theory, even one as elegant and appealing as the *critical volume* theory. In the present case this point is illustrated by the difference in antiHPNS potencies displayed by the inert gas anesthetics against tremors—where the whole effect is marginal—and against convulsions. Similar discrepancies arise in respect to age, to compression rate dependence, and to the action of drugs enhancing HPNS, and this whole subject will be elaborated upon in subsequent communications.

With respect to the application of these results to human diving practice, four points seem worthy of note. First, HPNS effects can be ameliorated to a significant degree by admixture of narcotically effective inert gas constituents with a basic heliox mixture. Second, this amelioration can be produced at high compression rates; in mice, 600 atm/hr does not seem to reduce the potency of $N_2O$ in this respect. Third, marked antiHPNS effects are produced by narcotic gas additions equivalent to less than 10 atm of $N_2$, and probably at levels of narcotic impairment considerably below the $N_2$ equivalent indicated. Finally, fourth, the present authors are less sanguine with respect to the effectiveness of such modified atmospheres against the *mild tremor* phase of HPNS than against the convulsions and (on the basis of EEG studies in monkeys) against the preconvulsive myoclonic jerks and the *coarse tremor* stage which precedes the generalized motor seizures.

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# Underwater Physiology

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# EXPERIMENTAL STUDIES ON THE HIGH PRESSURE HYPEREXCITABILITY SYNDROME IN VARIOUS MAMMALIAN SPECIES

*R. W. Brauer, R. O. Way, M. R. Jordan, and D. E. Parrish*

In 1965 we began a series of investigations to establish the relative narcotic potency of $H_2$, He, and $N_2$, a comparison that is of considerable theoretical interest. Early experiments using rhesus monkeys revealed that under pressures at which early narcotic manifestations of either He or $H_2$ might be expected, the reaction was not narcosis but, rather, severe convulsive seizures. There was a suggestion that such seizures might be less frequent on $H_2$ than on He, and that they might occur at slightly higher pressures (3). Subsequently, a similar response pattern was observed to occur in mice at somewhat higher pressures than in the monkeys. Furthermore, $H_2$ produced narcosis rather than convulsions in a high proportion (between 80 and 90%) of the strain of mice we used (7).

Since convulsions preclude meaningful quantitative evaluation of the relative narcotic potency of He and $H_2$ at high pressure, an alternative technique was developed based on the concept of linear additivity of the narcotic effects of inert gases in binary mixtures. This technique led us to use a series of He–$N_2$ and $H_2$–$N_2$ mixtures to determine their relative narcotic potency by mathematical analysis of the resulting curves (Fig. 1) (6). Helium was thus shown to exert a negligible narcotic effect, whereas $H_2$ was shown to be about one-fourth as narcotic as $N_2$ is. A correlation of these results with other available data is shown in Fig. 2, demonstrating that narcotic potency is somehow related to molecular interaction, possibly of a type involving bonding based on the induction of dipole moments in the inert gas molecule [cf. Featherstone and Muehlbaecher (10)].

The syndrome of tremors and convulsions observed in monkeys and mice will be referred to hereinafter as the *high pressure hyperexcitability syndrome* (HPH syndrome). In earlier experiments, we have observed the same general pattern of response in a number of other species of animals (Table I). Susceptibility to this syndrome appears to be greatest in the primates and to bear some rough relation to the extent to which the CNS has evolved. We have studied the syndrome more fully, to date, in the mouse and squirrel monkey than in other animals, and the following paragraphs contain a resumé of our findings.

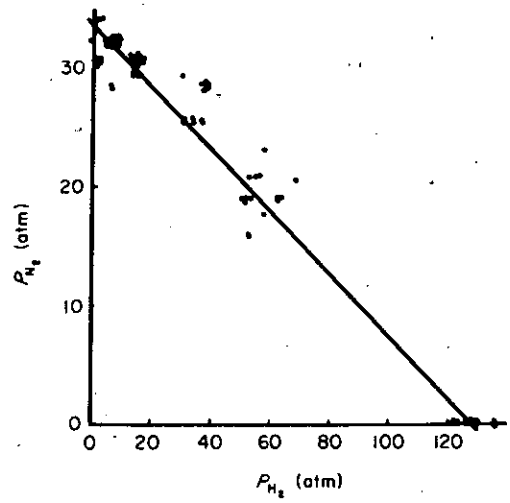


FIG. 1. Relation between the $P_{N_2}$ and $P_{H_2}$ at the point where loss of righting reflexes occurs in CD-1 mice compressed with mixtures containing these gases in various proportions, the $P_{O_2}$ being held constant at 0.5 atm.

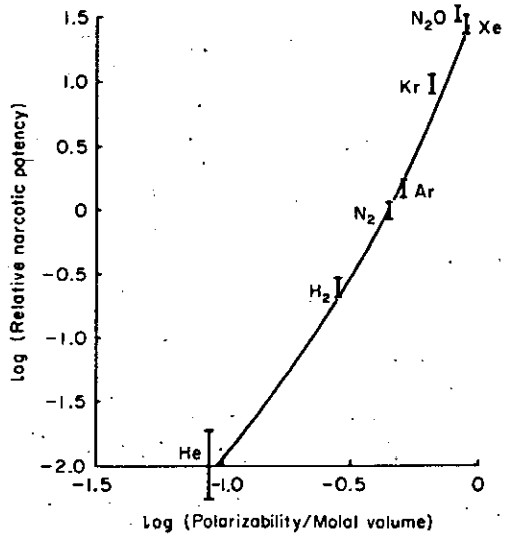


FIG. 2. The relative narcotic potency of He, $H_2$, and $N_2O$ obtained by methods used in Fig. 1, together with data of other workers using other inert gases.

TABLE I

CONVULSION PRESSURE IN SEVERAL SPECIES
($He–O_2$, 22.8 atm/hr)

| Species | Pressure at first convulsion (atm) |
|---|---|
| Birds | |
| *Serinus canarius* | 101 |
| Marsupials | |
| *Didelphis virginiana* | 81 |
| Rodents | |
| *Mus musculus* spp. | 80–110 |
| CD–1, 5 days old | 63 |
| CD–1, adult | 98 |
| *Epimys rattus* Norv. (S-D) | 110 |
| *Oryclolagus cuniculus* | 99 |
| Carnivores | |
| *Procyon lotor* | 82 |
| Primates | |
| *Saimiri sciureus* | 61 |
| *Simia rhesus* | 57 |
| *Homo sapiens* | 22 |

## Observations in Mice

We tried from the beginning to exclude from consideration, as far as it was possible, any trivial response to artifacts that inadequate environmental control might cause. The systems we used allowed precise control of $P_{O_2}$ at any desired level. The systems also assured negligible $CO_2$ tensions throughout the experiments, and permitted adequate control of chamber temperature to $\pm$ 1°C. In all the experiments described hereafter, chamber temperature was kept between 30 and 33°C, which appears to be near the middle of the comfort range for mice in He or $H_2$ environments. In monkeys, this temperature range allows maintenance of constant euthermia, even in immobilized animals. To test the possibility that, in the relatively dense atmosphere encountered at the high pressures required to produce the HPH syndrome, hypoxia due to respiratory causes is not a factor, compressions were conducted using gas mixtures containing several different $O_2$ concentrations (4).

The convulsion threshold pressure was found to be independent of $P_{O_2}$ in the range of 0.4 atm to approximately 2 atm (Fig. 3). At 2.4 atm, a significant depression of the convulsion threshold pressure was observed, suggesting synergism between the convulsant effects of $O_2$ and high pressure. Indeed, 2.4 atm of $O_2$ caused convulsions in our CD-1 mice only after 200 min of exposure, whereas 60 atm of He caused convulsions within 5 min. Synergism between the HPH syndrome and convulsant agents appears to be the rule rather than the exception.

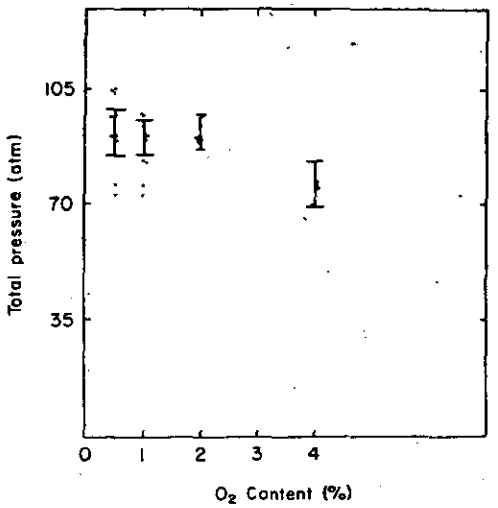


FIG. 3. Convulsion threshold pressures in CD-1 mice breathing He–$O_2$ mixtures of various $O_2$ content.

A further example of this type of effect is the depression of electroshock convulsion thresholds as a function of atmospheric pressures (Fig. 4).

The high gas density at which the HPH syndrome occurs may possibly interfere not only with $O_2$ transfer in the lung but also with $CO_2$ elimination. However, administration of an amine buffer in biologically effective doses fails to alter the mean convulsion threshold pres-

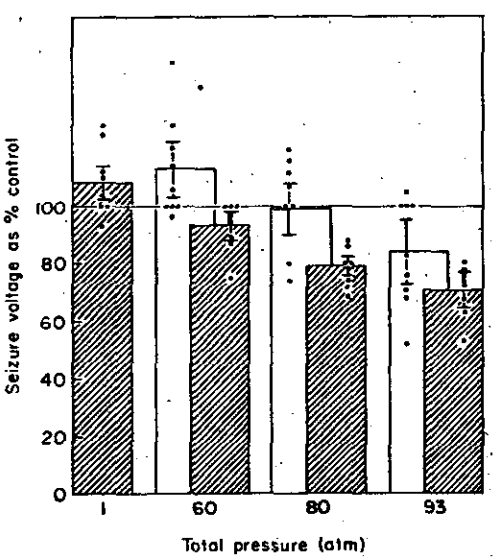


FIG. 4. Modification of electroshock convulsion threshold in CD-1 mice. ($P_{O_2}$ is 0.5–0.6 atm throughout.) (▨) He–$O_2$; (□) $H_2$–$O_2$.

TABLE II

SUSCEPTIBILITY OF MICE TO THREE CONVULSANT CONDITIONS

| | $He–O_2$ $EP_{50}$ atm | | $O_2$ $T_{50}$ min | | Audiogenic % not convulsing |
|---|---|---|---|---|---|
| BALB/CJ | 89 | BALB/CJ | 10 | BALB/CJ | 35 |
| DBA/2J | 103 | DBA/2J | 17 | DBA/2J | 0 |
| C57BL/6J | 106 | C57BL/6J | 43 | C57BL/6J | 75 |
| 129/J | 116 | 129/J | 35 | 129/J | 17.5 |
| CD–1 | 99 | CD–1 | 20 | | |
| A/J | 82 | A/J | 15 | | |

sure in mice, rendering this interpretation improbable (7). The relationship between gas density and altered respiratory mechanics in the HPH syndrome will be reviewed hereinafter in the light of data comparing the effects of different gas mixtures.

Mice of six inbred strains were compared with respect to their susceptibility to high pressure convulsions, hyperoxic convulsions, and audiogenic seizures [cf. Fuller and Sjunsen (11)]. The results, shown in Table II, suggest that these three responses are not related to one another, and, in particular, that susceptibilities to audiogenic seizures and the HPH syndrome do not correlate. Worth noting in Table II are the wide differences among the mouse strains in the animals' susceptibility to the HPH syndrome. These differences probably explain why this phenomenon did not emerge in earlier experimentation with mice compressed between 130 and 150 atm (15, 16).

Generalized intention tremors, and possibly some degree of spontaneous myoclonic seizure, occur in humans subjected to high pressures of $He–O_2$ (1), but the actual depth at which these effects are first noted depends greatly upon the compression rate. To ascertain to what extent in mice these He tremors might be related to the HPH syndrome, the animals' convulsion thresholds in a $He–O_2$ environment at $P_{O_2}$ of 0.50 atm were compared at compression rates of 40 atm/hr and 5.1 atm/hr. The mean convulsion threshold at the faster compression rate was 98 atm, while at the slower rate it was 133 atm. The onset of visible tremors was postponed from about 50 atm (at the faster rate) to near 80 atm (at the slower rate). Considering our observation that severe tremors also occur when $H_2$ is used in the breathing mixture and that convulsions are only seen at very high pressures (or not at all), our tentative conclusion is that the underlying cause of convulsive seizures may be different from the one causing the HPH syndrome when He is contained in the breathing mixture.

In the mice as in the rhesus monkeys, $H_2$ produced fewer convulsions, and the seizures occurred at a higher mean pressure than when $He–O_2$ mixtures were used. These differences might be attributed either to the physical properties of the two gas mixtures (and hence to the smaller $H_2$ resistance) or to the higher narcotic potency of $H_2$. To clarify this matter, we determined the convulsion threshold of mice compressed with graded binary inert gas mixtures—$He–H_2$, $He–N_2$, and $He–N_2O$. In each case, an increased concentration in the mixtures of the narcotically active components resulted in an elevation of the mean convulsion threshold (Fig. 5). During compression, when the narcotic component reached a certain concentration at 130

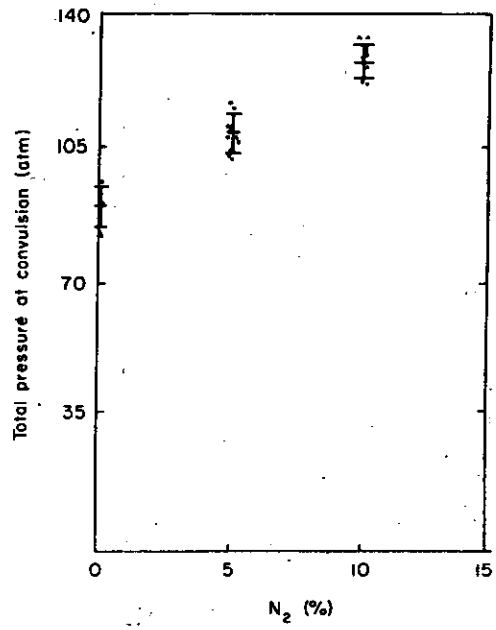


FIG. 5. Modification of convulsion thresholds in $He–O_2$ atm as function of the amount of $N_2$ added to the breathing mixture. Similar relations have been observed with $H_2$ or with $N_2O$ admixture. Convulsions are no longer observed when 12% or more of $N_2$ is added so that the maximum pressure at which convulsions are observed before the onset of narcosis is approximately 130 atm. The gas concentration which produces 50% of this maximum convulsion threshold elevation is used for the calculation of relative anticonvulsant potency of the gases shown in Table III.

atm and no convulsions occurred, the majority of the animals showed loss of righting reflexes. Higher pressures then failed to induce convulsions.

Increasing the concentration of $H_2$, $N_2$, or $N_2O$ in the $He–O_2$ mixture to a pressure midway between the pressure at which convulsions typically occurred in the $He–O_2$ mixture and the pressure at which convulsion frequency had dropped below 10% was used to calculate the

TABLE III

RELATIVE BIOLOGICAL EFFECTIVENESS OF METABOLICALLY INERT GASES

| | Index of comparison (CD-1 mice ♂) | |
|---|---|---|
| | Loss of righting reflex | Elevation of convulsion pressure (He–0.5 atm $O_2$) |
| $H_2$ | 0.27 | 0.25 |
| $N_2$ | 1.00 | 1.00 |
| $N_2O$ | 28 | 35 |

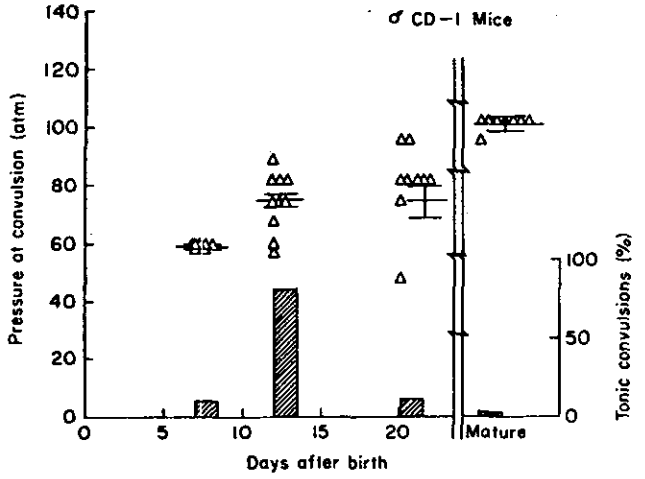


FIG. 6. Modification of convulsion thresholds with age in mice compressed with He–$O_2$ mixtures ($P_{O_2}$ = 0.4–0.5 atm). The vertical bars refer only to the tonic seizure pattern.

convulsive potency of the three gases. Table III shows the results of such calculations, using loss of righting reflexes and convulsions as the indicators of narcotic potency. Since the two sets of values agree, one may conclude that indeed the narcotic potency of a specific gas is involved in the elevation of convulsion thresholds.

One may further conclude that modification of respiratory resistance—either downward by substituting $H_2$ for He, or upward by partial substitution of $N_2$ for He—fails to affect the convulsion threshold, except insofar as the gas acts as a CNS depressant. This latter conclusion agrees with the observations of other investigators, who suggest that nonvolatile CNS depressants also can counteract certain manifestations of HPH in mice and newts (17.) High pressure convulsions in the gill-breathing newt, furthermore, suggest that such responses are caused by hydrostatic pressure, as such, or by hydrostatic pressure changes; and that the convulsions should not be attributed simply to the gaseous environment in which pressure is exerted. These observations are not restricted to the newt—we have observed similar responses in mice breathing oxygenated fluorocarbon liquid, and our findings have been confirmed and extended by others (14).

A final series of tests shows that susceptibility to HPH convulsions is markedly greater in very young mice than in adults (Fig. 6), and that susceptibility decreases after the first 3 weeks of life. There is a curious change in the pattern of the convulsions. In the adult, the seizures are characteristically clonic; a tonic phase is rarely observed, if at all. A similar pattern occurs in very young mice. In numerous tests, however, 13- to 15-day-old CD-1 mice demonstrated a strong tendency toward tonic hyperextension seizures. A similar pattern was observed in adult mice only when the inert gas mixture contained 0.15% $N_2O$ in He. These observations suggest that the seizures may originate not in the dendritic surface layer of the cortex (which is poorly developed in the young animal) but, rather, in some of the older, deeper layers of the brain. The significance of these curious changes in convulsive patterns with age remains to be determined by future investigations.

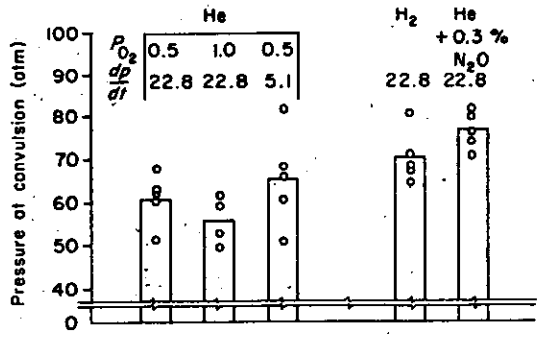


FIG. 7. Onset of convulsions in squirrel monkeys in various high pressure atmospheres as a function of $P_{O_2}$ and compression rate.

## Observations in Squirrel Monkeys

Elevating the $O_2$ pressure from 0.5 to 1.0 atm lowered the convulsion threshold of the squirrel monkey very slightly, if at all (Fig. 7). Slowing the compression rate from 22.8 to 5 atm/hr produced a slight but probably significant increase in convulsion thresholds, quite similar to the responses observed in mice (5). Substituting He for $H_2$ raised the mean convulsion thresholds in the squirrel monkeys as it did in mice. Addition of 0.3% $N_2O$ to He produced a similar effect. In general, the responses of the squirrel monkey and the mouse closely

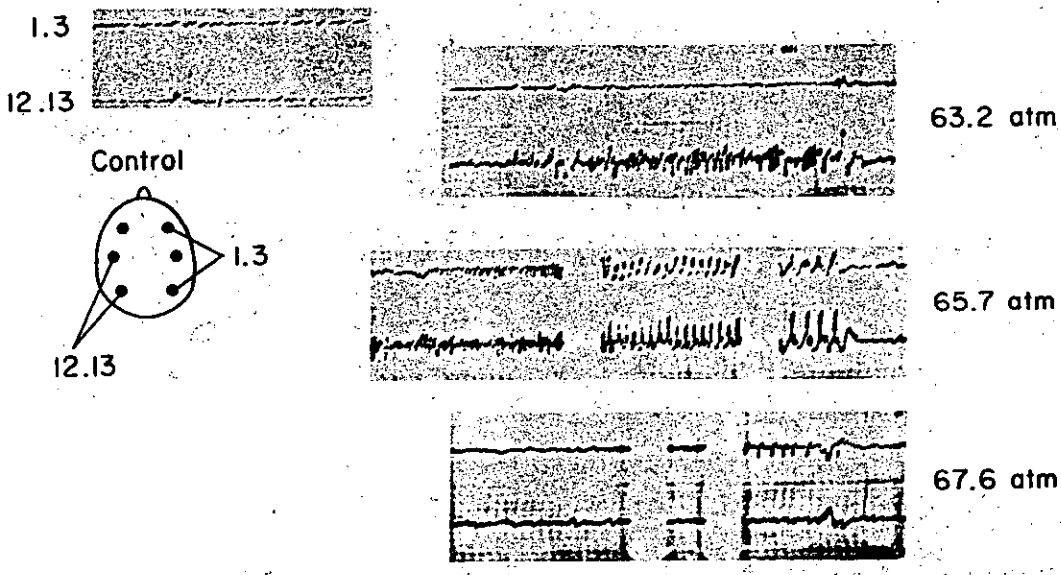


FIG. 8. EEG showing spontaneous seizures in a squirrel monkey compressed with He–$O_2$ at a $P_{O_2}$ of 0.45 atm and a compression rate of 22.8 atm/hr.

corresponded, except that the monkey's convulsive seizures occurred at a lower pressure. There appears to be a marked difference between the lower mammalian species and the primates, judging from the results shown in Table I.

We studied the EEG changes associated with the monkeys' convulsions by implanting extradural electrodes. After at least a week's recovery, the monkeys were observed either in an unrestrained state or on a specially constructed restraining couch, the latter allowing for more detailed measurements. Compression, regardless of rate, has been associated with the eventual development of spiking and electrical seizure activity in all the animals (Fig. 8). At 63.2 atm, a localized seizure occurred; at 65.7 atm, a seizure started in the left temporo-occipital region and quickly became generalized, terminating in a postictal depression. The tracing at 67.6 atm illustrates that from this point forward, some measure of seizure activity was almost continuously present at one point or another in the brain.

Characteristically, tremors preceded any marked EEG change. The first clearly recognizable change was focal spiking, which at the outset was unaccompanied by any recognizable myoclonus. As the experiment progressed, focal spiking became more marked and electrical activity from epileptogenic foci sometimes appeared. Brief myoclonic seizures occurred along with the focal spiking. This suggests that a distinction may be made between the fine tremors associated with voluntary movements that have no concomitant in the EEG (which may be similar to He tremors in man), and the coarse tremors localized in a circumscribed muscle group that are not obviously associated with voluntary movements. As pressures were raised,

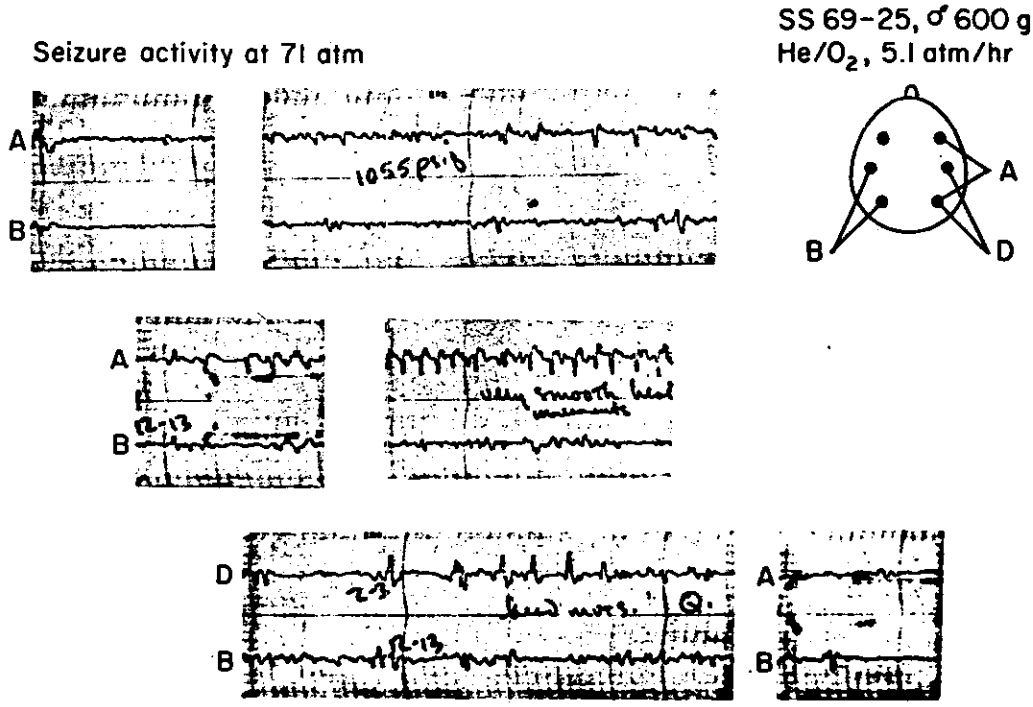


FIG. 9. EEG's of seizures associated with very limited motor activity resembling a petit mal seizure.

focal seizure activity became prolonged and more generalized. Several types of generalized seizures occurred occasionally and spontaneously at this point. The electrical seizure pattern either appeared simultaneously throughout the cortex, or by the spreading of a focal discharge (Figs. 8 and 9).

The EKG's taken through this period revealed no marked changes in heart rate or pattern, even just before generalized motor seizures began. Recovery after all but the most severe grand mal seizures was prompt. Generalized seizures were usually followed by postictal electrical pauses lasting 20–60 sec and by gradual return to a normal EEG. Once a generalized seizure began and compression continued, EEG seizure activity never subsided completely. Further occurrences of generalized seizures appeared to be dependent in part upon the degree of damage done during the first severe attack. A generalized seizure was sometimes followed by a 30-min period of relative quiescence marked by scattered focal spiking on the EEG, then by increasing hyperexcitability, and then perhaps by a buildup to another generalized seizure. If pressure was maintained at the level at which the first convulsion took place, convulsive

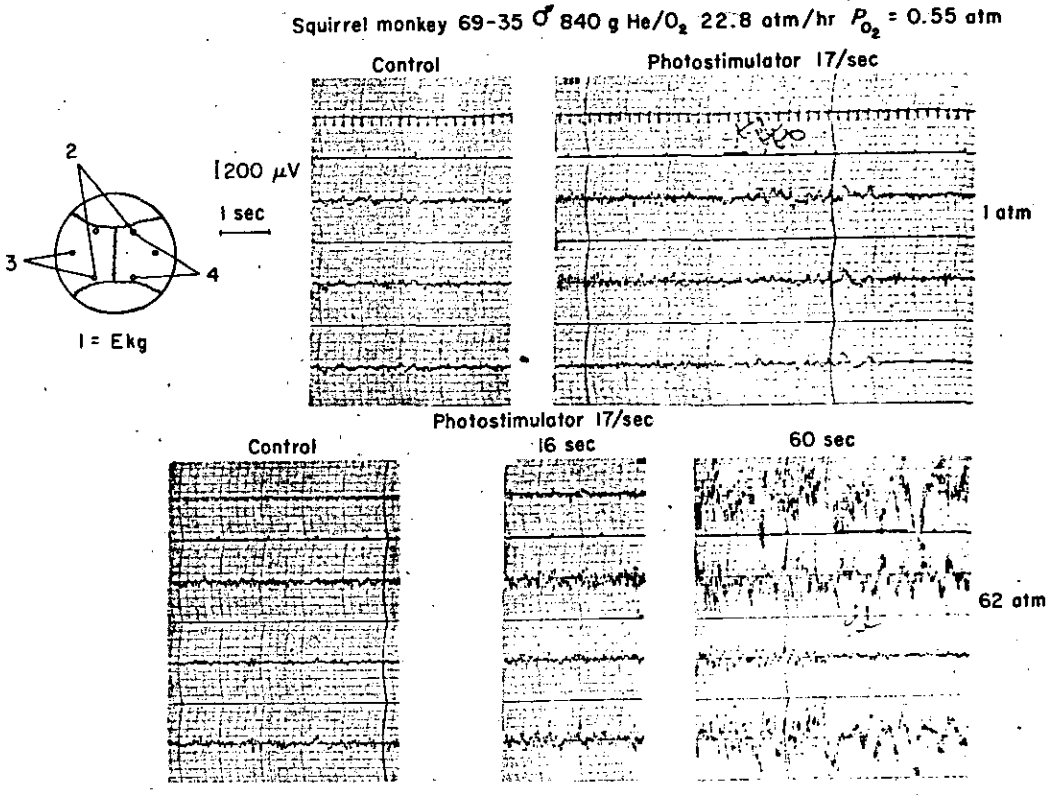


FIG. 10. Modification of the response to repetitive photostimulation as a result of compression. In the upper diagram the characteristic self-limiting response in the normal animal; in the lower tracing, marked recruitment, spiking, and eventual development of a grand mal seizure at 62 atm.

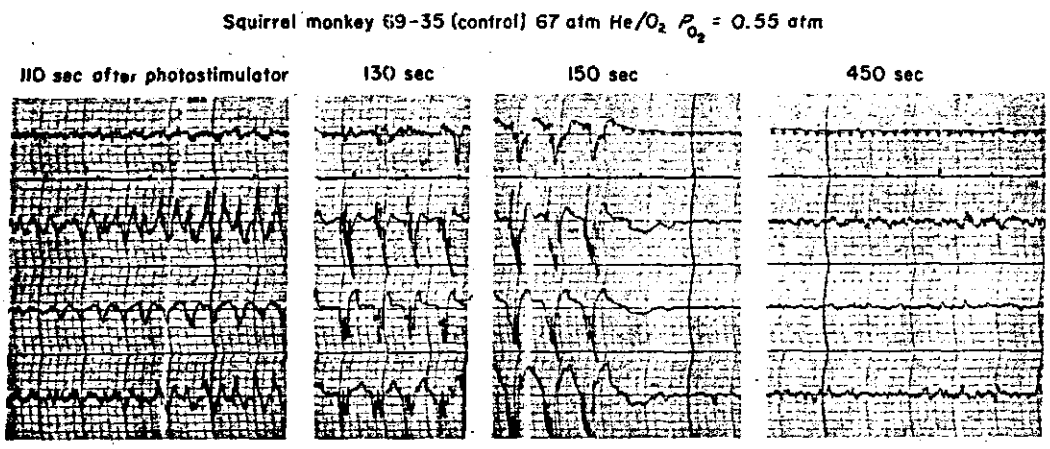


FIG. 11. Two minutes after the end of photostimulation shown in Fig. 10 there is a secondary buildup to a generalized petit mal seizure followed by a postictal period, and resumption of spiking activity 5 min later.

activity tended to subside after a few attacks; but seizures recurred as long as 12 hr after the first attack, and were accompanied by hyperexcitability a large part of the time.

While this paper was in preparation, we learned of two experiments conducted by Dr. X. Fructus and Dr. R. Naquet of Marseilles, France. In each experiment, a baboon (Papio papio) was compressed in an $He–O_2$ environment very slowly (approximately 3 atm/hr). The animals were held for 12 hr, one at a pressure of 60 atm and the other, 100 atm. The latter animal showed characteristic epileptiform EEG changes and began motor seizures at 92 atm. There then followed the pattern of quiescence and resumption of convulsive activity observed in our experimentation with squirrel monkeys. This animal died during decompression, and the preliminary analysis of the EEG and EKG suggests that death was caused by CNS damage that was not necessarily associated with the decompression sequence. The second animal was reported to have shown "alarming CNS changes" at depth, and it also died during decompression. A more complete analysis of these data is not yet available.

Experiments by Killam, Killam, and Naquet (13) suggest that generalized seizures can be induced in a given animal by repetitive photostimulation at pressures significantly below those that could reasonably be expected to provoke a spontaneous convulsion (Figs. 10 and 11). Above 50 atm, photostimulation produces an abnormal EEG pattern of numerous high voltage, high frequency discharges. If photostimulation is discontinued at this point, a few seconds of persistent self-sustained spiking activity may follow. At slightly higher pressures, recruitment and buildup of response amplitude become pronounced, and myoclonus occurs with each spike. In 30–40 sec this sequence tends to build up to a self-sustaining seizure. After the initial seizure, a brief period of near quiescence may ensue, followed, without further stimulus, by gradual recovery and then by a buildup to a second seizure, which now may be petit mal rather than grand mal.

EEG changes in squirrel monkeys exposed to high pressure $He–O_2$ environments appear in many respects to resemble those of idiopathic epilepsy. At the pressures we chose, significant changes may have occurred in the cortex. These changes may have triggered both the synchronous repetitive discharges seen in the EEG at various foci and the spread of seizure

activity. Future investigations must determine if the predominant site of the HPH syndrome is in the outer layers of the cortex, or if the responses reflect paroxysmal activity in deeper structures, such as the thalamus or hippocampus.

We have speculated very little up to this point about the biophysical mechanisms that might induce the HPH syndrome. Some suggestions regarding this aspect of the problem might be made here. There is a strong possibility, we feel, that the observed changes in CNS excitability are attributable either to the effect of hydrostatic pressure, as such, upon the membranes or upon the energy metabolism of CNS neurons; or to the magnitude of hydrostatic pressure used. Hydrostatic pressures from 50 to 150 atm are now recognized as being high enough to produce significant biological changes. Thus the Ussing frog skin preparation responds to hydrostatic pressures of 50 atm by a marked increase in membrane potential. This potential appears to be associated with increased ability of sodium ions to permeate one part of the composite membrane (8). If such changes were to occur in the CNS, they obviously could cause depolarization of neuronal membranes, thereby increasing excitability and facilitating impulse spread.

Changes have been noted in polymerization of certain fibrous proteins at 50–150 atm (12). The $O_2$–hemoglobin dissociation curve is displaced to the right at similar pressures (18), suggesting a possible, significant change in protein/small molecule interaction in this pressure range. It is far too early to single out any one of these phenomena as having particular significance in the HPH syndrome, but these examples suggest that they must have some importance. Future investigation into these relationships should be highly rewarding.

A second point is that different species possibly respond to high pressures in ways that differ qualitatively rather than quantitatively. Recent findings (9) suggest that in sheep CNS depression rather than the HPH syndrome may be the characteristic response to high pressures. The $P_{O_2}$ of about 0.5 atm in our present experiments is above the values producing the symptoms described in Professor Chouteau's paper published in this volume. Other effects must also be taken into account—e.g., different compression rates, and the amount of rumen gases that might possibly be absorbed at these high pressures. Speculation must of course be replaced by experimentation.

Concerning the relationship between our findings in animals and the physiology of man under deep-diving conditions, several observations should be mentioned. In a series of experimental chamber dives* to pressures exceeding that of 1000 FSW, EEG changes were observed in each of the four human subjects studied (2). The changes consisted of θ wave activity, especially in the occipitotemporal region; they appeared in the more susceptible subjects from approximately 30 atm onward. The phenomenon appeared to be reproducible, the relative susceptibilities of the different individuals seeming to bear a constant relation to one another throughout the series of dives. The EEG changes were concomitant with such behavioral changes as decreased attention, drowsiness (not unlike the pattern described as *microsleep*), and, at the highest pressures—equivalent to 1150–1190 FSW—some degree of confusion and motor disturbance. These last manifestations seemed to exceed those usually associated with He tremors, and were observed in all subjects when pressure reached 750 FSW and greater. Voluntary hyperventilation (2 min) at 28 and 35 atm failed to alter the EEG.

* Jointly performed in 1968 by the French National Research Council, the Compagnie Maritime d'Expertise of Marseilles, and the Wrightsville Marine Bio-Medical Laboratory.

These experiments suggest that, with the compression schedule used, man may begin to show evidence of the high pressure neurological syndrome at about 36 bar. No attempt was made to set a record in the experiments, of course. Rather, we had hoped to produce in the human subjects controllable symptoms relating to the sequence of CNS changes known to occur in animals under high pressures. The series was terminated sooner than we intended and before the anticipated severe symptoms developed, because one subject displayed an EEG change that could have meant a possible destructive hypoxic or ischemic condition in the CNS if exposure had been continued.

Before such experiments are resumed, it is essential that additional information be assembled. Data are needed regarding not only changes in blood gas composition of primates that are sufficiently compressed to evoke neurological changes, but also the degree of reversibility of such changes. To this end, decompression procedures have been developed that allowed us to recover safely six monkeys subjected to various time exposures at pressures up to 75 atm in He and $H_2$. These animals appeared grossly normal once they recovered from the fatigue of their 2- to 3-day exposure. They are being allowed recovery periods lasting 1–4 months before they are recompressed to establish new convulsion thresholds.

While it is too early for us to formulate firm conclusions, other studies with mice suggest that previously exposed and decompressed animals may prove much more sensitive to the HPH syndrome on their second exposure than on their first. If this is so, the heightened sensitivity implies residual CNS damage, and may provide a standard against which safe compression procedures can be planned in the future.

ACKNOWLEDGMENTS

This paper was supported by research grant NIH 5-RO1-GM154440-02 and by research grants from the United Medical Research Foundation, Inc., and the Z. Smith Reynolds Foundation. We wish to acknowledge the help of Dr. Heinz Schreiner, Director of Research, Ocean Systems, Inc., and of the Linde Corp. (Division of the Union Carbide Corp.) for making available part of the helium and helium–oxygen mixtures used in this work. The authors also wish to thank Dr. John B. Storer, formerly of the Jackson Memorial Laboratory, Miami, Fla., for his advice regarding the mice strains used in our experiment, and for making the animals available to us. The authors express their warm thanks to Col. Michael M. Conrad for making available the original design of a restraining couch used by the United States Air Force.

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FEDERATION PROCEEDINGS 26(2): 720, 1967



SEPARATION OF ANESTHETIC AND CONVULSANT EFFECTS IN MICE BREATHING He AND $H_2$ CONTAINING ATMOSPHERE AT 50 to 150 ATM. R.W. Brauer, R.O. Way* and R. Perry*
Wrightsville Marine Biomedical Lab., and Department of Physiology, Duke University, Wilmington, N.C.

Exposure to 45-47 atm. of He and $O_2$ at partial pressures of 0.5 to 1 atm., causes convulsions in Rhesus monkeys (Brauer Johnsen and Redding). Using $H_2$ in place of He convulsions occurred at slightly higher total pressures. Anesthetic effects of either gas were not clearly established. In CB1 mice, convulsions on He occur invariably at 90-105 atm. With $H_2$ as the inert gas convulsions occur at pressures of 105-110 atm. in 50% of the animals. Reversible loss of righting reflexes ("anesthesia") occurred in all $H_2$ animals at 99-110 atm., but was not seen with He. Addition 9% $N_2$ to the $He-O_2$ breathing gas prevented convulsions in 40% of the animals. Above 16% $N_2$ no convulsions were seen. When $N_2$ concentrations exceeded 30%, anesthesia resulted at 90-130 atm. The anesthetic potency of $H_2$ thus is near 40% that of $N_2$, as predicted by its oil solubility. The convulsions probably represent an effect of hydrostatic pressure on the CNS. Some degree of motor impairment is seen above 60 atm. in all animals.

# 21

*Ralph W. Brauer, Ph.D., Robin O. Way and Robert A. Perry*

# Narcotic Effects of Helium and Hydrogen in Mice and Hyperexcitability Phenomena at Simulated Depths of 1500 to 4000 Feet of Sea Water*

Recent interest has been shown in the possible correlation of physical properties with the anesthetic potency of metabolically inert gases. This interest has focused on those gases whose physical properties differ from the usual sequence of variables. Table 21.1 shows that hydrogen is one of these gases of special interest: the physical properties which can be correlated with molecular size as such place it at one extreme of the series of metabolically inert gases, while the properties which reflect the tendency to molecular interaction place it much lower in the series, closer to nitrogen than to helium. Thus, determination of the relative anesthetic potencies of helium, hydrogen and nitrogen is of considerable theoretical interest. As technological advances place progressively greater diving depths within reach, the physiological factors limiting extreme diving depths for exposed man become of paramount concern. A central question here is the extent to which this limit is affected by the pharmacological properties of the inert gases used in gas mixtures for such dives to dilute oxygen and to counterbalance hydrostatic pressure.

Electroencephalographic studies in rhesus monkeys (1) have shown that this species responds to either helium or hydrogen based atmospheres by convulsions of a grand mal type when pressures reach approx-

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TABLE 21.1

*Physical properties of gases*

Group I

| Gas | Molecular weight | Molal volume* | van der Waals constant "b" | Velocity of sound in gas | Thermal conductivity at 0°C |
|---|---|---|---|---|---|
| | | *ml/mole* | | *m/sec, STP* | |
| $H_2$ | 2.00 | 26.4 | 26.5 | 1300 | 39.6 |
| He | 4.00 | 27.4 | 23.6 | 970 | 33.6 |
| Ne | 20.18 | | | 430 | |
| A | 39.94 | 28.1 | 32.2 | 320 | 3.88 |
| $N_2$ | 28.02 | 32.8 | 38.3 | 330 | 5.68 |
| Kr | 82.9 | 38.9 | 39.7 | | |
| Xe | 130.2 | 47.5 | 50.8 | | |

Group II

| Gas | Polarizability | Polarizability molal volume | van der Waals constant "a" | Solubility in olive oil | Oil/water partition coefficient |
|---|---|---|---|---|---|
| | $cm^3 \times 10^{24}$ | $cm^3/l/mole \times 10^{22}$ | | *ml/l, 37°C* | |
| He | <0.2 | 0.09 | 0.035 | 15 | 1.7 |
| Ne | 0.4 | 0.23 | | | |
| $H_2$ | 0.8 | 0.29 | 0.25 | 50 | 2.3 |
| $N_2$ | 2.0 | 0.45 | 1.36 | 67 | 3.5 |
| A | 1.6 | 0.52 | 1.36 | 140 | 4.0 |
| Kr | 2.8 | 0.65 | 2.35 | 430 | 7.5 |
| Xe | 4.4 | 0.82 | 4.15 | 1700 | 14.5 |

* Liquid at boiling point.

imately 50 atm (table 21.2). With nitrogen-oxygen mixtures, convincing electroencephalographic evidence of deep narcosis was observed at approximately 28 atm in the same rhesus monkeys; when either helium or hydrogen took the place of nitrogen comparable effects were not seen even at pressures of 110 atm. In view of the marked convulsions which dominate the clinical picture in monkeys exposed to such pressure, the duration of such exposures was of necessity quite limited. The CNS depression inferred from the EEG in a number of these animals was not readily distinguished from postictal depression. A degree of pharmacological differentiation between He and $H_2$ was seen in the fact that, in contrast to He, only 60% of the animals showed convulsions on $H_2$ as well as in a marginally greater pressure (10–15%) at which convulsions occurred on hydrogen in those animals which responded in this manner (see table 21.2, both mixtures).

This body of data did not permit discrimination between two alternatives. The convulsions may have resulted from pharmacological activity of the inert gas at the high concentrations reached, the effect

representing possibly an extension of hyperactivity such as forms part of the induction phase of xenon (2) and possibly of $N_2O$ anesthesia (*cf.* Faulconer, Anesthesiol. *10:* 601, 1949). On this concept, $H_2$ would have been proved to be less potent than He as a CNS affecting agent. Alternatively, if the convulsions were not related to the pharmacological activity of the gases but resulted from some other physical cause, such as the effect of high hydrostatic pressures in altering excitability of nerve or muscle (*cf.* 3), the difference in pressure required for convulsions and the lower convulsion incidence must be read as an indication that hydrogen is more active in suppressing this particular effect. A third possibility, that the convulsions reflected anoxia or the accumulation of $CO_2$ secondary to disturbed respiratory mechanics, was entertained but considered unlikely after examination of the total experimental material available.

A series of experiments has been conducted using mice as test animals. It was hoped that in the smaller animal the much more rapid tissue gas equilibration times would permit attainment of pharmacologically effective concentrations of the inert gas within sufficiently short times to allow elucidation of their pharmacological effects, if such effects were a prominent element of the phenomenology observed. In addition,

TABLE 21.2

*Convulsions in rhesus monkeys breathing gas mixtures at elevated pressures*

| Monkey no. | Descent rate | $P_{conv}$ | Time at $P_{conv}$ | $P_{CO_2}$ | $P_{O_2}$ |
|---|---|---|---|---|---|
| | *ft/min* | *atm* | *min* | *atm* | *atm* |
| | | | $He / O_2$ mixture | | |
| 1 | 160 | 52 | 2 | 0.027 | 1.04 |
| 5 | 200 | 42 | 5 | 0.028 | 0.84 |
| 7 | 200 | 49 | 2 | | 0.96 |
| 8 | 160 | 49 | 10 | 0.036 | 1.01 |
| 9 | 100 | 85 | 3.5 | 0.076 | 1.03 |
| 16 | 33 | 62 | 2 | 0.057 | 1.15 |
| 17 | 25 | 71 | 2 | 0.025 | 0.51 |
| 20 | 55 | 52 | 2 | 0.011 | 0.34 |
| 21 | 25 | 57 | 2 | 0.037 | 0.45 |
| | | | $H_2 / O_2$ mixture | | |
| 2 | 200 | None by 64 | 14 | | 0.94 |
| 4 | 200 | None by 65 | 56<br>240 | 0.104 | 0.96 |
| 6 | 210 | 64 | 0.5 | 0.043 | 1.00 |
| 10 | 180 | None at 77 | 17 | 0.036 | 1.00 |
| 11 | 200 | None at 102 | 30 | 0.077 | 1.04 |
| 12 | 200 | 63 | 0.5 | 0.036 | 0.65 |
| 18 | 35 | 68 | 2 | 0.018 | 0.48 |
| 19 | 60 | 96 | 2 | 0.025 | 1.04 |

the smaller test animal permits the use of a much smaller test chamber than had been used for the rhesus monkeys. This smaller chamber was more readily provided with an observation window, and made practicable maintenance of gas flow rates such that composition of the chamber gas with respect to inert gas and oxygen concentrations never deviated significantly from those of the gas supplied to the chamber.

## EXPERIMENTAL METHODS

Female mice of the $CB_1$ strain weighing 28 to 32 g were employed throughout this work. They were exposed in pairs in a cylindrical steel chamber, 10 by 23 cm and equipped with a window at one end.* Gas was supplied to the chamber and distributed by suitable baffling to ventilate the entire chamber volume. The outflow line was vented through a back pressure regulator which was used to set the chamber pressure. Gases were supplied to the chamber from premixed analyzed supply cylinders. The chamber was ventilated continuously and the rate of flow was adjusted so that the chamber atmosphere was turned over at least once every minute. Gas samples were taken periodically from the chamber effluent. Analyses performed by gas chromatography confirmed that under these conditions oxygen concentrations in the chamber did not deviate significantly from those in the gas mixture supplied, with $CO_2$ tensions in the chamber maintained below 0.02 atm at all times.

Chamber temperature was determined by a mercury thermometer inserted in the chamber and calibrated for various chamber pressures. Equilibrium chamber temperature was maintained between 30 and 32.5°C throughout. The time course of temperatures during a typical compression sequence was followed by means of a thermistor. Maximal heating during the compression stages raised chamber atmosphere temperatures to 2.5°C above the equilibrium level. Such temperature excursions were reversed within 3 min. In the helium or hydrogen atmospheres, this temperature range seemed optimal for the mice: on hydrogen in particular, shivering disappeared at temperature above 25°C; temperatures greater than 36°C produced visible distress. Experiments were conducted along three standarized compression profiles shown in table 21.3. The most frequently used scheme consisted of a series of compression steps, the compression rate being held at 7 atm

* The chambers were made available for our work by the Shell Development Company, Emeryville, Calif. The authors wish to express their sincere appreciation to Mr. W. R. Harp, Jr. and to Mr. Ed Kelly of that company for their assistance in this connection. The mixed gases were supplied by Precision Gas Products, Inc., Linden, N.J. Analyses performed under contract by Precision Gas Products, Inc., Linden, N.J.

per min, separated by stops when pressure was held at a constant level. The maximal pressure obtained in any one experiment was variable, and was determined by the biological effects observed.

Two other compression profiles were employed, each in one series of experiments. Schedule 2 was identical with the first scheme shown in table 21.3, except that the duration of all early stops was reduced so that total compression time to convulsion depth should be sufficiently short to allow satisfactory activity of the injected amino buffer. Schedule 3 differed from that of table 21.1 in that compression rates were only 1.4 atm per min instead of 7 atm per min. This experiment was conducted to provide results as part of the present series which should be directly comparable to the work reported by MacInnis *et al.* (4).

Animals were sacrificed by decompressing from pressures of 75 atm or greater to 1 atm in 20 to 30 seconds; preliminary trial showed that this procedure resulted in death of the animal within less than 10 seconds from the beginning of decompression.

TABLE 21.3

*Compression schedules*

| Stop at | Duration of stops | | |
|---|---|---|---|
| | Schedule 1 (6.9 atm/min) * | Schedule 2 (6.9 atm/min) | Schedule 3 (1.5 atm/min) |
| *atm* | *min* | | |
| 1† | 6 | 2 | 6 |
| 21 | 4 | 2 | 4 |
| 31‡ | 5 | 2 | 5 |
| 41 | 5 | 2 | 5 |
| 48 | 6 | 2 | 6 |
| 58.5§ | 10 | 2 | 10 |
| 62.5 | 10 | 2 | 10 |
| 68.5 | 10 | 2 | 10 |
| 82 | 10 | 10 | 10 |
| 89 | 10 | 10 | 10 |
| 96 | 10 | 10 | 10 |
| 102 | 10 | 10 | 10 |
| 109 | 10 | 10 | 10 |
| 116 | 10 | 10 | 10 |
| 125 | 10 | | 10 |

* Compression rate.

† Compression to this point on gas mixture containing 4% oxygen.

‡ Compression to this point on gas mixture containing 2% oxygen.

§ Compression to this point on gas mixture containing 1% oxygen. Compression beyond this point employed 0.5% oxygen.

### EFFECTS IN MICE

Evaluation of the results was made visually by two observers using a set of standard responses established in preliminary trials. Three phenomena in particular were observed with such regularity, and provided such clear-cut endpoints, that they form the basis of the subsequent discussion. 1) Fasciculation—coarse, apparently uncoordinated tremors of head and extremities beginning in forelimbs and extending swiftly to hindlimbs and large body muscles ("doddering and ~~"~~aking"). 2) Convulsions usually preceded by a brief preconvulsive ~~r~~a characterized by hyperirritability, severe fasciculation and grow~~i~~g muscular rigidity culminating in a tonic-clonic convulsion, followed by gradual relaxation during which running movements of an apparently unconscious animal were prominent; such a convulsion would typically be followed by apparent recovery, and within 2 or 3 min by resumption of the cycle leading to further convulsions. This sequence continued for 45 min or until death of the animal. 3) Anesthesia (or better, narcosis)—loss of righting reflexes in animals which appear more or less flaccid, with deep and often slow respiration. This state has been shown to be reversible by lowering the chamber pressure with recovery of the animals in a few minutes.

Table 21.4 shows the results obtained with the three binary gas mixtures, helium-oxygen, hydrogen-oxygen and nitrogen-oxygen. Extremes of the range of response patterns are observed on the helium and the nitrogen mixtures. In the case of the former, fasciculation was observed in all animals, generally commencing at about 58 atm total pressure. Likewise, convulsions of the type just described were observed in all animals by the time total pressures of 102 atm had been reached, with a maximal frequency of onset at 89 atm. None of the animals could be carried on helium to the point where anesthesia was observed.

By contrast, in the nitrogen series, no fasciculation or convulsions were observed in any of the animals. Instead, narcosis was seen in all animals at total pressures between 41.5 and 48.5 atm, somewhat higher than the values observed for comparable exposure times but for a less definitive endpoint by Marshall (5).

Hydrogen was intermediate between these two gases. Fasciculation occurred in all animals, but in half of them the point of onset was higher than was seen in the majority of the helium exposed animals. Convulsions were observed in 25% in the hydrogen exposed animals, but required pressures perceptibly higher than those seen in the helium series. Narcosis was observed in nine out of 12 hydrogen exposed animals at pressures of 89 to 109 atm.

### HYPEREXCITABILITY EFFECTS

Early results suggested that there might be some correlation between the point of onset of fasciculation in the helium-oxygen exposed animals

and chamber temperature. A series of 10 animals was accordingly tested at chamber temperatures from 18 to 35°C. At 18°C, shivering was observed in the mice, beginning almost as soon as the air in the chamber had been displaced by helium, and was well established by the time the chamber pressure had reached 8 atm. This response disappeared at chamber temperature of 25°C. Above this point, neither the pressure of onset of fasciculation nor the point of onset of the convulsion appeared to vary with changes in chamber atmosphere temperature within the range of values employed.

The possibility was considered that the convulsions might be correlated with chamber oxygen tension. To test this possibility, experiments with helium-oxygen mixtures were conducted at two levels of oxygen content, 1.0 and 0.5%. The results of these experiments failed to show any systematic difference in the point of onset of convulsions on the two mixtures, the majority of responses in both cases occurring at 89

TABLE 21.4

*Physiological effects observed at high pressures in $CB_1$ mice breathing He, $N_2$ or $H_2$ atmospheres*

| Inert gas | Oxygen content | Pressure at response and proportion of mice responding | | | | | |
|---|---|---|---|---|---|---|---|
| | | Fasciculation | | Convulsions | | Anesthia | |
| | | Pressure | Proportion* | Pressure | Proportion | Pressure | Proportion |
| | % | atm | | | | | |
| He | 0.5 | 58.5 | 1/11 | 75 | 1/11 | 102 | 0/11 |
| | | 75 | 2/111 | 89 | 6/11 | | |
| | | | | 96 | 2/11 | | |
| | | | | 102 | 2/11 | | |
| He | 1/0 | 58.5 | 9/9 | 82 | 1/9 | 89 | 0/9 |
| | | | | 89 | 7/9 | | |
| | | | | 96 | 1/9 | | |
| $N_2$ | 1.0 | 96 | 0/10 | 96 | 0/10 | 41.5 | 6/10 |
| | | | | | | 45 | 2/10 |
| | | | | | | 48.5 | 2/10 |
| $H_2$ | 0.5 | 58.5 | 6/12 | 102 | 1/12 | 96 | 4/12 |
| | | 68.5 | 6/12 | 109 | 2/12 | 102 | 2/12 |
| | | | | | | 109 | 3/12 |
| | | | | 109 | 9/12 | 109 | 3/12 |
| He plus $N_2$† | 0.5 | 62.5 | 2/8 | 129 | 0/8 | 89 | 1/8 |
| | | 68.5 | 4/8 | | | 102 | 1/8 |
| | | 75 | 2/8 | | | 109 | 1/8 |
| | | | | | | 116 | 1/8 |
| | | | | | | 116 | 4/8 |

* Given as number responding/total.

† He, 75.5%; $N_2$, 24%.

atm, *i.e.*, at $O_2$ partial pressures of 0.45 and 0.89 atm respectively (table 21.4). These experiments make it improbable that either hypoxia or oxygen toxicity can be primary factors in the induction of convulsions in the present series of experiments.

To ascertain whether $CO_2$ accumulation might be an important factor in the genesis of the convulsions, eight mice were pretreated by intraperitoneal injection of 1 ml of 0.3 M THAM, a dose shown to be effective in delaying $O_2$ convulsions (6). To test this point, six mice were injected with THAM. After 30 min, injected and saline control animals were exposed to 5.5 atm $O_2$ and the time of onset of convulsions noted. The average time to convulsions was 16 min in the controls and 33 min in the THAM treated mice, the difference by ranking test being significant at the 5% level ($0.01 < p << 0.05$). Thus the period of effective protection by the dose of THAM employed was well in excess of that required to compress the animals on the foreshortened schedule 2. Compression studies using He and 1% $O_2$ with this schedule were conducted pairing each of the THAM treated mice with a saline treated control. Convulsions occurred at the following pressures:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Control | 89 | 82 | 82 | 109 | 75 | 95 | 86 |
| THAM | 75 | 89 | 82 | 109 | 96 | 96 | 88 |

There is no significant difference between these two series. Thus, $P_{CO_2}$, like $P_{O_2}$, does not appear to be a major factor in the induction of the convulsions observed in this present study.

After completing the basic experiments described above, the authors were given an opportunity to examine a manuscript by MacInnis and collaborators describing observations on Wistar mice exposed in $He/O_2$ atmosphere to pressures up to 135 atm (4).* Since these experiments, while demonstrating phenomena similar to those here referred to as fasciculation, failed to reveal dramatic convulsions of the type observed in the present series, it was felt important to replicate as far as possible the precise conditions of those experiments. Apart from the use of different strains, the principal discrepancy between the experimental techniques used in the two laboratories appeared to be that slower compression rate was employed by MacInnis (4); therefore, a test series was conducted in which mice of the strain used in our laboratory were compressed at a rate comparable to that used by MacInnis. The compression schedule was schedule 3. On this scheme the pressure at which fasciculation began was the same as with either of the other compression schemes. However, the onset of convulsions seemed to be delayed somewhat. Table 21.5 summarizes the results for the onset of convulsions on the three compression schedules employed. There is some suggestion

* The authors wish to thank Dr. J. MacInnis for making this paper available.

in these data that shortening the stops may result in earlier onset of convulsions; conversely, the slower compression rate appears to result in more frequent onset of the convulsions at higher pressures. Nonetheless, all animals exposed showed convulsions. We conclude tentatively that the difference between our results and those of MacInnis represents primarily a strain difference in CNS susceptibility. In this view we are confirmed by preliminary experiments which led to selection of the $CB_1$ mice for the present study. Among several other strains $CB_1$ mice appeared to be perceptibly less susceptible to convulsions under our exposure conditions than either DK+, EB+ or CBA strains.

## HELIUM-NITROGEN MIXTURES SIMULATING THE EFFECTS OF HYDROGEN: ANTICONVULSANT EFFECTS OF $N_2$

The data presented so far suggest that hydrogen occupies a position intermediate between helium and nitrogen with respect to its effect upon the mouse. It appeared of interest, therefore, to test the possibility that mixtures of helium and nitrogen could be prepared which generally would resemble the behavior of hydrogen. A mixture containing 75.5% He, 24% $N_2$ and 0.5% $O_2$ was found to come rather close to such simulation, and the results obtained with this are included in Table 21.3. On such a mixture, generalized fasciculation is a prominent part of the syndrome observed, although its onset may be slightly later than on pure helium-oxygen mixtures, resembling in this respect the effects of hydrogen. Narcosis also occurs in the majority of animals on this He-$N_2$ mixture, but requires slightly higher pressures than on $H_2$-$O_2$. A significant difference between He-24.5% $N_2$ and hydrogen may exist with respect to convulsion incidence. On $H_2$-$O_2$, 25% of the animals showed convulsions, but even at the highest pressures attained on the helium-nitrogen mixture no animals showed this particular response. This anticonvulsant effect of nitrogen is detectable even at considerably lower nitrogen concentrations. While with pure He as the inert phase all mice had undergone convulsions (*cf.* table 21.4) when pressures had reached about 110 atm, 9.9% $N_2$ in He yielded convulsions in only five of 10 mice at 95 atm, and no further convulsions at 108 to 135 atm. On 13% $N_2$ no convulsions were seen in six animals at pressures to 135 atm. At these concentrations narcosis likewise failed to occur even at the highest pressures tested.

## RELATIVE ANESTHETIC POTENCIES OF He, $H_2$ AND $N_2$

It is interesting to attempt to derive on the basis of these data the relative anesthetic potencies of helium and hydrogen. If one assumes that pressure effects as such can be neglected in the comparison of the narcotic effectiveness, one may note that partial pressures of hydrogen ap-

proximately 2.5 times as high as those of nitrogen are required to induce narcosis in these mice; the anesthetic potency of hydrogen thus appears to be in the neighborhood of 40% that of nitrogen. If the helium-nitrogen mixture containing 23% of nitrogen can be considered approximately equivalent to hydrogen, this fact and the narcotic potency ratio between nitrogen and hydrogen just calculated lead to the conclusion that, in the test mixture, the helium present must account for narcotic potency roughly equivalent to that of 17 atm of nitrogen. Since the helium content of this test mixture is approximately equivalent to 78 atm, such a calculation leads to an estimate for the potency of helium as approximately one-fifth that of nitrogen (1:4.6). These observations thus suggest that the ratios of narcotic potencies of nitrogen, hydrogen and helium are close to 1.0:0.4:0.2. Such calculation involves the assumption of linear additivity of anesthetic effects; furthermore it assumes that the only agents at work are the effective partial pressures of the several gases. Such a ratio therefore can be taken as no more than a tentative classification requiring further experimental verification.

One step in this direction was to test the hypothesis of linear additivity of anesthetic effects of inert gases. Mathematically this hypothesis can be developed as follows.

If a given level of central nervous system depression is produced by a standard gas, $s$, whose anesthetic potency is taken to be unity, at a partial pressure of ${}^{a}P_s$ atm, the relative anesthetic potency ${}^{a}\Pi_n$ of any other gas, $n$, acting in the same manner is given by ${}^{a}\Pi_n = {}^{a}P_s/{}^{a}P_n$, where ${}^{a}P_n$ is the partial pressure of gas at which the level of CNS depression is comparable to that produced by the standard at ${}^{a}P_s$. If the effects are linearly additive, comparable anesthetic effects can be produced by a mixture of gases when ${}^{a}P_s = \sum_{n=1}^{n} {}^{a}\Pi_n P_n$, where $P_n$ is the partial pressure of the $n$th gas in the mixture. When the conditions are such that deviations from ideal gas behavior can be ignored, this equation can be rewritten in terms of ${}^{a}P_T$, the total effective gas pressure of the mixture when anesthesia is attained, and $r_n$, the mole fraction of each gas is the mixture:

$$ {}^{a}P_s = {}^{a}P_T \sum_{1}^{n} r_n {}^{a}\Pi_n $$

For a binary system this equation becomes ${}^{a}P_s = {}^{a}P_T(\alpha {}^{a}\Pi_1 + (1 - \alpha){}^{a}\Pi_2)$, and if the standard gas is one of the two components, *i.e.*, ${}^{a}\Pi_2 = 1.0$, ${}^{a}P_s = {}^{a}P_T(\alpha {}^{a}\Pi_1 + 1 - \alpha)$ or ${}^{a}P_s/{}^{a}P_T = \alpha {}^{a}\Pi_1 + (1 - \alpha)$. Thus a plot of $({}^{a}P_T)^{-1}$ against $\alpha$ should be a straight line of slope ${}^{a}\Pi_1 - 1$ and pass through $({}^{a}P_T)^{-1} = ({}^{a}P_s)^{-1}$ when $\alpha$ is 0, and through $({}^{a}P_T)^{-1} = {}^{a}\Pi_1/{}^{a}P_s$ when $\alpha = 1$.

To test this hypothesis, a series of mixtures was prepared using He and $N_2$, and $H_2$ and $N_2$ in varying proportions, together with 1% O.

For each the point was determined at which it induced anesthesia in $CB_1$ mice in the sense defined above under Methods. The results plotted in the manner just outlined are presented in figure 21.1. The data appear compatible with the hypothesis of linear additivity, although the scatter of the values is sufficient to preclude any real determination as to possible deviations of the exponent from 1.0. The data were analyzed by accepting the linear hypothesis and fitting lines through the mean value for 100% $N_2$ by the least square method. The helium, and to a smaller extent the hydrogen series, showed increased scatter when $P_T$ exceeded the fasciculation threshold ($\sim$55 atm) and became blurred by hyperexcitability effects when the nitrogen admixture was so small that total pressures above 110 atm were required for anesthesia. Extrapolation is nonetheless possible and allows calculation of relative anesthetic potencies for the three gases. If $^{e}\Pi$ is taken to be 1.0 for nitrogen, $^{e}\Pi_{He} = 0.184 \pm 0.089$ and $^{e}\Pi_{H_2} = 0.405 \pm 0.060$. The difference between these values, tested by $t$ test, is highly significant ($0.01 > p > 0.02$). These figures appear to establish conclusively the rank order of anesthetic potencies for He and $H_2$.

These figures appear well in line with general predictions made on the basis of measurements of oil solubility (7), or the polarizibility to volume ratios (table 21.1) (8), and thus confirm the view that the factors which determine the narcotic potency of these inert gases are closely related to those physical properties listed in table 21.1B as correlated with the van der Waals interaction coefficient "a."

## NATURE OF THE HYPEREXCITABILITY EFFECTS ABOVE 100 ATM—HYDROSTATIC PRESSURE EFFECTS

However tentative these numerical values may be, the experimental data resolve the question of the relation between the narcotic effects of these inert gases and the hyperexcitability phenomena observed. There seems to be no room for doubt that the convulsions are negatively correlated with the narcotic potency of the inert gas employed. Fasciculation

TABLE 21.5

*Effect of compression schedule on pressure of onset of convulsions*

| Compression schedule | Proportion of mice having first convulsion at | | | | | |
|---|---|---|---|---|---|---|
| | 75 atm | 82 atm | 89 atm | 96 atm | 104 atm | 107 atm |
| 2 | 3/13* | 2/13 | 4/13 | 2/13 | 0 | 2/13 |
| 1 | 1/20 | 1/20 | 13/20 | 3/20 | 2/20 | 0 |
| 3 | 0 | 0 | 0 | 1/7 | 4/7 | 2/7 |

* Given as number convulsing/total.

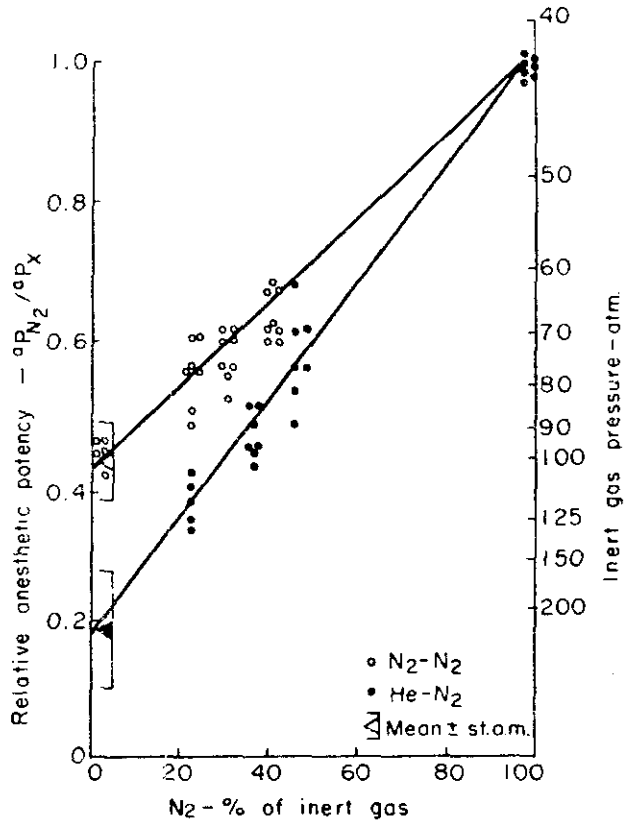


*Figure 21.1.* Pressures at which anesthesia is produced by helium-nitrogen or hydrogen-nitrogen mixtures as a function of nitrogen content. See text for discussion of the hypothesis underlying calculation of regression lines. Animals used were $CB_1$ mice.

seems to be virtually independent thereof, except in the case of nitrogen, in which deep anesthesia supervenes well before the point of onset of fasciculation. The experimental data furthermore suffice to render most improbable any intimate relation of the hyperexcitability phenomena either with oxygen tension in the chamber atmospheres or with possible $CO_2$ accumulation in the animals. Finally, in these mice admixture of $N_2$ with helium produces an atmosphere resembling in its effects a hydrogen atmosphere rendering improbable any interpretation based on the breathing resistance of the gas mixtures at the high pressures as the primary factor in the induction of the hyperexcitability syndrome or the anesthesia.

These several considerations thus lead to the conclusion that convulsions and fasciculation observed at the elevated pressures attained in

these experiments reflect neuromuscular or central nervous system hyperirritability due to some factor which is neither related to the narcotic potency of the inert gases employed, nor primarily linked to temperature, oxygen or $CO_2$ effects. We suggest that the best interpretation of these phenomena is that they reflect the direct effects of hydrostatic pressure upon excitable systems.

This conclusion appears even more reasonable as observations of the effects of hydrostatic pressures on nerve conduction and muscle contraction place the zone in which such effects begin to be observed even in isolated systems close to that obtained in the present experiments. Thus, induction of contracture in frog gastrocnemius was observed after brief exposures to 200 atm (9). In the striated retractor penis muscle of the turtle, a pressure of 2000 p.s.i. (135 atm) at 4°C similarly initiated contracture (10). Marked increases in twitch tension of the frog gastrocnemius were reported at 1000 p.s.i. (68 atm) (11), and in a similar pressure range profound changes in cardiac muscle of the same species have been described (12, 13). Changes in nerve conduction in the same general pressure range have been recognized ever since the early report by Grundfest and Cattell (14). More recently, it has been reported that single nerve fibers show marked increase of duration of action current at pressures as low as 2500 p.s.i. (170 atm) (15), and the same pressure causes a marked enhancement in sodium gain and potassium loss in this preparation, resembling in this respect the reaction to anoxia and to veratrine (16). Without entering into further discussion as to the nature of these changes in properties of excitable tissue exposed to high hydrostatic pressures, data available from the literature suggest that marked effects can be expected even in simple systems in the pressure range here observed.

## TENTATIVE EXTRAPOLATION TO MAN

In the mice studied in the present communication, hyperexcitability effects supervene at pressures equivalent to depths of approximately 1700 feet of sea water for fasiculation, and the more dramatic convulsion episodes supervene at pressures near 3000 feet. Comparison of these results with data previously obtained in the rhesus monkey (1) showed that in this species convulsions occurred at a mere 1700 feet equivalent depth, suggesting that sensitivity of the CNS to the effects of these exposures is greater in species with a more highly developed CNS. British observers have recently turned up phenomena, not unlike a mild form of those here, characterized as fasciculation in man at depths equivalent to 800 feet (17). It is our impression that these three sets of data are mutually consistent, and that they suggest that we are here in the presence of a major factor hitherto not considered significant but now shown

likely to limit maximal depths to which unprotected man can penetrate the ocean to levels not far in excess of 1000 feet.

In considering future implications of these observations, it appears to us highly significant that, in admixture with helium, quite low concentrations of nitrogen (10 12%) suffice to inhibit markedly the convulsions in our experimental animals. At the same time the failure of such conditions to affect the onset of fasciculation suggest to us that convulsions and fasciculation may be separate manifestations of hydrostatic pressure hyperexcitability acting at *different levels of organization*. Further exploration of the pharmacology of these phenomena should be highly rewarding.

## SUMMARY

Comparison of the effects of nitrogen, hydrogen and helium as the metabolically inert gas in synthetic atmospheres shows that in mice the approximate relative narcotic potencies of the three gases are as 1:0.4:0.2. The pressures attained in this work are sufficiently high to elicit a series of effects, including skeletal muscle fasciculation and convulsions, which are attributed tentatively to hydrostatic pressure effects on excitable tissues. Mixed helium-nitrogen atmospheres can be prepared to simulate the physiological properties of hydrogen atmospheres, and allow partial control of the hyperexcitability effects seen at the high pressures. The behavior of a series of such binary mixtures is compatible with the hypothesis of linear additivity of anesthetic effects of the metabolically inert gases. Analysis of such data provides a general method for estimating the anesthetic potencies of the lighter gases, for which anesthetic concentrations lie in a partial pressure range where hyperexcitability phenomena dominate the picture. Relative anesthetic potencies for $N_2$, $H_2$ and He determined in this fashion are 1.0, 0.405 $\pm$ 0.060 and 0.184 $\pm$ 0.089. The bearing of these data on the formulation of a theory of inert gas narcosis and their relevance to high pressure tolerance of man are discussed.

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## DISCUSSION AFTER PRESENTATION

*Dr. Paul:* Unfortunately we have time for only one question.

*Dr. Eastwood:* There are so many things to comment on in this paper that it is going to be hard to make only one question. We knew that Dr. Albert Faulconer convulsed under hyperbaric nitrous oxide. Also, I assume that there are cells that would be depressed other than lymphocytes in these animals including the leucocytes, the bone marrow and so on. I understand that the bone marrow can be completely destroyed with a short hyperbaric exposure in the rat. Was this your finding?

*Dr. Brauer:* We are of course aware of the Faulconer data and, in fact, a good deal of the ancillary material in my presentation was to eliminate the question that the anesthetic potency and the convulsion producing potency of these gases could be correlated. With our gases they are not correlated. Whether in the case of nitrous oxide the mechanisms underlying these two effects could have something in common is another question. Now with respect to the cell population data, our findings allow us to say at the moment that we get a rapid drop in lymphocytes, rather too rapid, incidentally, for simple mitotic inhibition, and that in several other cell systems we have looked at, we have indications of inhibition of mitotic activity. We have no evidence of cytolytic factors except possibly with the lymphocytes.

# La limitation hypoxique de la Plongée profonde de longue durée

par

J. CHOUTEAU et G. IMBERT

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# La limitation hypoxique de la Plongée profonde de longue durée

par

J. CHOUTEAU et G. IMBERT

(*)

Les plongées profondes ne peuvent être *envisagées autrement que comme des plongées* de longue durée. En premier lieu, les temps de décompression sont inévitablement allongés. En outre, la nécessité commence aujourd'hui à être clairement aperçue d'utiliser de faibles vitesses de mise en pression lorsqu'on se propose d'atteindre plusieurs dizaines de bars (c'est-à-dire plusieurs centaines de mètres de profondeur). Pratiquement se sont imposées les techniques de la plongée à saturation, proposées par le Cpt BOND aux U.S.A. et mises en œuvre pour la première fois par le Cdt COUSTEAU en 1962.

1°) Parce que par nature, elles offrent *des coefficients* de temps utile élevés, autrement dit parce que le temps de séjour au fond et la durée globale de la plongée sont dans un rapport tendant à se rapprocher de l'unité (CHOUTEAU et al. 1966) ;

2°) parce que la plongée à grande profondeur nécessite l'utilisation d'hélium comme diluant de l'oxygène pour éviter les phénomènes narcotiques provoqués par l'inhalation d'azote sous pression élevée. Ce gaz, plus léger, est également plus diffusible, ce qui entraîne une charge rapide des tissus en gaz inertes et conduit, de toute manière, à une saturation précoce de l'organisme.

Les expériences « princeps » de la plongée à saturation conduites sur l'animal, surtout le rat (WORKMAN, BOND et MAZZONE 1962, BARTHELEMY 1963) ont immédiatement démontré que les risques léthaux qu'elle entraîne sur des périodes prolongées, résultent principalement de l'inhalation d'oxygène sous des pressions partielles élevées. Les lésions du parenchyme pulmonaire (et suivant des données plus récentes, de la couche superficielle de surfactant) provoquées par l'hyperoxie chronique (LORRAIN-SMITH, 1889) semblent de plus favorisées par l'effet atélectasiant de l'élévation de la masse spécifique du mélange respiré. Ceci conduit à utiliser des atmosphères synthétiques dans lesquelles la fraction d'oxygène ($F_{IO_2}$) est diminuée proportionnellement à la pression absolue (P) de telle manière que soit réalisée une pression partielle normoxique ($P_{IO_2}$ = 210 mb). Par exemple à 21 bars (200 mètres), cette condition est remplie par un mélange contenant 1 % *d'oxygène et 99 % d'hélium.*

Ce principe autorisait la réalisation des premières expériences humaines à saturation en mer, à petites ou à moyennes profondeurs, avec les opérations Précontinent du Cdt COUSTEAU et le programme Sea Lab de l'U.S. Navy.

Par ailleurs des expériences conduites sur des souris dans de petites enceintes hyperbares montraient que le mélange oxygène-hélium normoxique permettait la survie à des pressions de l'ordre d'une centaine de bars (voir en particulier, Mc INNIS, DICKSON et LAMBERTSEN, 1967). A ces très hautes pressions, les auteurs constataient certaines anomalies cliniques, notamment une réduction de l'activité spontanée et des troubles moteurs localisés dans le train postérieur pour lesquels ils n'avançaient cependant aucune interprétation.

Les considérations qui précèdent ont servi de base à notre programme expérimental ayant pour but de définir les limites en profondeur et en durée de la plongée à saturation en atmosphère oxygène-hélium, commencé en 1965 après l'expérience Précontinent III.

## EXPERIENCES GLOBALES DE SURVIE

### effectuées sur gros mammifères

Les dimensions de nos caissons hyperbares permettent d'y installer des animaux de taille comparable à celle de l'Homme,

(*) Laboratoire de Physiologie Appliquée de l'Université de Provence - Centre Saint-Charles - Marseille (3e), et Laboratoire de Physiologie des Hautes Pressions, Centre d'Etudes Marines Avancées, Cap Janet, Marseille.

des *Caprins notamment*. Par ailleurs, les systèmes de régénération et de contrôle qui leurs sont associés permettent des régulations de la composition des atmosphères et des conditions physiques de l'environnement. Ces paramètres peuvent être modifiés indépendamment et maintenus dans un intervalle de valeurs choisies. Dans ces conditions les effets observés sont interprétables en fonction de chaque variable : *pression absolue*, $PIO_2$, $PICO_2$, *hygrométrie*, température, composition en gaz inertes. Des systèmes de régénération spéciaux assurent l'élimination des polluants ammoniacaux ou organiques et du méthane produit en quantités importantes par les Ruminants.

Deux principes méthodologiques communs à toutes nos expériences sont à souligner :

- lors des expériences profondes en mélange oxygène-hélium, de nombreuses précautions sont prises pour éviter la contamination de l'atmosphère respirée par de l'azote : dans nos expériences $PIN_2$ est *maintenu inférieur* à 50 mb :

- nous utilisons invariablement lors des expériences animales une vitesse de montée en pression inférieure ou *égale à 0,1* bar/mn. La compression est de plus ralentie par des paliers effectués à intervalles *réguliers et progressivement* allongés. A l'origine, ce procédé nous a été imposé par les difficultés des Caprins à réaliser la compensation des pressions dans les cavités internes. En particulier l'équipression dans la cavité ruménale nécessite la déglutition de bols gazeux qui se révèle assez pénible pour le sujet. Par *la suite* nous l'avons retenu comme principe général pour limiter le stress que déclenche *la compression indépendamment* de la pression maximum atteinte. Au-delà de 40 bars, des paliers de plusieurs heures à plusieurs dizaines d'heures sont généralement effectués toutes les 10 bars en vue de l'analyse comportementale et clinique ou de mesures électrophysiologiques.

Nous présentons ci-dessous un essai de synthèse des résultats qui ont été obtenus au cours d'expériences profondes, entre 40 et 111 bars sur une quinzaine de sujets utilisés isolément ou en groupe. La durée globale des expositions varie de 2 jours à 2 semaines. Tous les sujets étaient des boucs castrés, âgés de 2 à 5 ans, pesant 55 à 75 kg et préalablement conditionnés au mode *spécial d'alimentation et à l'environnement* instrumental.

1) Lors de la respiration d'un mélange oxygène-hélium normoxique ($PIO_2$ = 210 mb) nous observons au-delà d'un certain seuil de pression des perturbations qui se manifestent dans leur forme fruste par une diminution plus ou moins marquée de l'activité spontanée et une inhibition des comportements habituels des sujets. Ces troubles peuvent prendre brutalement une forme aiguë se traduisant sur le plan neuro-musculaire par *des parésies intéressant* d'abord le train postérieur. Dans une attitude caractéristique le sujet, debout, les membres postérieurs en extension, ébauche un comportement de fuite en agitant les membres antérieurs. L'équilibre est compromis et l'animal tombe sur le flanc en décubitus latéral complet. Ensuite survient une phase de paralysie flasque entrecoupée de brèves périodes d'hypertonie des *membres et du cou. La mort est précédée de* spasmes inspiratoires prolongés. Ces troubles sont reversibles par des relèvements de 20 à 50 % de la valeur de $PIO_2$ ; il est d'ailleurs possible d'effectuer des cycles en laissant redescendre la valeur de $PIO_2$ puis en la rétablissant à la valeur supérieure par injection d'oxygène. Les sujets passent par des phases de prostration et des phases d'activité (CHOUTEAU et coll., 1967).

Une valeur supérieure de $PIO_2$ permet éventuellement de soumettre les sujets à une nouvelle augmentation de la pression absolue jusqu'à ce que surviennent de nouveaux troubles également réversibles par *relèvement de* $PIO_2$.

Un tel procédé a permis de comprimer 3 boucs jusqu'à 101 bars, au terme d'une expérience d'une durée globale de 12 jours (CHOUTEAU, IMBERT et ALINAT, 1969) et après plusieurs manifestations aiguës : *à 71 bars (relèvement de* $PIO_2$ de 220 à 280 mb, puis de 270 à 300 mb) et à 91 bars (relèvement de 350 à 500 mb). Soulignons le fait qu'à 81 bars (350 mb) le comportement des animaux était normal. A 101 bars (650 mb), une crise mortelle est survenue au bout de 10 heures chez un sujet resté *jusqu'alors indemne*.

Leur reversibilité par relèvement de $PIO_2$, d'une part, et une analogie clinique certaine avec les crises convulsives anoxiques, d'autre part, nous ont conduit à attribuer ces troubles à un effet de type *hypoxique (CHOUTEAU 1967, 1968)*. Nous verrons plus loin quels sont les arguments directs qui permettent de confirmer cette interprétation. Quoiqu'il en soit, il semble que le mélange respiratoire normoxique ($PIO_2$ = 210 mb) se comporte comme un mélange hypoxique au-delà d'une certaine profondeur.

Ces troubles ont été retrouvés dans des conditions similaires chez d'autres espèces en particulier le porc (101 bars, $PIO_2$ = 450 mb) et le babouin Papio papio (91 bars,

420 mb). Chez le porc les manifestations sont identiques à celles décrites chez les caprins. Chez les babouins la forme clinique est de type épileptique ; nous avons pu, après relèvement de $PIO_2$ à 800 mb, obtenir une récupération complète de l'animal et le ramener à la pression atmosphérique par une décompression de 90 heures sans répétition de la crise épileptique. L'animal survit encore après 9 mois. Notons que lors de cette expérience dans laquelle étaient simultanément utilisés un babouin intact et un bouc porteur d'électrodes à demeure. Les manifestations aiguës sont survenues simultanément chez les deux sujets. Le relèvement de $PIO_2$ n'a cependant assuré que la survie du babouin.

2) Dans certaines expériences en mélange oxygène-hélium conduites jusqu'à la limite de survie (90-111 bars), nous avons utilisé des sujets porteurs d'électrodes implantées à demeure permettant l'enregistrement simultané de l'E.E.G., de l'E.C.G., de l'E.M.G. de muscles posturaux (quadriceps fémoral, triceps brachial), respiratoire (diaphragme) ou lisse (paroi gastrique) et de la température interne. Les enregistrements confirment la brutalité de la crise hypoxique qui s'est avérée mortelle dans chaque cas. Les perturbations E.E.G. s'installent au moment de la chute de l'animal et consistent essentiellement en ondes lentes de grande amplitude (delta) significatives de l'hypoxie corticale. Elles précèdent le *silence électrique* définitif mais peuvent être entrecoupées de phases moins synchronisées au cours de la période de paralysie flasque. Les spasmes inspiratoires (E.M.G. du diaphragme) correspondent aux phases d'hypertonie des membres (E.M.G. des muscles posturaux). La fréquence cardiaque est considérablement augmentée, le cœur ne ralentissant qu'au cours de la dernière minute.

Nous attendions surtout des enregistrements polygraphiques continus, la mise en évidence de signes de souffrance physiologique précédant et annonçant les manifestations aiguës. Nous avons constaté au-delà de 61 bars une augmentation régulière avec la pression des fréquences cardiaque et respiratoire et de l'activité musculaire tonique. L'activité comportementale tend à se réduire bien que le sujet reste debout (hypertonie musculaire et raideur des articulations) et bien que les périodes de somnolence E.E.G. diminuent significativement en nombre et en durée. Ces manifestations nous semblent cependant davantage liées à la compression qu'à la pression absolue car elles sont amplifiées au moment des changements de palier. Les expériences réalisées sont de durées relativement courtes (2 à 3 jours) et nous manquons pour le moment d'enregistrements au cours de séjours prolongés. Plus spécifiquement liées à la pression, nous constatons d'une part une augmentation progressive du recrutement dans le diaphragme et d'autre part des perturbations de la motricité gastrique :

a) Le recrutement diaphragmatique correspond évidemment à l'accroissement de l'effort inspiratoire résultant de l'augmentation de la masse spécifique du mélange respiré. Cet accroissement n'est cependant pas suffisant pour déborder les possibilités de l'appareil ventilatoire du sujet même à 111 bars, qui constitue la pression extrême expérimentée.

b) Les troubles de la motricité gastrique sont révélés par l'électromyographie de la paroi du réseau, la poche la plus antérieure du complexe gastrique des Ruminants. Chez ces animaux la motricité gastrique est organisée au niveau de centres réflexes bulbaires déchargeant par la voie vagale suivant des cycles de contractions ruméno-réticulaires qui assurent l'homogénéisation du contenu stomacal. La fréquence, la régularité et la morphologie des contractions bi ou triphasiques du réseau sont étroitement corrélées au comportement et à l'état psychosomatique du sujet (Ruckebusch, 1968). Nous avons constaté une tendance au ralentissement général du rythme des contractions, même pendant les phases d'activité comportementale de niveau élevé. Aux pressions extrêmes, voisines des limites, surviennent des arrêts complets se prolongeant plusieurs dizaines de minutes et réversibles par des relèvements de $PIO_2$.

Ces modifications sont observées plusieurs heures avant la crise fatale et les perturbations de l'E.E.G. Les mécanismes de cette inhibition gastrique restent pour le moment inconnus. Quoiqu'il en soit, cette observation comporte un aspect pratique évident : c'est au niveau des fonctions végétatives qu'il faut rechercher les signes cliniques susceptibles d'avertir de l'imminence de troubles aigus de type hypoxique.

3°) La nécessité de relever $PIO_2$ lors des séjours sous pressions élevées comporte le risque de provoquer au delà d'une certaine valeur des troubles hyperoxiques de type Lorrain-Smith.

Le délai d'installation des lésions pulmonaires est d'autant plus court que $PIO_2$ est plus élevé. Lors de la respiration d'oxygène pur à la pression atmosphérique les premiers signes apparaissent chez l'Homme en 70 heures. Pour des $PIO_2$ plus faibles ce délai augmente rapidement et au dessous de 400 mb des expositions très prolongées peuvent être effectuées (Barthelemy 1963, Fructus et Chouteau 1963). Cette relation $PIO_2$/temps conditionne la du-

rée et la profondeur de la plongée à saturation lorsqu'une valeur de $PIO_2$ supérieure à 400 mb est nécessaire. Cette relation est bien connue aux faibles profondeurs donc aux pressions voisines de la pression atmosphérique (voir en particulier LAMBERTSEN 1965), mais il n'est pas certain « a priori » qu'elle ne se modifie pas sous pression élevée et que notamment, le seuil d'immunité se maintienne à 400 mb. Trois hypothèses sont possibles.

a) Le seuil de normoxie étant augmenté, on pourrait espérer que le seuil d'hyperoxie chronique l'est également. A la limite un compromis serait possible et permettrait d'envisager d'augmenter la profondeur et la durée des séjours.

b) Si le seuil d'hyperoxie n'est pas modifié, la plongée à saturation se trouve naturellement limitée au seuil de pression où le relèvement nécessaire de $PIO_2$ atteint la valeur hyperoxique.

c) Enfin on peut craindre que les effets toxiques de l'oxygène puissent être potentialisés par la pression ou les conditions d'environnement associées à la plongée. Dans ce cas le seuil d'hyperoxie peut être abaissé alors que celui de normoxie est relevé. La plongée à saturation se trouve alors limitée en profondeur et en durée par deux effets concourant à réduire l'intervalle des $PIO_2$ admissibles.

Les résultats expérimentaux dont nous disposons pour l'instant semblent éliminer la première hypothèse.

Nous avons vu plus haut qu'avec $PIO_2$ = 350-400 mb, valeur ne devant pas entraîner de risque hyperoxique, le comportement des animaux est normal à 81 bars (800 mètres). Nous avons voulu vérifier ce fait au cours d'expositions prolongées de longue durée (8 à 10 jours) suivies de décompression. Six boucs ont été soumis à ces conditions au cours de deux expériences de plongée fictive.

- Au cours de la première expérience, après 48 heures de séjour à 81 bars, les animaux étaient asthéniques et inactifs et surtout présentaient des troubles digestifs (diarrhée, météorisation) associés à des déviations du comportement alimentaire (mallophagie, boulimie). Une décompression de 10 bars a permis d'obtenir une nette amélioration sur tous les plans et après 5 jours à 71 bars, les animaux ont été recomprimés à 81 bars. Le deuxième séjour à 81 bars n'a été que de 36 heures, les troubles réapparaissant surtout chez l'un des animaux. Ce sujet est mort quelques heures après le début de la décompression (46 bars) mais les deux autres ont pu être ramenés à la pression atmosphérique en bon état (durée de la décompression exponentielle : 72 heures). Les troubles digestifs observés sont surtout imputables à un défaut de conditionnement alimentaire des sujets dans la phase préliminaire.

- Au cours de la deuxième expérience, trois boucs ont séjourné 8 jours à 81 bars. Par suite de divers incidents techniques et d'une souillure de notre hélium par de l'oxygène, les animaux ont été soumis durant environ 76 heures à des valeurs de $PIO_2$ supérieures à 420 mb ($PIO_2$ maximum : 480 mb). Le comportement des sujets était excellent à la fin du séjour à 81 bars et pendant la première partie de la décompression effectuée suivant un thème plus conservateur que celui de la première expérience. A partir de 61 bars, les trois sujets ont présenté des signes de maladie de la décompression qui se sont aggravés rapidement. Nous avons obtenu une légère rémission en effectuant des paliers, en réduisant la vitesse et en augmentant $PIO_2$ aux alentours de 600 mb et plus. Cette valeur de $PIO_2$ a été maintenue durant toute la suite de la décompression, donc pendant 80 heures environ. Dans des conditions très difficiles, les animaux ont atteint une pression de 4 bars, niveau auquel de l'air est substitué au mélange oxygène-hélium. Le passage à l'air, en augmentant la densité de l'atmosphère, a entraîné d'importantes difficultés respiratoires et la mort des trois sujets dans un tableau asphyxique. L'autopsie a mis en évidence une pneumonie à l'oxygène gravissime. L'état des poumons explique la maladie de décompression par une diminution très importante de la capacité de diffusion. Les sujets ont été victimes d'un enchaînement de troubles dont il faut rechercher l'origine dans les périodes d'hyperoxie qui se situent au cours de la mise en pression et du séjour à 81 bars, pendant lesquels, au total, le comportement et l'état des animaux avaient été satisfaisants. Le maintien d'une valeur de $PIO_2$ encore plus élevée durant la décompression a finalement aggravé tous les troubles. Il semble donc qu'un dépassement relativement faible de la valeur limite de 400-420 mb de $PIO_2$ entraîne des troubles hyperoxiques même en respiration discontinue contrairement aux données classiques à la pression atmosphérique. On pourrait penser que cela est dû à un effet potentialisant des hautes pressions ou éventuellement d'un autre paramètre de l'environnement.

4°) Des expériences plus récentes effectuées sur des porcs au G.E.R.S. ont effectivement montré l'importance de l'hygrométrie

en tant que facteur étiologique synergique de l'oxygène. Quatre sujets, pesant 40 à 45 kg, ont été soumis avec des protocoles pratiquement identiques à des plongées fictives à 76 bars d'une durée globale d'une semaine, $PIO_2$ étant régulé à 500 mb. Dans une première série l'hygrométrie relative était de 45 à 50 % (température 32°C) et les animaux n'ont présenté aucun trouble. Dans la seconde série l'hygrométrie était maintenue à 80 %, valeur correspondant en moyenne à celle entretenue au cours des expériences à 81 bars sur les boucs. Le sujet a présenté *des difficultés respiratoires* (« tirage »). Au retour en surface, l'autopsie a montré des signes importants de pneumonie à l'oxygène. Il semble donc bien que l'association d'une hygrométrie élevée et d'une valeur de $PIO_2$ supérieure à 420 mb entraîne des lésions hyperoxiques. On peut donc espérer reculer les limites de toxicité de l'oxygène sur le parenchyme pulmonaire en entretenant une hygrométrie inférieure à 50 %.

D'autre part nous avons constaté chez les Caprins, un recul constant du seuil *d'apparition des manifestations* hypoxiques par une amélioration progressive des conditions expérimentales (Chouteau, Imbert et Alinat 1969). Avec $PIO_2$ = 210 à 220 mb, les troubles survenaient à 51 bars lors de la première expérience (humidité relative à 100 %), à 71 bars à partir des expériences suivantes (humidité relative 60 à 70 %). L'importance de l'hygrométrie non seulement dans la genèse des phénomènes hyperoxiques mais également dans celle des phénomènes hypoxiques a d'abord été vérifiée fortuitement. Des troubles de type hypoxique sont apparus à 71 bars ($PIO_2$ = 310 mb) chez un bouc lors d'une remontée de l'hygrométrie à 100 %. La remise en service du filtre épurateur, suivi d'une chute rapide à 40 % a entraîné la récupération totale sans relèvement de $PIO_2$.

L'importance et le rôle qu'il convient d'attribuer à ce nouveau facteur ne pourront être clairement compris que lorsque seront élucidés les mécanismes impliqués *dans l'ensemble des phénomènes que nous* venons d'exposer.

## MECANISMES DE L'EFFET HYPOXIQUE

La manifestation de troubles hypoxiques lors de la respiration d'un mélange normoxique sous pression semble un facteur fondamental de la limitation de la plongée profonde. Son origine et ses rapports avec la narcose aux gaz inertes méritent d'être discutés.

1°) L'effet hypoxique ne semble pas tirer son origine d'une hypoventilation alvéolaire résultant de l'augmentation de la masse spécifique du mélange respiratoire sous pression. Celle-ci devrait s'accompagner d'une hypercapnie importante dont les signes ne devraient pas disparaître par augmentation de $PIO_2$ (Chouteau et al. 1968). D'autre part des expériences d'anoxie ont été effectuées sur les Caprins à la pression atmosphérique ($PIO_2$ compris entre 120 et 40 mb). Elles ont confirmé, en dehors de toute intoxication au gaz carbonique, l'identité des signes cliniques et électrographiques.

2°) Nous pensons que l'hypoxie résulte d'une perturbation des échanges gazeux alvéolo-capillaires induisant une hypoxémie. Ces perturbations correspondent soit à une diminution de la capacité de diffusion pour l'oxygène (barrière de diffusion, bloc alvéolo-capillaire), soit d'une très grande inhomogénéité des rapports ventilation-perfusion. Les deux hypothèses ne s'excluent d'ailleurs pas l'une, l'autre.

Une série d'expériences en collaboration avec le Certsm a été effectuée sur des lapins (27 sujets) anesthésiés à l'uréthane et porteurs d'une électrode ampéro-polarographique à $PIO_2$ dans la crosse aortique. Ces animaux ont été comprimés dans des caissons de dimensions réduites avec des mélanges normoxiques oxygène-hélium et également oxygène-azote, oxygène-argon et oxygène-néon. On observe au-delà d'un certain seuil de pression variable avec la nature du gaz diluant une chute significative de $PAO_2$ réversible par relèvement de $PIO_2$ et/ou décompression.

Cette chute de $PAO_2$ intervient obligatoirement lorsque la masse spécifique du mélange *respiré dépasse* 25 g/l c'est-à-dire à une pression d'autant plus basse que le gaz utilisé comme diluant de l'oxygène est plus lourd. Les effets de l'hélium sont plus marqués que ceux obtenus avec les autres gaz inertes :

- la chute de $PAO_2$ intervient pour une masse spécifique plus faible, environ moitié, c'est-à-dire vers 91 bars ;

- la chute est extrêmement importante, alors qu'avec les autres gaz elle reste comprise entre 20 et 40 % de la valeur initiale ;

- la réversibilité obtenue par relèvement de $PIO_2$ n'est que temporaire, alors qu'elle est définitive dans le cas des autres gaz. Seule la décompression rétablit $PAO_2$ normal.

Cette chute de $PAO_2$ notamment en mélange normoxique oxygène-hélium est suffisamment importante pour expliquer les *perturbations sévères observées* chez l'animal normal.

Nous n'avons jamais utilisé les mélanges oxygène-néon ni oxygène-argon pour des expériences de plongée fictive chez l'animal intact. Par contre nous avons effectué des expositions prolongées à un mélange azote-oxygène *normoxique* jusqu'à 21 bars, chez des Caprins (8 sujets) et sur des babouins (3 sujets).

Nous avons obtenu, chez les Caprins notamment, des phénomènes *aigus analogues* quoique moins sévères que ceux que nous avons décrits *en atmosphère* oxygène-hélium, réversibles par relèvement de $PIO_2$ et survenant entre 12 et 17 bars. Nous n'avons pas obtenu de manifestation paroxystique chez les babouins, analogue à celle que nous avons décrite plus haut en atmosphère oxygène-hélium. Cependant dans le cas de l'azote, la séméiologie est compliquée par les perturbations entraînées par la narcose.

3°) La narcose aux gaz inertes est attribuée à une hypoxie cellulaire de type histotoxique due à l'augmentation de pression *partielle en gaz neutres* (BENNETT 1966). Les tensions élevées de gaz neutres dissous par les phospholipides des membranes cellulaires seraient responsables d'une limitation de la diffusion de l'oxygène et de perturbations des échanges ioniques ($Na^+$ et $K^+$ essentiellement). Les effets narcotiques des gaz neutres semblent en effet fonction de leur coefficient de partage entre l'eau et les graisses, suivant la *théorie générale* de l'anesthésie volatile (MEYER, OVERTON) et de *leur solubilité générale* dans les lipides (expliquant que l'argon soit plus narcotique que l'azote à coefficients de partage similaires). Ces propriétés de solubilité permettent de classer les gaz neutres dans un ordre croissant de pouvoirs narcotiques, lorsque ces derniers sont connus : Xe, Kr, Ar, $N_2$, et laissent prévoir dans le cas de l'hélium les premières manifestations entre 50 et 80 bars. En réalité, les phénomènes que nous avons observés dans ce *domaine de pressions en* mélange oxygène-hélium ne semblent pas *correspondre à un début* de narcose aux gaz inertes :

a) les perturbations mises en évidence par les enregistrements polygraphiques *effectués sur les Caprins* jusqu'à 111 bars (1100 mètres fictifs), ne présentent aucun caractère de narcose telle qu'elle peut être constatée avec les mêmes types d'enregistrement entre 11 et 21 bars en atmosphère oxygène-azote normoxique ;

b) la *faible augmentation* de $PIO_2$ qui permet de corriger les troubles ne devrait pas être efficace aussi immédiatement sur une hypoxie de type histio-toxique ;

c) lors d'expositions de *longue durée* en atmosphère $O_2$-$N_2$, l'augmentation de $PIO_2$ *n'influence qu'une* partie des comportements anormaux des sujets. Des constatations de ce type ont été effectuées au cours d'expositions de longue durée de boucs (15 jours à 11-12 bars) et surtout chez des babouins préparés en « chroniques » pour des mesures réflexologiques (jusqu'à 21 bars). Chez ces derniers nous avons pu observer que certaines perturbations réflexologiques peuvent être corrigées par un relèvement de $PIO_2$ de 210 à 390 mb. C'est le cas notamment d'une hyper-réflexie tendineuse bilatérale bien établie en profondeur. Par contre, d'autres manifestations sont peu ou pas modifiées par l'injection d'oxygène comme les perturbations comportementales (prostration au delà de 16 bars), électroencéphalographiques (activité thêta) ou réflexologiques (diminution de la latence sommitale des réponses polysynaptiques).

Ces résultats ne peuvent s'interpréter qu'en admettant en atmosphère oxygène-azote sous pression, l'intrication de phénomènes narcotiques peu sensibles à $PIO_2$ et de phénomènes en relation avec l'existence d'une hypoxémie discrète (l'effet hypoxique étant moins marqué qu'en atmosphère oxygène-hélium).

Cependant les deux facteurs ne peuvent pas être nettement séparés dans leurs conséquences en raison de leurs interactions mutuelles :

- on peut envisager en effet que la réduction de l'activité spontanée due à la narcose entraîne une diminution des besoins du sujet en oxygène et du risque hypoxique,

- inversement les effets activateurs de l'hypoxémie sur le S.N.C. sont bien connus (HUGELIN et al. 1959) et doivent développer une action antagoniste de la narcose. Par ailleurs, dans le cas d'un gaz non narcotique comme l'hélium, cette donnée ne doit pas être oubliée dans l'interprétation d'un éventuel « effet excitant » des hautes pressions (BRAUER).

Ces phénomènes sont encore compliqués par l'intervention de facteurs mal connus d'adaptation à la narcose aux gaz inertes notamment au cours des expositions prolongées. Au delà de 7 à 8 bars (60 à 70 mètres), la narcose à l'azote n'a fait l'objet d'études systématiques que lors d'expositions de courtes durées.

4°) Une autre source de perturbations qui a été à peine évoquée car elle dépasse le cadre que nous nous sommes imposé, découle des effets des compressions rapides. La vitesse de mise en pression est responsable d'un ensemble de troubles que certains A. ont décrits chez l'Homme sous le nom de « Syndrome Nerveux des Hautes

Pressions » (FRUCTUS et al. 1969). Ces manifestations se traduisent essentiellement par des tremblements (« helium tremor » décrits par P.B. BENNETT 1967), des nausées, des vertiges et une somnolence incoercible. Au syndrome neurologique et électrographique (activités thêta), s'associent éventuellement des douleurs articulaires (« No joint Juice Syndrom »).

Par contre il ne semble pas qu'il y ait lieu d'y rattacher les crises épileptiques décrites chez le singe lors de plongées profondes en atmosphère oxygène-hélium (BRAUER 1970). Comme nous l'avons vu plus haut, ce type de crise se manifeste chez le babouin simultanément aux crises hypoxiques chez le bouc. Elles se rattachent spécifiquement à la pathologie décrite chez les Caprins, le Porc et les Rongeurs dont elles constituent la traduction chez une espèce dont la susceptibilité épileptique à l'hypoxie est connue (BOSTEM et LESEVRE 1968).

L'origine des troubles, dont la gravité est proportionnelle à la vitesse de compression, doit être liée à des dysbarismes s'établissant au cours de la mise en pression, en raison de l'inégalité des vitesses de saturation en gaz neutres des divers compartiments. Pour LANGMUR et KYLSTRA (1968), ces effets seraient provoqués par la pression osmotique développée entre compartiments voisins inégalement saturés en gaz neutres. Les perturbations des échanges membranaires aqueux et ioniques pourraient expliquer les divers symptômes observés.

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En résumé, l'ensemble des troubles entraînés par la plongée profonde semblent en relation avec des perturbations des échanges entre compartiments entrainés par la présence de fortes tensions en gaz neutres. En ce qui concerne les facteurs les plus importants de limitation, une bonne partie des phénomènes semble consommé au niveau de la membrane alvéolo-capillaire.

Dans le cas de l'hypoxie aiguë, comme dans le cas de l'hyperoxie chronique, c'est une diminution de la capacité de diffusion pulmonaire à l'oxygène qui est responsable des perturbations gravissimes que nous avons laissé établir chez les animaux. On peut supposer l'existence d'autres barrières de diffusion qui jouent cependant un rôle moindre.

Les mécanismes mis en jeu dans la formation du bloc de diffusion alvéolo-capillaire ne sont réellement connus ni dans le cas de l'hypoxie, ni dans celui de l'hyperoxie. Certains facteurs, comme l'hygrométrie, semblent intervenir dans les deux phénomènes. Dans les deux cas, une atteinte spécifique du surfactant pulmonaire, riche en phospholipides, ou des organites impliqués dans sa formation (corps lamellaires) doit jouer un rôle important. La disparition du surfactant, son altération ou une modification de ses propriétés par les fortes pressions de gaz neutres, peuvent favoriser les alectasies et les processus congestifs et œdémateux entrainant des perturbations des rapports ventilation-perfusion ou simplement un ralentissement de la diffusion des gaz liposolubles comme l'oxygène. Dans le cas de l'hyperoxie ce type de modifications a pu être observé en microscopie électronique (KISTLER et al. 1967) ainsi que des variations des propriétés tensio-actives du surfactant pulmonaire (CALDWELL et al. 1965). Nous avons mis ces propriétés à l'étude sous hautes pressions d'hélium.

Sur le plan pratique, une étude systématique du facteur hygrométrique est également mise en œuvre pour optimiser les conditions d'environnement de la plongée profonde. Dans ce domaine certains progrès peuvent encore être attendus, mais resteront probablement limités.

Si les résultats obtenus sur l'animal sont transposables à l'homme et en gardant une marge de sécurité suffisante, la plongée humaine profonde et de longue durée doit avoir une limite qui n'est pas très éloignée des plongées-record effectuées récemment (53 bars, -520 mètres, COMEX, 1967). Au delà, seulement des incursions de brèves durées pourront être envisagées. Il convient toutefois de noter que ces incursions seront elles-mêmes probablement limitées à une dizaine de bars (correspondant à une centaine de mètres) à partir de la profondeur de saturation) par les phénomènes dysbariques que nous avons brièvement discutés.

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(Aus dem Physiologischen Institut der Universität Bonn.)

# Über das Verhalten des Zentralnervensystems (Rückenmarksfrosch) unter der Einwirkung hoher Drucke[1].

Von

**U. Ebbecke.**

*(Eingegangen am 10. März 1936.)*

Hängt man einen Rückenmarksfrosch in eine mit Wasser oder Salzlösung gefüllte Druckbombe und steigert in ihr den Druck, so treten bei einer bestimmten Druckhöhe klonische, unregelmäßige rhythmische Bewegungen der Extremitäten auf, die bei weiterer Drucksteigerung stillgestellt werden. Es handelt sich um eine neue Form der durch Kompression erzeugten Reiz- und Lähmungswirkung, die im folgenden näher betrachtet und analysiert werden soll.

Die Versuchsvorrichtung ist in bezug auf Druckpumpe und Druckbombe die gleiche, wie sie für die Viscositätsmessungen benutzt wurde, so daß auf jene Arbeit verwiesen werden kann[2]. Die beiden, die Durchleuchtung und Beobachtung ermöglichenden Fensterpaare der Viscosimeterbombe mit ihrem Abstand von 50 mm erlauben bei passender Aufhängung des Präparats, im unteren Fenster die Zehen oder Pfoten, im obern die Oberschenkel des Frosches zu sehen. Um Verunreinigung und Vermischung von Füllflüssigkeit und Präparatflüssigkeit zu vermeiden, kam das Präparat in ein Reagenzglas von weitem Lumen (25 cm Durchmesser), nachdem die sonst überstehenden vorderen Extremitäten abgeschnitten waren. In vielen Fällen wurden auch die vordere Bauch- und Brustwand und sämtliche Eingeweide entfernt.

Die Bewegungen, die in der Regel zwischen 150 und 200 Atm. am besten zu sehen sind, bestehen in einem unregelmäßigen Hin und Her von Flexion und Extension, Adduktion und Abduktion, das zuweilen nur die Zehen oder den Fuß, meist aber zugleich auch Unter- und Oberschenkel ergreift. Man sieht die Pfote abwechselnd hochgezogen werden und zurücksinken oder von einer Seite zur andern an dem Fenster vorbeischlagen. Das Präparat fängt unter dem Druck an, oft recht heftig zu zappeln, um sofort bei Druckablaß wieder in die hängende Ruhelage zurückzukehren. Niemals wurde eine längerdauernde Beinanziehung oder Streckung beobachtet. Zuweilen erinnern die Bewegungen an Sprung- und Schwimmbewegungen.

Die Druckschwelle für die rhythmisch klonische Reizung liegt meist bei 100—150 Atm., in seltenen Fällen schon bei 50 Atm. Die erste schwächste Reizwirkung ist gewöhnlich eine einmalige leichte Bewegung des Fußes oder Beines, das danach bei fortbestehendem Druck in Ruhe bleibt (Anfangswirkung). (Daß es sich nicht etwa um mechanische, durch Flüssigkeitsströmungen in der Bombe entstandene Verschiebungen

[1] Ausgeführt mit Unterstützung der deutschen Forschungsgemeinschaft. —
[2] *Ebbecke:* Pflügers Arch. (erscheint demnächst).

handeln kann, ist leicht daran zu sehen, daß ein totes Präparat bei Druckanstieg und -abstieg völlig in Ruhe bleibt.) Mehrfach wiederholte und besonders höhere Drucke setzen die Reizschwelle herauf. Ob der Druckanstieg schneller oder langsamer erfolgt, scheint keinen wesentlichen Einfluß auf die Höhe der Druckschwelle zu haben. Dagegen sind die individuellen Unterschiede von Präparat zu Präparat recht groß.

Die Bewegungen setzen meist ohne merkliche Verzögerung bei Erreichen einer genügenden Druckhöhe ein, und nur in wenigen Fällen vergeht eine kurze Latenzzeit, bis die Bewegungen in Gang kommen, oder während der sie an Heftigkeit zunehmen. In dem Druckbereich von 200—250 Atm. pflegen die Bewegungen ihre größte Stärke und auch ihre größte Dauer zu erreichen. Statt der Anfangswirkung macht der kontinuierlich bestehende Druck nun eine Dauerreizung, die sich je nach dem Kräftezustand des Präparats unter Umständen 2—3 Min. lang fortsetzt, meist freilich schon nach 20—30 Sek. sich abschwächt und verliert. Bei den längeren Bewegungsserien kommt gelegentlich ein recht regelmäßiger Rhythmus zum Vorschein, und in einem Fall konnten 93 in gleichem Takt aufeinanderfolgende Zehenbewegungen von der Frequenz 41 in der Minute gezählt werden, die an Regelmäßigkeit einem Herzrhythmus oder Medusenrhythmus nicht nachstanden.

Übersteigt der Druck den durchschnittlich optimalen Bereich zwischen 150 und 250 Atm., so kann die Frequenz bei den Bewegungsserien zunächst noch zunehmen, unter Umständen bis zum feinschlägigen Zittern, die Amplitude, das Ausmaß der Bewegungen nimmt aber in allen Fällen ab, und besonders verkürzt sich die Dauer der Bewegungen, so daß Drucke von 300 Atm. und darüber wiederum so wie die schwächsten Drucke nur noch Anfangswirkung haben. Der Unterschied von jenen ist aber ihre lähmende und schädigende Wirkung, die schon nach kurzem Bestehen schlecht oder gar nicht reversibel wird. Wird der Druck stufenweise von 200 auf 300 Atm. gesteigert, so kann man eine in Gang befindliche Bewegungsreihe durch den Druckanstieg plötzlich zum Stillstand bringen. Steigt der Druck rasch von 0—300 oder 400 Atm., so scheinen ein oder einige wenige der Lähmung vorangehende Schläge niemals zu fehlen. Schon nach einem 300-Druck von 20—30 Sek. kann das Präparat so geschädigt sein, daß es nun auch auf einen vorher wirksamen 200-Druck kaum oder gar nicht anspricht und, außerhalb der Bombe geprüft, sich als unerregbar und tot erweist. In anderen Fällen zeigt ein Präparat, nach einem kurzdauernden 300-Druck aus der Bombe herausgenommen, erhaltene, wenn auch herabgesetzte Reflexerregbarkeit, die sich nachträglich noch etwas erholen kann, und es kommt vor, daß ein Präparat, das bei 300 Atm. in Ruhe war, bei Drucksenkung auf 200 Atm. wieder einige Schläge macht als Zeichen für die reversible Natur der Lähmung. Im übrigen fehlt jede eigene Wirkung eines

plötzlichen Druckabfalls und konnten keine Entlastungsreizwirkungen beobachtet werden.

Wenn im vorhergehenden die auf Druck eintretenden klonischen Bewegungen in ihrer Druckabhängigkeit und ihrem zeitlichen Verlauf geschildert sind, so ist nun die Frage nach dem Angriffspunkt der Reiz- und Lähmungswirkung zu erörtern. Ein Präparat mit ausgebohrtem Rückenmark zeigt keinerlei vergleichbare Erscheinungen, und schon daraus geht hervor, daß das Erhaltensein der Rückenmarkszentren Vorbedingung ist. Bei den zahlreichen früher angestellten Versuchen an quergestreiften Muskeln und Nervmuskelpräparaten hatten niemals rhythmische, durch den Druck allein hervorgerufene Reizwirkungen gefunden werden können, sondern immer nur stetige, während der Druckdauer gleichmäßig anhaltende Reiz- oder Lähmungswirkungen, die außerdem zu ihrem Zustandekommen bedeutend höherer Druckwerte bedurften. Bei der Kompressionsverkürzung liegt die Schwelle für die mit optischer Vergrößerung registrierte schwächste Bewegung zwischen 150 und 200 Atm., aber erst jenseits 300 oder 400 Atm. wird die Verkürzung mit bloßem Auge gut sichtbar. Noch deutlicher wird der Gegensatz, wenn an einem in bezug auf das Rückenmark toten Froschpräparat durch einen Druck von 600—800 Atm. die völlige Streckstarre und Steifheit der Extremitäten hervorgerufen wird, die eine nur äußerliche Ähnlichkeit mit einem Strychninkrampf, aber keinerlei Verwandtschaft mit dieser klonischen, eher den Phenolkrämpfen vergleichbaren Bewegungsunruhe aufweist. Der Skeletmuskel kommt hiernach für den Angriff der Reizwirkung nicht in Betracht, ebensowenig aber auch die periphere Nervenfaser, an der immer nur Erregbarkeitsänderungen, aber keine selbständigen Impulse durch den Druck hervorgerufen werden, und die nach den das Rückenmarkspräparat lähmenden Drucken von 300 Atm. in voller Funktionsfähigkeit überleben, wie die elektrische oder mechanische Nervenreizung zeigt. Auf die gut erhaltene Reizbarkeit der Nervenfaser ist wohl auch der Befund zurückzuführen, daß an einem Präparat, das weder innerhalb der Bombe durch Druck noch außerhalb der Bombe durch Hautreize zu Reflexen oder reflexähnlichen Bewegungen zu veranlassen ist, beim Ausbohren des anscheinend toten Rückenmarks noch — eben durch mechanische Reizung von Nervenbahnen — kurzdauernde unregelmäßige Bewegungen auftreten. Können somit der Skeletmuskel und die periphere Nervenfaser innerhalb und außerhalb des Rückenmarks als Ausgangspunkt der rhythmischen Reizwirkung ausgeschlossen werden, so bliebe noch die Möglichkeit, daß die Receptoren der Peripherie am Anfang des Reflexbogens für die Art des Reizerfolgs verantwortlich wären. Aber auch diese Annahme läßt sich widerlegen.

Die Mehrzahl der Versuche, über die im vorhergehenden berichtet war, wurde an Rückenmarkspräparaten nach Dekapitation, Amputation der Vorderextremitäten und Eviszeration vorgenommen. Zwischen

eviszerierten Präparaten, bei denen außer den Schenkeln nur noch die Wirbelsäule mit anschließender Haut erhalten war, und den gewöhnlichen Rückenmarkspräparaten fand sich kein wesentlicher Unterschied. Die eviszerierten Präparate, die bequemer mit Hilfe einer um die Wirbelsäule gebundenen Schlinge an dem über die Reagenzglasöffnung gestülpten Haltering anzubinden und anzuhängen waren, bewiesen, daß eine Reizwirkung von seiten der Eingeweideorgane, etwa von der lufthaltigen Lunge her, durch Veränderung des Kreislaufes oder durch unphysiologische Flüssigkeiten, nicht im Spiele war. Um die Möglichkeit, daß die Reizwirkungen von den Receptoren der Haut ausgingen, zu untersuchen, wurde das Präparat enthäutet. Die Präparation war also die gleiche wie bei der Herstellung eines Nervschenkelpräparats, nur daß der Wirbelkanal nicht ausgebohrt war. Ist die Enthäutung vollständig, so ist durch Kneifen der Zehen kein Reflex mehr auszulösen, und nur faradische Reizung der Pfote, ihrer afferenten Nervenäste und -stämme ist noch wirksam. Es genügt ein kleiner Rest von Zehenhaut zur Auslösung der vollständigen ausgebreiteten Reflexe, die dann durch Abziehen des Hautrestes oder Abschneiden der Zehe beseitigt werden. Auch an diesem enthäuteten, seiner Receptoren völlig beraubten Rückenmarkspräparat konnten noch gute, kräftige und anhaltende Bewegungsserien durch Kompression in der Bombe erzielt werden.

Als Angriffspunkt der Kompressionswirkung ist daher das Zentralnervensystem selbst anzusehen, was nicht nur per exclusionem, sondern auch der Natur der Reizwirkung nach wahrscheinlich ist. Denn es handelt sich um typisch koordinierte, an Lauf-, Spring- und Schwimmbewegungen erinnernde Bewegungen, bei denen ein geordnetes Zusammenwirken vieler Muskelgruppen an Hüft-, Knie- und Fußgelenk vorliegt, wie es nur durch zentralnervöse Steuerung mit ihrer reziproken Innervation, mit ihrem Wechselspiel von Erregung und Hemmung, mit der synergistischen und antagonistischen Verknüpfung in Simultan- und Sukzessivinduktion erreichbar ist. Freilich ist es, da die Reizwirkung der Kompression in ungeordneter Weise das ganze Rückenmark gleichzeitig ergreift, einigermaßen zufällig, welche Innervationskomplexe und Zellgruppen als erste ansprechen, oder wie sich die verschiedenen Innervationen durchkreuzen, so daß die Bewegungen weniger sinnvoll erscheinen als ein gewöhnlicher Reflex und mehr den klonischen Bewegungen eines Phenolfrosches vergleichbar sind. Ein Analogon bieten auch die in einer vorangehenden Arbeit beschriebenen Wirkungen auf das Magenpräparat: Schwache Drucke regen die ihm eigentümliche und innewohnende Bewegungsrhythmik an oder rufen sie hervor, stärkere Drucke lähmen sie, und erst die stärksten bringen die Muskeln durch direkte Muskelreizung zur Kompressionsverkürzung. Schließlich sind neben der Phenolwirkung auch die rhythmischen Bewegungen zum Vergleich heranzuziehen, die in tiefer Narkose „spontan" auftreten können und von mehreren Autoren untersucht sind *(Graham Brown, Storm van Leeuwen, Ebbecke, Blume)*.

Wenn es demnach das Zentralnervensystem selbst ist, das in diesen Versuchen in der ihm eigentümlichen Weise auf die Kompressionswirkung reagiert, so führen die Versuche zu folgenden Schlußsätzen.

Die Kompression durch Drucke zwischen 100 und 300 Atm. wirkt auf das Zentralnervensystem als Reiz. Der kontinuierlich und stetig einwirkende Druckreiz wird vom Zentralnervensystem infolge der ihm innewohnenden Rhythmik, in Analogie zu dem Verhalten anderer rhythmisch arbeitender Organe und Organismen (Herz, Magen, Medusen) mit rhythmischer Reaktion beantwortet. Schon verhältnismäßig niedrige Drucke von 300 Atm., die für Muskeln und periphere Nerven keine Schädigung setzen und auch andere rhythmische Organe wie Herz und Magen noch intakt lassen, vermögen das Zentralnervensystem erst reversibel, sehr bald aber auch irreversibel zu schädigen. Das Zentralnervensystem ist gegenüber der Druckeinwirkung von allen untersuchten Organen das wenigst resistente.

Der Befund wirft ein Licht auf frühere Untersuchungen über die Druckeinwirkung an ganzen Fischen, bei denen sich zeigte, daß sie unter einem Druck von 400 oder schon 300 Atm. unter den Symptomen einer Erstickung (weit geöffnetes Maul und Kiemendeckel, kongestionierte Kiemen) bei sonst intakten inneren Organen schnell eingehen, was hiernach ebenfalls als zentralnervöse Lähmung und Schädigung zu deuten wäre.

## Zusammenfassung.

Ein Rückenmarkspräparat vom Frosch, das in die Druckbombe gehängt und bei Drucken von einigen hundert Atmosphären durch Fenster der Bombenwand beobachtet wird, zeigt, von 50—100 Atm. beginnend, am deutlichsten zwischen 150 und 250 Atm. rhythmisch-klonische Bewegungen der Extremitäten, die etwa den Phenol- und Narkosebewegungen vergleichbar sind und als Reaktion auf den gleichmäßig stetigen Druckreiz die dem Zentralnervensystem eigentümliche innere Rhythmik kennzeichnen. Drucke von 300 Atm., die für Muskel und peripheren Nerv unschädlich sind, lähmen das Zentralnervensystem erst reversibel, sehr bald aber irreversibel. Das Zentralnervensystem ist demnach für die Reiz- und Lähmungswirkungen der Kompression besonders empfindlich.

# BULLETIN

# MEDSUBHYP

SOCIÉTÉ FRANÇAISE DE MÉDECINE
SUBAQUATIQUE ET HYPERBARE

SERVICE D'HYPERBARIE - HOPITAL SALVATOR 13 MARSEILLE (9E)

N° 9 MARS 1973

Compte rendu des travaux communiqués lors de la seance du 20 octobre 1972 et de la table ronde du 19 Janvier 1973

ÉDITÉ PAR LA COMEX TRAVERSE DE LA JARRE 13275 MARSEILLE- CEDEX 2

# REFLEXIONS SUR LA COURBE DE COMPRESSION DES PLONGEES TRES PROFONDES

X. Fructus, C. Agarate et J. C. Rostain

Bull. Med. Sub. Hyp. 9: 2 - 6 (1973)

REFLEXIONS SUR LA COURBE DE COMPRESSION DES PLONGEES TRES PROFONDES(-)FRUCTUS X, (--), AGARATE C,(--) ROSTAIN J.C.(---)

Maintenant que nous sommes assurés de l'existence du SNHP chez l'homme, décrit et retrouvé non seulement par nous, à plusieurs reprises mais aussi par BENNET lors de la 1500 ft d'Alverstoke en Mars 1970, nous pouvons analyser plus objectivement le rôle favorisant de la vitesse de compression.

Lors de la première 365 mètres (PHYSALIE III - 1968) la vitesse de compression était en moyenne de 3m/minute ; les signes cliniques et électriques du SNHP apparurent dans la zone des 250 mètres pour s'accentuer de façon inquiétante au dessous de 350 mètres.

Une compression à peine moins rapide lors de plusieurs expériences réalisées, tant chez nous qu'à Alverstocke, dans la zone des 300-350 m n'avait pourtant pas paru affecter notablement les plongeurs. Ce qui ne nous a pas empêché de prendre quelques précautions pour comprimer les océanautes lors de la première phase de JANUS II Mai 1970 à 200 mètres seulement 5 minutes pour les premiers cent mètres - 20 min de 100 à 150 - palier de 10 minutes à 150 - descente de 150 à 200 mètres en 35 minutes - malgré ces précautions si les sujets n'objectivèrent pas un SNHP ils présentèrent des vertiges des signes articulaires et une fatigue marquée à l'arrivée au fond.

Tout cela s'accentuant lors de la première descente (type ludion) de 200 à 250 mètres et ayant totalement disparu lors du 2° ludion 10 heures plus tard.

A partir de cette observation nous décidâmes de mettre à l'étude une courbe de compression - Pour cela il fallait se fonder sur une hypothèse de travail - Nous adoptâmes celle du "dysbarisme osmotique" défendue par Kylstra, sans nous douter que 18 mois plus tard nous serions en mesure de retrouver expérimentalement des perturbations osmotiques dans le plasma des sujets soumis à de hautes pressions d'hélium.

Le dysbarisme osmotique fait intervenir le déséquilibre existant entre la saturation en gaz inertes des tissus rapides tels que le sang et celle des tissus plus lents, lors des variations rapides de pression. Ce déséquilibre peut avoir des effets non négligeables au niveau de certaines formations ou de certains compartiments liquidiens (appareil cochléo-vestibulaire, L.C.R., articulations)

Hypothèse, certes, mais hypothèse pratique, car tout autre processus d'adaptation biologique favorisé par une compression lente, ou très lente, serait difficilement quantifiable autrement que par une expérimentation systématique, difficile à réaliser chez l'homme.

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(-) Travail réalisé au CENTRE EXPERIMENTAL HYPERBARE de la COMEX - MARSEILLE

(--) C.N.E.X.O. - COMEX - 13275 MARSEILLE CEDEX II

(---) C.N.R.S. - I.N.P.3 - 32 Ch Joseph Aiguier 13009 - MARSEILLE

Nous avons donc admis qu'il pourrait exister une valeur limité des différences de pression de gaz dissous au-delà de laquelle le déséquilibre osmotique ferait apparaitre des troubles: vertiges, tremblements, S.N.H.P, syndrome articulaire des hautes pressions.

Cette valeur limite, ou gradient admissible, pouvait être de l'ordre de 100 mètres d'après notre expérience pratique; expérience fondée dans le domaine opérationnel sur des milliers de plongées profondes à l'héliox.

L'un entre nous a donc calculé la vitesse de compression compatible avec le maintien d'un gradient constant - Cela donnait pour " JANUS II " une compression rapide de 0 à 100 mètres d'une "descente" en 5 heures de 100 à 200 mètres (20 m/Heure)

Avant le 1° ludion (200-250 m en 10 minutes) 1pause de 4 heures était respectée.

Résultats relativement satisfaisant lors de la 2° expérience JANUS II (Phase II) mais incomplets tout de même - D'où réduction des gradients pour les expériences suivantes (Phase II B et III Gradient d'environ 85 mètres au départ d'où pressurisation à 15 m/h (8h de 80 à 200m) Pause minimale de 6 heures à 200 mètres pour réduire le gradient initial à 30 mètres avant la première plongée - travail à 250 m ce qui portera le gradient total à 30 + 50 = 80 mètres.

Les résultats, excellents, nous confirmèrent l'efficacité de cette méthode de travail.

En Septembre 70, nous pûmes, nous référant à la 1500 ft (457m) d'Alverstoke, calculer les gradients de sous-saturation du tissu considéré comme le plus long pour l'hélium (240 minutes à l'arrivée aux différents paliers). Cela donna:

180 m à 600 ft
125,5 m à 1000 ft
78,5 à 1300 ft
57,5 m à 1500 ft

Or les constatations cliniques de BENNET à l'arrivée des plongeurs à ces niveaux successifs montraient que ces valeurs de gradient était encore trop fortes et devaient être réduites.

Il s'en dégageait aussi la notion de variabilité du gradient admissible: un gradient de 80 mètres, admissible à 250m (JANUS II) est trop important à 400 m et doit être inférieur à 57,5 mètres dans la tranche des 450m.

La méthode à gradient constant de JANUS II s'avérait donc inadéquate pour les profondeurs où doit justement apparaitre le SNHP. Ainsi nous admettions que la fonction $\hat{G}(P)$ est une fonction décroissante de la profondeur.

C'est à partir de cette idée que l'un d'entre nous calcula la courbe de compression de PHYSALIE V - 520 m- plongée fictive réalisée par 2 plongeurs de la Comex en Novembre 1970-

La table de compression présentait les pentes remarquables suivantes =

de 0 à 108 m.....60 m/h
de 238 à 307 m.....10 m/h
de 462 à 478 m..... 5 m/h
de 503 à 512 m..... 4 m/h

Pour des raisons d'ordre pratique et expérimental, la courbe de compression, ainci déterminée a été interrompue par des paliers de longue durée (16 heures environ) aux profondeurs de 350 et 460 mètres.

Ces paliers nous permirent:

- de mesurer l'influence d'un arrêt de la compression sur l'atténuation de symptômes éventuels du S.N.H.P. qui seraient apparus lors de la phase de compression précédente.

- d'effectuer, à profondeur constante, les différents tests et mesures physiologiques destinés à étudier, en détail, les réactions d'adaptation des plongeurs à ces niveaux intermédiaires.

- d'éviter les variations de pression pendant le sommeil: les modifications E.E.G. dues au S.N.H.P. pouvant ne pas être révélées au cours du sommeil.

De faire suivre chacun de ces paliers par une phase de compression "rapide" (1 mètre par minute) permettant ainsi, de tester, en deux points, la validité de la fonction G (P) choisie tout en s'affranchissant de l'incertitude subsistant dans le choix de la période du tissu "guide".

Le gradient admis étant de 50 m de 350 m à 400m, et 30m de 460m à 490m le programme réel de compression de "PHYSALIE V" s'est donc établi comme suit:

| | |
|---|---|
| de 0 à 108 mètres | 1 minute/mètre |
| de 108 à 135 mètres | 4 minutes/mètre |
| de 135 à 238 mètres | 5 minutes/mètre |
| de 238 à 307 mètres | 6 minutes/mètre |
| de 307 à 350 mètres | 7 minutes/mètre |

palier de 16 heures à 350 mètres

| | |
|---|---|
| de 350 à 400 mètres | 1 minute/mètre |
| de 400 à 421 mètres | 9 minutes/mètre |
| de 421 à 444 mètres | 10 minutes/mètre |
| de 444 à 460 mètres | 11 minutes/mètre |

Palier de 16 heures 15 à 460 mètres

| | |
|---|---|
| de 460 à 490 mètres | 1 minute/mètre |
| de 490 à 491 mètres | 13 minutes/mètre |
| de 491 à 503 mètres | 14 minutes/mètre |
| de 503 à 512 mètres | 15 minutes/mètre |
| de 512 à 518 mètres | 16 minutes/mètre |

La fonction G (P) théorique résultant de ce programme de compression pour un tissu de période 240 minutes est représentée sur la (Fig 1)

Les résultats furent appréciables - la courbe de compression avait permis à 2 plongeurs d'atteindre la profondeur fictive de 1700 ft et d'y rester 77 minutes. 77 minutes parce que nous tenions à respecter notre schéma initial. En fait les expériences ultérieures nous font penser que ce séjour aurait pu être prolongé. Toutefois, le SNHP était apparu dans la zone des 350 mètres, modéré mais évident, et s'accentuait à chaque descente rapide(de 350 m à 400m et de 460m à 490 m.) Les paliers étaient trop courts pour amener une régression notable des troubles. Nos gradients admissibles étaient sans doute encore trop optimiste. En décembre 71, la plongée fictive "Saturation III" effectuée au CEMA, sous la direction de J. Chouteau, nous confirmait l'influence favorable des paliers, surtout aux grandes profondeurs, le séjour des deux océanautes ayant été de près de 19 h à 500 mètres.

C'est en Février 72 que nous réalisâmes notre 500 mètres,"Sagittaire II" destinée à tester avec précisions l'évolution du SNHP au cours d'un séjour prolongé à cette profondeur.

La courbe de compression, sans paliers intermédiaires, était fondée sur les valeurs adoptées pour celle de "PHYSALIE V" (Fig II) "PHYSALIE V" ayant montré que les gradients adoptés étaient encore trop importants, nous comptions bien voir le SNHP se manifester, ce qui nous permettrait de suivre et de contrôler son évolution.

Les troubles cliniques et les modifications EEG, apparus en cours de descente à partir de 300 mètres, s'amplifièrent jusqu'à 500 mètres. Le syndrome clinique ne régressant que partiellement à partir de la 40° heure à cette profondeur - la plongée expérimentale Sagittaire II nous a permis de faire deux constatations importantes.

- D'une part que la courbe de compression devait être remaniée pour reculer encore le seuil d'apparition du syndrome au cours de la descente.

- D'autre part que celui-ci, une fois installé était difficilement résorbable par un séjour prolongé sous des pressions d'héliox, dépassant 36 ATA. Mais ne généralisons pas trop car notre expérience est encore limitée et les constatations qui précèdent ne sont valables que pour les deux sujets en cause, la profondeur fictive de 500 mètres et un séjour de 100 heures-

Il nous a semblé possible d'améliorer la courbe de compression par trois modifications importantes = (Fig II)

- Réduction de la valeur du gradient admissible aux diverses profondeurs;

- Paliers prolongés dans le début de la zone des profondeurs critiques;

C'est dans cette optique que nous avons réalisé 'PHYSALIE VI".

Pas de compression rapide au départ.

1° phase = gradient maximum: 56m,50 à 160 m et de 39 m à l'arrivée à 350 m
2° phase = gradient maximum: 27m à 430 m - 19,50m à 535 m - palier de 14 heures
3° phase = gradient maximum: 14 m à 565 m - palier de 14 heures
4°, phase = gradient maximum: 12m50 à 610m

les pentes de compression allant de 4 minutes/m au démarrage, à 27 min/m de 605 à 610m

Les résultats des très nombreux tests et enregistrements réalisés au cours de cette plongée fictive feront l'objet d'autres publications

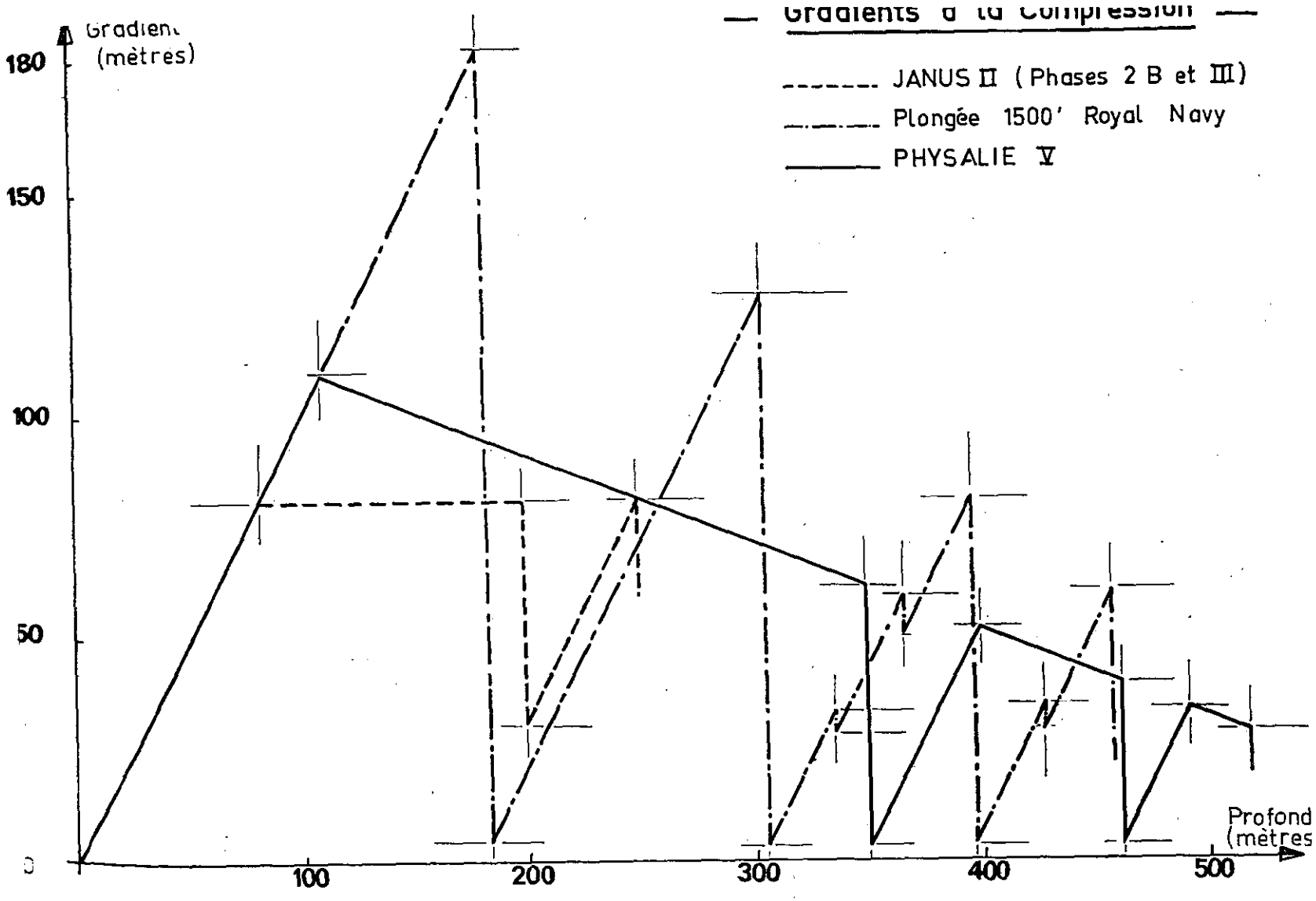
Retenons seulement les constatations suivantes :

- Apparition de quelques légers symptomes à l'arrivée à 350 m - Résorption au bout de 48 heures;

- Accentuation et développement du SNHP à partir de 565 mètres

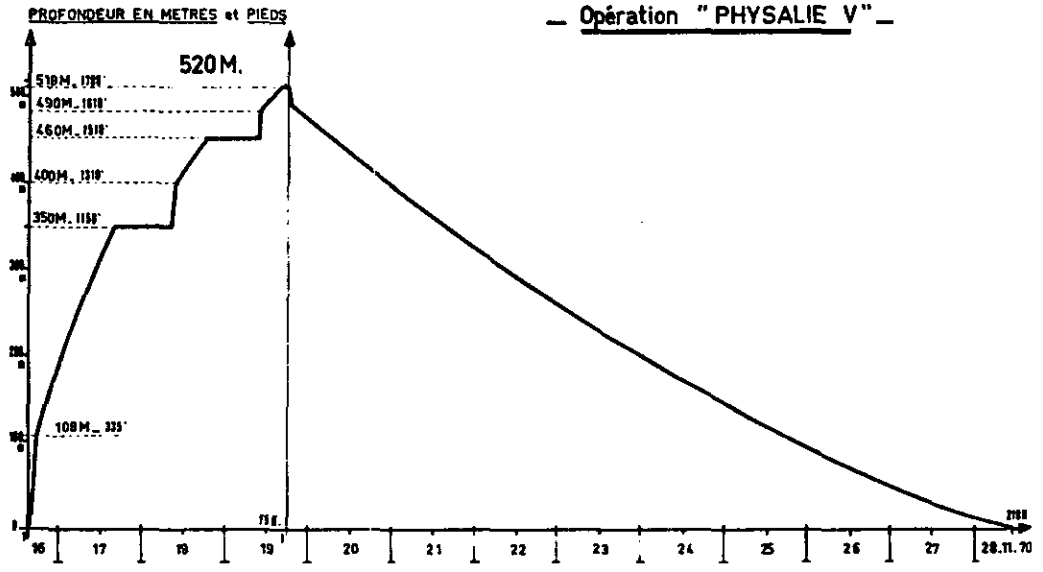
Si nous avons pu continuer la descente c'est qu'au total les manifestations du S.N.H.P n'étaient pas plus importantes que celles observées à 520 mètres lors de "PHYSALIE V".

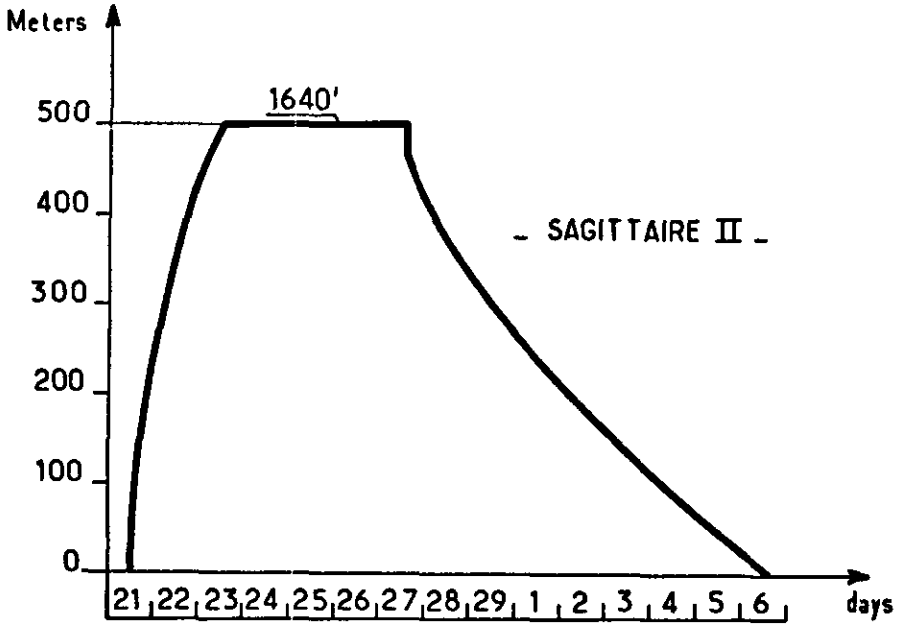
En conclusion, une étude minutieuse de la courbe de compression, fondée sur les résultats des expériences successives, nous a permis de minimiser le S.N.H.P., sans pour autant le faire disparaitre.

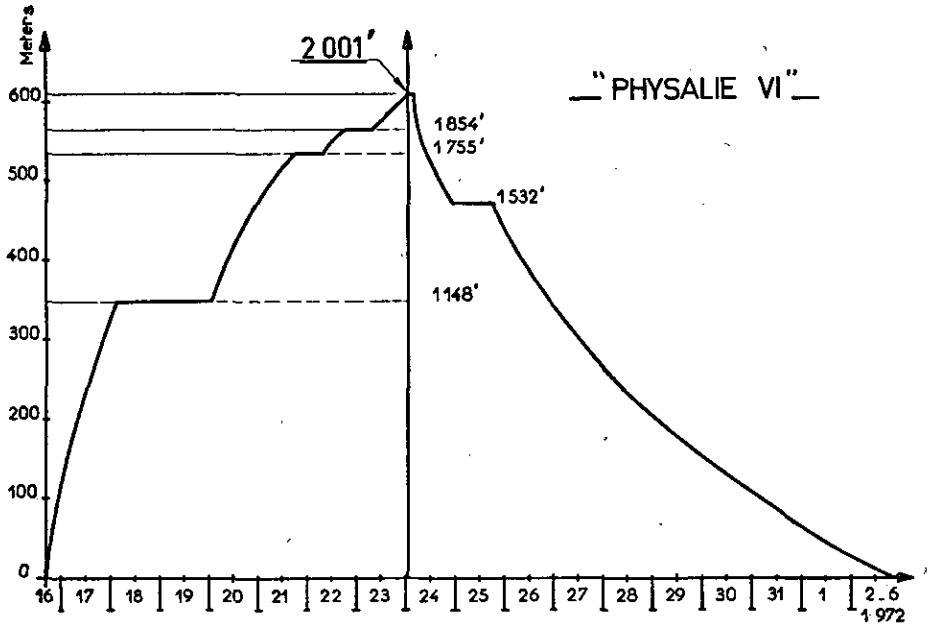

Gradients à la Compression
JANUS II (Phases 2 B et III)
Plongée 1500' Royal Navy
PHYSALIE V
Gradient (mètres)
180
150
100
50
0
100
200
300
400
500
Profond (mètres

La plongée très profonde du 16 au 28.11.1970

_ Opération "PHYSALIE V" _




Meters
600
500
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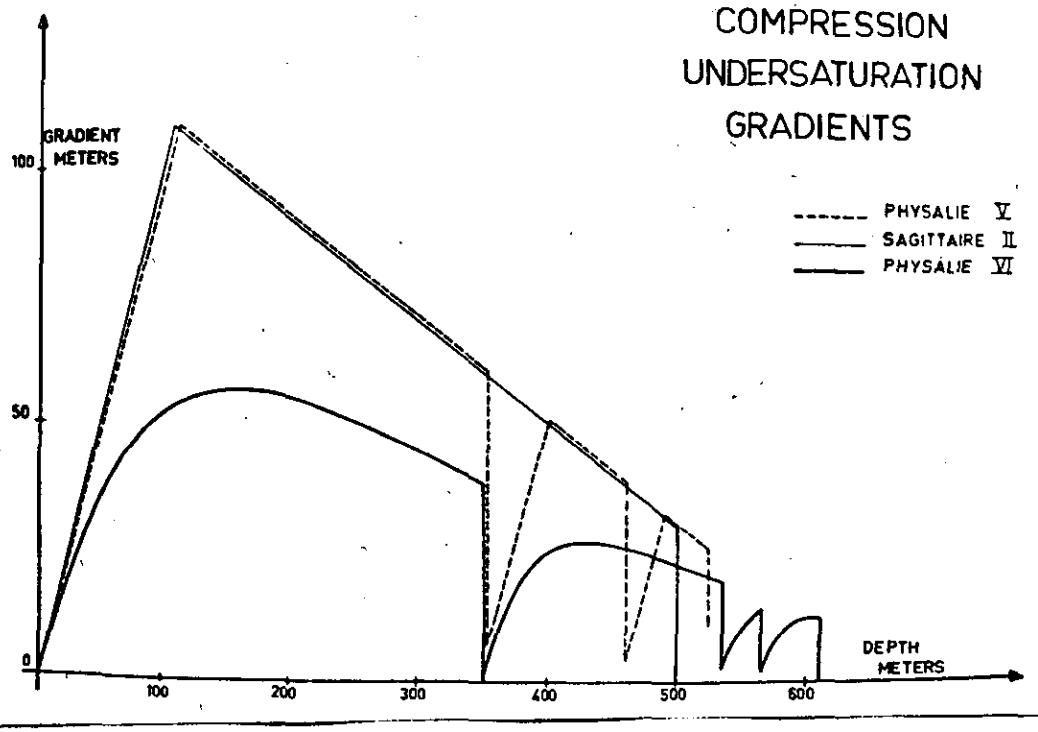
2 001'
1854'
1755'
1532'
1148'
"PHYSALIE VI"
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
1
2-6
1972


COMPRESSION
UNDERSATURATION
GRADIENTS
GRADIENT METERS
100
50
0
PHYSALIE V
SAGITTAIRE II
PHYSALIE VI
100
200
300
400
500
600
DEPTH METERS

SCIENCE 158:793-794. 1967

## Hydraulic Compression of Mice to 166 Atmospheres

Abstract. *Hydraulic uniform compression elicited tremors, uncoordinated limb movements, and tonic convulsions in liquid-breathing mice at pressures ranging from 50 to 100 atmospheres. Such abnormal muscular activity was observed neither in control animals nor in mice caudally to a spinal transection. Uniform compression of isolated preparations of mouse muscle in saline failed to contract at pressures up to 200 atmospheres.*

The effects of pressure on marine organisms, isolated organs, and cells have been studied since 1884 (*1*), and a concise review of pressure physiology has recently been written by Fenn (*2*). The response to uniform compression of gas-breathing animals may be modified or obscured by the pharmacological properties of compressed gases, and pressure effects in intact mammals have only been postulated thus far on the basis of indirect evidence and extrapolation (*3*, *4*). Since mice with liquid-filled airspaces have been reported to survive submerged in hyperbarically oxygenated salt solutions (*5*) and in a synthetic liquid equilibrated with oxygen at atmospheric pressure (*6*), it has become possible to study the effects of increased ambient pressure per se in mammals directly. One can observe the behavior of intact mammals subjected to great hydrostatic pressures and compare it with the behavior of control animals at normal atmospheric pressure under otherwise identical conditions. We report here the preliminary results of a series of such experiments in which adult Swiss mice were used.

The mice were placed in a small (150-ml) pressure chamber consisting of a thick-walled perspex cylinder sealed between two circular aluminum plates which are held together by steel bolts. The mouse enters into the chamber through a hole in the top plate which is then closed by means of a plug incorporating a valve. Gas or

liquid is introduced into the chamber from the bottom through a three-way valve, one end of which is connected with a hydraulic pump (*7*). The chamber containing the mouse is flushed thoroughly with oxygen and then flooded with oxygen-equilibrated FX-80 fluorocarbon liquid (*8*), replacing gas which escapes through the vent. Once the system is completely filled with liquid, the vent-valve is closed and the pressure in the chamber is raised by activating the hydraulic pump. The measured partial pressures of oxygen in the fluorocarbon liquid were 700 mm-Hg or less; the temperature of the liquid ranged from 17° to 25°C. Since the solubility of oxygen in FX-80 fluorocarbon liquid (at standard temperature, pressure and density) is approximately $9 \times 10^{-4}$ cm$^3$/cm$^3$ per millimeter of Hg at 25°C, the liquid contained, roughly, 60 percent (by volume) of oxygen at the beginning of each experiment.

Eight control mice were kept at normal ambient pressure in the liquid-filled pressure chamber up to 1 hour; pressure experiments were completed within ½ hour.

Forty liquid-breathing mice were subjected to hydrostatic pressures up to 166 atm. The first pressure effect observed in most animals was trembling of the limbs, and voluntary movements became jerky and uncoordinated. These phenomena occurred at pressures ranging from 50 to 80 atm. When the pressure was increased further, the mouse was seen to clench its paws tightly, and almost immediately afterward the neck bent sharply and the upper portion of the body arched so that the lower jaw almost touched the chest. The hindlimbs and forelimbs stretched caudally in full extension. After a few seconds, the limbs bent slightly again and the forepaws seemed to be drawn together. Respiration ceased and the mouse appeared to be dead. These tonic convulsions occurred at pressures ranging from 50 to 100 atm. If the pressure is kept constant when the mice develop these muscle spasms, some of the animals recover: the muscles seem to relax slowly and gradually, and after approximately 1 minute the mouse appears to be normal again. Raising the pressure by another 5 atm or so provokes the next, often irreversible, tonic convulsion. These tremors, uncoordinated limb movements, and tonic convulsions were not observed in control animals.

Three mice were compressed with helium to 100 atm. Tremors and uncoordinated movements, but no tonic convulsions, were observed. Five mice were precooled in a water bath until the rectal temperature had dropped to approximately 20°C. When the animals were then compressed with helium, tonic convulsions, similar to the ones observed in hydraulically compressed mice, occurred in three animals at pressures ranging from 69 to 86 atm. Three fresh preparations of mouse hindlimbs failed to contract when hydraulically compressed in Ringer solution at 20°C up to 200 atm, while the muscles readily contracted after electrical stimulation, before as well as after compression. In three mice with transected spinal cords, typical pressure-contractions occurred cranially to the lesions, whereas the muscles caudally to the lesions remained flaccid.

One fluorocarbon-breathing mouse survived uniform compression to 100 atm for 30 seconds; it was decompressed in 3 seconds, resumed air-breathing, and was alive and in apparent good health 1 month after the experiment. Such a rate of decompression is equivalent to surfacing from 3000 feet (1000 m) underwater at a vertical speed of 700 miles/hr (1200 km/hr) without signs of decompression sickness. This confirms tolerance to rapid decompression of fluorocarbon-breathing mice reported earlier (*9*).

Kylstra *et al.* (*5*) have previously described reversible tonic convulsions in hyperbarically oxygenated saline-breathing mice at pressures between 20 and 70 atm and survival of a liquid-breathing mouse at 160 atm, but the inspired gas tensions were not adequately controlled in these experiments. Brauer and co-workers (*10*) recorded abnormal electroencephalographic tracings in monkeys that were compressed with mixtures of helium and oxygen at 45 to 47 atm. MacInnis *et al.* (*11*) saw tremors in mice breathing mixtures of helium and oxygen at pressures between 75 and 80 atm, but no convulsions at pressures up to 122 atm. It is possible that pharmacological properties of compressed helium inhibited convulsions in their animals. Moreover, the temperature of the chamber was carefully controlled and maintained at approximately 30°C, and compression was carried out very slowly so that maximum pressures were reached only after 3 hours. In our experiments maximum pressures were reached within 10 minutes; the body temperature of the mice dropped rapidly and approached the temperature of the liquid environment. Pressure-induced biological phenomena are temperature-dependent (*2*), and it seems likely that convulsions would occur at higher pressures in mammals with a normal body temperature than in hypothermic animals, as suggested by our observations in mice compressed in helium. Unfortunately, attempts to keep mice alive while submerged in hyperbarically oxygenated fluorocarbons at temperatures greater than 30°C have failed. Retention of carbon dioxide, resulting from inadequate alveolar ventilation and diffusion limitations (*12*), would seem to be the limiting factor.

Our observations in hydraulically compressed fluorocarbon - breathing mice clearly reveal profound biological changes brought about by uniform compression of intact mammals. The pressure-induced muscular activity seems to reflect changes in function of the central nervous system. Our results tend to support the conclusion reached by Miller and co-workers (*4*) that mammalian tolerance to high environmental pressures is probably limited to pressure per se rather than by the pharmacological effects of inert gases, such as helium and neon.

J. A. Kylstra, R. Nantz
J. Crowe, W. Wagner
H. A. Saltzman

*Departments of Medicine and Physiology, Duke University Medical Center, Durham, North Carolina*

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13. Supported, in part, by grants HE-07896 and HE-5662 from PHS.

7 September 1967

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Academic Press, New York & London. C. J. Lambertsen, Editor.

# EFFECTS OF HYDROSTATIC PRESSURE ON MAMMALS

*M. J. Lever, K. W. Miller, W. D. M. Paton, W. B. Strecti, and E. B. Smith*

The extent to which exposure to high hydrostatic pressures may limit man's underwater activities is as yet uncertain. The problem can be summarized in the form of three questions, one of which can be readily answered. The remaining two are the subject of much current research.

*1.* Does hydrostatic pressure affect animals deleteriously?
*2.* Do the narcotic effects of the gases breathed by mammals always make themselves felt before the effects of hydrostatic pressure do?
*3.* Can the effects of hydrostatic pressure on mammals be alleviated?

To answer the first question, we need only consider the results obtained when aquatic or amphibious animals are exposed to high hydrostatic pressures in the absence of potentially narcotic gases.

## Effects of Hydrostatic Pressure

The effects of hydrostatic pressure on a wide range of biological systems have been the subject of extensive investigations. As early as 1884 Regnard (11) initiated a series of studies, the main conclusion of which was that hydrostatic pressures in the range of 200–300 atm can cause animals' muscles to lose their excitability, leading to a rigid paralytic state. Higher pressures (~400 atm) proved lethal. Even greater pressure was required to inactivate simpler organisms. Research undertaken since that time has confirmed and extended these conclusions. The effect of pressure on nerve cells is to stimulate at pressures below 200–300 atm (3). At greater pressures the height of the action potential is reduced and the duration is extended.

These effects of hydrostatic pressure have recently been reviewed comprehensively (4). The inference is quite clear: hydrostatic pressure inactivates aquatic animals at pressures at levels of 200–300 atm, and its effects are fatal at about 400 atm.

## Mammals Exposed to High Hydrostatic Pressures

The "pressure barrier" for non-gas-breathing animals is approximately 300 atm. The barrier in the case of mammals is not so recognizable, as it is not always easy to distinguish be-

TABLE I

EXPERIMENTS EXPOSING MICE TO PRESSURES GREATER THAN 100 ATM[a]

| Worker | Number of animals | Maximum pressure (atm) | Approx. time to 100 atm | Onset pressure (atm) for | | | Comments |
|---|---|---|---|---|---|---|---|
| | | | | Tremors | Convulsions | Death | |
| MacInnis | 16 | 107 | 3 hr | 75–80 | — | — | Mice |
| *et al.* (7) | 24 | 122 | 3 hr | | | | recovered after 4 hr at pressure |
| Brauer | 11 | 102 | 1½–2 hr | 60–70 | 90 | — | |
| *et al.* (2) | 12 | 116 | 1½–2 hr | 60–70 | 109 | — | |
| Miller | 6 | 115 | 5 min | 80 | 110 | — | |
| *et al.* (10) | 4 | 140 | ½ hr | 55–80 | 110 | 126–143 | |
| Brauer | 12 | 116 | 1½–2 hr | 60–70 | 109 | — | $H_2$ |
| *et al.* (2) | 8 | 129 | 1½–2 hr | 65–75 | 129 | — | 75% He, 24% $N_2$ |
| Miller | 1 | 136 | ½ hr | 82 | — | 136 | Ne |
| *et al.* (10) | 1 | 125 | ½ hr | 90 | — | — | $He/N_2O$ |

[a] All experiments carried out at 30–32°C with $O_2$–He mixtures unless otherwise stated.

tween the effects of pressure per se and the narcotic effects of the gases breathed. Certainly when animals are exposed to high pressures of $N_2$, no effects are observed other than narcosis, which occurs at approximately 35–40 atm (9). It is probable that only three gases are suitable for studies of the effects of higher pressures: He, $H_2$, and Ne. There is now evidence that with He and Ne, the effects of pressure make themselves felt before narcosis sets in, whereas with $H_2$, pressure and narcotic effects appear to occur almost simultaneously.

Membery and Link (8) exposed mice to He–$O_2$ mixtures in the pressure range of 60–90 atm for up to 13 hr. They observed no adverse reactions, and the occasional deaths that did occur were attributed to hypoxia or decompression sickness. They noted that the mice shivered if the temperature of the chamber fell below 32°C. MacInnis *et al.* (7) exposed mice to pressures of 122 atm for 4 hr. (Table I). The rate of compression was less than 1 atm/min (somewhat slower than the rate used by Membery and Link). The mice appeared normal until pressures of 75–80 atm were reached, at which point slight tremors occurred. At higher pressures the tremors became coarse and persistent, and appeared to involve the whole body. The tremors ceased after 1 hr at pressure. At pressures above about 90 atm, the animals appeared to have some difficulty in breathing. Mice surviving the decompression procedure lived for several months.

Brauer *et al.* (1) showed that rhesus monkeys underwent convulsions of the grand mal type when pressures reached approximately 50 atm in both He–$O_2$ and $H_2$–$O_2$ breathing atmospheres. The pressures required to produce convulsions were marginally higher for $H_2$–$O_2$ mixtures and, in contrast to the animals breathing He–$O_2$, only half the monkeys convulsed.

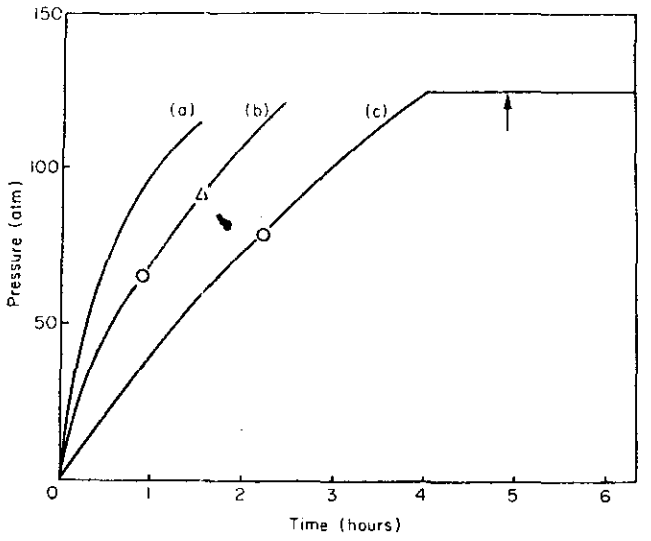


FIG. 1. Three compression schedules for mice. (*a*) Brauer *et al.* (2) (fast); (*b*) Brauer *et al.* (2) (normal); (*c*) MacInnis *et al.* (7). (○) Mean pressure at onset of tremors; (△) onset of convulsions; ( ↑ ) marks point at which tremors ceased. The pressure–time curves illustrated are schematic only.

Brauer and his co-workers extended these studies to mice (1, 2). Tremors began at about 60 atm, and convulsions were observed in all animals by 102 atm. Convulsions were not reported by MacInnis *et al.* The differences do not appear attributable to the somewhat faster compression rates used by Brauer in most of his experiments; it was therefore concluded that the discrepancies were due to the difference in the strains of mice used. The approximate compression schedules used by these workers are illustrated in Fig. 1.

Miller *et al.* (10), making a comparative study of Italian great newts and mice, attempted to confirm unequivocally the effects of the atmospheric environment under pressure. They first showed that the sensitivity of the mice and newts to anesthetics ($N_2$ and $N_2O$) at 30°C was comparable. The newts were shown to lose responsiveness between 165 and 245 atm, whether pressure was applied hydrostatically or by use of He or Ne. At pressures up to 125 atm, Ne (in one experiment only) and He failed to anesthetize mice; but at slightly higher pressures (135–145 atm) the effects were lethal. Within 5 min of reaching these pressures, the animals passed through a phase of prostration and respiratory difficulty to death. At pressures above 100 atm, distinct tremors were observed. It was concluded from these experiments that the effects of hydrostatic pressure appear both in newts and mice at pressures below those at which anesthesia occurs with He and Ne. The compression rates in this investigation were faster and the exposure times shorter than those used in the studies described in the preceding paragraphs.

In investigating the effects of pressure on mice breathing oxygenated liquids, Kylstra (6) observed tremors at 34 atm. At higher pressures (~70 atm) temporary cessation of breathing, caused by generalized muscular contraction, was observed. In other experiments, mice showed no apparent distress at 100 atm pressure, and in some animals "rhythmical respiratory movements of the chest" were evident at pressures as high as 160 atm.

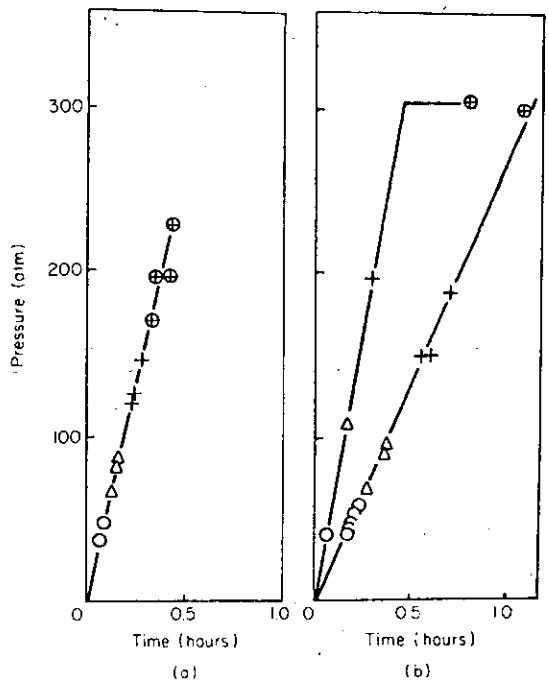


FIG. 2. Fast compression schedules for mice. (a) Chamber temperature, 30°C; (b) chamber temperature, 23°C. Oxygen tension, 1 atm. (○) Onset of tremors; (△) onset of convulsions; (+) death; (⊕) death of animals treated with pentobarbital.

Although the results of all these animal experiments are not entirely consistent, the main conclusions are clear. The effects of high pressure are fourfold:

*1. Uncoordinated tremors* ["fasciculation," as described by Brauer *et al.* (2)]. These have been observed by all workers except Membery and Link (8). The onset appears to be at pressures of 70 atm ± 10. There is some evidence that the tremors are dependent upon the rate of compression, although it is far from conclusive; and that the symptoms appear to remit after 30–60 min.

*2. Convulsions.* These have been most clearly observed by Brauer *et al.*, although the experiments of Miller *et al.* (10) did produce convulsions in a number of cases. The effect may depend upon the strain of mice used.

*3. Respiratory distress.* As MacInnis *et al.* (7) observed at pressures above 90 atm, the respiratory rate decreased and movement of the chest wall became obvious. Mouth breathing and gasping were observed. To what extent these effects were due to the increased density of the atmosphere or were caused by the effects of pressure on muscular activity cannot be stated.

*4. Paralysis.* Newts in the pressure range of 165–245 atm lost all spontaneous movements and frequently took up contorted postures. Spontaneous movement returned upon reduction of the pressure (10). Whether this paralysis was due to the effect of pressure on the nervous system or to pressure directly on the muscles is not known. In many experiments with mice,

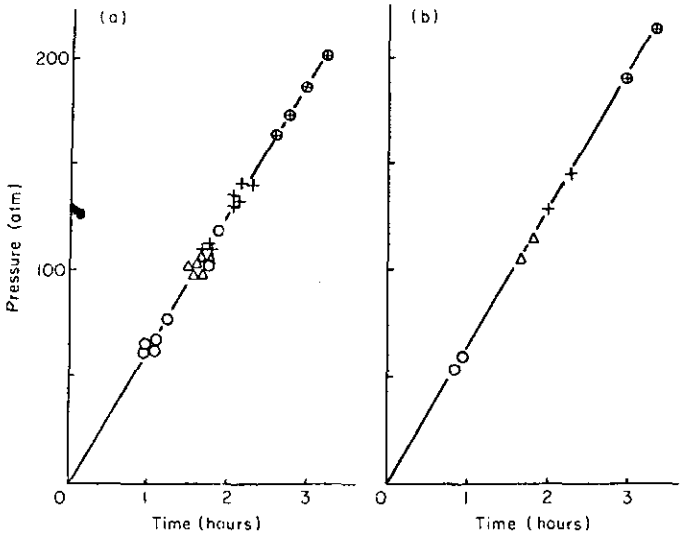


FIG. 3. Medium rate compression schedules for mice. (a) Chamber temperature, 30°C; (b) chamber temperature, 23°C. Oxygen tension, 1 atm. Symbols are the same as those in Fig. 2, except that ⊖ means death of animals in an anesthetic pressure of $N_2$.

the tremors and convulsions appeared to fade at higher pressures and most activity had ceased before death, suggesting paralysis.

The degree to which these symptoms depend upon the conditions of the particular experiment has been the subject of only a few isolated investigations. In general, it has been as-

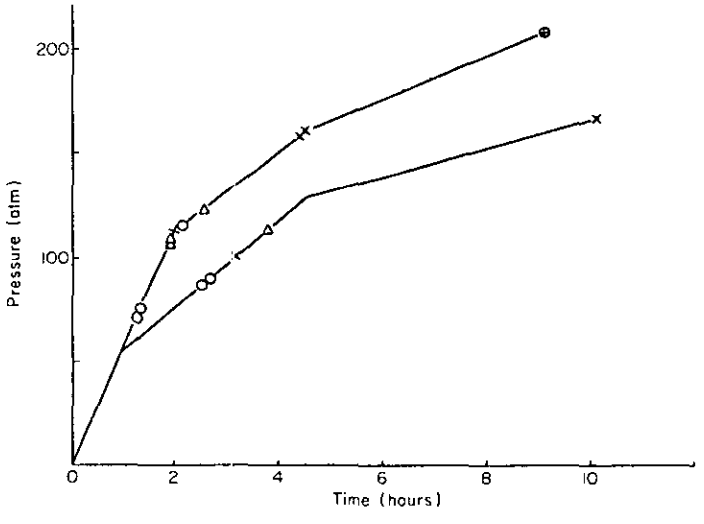


FIG. 4. Slow compression schedule for mice. Chamber temperature, 30°C; $O_2$ tension, 1 atm. Symbols are the same as those in Fig. 2.

TABLE II

EXPERIMENTS EXPOSING MICE TO PRESSURES GREATER THAN 100 ATM
(All experiments in $O_2$–He mixtures ($P_{O_2} \sim 1$ atm), unless otherwise stated)

| No. of animals | Max. pressure (atm) | Approx. time to 100 atm (hr) | Onset pressure (atm) for | | | Comments | |
|---|---|---|---|---|---|---|---|
| | | | Tremors | Convulsions | Death | | |
| 3 | 150 | 0.2 | 35- 50 | 70- 80 | 120–150 | | 30° C |
| 6 | 160 | 1.7 | 60–110 | 90–100 | 110–130 | | 30° C |
| 3 | 160 | 2.0 | 68- 75 | 100–120 | 110–160 | | 30° C |
| 2 | 165 | 3.0 | 85 | 112 | 104 and 165 | | 30° C |
| 2 | 105 | 1.2 | 60 | 105 | 105 | | 25° C |
| 4 | 200 | 0.1–0.5 | 40- 54 | 70–110 | 190–205 | | 22° C |
| 2 | 150 | 0.5 | 40- 50 | 90–100 | 150 | | 22° C |
| 2 | 150 | 1.7 | 50- 60 | 105–115 | 130–145 | | 22° C |
| 4 | 250 | 0.1–0.5 | — | — | 170–240 | Nembutal[a] | 30° C |
| 2 | 200 | 0.1–0.5 | — | — | 0/2 at 200 | Nembutal[a] | 30° C |
| 2 | 200 | 1.1 | — | — | 184 and 200 | Nembutal[a] | 30° C |
| 2 | 300 | 0.1–0.5 | — | — | 2/2 at 300 | Nembutal[a] | 22° C |
| 5 | 136 | 0.2 | — | — | 0/5 at 136 | Nembutal[a] | 22° C |
| 2 | 214 | 1.2 | — | — | 190 and 214[b] | Nembutal[a] | 22° C |
| 15 | 136 | 0.5 | — | — | 3/15 at 136 | $N_2O$[a] | 30° C |
| 5 | 136 | 0.5 | — | — | 5/5 at 136 | Ar[a] | 30° C |
| 2 | 170 | 1.2 | — | — | 160–170 | $N_2$[a] | 30° C |
| 2 | 206 | 2.0 | — | — | 120 and 206 | $N_2$[a] | 30° C |

[a] Anesthetic doses given.
[b] Animals cooled only when above 120 atm.

sumed that the adverse symptoms are reduced by maintaining fairly low $O_2$ tensions ($<0.5$ atm) and by utilizing slow compression, although neither of these suppositions was confirmed by Brauer's experiments. However, the range over which these $O_2$ tensions and rates of compression were varied may not have been sufficiently large to produce significant effects.

The results of our investigations (Figs. 2–4; Table II), in which the compression rates were varied by a factor of 10, suggest that the benefits of a slower compression are at best marginal in experiments carried out at room temperature. A preliminary study of the effect of temperature on animals exposed to high pressures did not produce statistically significant results. There is some evidence, however, that heat loss from the body is accelerated by high He pressures, and shivering has been reported by Membery and Link (8) when the chamber temperature fell below 32°C. In contrast to their observations, we have noted that death occurred at marginally higher pressures in mice when they were treated in vessels maintained at room temperature than when they were kept in vessels at 30°C temperature.

## Drugs and High Hydrostatic Pressures

As the answers to our first two questions indicate that direct effects of hydrostatic pressure may produce harmful symptoms in mammals, it is necessary to consider how far these symptoms may be alleviated by such means as drugs.

The most important early observation concerning the effects of drugs in modifying the response of organisms to hydrostatic pressure was that of Johnson and Flagler (5). They noted that applying pressure could restore the luminosity of luminous bacteria that had been exposed to an anesthetic agent; they then tried a similar experiment using tadpoles narcotized with alcohol. The effect of 2–5% alcohol was to narcotize the tadpoles so that they stopped swimming and fell to the bottom of the vessel. If a pressure of 130–300 atm was then applied, the animals resumed swimming. (The effect of pressure on unnarcotized animals was increased activity at 130 atm, followed by paralysis at about 300 atm.) Similar results occurred when animals were anesthetized with urethane; but pressure did not remove the effects of amyl carbamate.

In an attempt to see how far general anesthetics and other drugs can modify the effects of pressure on other animals, we initiated a study using newts and mice. In the case of newts, the results were clear-cut. Narcosis produced not only with a general anesthetic (halothane) but also with pentobarbital (Nembutal) could be instantaneously reversed by the application of hydrostatic pressures of between 100 and 200 atm. Furthermore, newts treated with pentobarbital remained active to much higher pressures than the untreated animals. In one case the righting reflex remained to over 300 atm (9990 FSW) although the animals exhibited abnormal muscular contractions at that pressure.

Experiments were performed on mice anesthetized with pentobarbital or $N_2O$. There was uncertainty about the results when pentobarbital was used, because the time course of the experiment approximated the time required for the control animals to recover from the anesthetic. At room temperature the righting reflex was restored between 70 and 100 atm after about 40 min. The three control animals recovered their righting reflex after 80, 80, and 60 min. We also noted the tremors that have been observed in untreated animals by other workers, but in this instance they appeared to start at lower pressures and to continue to higher pressures. However, the lethal pressures for mice treated with pentobarbital were raised. In two experiments in which the chamber was kept at room temperature, deaths of anesthetized animals occurred at 300 atm. At 30°C, death occurred in anesthetized mice between 160 and 240 atm, compared with 120 to 150 atm in unanesthetized animals (Fig. 2; Table II).

All these preliminary experiments were carried out with rapid compression rates and in small chambers. We have initiated a further series of experiments using a new high pressure chamber. The results obtained to date confirm our earlier observations. With compression times to maximum pressure as long as 4 and even 10 hr, death in animals that received no drugs occurred between 155 and 165 atm (5100 and 5450 FSW), while the lethal limit was raised to as high as 215 atm (7100 FSW) by the use of anesthetics (Figs. 3 and 4).

## Outlook for Man

Diving below 600 FSW on $O_2$–He breathing mixtures has resulted in tremors in man. However, there is evidence that with slow compression rates and with strict control of $O_2$ tension,

these tremors can be considerably alleviated, if not entirely eliminated. Recent reports of 4-hr dives to 1150 FSW (P. B. Bennett, private communication) suggest that the safe depth limit for man has not yet been reached. The animal experiments reported here suggest that at somewhat greater pressures severe problems will be encountered. A superficial examination of these experiments further suggests that this "pressure barrier" for man may exist at depths as shallow as 1500 FSW to 2000 FSW, since mice can develop severe tremors at these pressures. However, as long as the factors that determine the severity of animals' response to high pressures have not been critically evaluated, no reliable estimate of this limit can be made.

It is possible, however, that the apparent antagonism between anesthetic agents and high hydrostatic pressures may be important. Thus the addition of some $N_2$ to $O_2$–He mixtures at high pressures may prove beneficial. More extensive experimentation with animals is necessary before the potential and safety of such practices can be fully evaluated. A more detailed investigation of the effects of varying $O_2$ tension, compression rates, and temperature, together with a study of the influence of drugs on the condition of animals at high pressure, is at present in progress.

ACKNOWLEDGMENT

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# Inert Gas Narcosis, the High Pressure Neurological Syndrome, and the Critical Volume Hypothesis

Abstract. *The hypothesis that general anesthesia or pressure-induced convulsions occur when a hydrophobic region is expanded or compressed, respectively, by critical amounts is consistent with recent data obtained with mice. Calculations show that anesthesia occurs at an expansion of 1.1 percent and convulsions at a compression of 0.85 percent, the latter site of action being more compressible.*

The replacement of nitrogen by helium as the inert gas diluent in deep-diving breathing mixtures has removed the constraint of nitrogen narcosis (*1*), and simulated depths of 600 m (2000 feet, 61 atm) have been reached recently in France. However, a new barrier to deeper diving is the high pressure neurological syndrome, a hyperexcitability which first manifests itself in man at about 20 atm as a coarse tremor of the limbs (*2*). At higher pressures (60 to 100 atm) convulsions occur in experimental animals, including primates, and manned diving programs have consequently adopted cautious compression schedules (for example, 7½ days in the 600-m dive). Addition of narcotic gases to the breathing mixture has an ameliorating effect in animals (*3*).

Pressure reversal of anesthesia is another example of an effect of pressure on the central nervous system, and has led to the formulation of the critical volume hypothesis (*4*). This states that anesthesia occurs when the volume of a hydrophobic region is caused to expand beyond a certain critical volume by the absorption of an inert substance. An applied pressure opposes this expansion and reverses anesthesia. In this report, it is proposed that the hypothesis may be extended to include the high pressure neurological syndrome by assuming that convulsions occur when some hydrophobic region has been compressed beyond a certain critical amount by the application of pressure. Absorption of an inert gas will compensate for such compression and raise the convulsion threshold pressure. This extension of the critical volume hypothesis has the attraction of offering a unified description for the interaction between pressure and narcotic gases in the central nervous system with respect to hyperexcitability and anesthesia. It could also provide a theoretical foundation for the use of inert gas mixtures in deep diving. The few studies that have been made of the effect of anesthetics and pressure on simple membranes suggest that the hydrophobic region is membranous in nature (*5*, *6*).

The fractional expansion, $E$, that occurs when a gas at a partial pressure, $P_a$, dissolves in a bulk solvent is given by

$$E = V_a x_a P_a / \bar{V}_a \qquad (1)$$

where $\bar{V}_a$ is the partial molar volume of the gas in the solvent of molar volume $V_m$, and $x_a$ is the mole fraction solubility of the gas in that solvent when its partial pressure is 1 atm. In addition, physical compression of the liquid occurs according to its compressibility, $\beta$, and the total pressure, $P_T$ (fractional compression $= \beta P_T$). In fact, for the less soluble gases, helium and neon, the compression term is larger than the expansion term and net compression results; hence they are not anesthetics. For the more soluble anesthetic or narcotic gases, such as $N_2$, Ar, and $N_2O$, net expansion occurs (*4*). Equation 1 must be corrected for gas imperfections and for the slight dependence of solubility on total pressure. The nature of these corrections has been given in a previous paper (*4*), in which the critical volume hypothesis accounted for pressure reversal of anesthesia data for newts. Here, the treatment will be applied to mammals.

Quantitative data for the pressure reversal of anesthesia in mice are available for three gas mixtures—He : $N_2O$, Ne : $N_2O$, and $H_2$ : $N_2O$ (*7*)—while comparable data for the elevation of convulsion threshold are available for He : $N_2$, He : $N_2O$, and He : $H_2$ (*3*). The study of the high pressure neurological syndrome is complicated by the apparent dependence of the convulsion threshold on the strain of mice used and, to some extent, on the compression rate employed. While these variations deserve more detailed investigation, they are not large, and the data used in this study are internally consistent, having been obtained in one laboratory by a standardized procedure.

The expansion caused by dissolution of the inert gases (Eq. 1) was calculated for the experimental isonarcotic and isoconvulsion end points. This is shown in Fig. 1 as a function of pressure for the model solvent benzene. Such a plot should yield a linear relation where the slope gives the compressibility of the site of action and the intercept gives the critical volume

Table 1. Results of calculations according to the critical volume hypothesis for three solvent models for the pressure reversal of anesthesia (*8*) and the high pressure neurological syndrome (convulsions) (*3*) in mice. Physical parameters for these calculations have been given previously (*4*); in addition, the solubility of neon in carbon disulfide is $4.8 \times 10^{-6}$ mole fraction (*17*). For hydrogen $\bar{V}_2$ was taken as 35 ml/mole for all solvents (*18*). The Bunsen partition coefficient of hydrogen in olive oil was 0.04 (*9*). The compressibilities of olive oil, benzene, and carbon disulfide are 6, 9, and $7 \times 10^{-5}$ atm$^{-1}$, respectively (*4*). For the critical volume change and compressibility, values are means ± standard deviations.

| Solvent | Effect | Critical volume change (%) | Compressibility ($\times 10^5$ atm$^{-1}$) | Correlation coefficient |
|---|---|---|---|---|
| Olive oil | Anesthesia | +0.35 ± 0.03 | 3.2 ± 0.56 | .85 |
| | Convulsions | −0.39 ± 0.12 | 7.1 ± 1.20 | .91 |
| Benzene | Anesthesia | +1.1 ± 0.02 | 3.0 ± 0.39 | .91 |
| | Convulsions | −0.85 ± 0.14 | 13.9 ± 1.37 | .96 |
| Carbon disulfide | Anesthesia | +0.60 ± 0.04 | 3.8 ± 0.68 | .84 |
| | Convulsions | −0.60 ± 0.16 | 10.0 ± 1.59 | .92 |

change required for anesthesia or convulsions at 1 atm absolute. Results of the calculations for three solvents, which experience shows are good analogs of the anesthetic site (*8*), are summarized in Table 1. All three model solvents produce a good fit of the data for both anesthesia and convulsions.

The most striking conclusion from Table 1 is that a particular model solvent gives a self-consistent description in terms of the critical volume hypothesis for the volume changes associated with anesthesia and convulsions; that is, a particular positive or negative change in volume at the sites of action is critical and results in profound effects in the central nervous system. The predicted percentage expansions vary somewhat depending on the solubility and molar volumes of the solvents. The compressibilities are close to those observed experimentally in each case, although the site mediating convulsions is two to five times the more compressible of the two, indicating that two separate sites of action exist for anesthesia and convulsions. Further discussion of the differences between the solvents seems unlikely to be profitable, and it would be more interesting to know the results of such calculations for real membranes, but the few physical data available (*9*) only allow one to conclude that the volume changes given by these solvents are of the order of magnitude to be expected in real membrane systems.

A further evaluation of the physical parameters of the site of action, which is independent of gas solubility data, may be made by using results of recent experiments (*10*) in which mice breathing an oxygenated fluorocarbon fluid were compressed hydraulically to produce convulsions. These experiments were conducted at a number of reduced rectal temperatures, allowing a short extrapolation to 37°C, which gives a convulsion threshold of 62 atm at compression rates comparable to those in Table 1. If we assume that the compressibility of the convulsive site is that given by each of the model solvents (Table 1), then these data yield critical volume changes of −0.44, −0.86, and −0.62 percent for olive oil, benzene, and carbon disulfide, respectively—values in good agreement with those in Table 1. These liquid breathing experiments raise a further

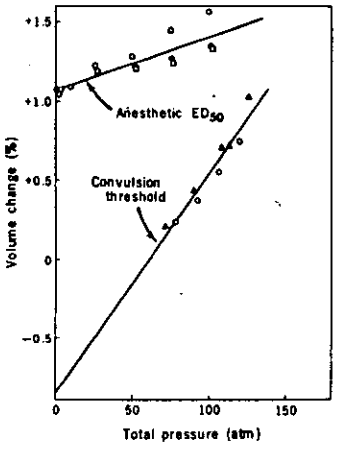


Fig. 1. Calculated expansion of benzene (Eq. 1) (*4*) caused by mixtures under isoanesthetic (*8*) and isoconvulsive (*3*) conditions at various pressures. The intercepts yield the critical volume changes, and the slopes, the compressibilities. The anesthetic $ED_{50}$ is the dose effective in anesthetizing 50 percent of a group of animals.

intriguing possibility. Liquids that have been compressed to remove all gas nuclei may be subjected to negative pressures of several hundred atmospheres without cavitation (*11*). Would a similarly treated mouse thus be anesthetized by negative pressures of the order of 50 to 100 atm?

For diving practice, the unified critical volume hypothesis suggests that the composition of the breathing mixture should be adjusted so as to produce no volume change at the site of action. Reversal of nitrogen narcosis by helium pressure has been observed in man (*12*), while the amelioration of the high pressure neurological syndrome in divers by adding anesthetic gas to their breathing mixtures is the object of active investigation (*3*). However, since the site for convulsions appears to be two to five times more compressible, it is clearly not possible to completely prevent volume changes at both sites by titrating the inert gas against the absolute pressure. Nonetheless, minimization of the changes should enable divers to maintain performance levels at considerably greater depths than those they currently achieve breathing helium-oxygen. Ultimately, it should be considered that the sites of action referred to here may only be the most sensitive of a spectrum of sites, as is suggested by the respiratory and cardiac problems encountered in mammals above 100 atm (*13*). This possibility, together with the different compressibilities in Table 1, suggests that more specific pharmacological intervention will eventually be required if man is to achieve depths of ever greater magnitude.

The success of the critical volume hypothesis in providing a self-consistent explanation of the interaction of anesthetic gases and pressure is rather remarkable. Although it cannot be ruled out that such success arises by chance, the hypothesis provides specific predictions about the sites of action which are accessible to experimental tests at a biophysical level. It seems, at present, most probable that the sites of action are situated in the lipid bilayers of some membranes (*14*). This interaction in itself is probably not directly responsible for the effects observed; rather, one might suppose that the membrane perturbations influence the functions of some membrane proteins in the neurological apparatus. Evidence for such a view may be found in stud-

ies of the red blood cell membrane (*5*), rat phrenic nerve (*15*), and the behaviors of simple antibiotic ionophores, such as valinomycin (*6, 14*) and gramicidin (*16*). Measurement of the appropriate membrane properties should enable this interpretation of the critical volume hypothesis to be examined in more detail.

KEITH W. MILLER
*Harvard Medical School, Departments of Pharmacology* and *Anesthesia, Massachusetts General Hospital, Boston 02114*

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6 SEPTEMBER 1974

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## Animals at Very High Pressures of Helium and Neon

Abstract. *At pressures up to 125 atmospheres, helium failed to anesthetize mice; at slightly higher pressures (135 to 145 atmospheres) it proved lethal. With Italian newts* (Triturus italicus), *whose sensitivity to anesthesia by nitrogen is similar to that of mice, responsiveness was lost at pressures between 165 and 245 atmospheres, whether the pressure was achieved with helium or neon, or hydrostatically. It was concluded that the anesthetic pressures of helium and neon, for mice and newts, are higher than the tolerable mechanical pressures.*

While the effects of very high pressures (of the order of 100 atm or above) on isolated tissues and on vegetable materials have been studied extensively (*1, 2*), experiments with living animals have been fewer. Carpenter (*3*), by extrapolation according to the dose-response relation observed with other gases, estimated the $ED_{50}$ (dose that was 50 percent effective) for helium anesthesia to be > 163 atm. His maximum pressure was, however, very considerably below this. Membery and Link (*4*) reached a similar conclusion up to their maximum working pressure of 90 atm. Recent experiments with monkeys showed that at a pressure of 67 atm for a mixture of oxygen and helium severe convulsions occurred, as indicated by electroencephalographic recordings, whereas no such effects were produced by a mixture of oxygen and hydrogen under similar conditions (*5*).

In this work we report some preliminary observations made at high pressures. Male white mice (C. D. Tuck No. 1 uniform strain) and Italian great newts (*Triturus italicus*) have been studied at pressures up to 245 atm. A 300-ml stainless steel pressure vessel fitted with a perspex port was used. In all experiments the vessel was flushed with oxygen before the inert gas was added under pressure, and strict precautions were taken to control the carbon dioxide partial pressure. The environmental temperature was controlled by placing the chamber in a water bath. Anesthetic end-points were determined by the rolling-response (RR) method, based on the ability of the animal to remain upright when the chamber was rotated. A more detailed description of the experimental technique will be given elsewhere (*6*).



At an environmental temperature of 30°C, no loss of RR occurred with mice in mixtures of oxygen and helium at pressures less than 125 atm. At 110 atm and 20°C, five animals lost their RR, but this was restored when the pressure vessel was warmed to 30°C. However, at pressures above about 100 atm distinct tremors were observed in the animals and respiration appeared very labored. Attempts to reach higher pressures showed that these pressures were lethal, although they were only slightly higher (in the range 135 to 145 atm). Within 5 minutes of reaching the higher pressures, animals passed rapidly through a phase of prostration and respiratory difficulty to death, in a way unlike that induced by anesthetics.

A test was made for a subliminal anesthetic effect of very high pressures of helium by combining these with subanesthetic pressures of nitrous oxide ($ED_{50}$ ~ 1.5 atm; see *6*). These experiments were generally unsuccessful, since the mice died on compression. This may have been due to a secondary effect of the gas—the abrupt rise in pressure with helium causing a compression of nitrous oxide in the animals' pulmonary air spaces and producing a transient lethal nitrous oxide tension. In one case, however, the animal survived and showed no signs of anesthesia in an atmosphere of nitrous oxide (1.2 atm) and helium (125 atm); thus 125 atm of helium failed to contribute 20 to 30 percent of an anesthetic dose.

In one experiment with neon, a mouse showed no loss of RR at 110 atm and an environmental temperature of 30°C. As with helium, the mouse died when the pressure was raised to 135 atm.

Further studies were performed on Italian great newts. The use of these animals avoided some of the technical difficulties experienced with mice and made it possible to study not only the effect of high gas pressure, but also that of hydrostatic pressure alone. For the latter studies the chamber and its inlet valve were completely filled with water, and pressure was applied through the gas supply line. The anesthetic pressure of nitrogen for these animals was found to be 40 ± 8 atm (standard deviation) at 30°C (*7*), compared with 34 ± 5 atm (S.D.) for mice (*6*). We found that the RR was lost between 165 and 245 atm, irrespective of whether the pressure was applied with the use of helium (3 experiments) or neon (4 experiments), or hydrostatically (4 experiments). The animals exposed to these pressures lost all spontaneous movement and frequently took up contorted postures. After exposures to hydrostatic pressures for 15 to 30 minutes, spontaneous movement was restored when the pressures were reduced. These animals were kept for 12 hours and no ill effects were observed. (No attempts were made to investigate survival of animals exposed to high gas pressures, since profuse bubble formation occurred on decompression.)



The conclusion suggested by these preliminary experiments is that the loss of activity in all cases resulted from the effects of high pressure alone. If helium and neon are capable of anesthetic action [and according to the clathrate theory (*8, 9*) they should not be], then their anesthetic pressures must be greater for mice and newts than the limiting mechanical pressure which the tissues of these animals can tolerate. This view is supported by Carpenter's studies of the anticonvulsant action of helium in mice. He estimated, by extrapolation, an $ED_{50}$ of 163 atm, and comparison of anticonvulsant end-points with end-points such as loss of righting reflex (*6*) suggests that the partial pressure of helium required to remove RR would be above, possibly substantially above, 250 atm. This is in keeping with the single experiment with nitrous oxide and helium, where 125 atm of helium did not contribute the fraction of an anesthetic dose required to reach the end-point. More detailed experiments will be required to assess the nature of the sickness produced in these animals by high pressure.

K. W. Miller, W. D. M. Paton
W. B. Streett, E. B. Smith
*Departments of Pharmacology, Physical Chemistry,* and *Inorganic Chemistry, University of Oxford, Oxford, England*

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# PULMONARY MECHANICAL FUNCTIONS IN MAN BREATHING DENSE GAS MIXTURES AT HIGH AMBIENT PRESSURES—PREDICTIVE STUDIES III

*R. E. Peterson and W. B. Wright**

As naval and commercial interest in the sea, particularly concerned with rescue and oil resources, extends to greater and greater depths, the extension of the known limits of man's ability to dive becomes of practical as well as theoretical interest. A factor frequently proposed as limiting man's functional diving depth is pulmonary performance in dense atmospheres. Past studies have shown that the greater gas density associated with descent results in an increase in resistance to pulmonary gas flow and work of breathing, and a depression in maximum respiratory gas flow rates. It has been suggested that the useful work of a diver might therefore be limited by inadequate ventilation resulting either from weakness or fatigue of respiratory muscles or from an effort-independent limitation in expiratory flow.

The purpose of this study was to determine the environmental conditions which would restrict ventilation and gas exchange sufficiently to render useful work impossible and to investigate the source of that restriction. The breathing gas densities required for this could be achieved only by employing inert gases more dense than helium. Correlation of effects upon pulmonary mechanical function of high density breathing gas under moderate pressure conditions with low density breathing gas under extreme pressure conditions was desired to validate predictions of ventilatory limitations of helium breathing at pressures greater than can be achieved in pressure chamber simulation of deep diving.

## Methods

These experiments concerning pulmonary function were conducted as part of the comprehensive study of the effects of oxygenated helium, crude neon (76.8% neon and 23.2% helium) and nitrogen at depths ranging from sea level to 1200 fsw (6, 8, 9).

The description of overall program, the chamber systems used, the subjects (II, X), and the general exposure profile are described elsewhere (8). Details pertinent only to pulmonary function will be described here.

Direct comparisons of the three diluent gases (nitrogen, crude neon and helium) were planned at densities of 1.2, 4.7 and 6.2 gm/L in order to validate extrapolation between equal density situations at different ambient pressures. The densities were calculated for a body temperature of 37 °C, an absolute pressure of 760 mm Hg plus the gauge pressure, and a constant 0.21 ata partial pressure of oxygen. Use of the high density inert gases neon and

*The authors, in presenting for this Symposium part of the results of a collaborative study, represent their direct co-investigators in the project.

nitrogen was planned at relatively high pressures to provide the basis for extrapolating results to helium breathing at pressures greater than those studied or even attainable in existing "man-rated" pressure chambers.

Table I shows the density values of the gas mixtures actually employed during each of the experimental conditions. The deviations from the planned exposures were due to: 1) contamination of the helium–oxygen chamber atmosphere with traces of other experimental gases; and 2) deviations from an oxygen partial pressure of 0.21 ata.

At each experimental condition, measurements were made during the following three pulmonary function maneuvers: 15 second maximum voluntary ventilations (MVV), forced expiratory vital capacities (FVC), and tidal breathing (TB). Transpulmonary pressure (esophageal balloon) and instantaneous gas flow (specially-designed pneumotachograph system [5]) were simultaneously recorded on a strip chart recorder and sampled and stored on magnetic tape by a digital computer (PDP-12). The esophageal balloon system was calibrated with a water manometer, while the pneumotachograph system was calibrated with a high-flow Brooks rotameter accurate to ±1% of the instantaneous flow. Calibrations were made both before and after each measurement condition.

When the experimental gas differed from the chamber gas, it was breathed by mask for 5 minutes before each experimental session started and during the time between measurement maneuvers. Before each maneuver the breathing system—including the pneumotachograph, low resistance valves, hoses and dump bag—was thoroughly flushed with the experimental breathing gas.

Data analysis of the three maneuvers cited was subsequently performed on a PDP-6

TABLE I

DESCRIPTION OF ACTUAL EXPERIMENTAL CONDITIONS INCLUDING VISCOSITY (μPOISE) AND DENSITY*

| Nitrogen Viscosity = 182 | | Crude Neon† Viscosity = 307 | | Helium Viscosity = 201 | |
|---|---|---|---|---|---|
| Depth (fsw) | Density (gm/L) | Depth (fsw) | Density (gm/L) | Depth (fsw) | Density (gm/L) |
| | | | | 0 | 0.39 |
| | | 0 | 0.78 | | |
| 0 | 1.15 | 18 | 1.07 | 167 | 1.20 |
| | | | | 400 | 3.08 |
| 100 | 4.48 | 200 | 4.73 | | |
| 141 | 5.86 | | | 900 | 5.65 |
| | | 272 | 6.18 | | |
| 200 | 7.82 | | | 1200 | 7.15 |
| | | 400 | 8.42 | | |
| 300 | 11.15 | | | | |
| 400 | 14.49 | 700 | 14.37 | | |
| | | 900 | 18.34 | | |
| | | 1200 | 25.21 | | |

*Values at body temperature for the breathing mixtures used at each depth.
†Crude neon used was 76.8% neon, 23.2% helium.

digital computer (20). The gas flow values from the MVV maneuver were integrated numerically over time to give the maximum voluntary ventilation rates. The maximum expiratory flows were ascertained from the FVC maneuvers, and the flows from these maneuvers were also integrated over time to determine the lung volumes at which each of the flows occurred. The tidal breathing maneuvers were used to determine flow resistance at each condition. This was done by subtracting the calculated dynamic compliance and calculated inertance (derived by the method of Mead [14]) from the transpulmonary pressure and dividing that value by the measured gas flow (16). Reported values of resistance are actually averages of resistances obtained for flows ±0.125 L/sec about the given flow. Thus, for example, the resistances specified for a flow of 1 L/sec really include resistances for flows from 0.875 through 1.125 L/sec. Inspiration and expiration are treated separately.

## Results

As the density of the breathing gas increased, airway resistance—particularly during expiration—increased, while the maximum voluntary ventilation and maximum expiratory flow decreased. The magnitude of these effects appeared to be influenced by the density and not by the particular diluent gas–pressure combination which provided that density. In spite of these changes in pulmonary function, even the greatest gas density did not prevent substantial ventilation for short periods of time. The specific influences observed in each of the experimental maneuvers are described below.

### Forced Expiratory Vital Capacity

As the density of the gas breathed increased from sea level values to about 5 gm/L, peak expiratory flows of both subjects fell rapidly. At greater densities, the rate of reduction in peak flows was much less. Thus about 70% of the total flow reduction caused by increasing density from 1 gm/L to 25 gm/L had occurred by a density of 5 gm/l. Figure 1 shows the values of peak expiratory flows as a function of gas density.

The function which best relates peak flows to density is a power function:

$$\dot{V}_{E\,max} = A\varrho^{B} \tag{1}$$

Values for the coefficients ($A$) and exponents ($B$) calculated by the least-squares method for this function are 8.116 and −0.257 for subject II and 10.488 and −0.328 for subject X. Peak expiratory flow occurred at about 92% of the vital capacity for each subject, except at the very lowest densities (those attained by administering helium or neon under normal sea level conditions) where the peak flow was reached at about 82% of the vital capacity. The decrease in peak flow is apparently a function of density alone, as the values for each gas appear to be randomly distributed about the regression lines rather than stratified according to species (Fig. 1).

### Maximum Voluntary Ventilation

The relationships of the maximum breathing capacity of each subject to density are shown in Fig. 2. As with peak expiratory flow, the striking feature of these results is that, at high density, there was almost no further reduction in short-term ventilatory ability as gas density

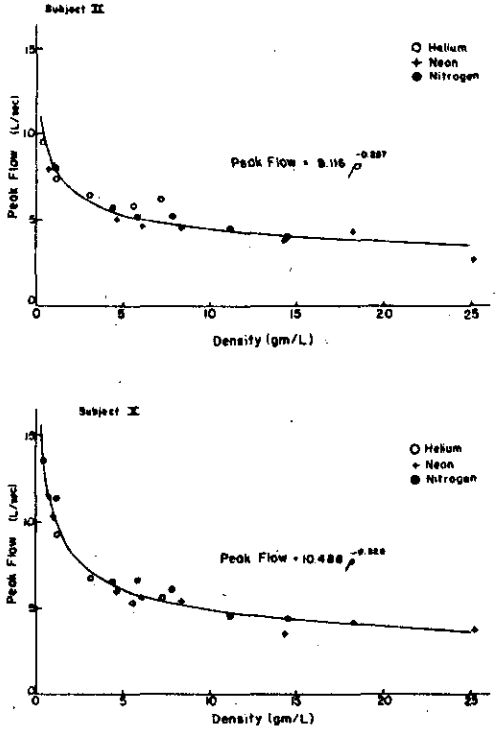


FIG. 1. Peak expiratory flow as a function of density.

increased. At an extreme density of 25 gm/L the maximum breathing capacity of the subjects was still about 50 L/min.

The function which best relates the results of the MVV measurements to the different experimental conditions was also found to be a power function:

$$\text{MVV} = A\varrho^{B} \tag{2}$$

Values for the coefficients ($A$) and the exponents ($B$) calculated by the least-squares method for this function are 117.9 and $-0.270$ for Subject II and 139.0 and $-0.298$ for Subject X, respectively.

## TIDAL BREATHING

The results from the tidal breathing maneuver include values for non-elastic or gas flow resistance and inertance. Linear regression lines relating inspiratory and expiratory non-elastic resistances to density for the flow ranges with median values of 1 and 2 L/sec are shown in Fig. 3.

At a flow rate of 1 L/sec, the inspiratory and expiratory resistances were nearly the same in the low density conditions. However, expiratory resistance increased to a much greater extent than did inspiratory resistance as the density of the breathing mixture was increased.

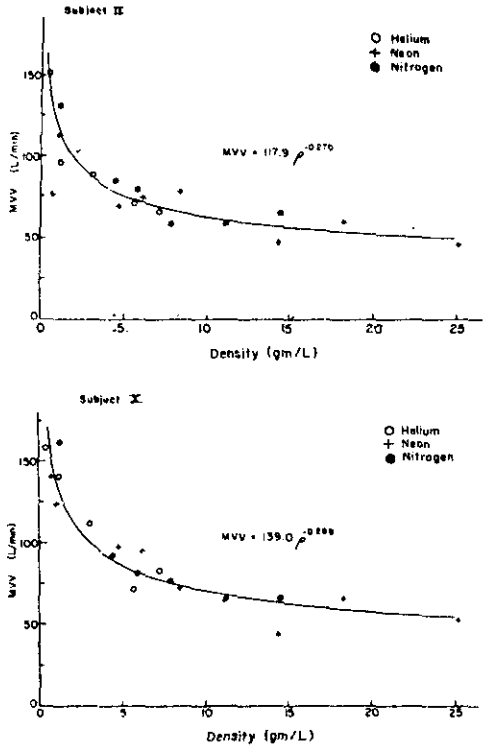


FIG. 2. Maximum voluntary ventilation as a function of density.

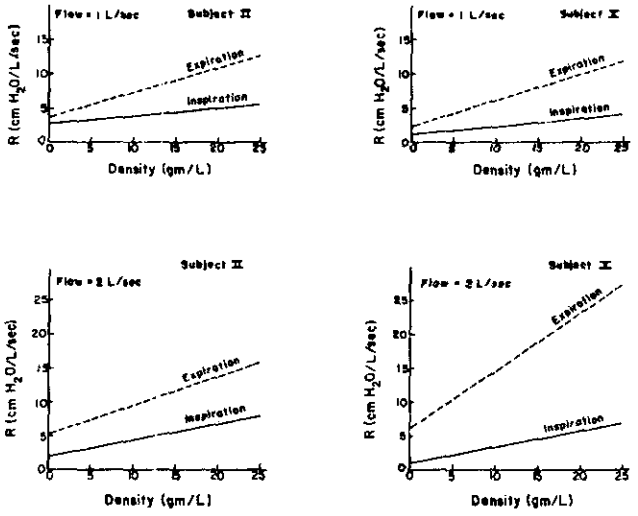


FIG. 3. Non-elastic resistances during inspiration and expiration at flows of 1 and 2 L/sec as a function of density.

At a flow rate of 2 L/sec, the same general pattern was followed. However, expiratory resistance was several times as large as inspiratory resistance for the lower density conditions, and the rate of resistance increase with density was twice the increase at the lower flow rate.

As with the MVV and maximum expiratory flows, there are no obvious differences in the non-elastic resistance-density relationships for the different inert gases. However, the data have considerably more scatter than the FVC and MVV data have.

The inertial pressure drops necessary for the calculation of non-elastic resistance were based upon the instantaneous acceleration and the value of inertance for each specific experimental condition. The inertance values used were derived from a least-squares linear regression analysis relating inertance to density. The parameters describing the relationship are shown in Fig. 4 with the inertance values for the individual experimental conditions.

## Discussion

The flow resistance, maximum voluntary ventilation and maximum expiratory flow measurements made in this study appreciably extend the breathing gas density span over which such measurements have been made. Qualitatively, these results match previous work. Flow

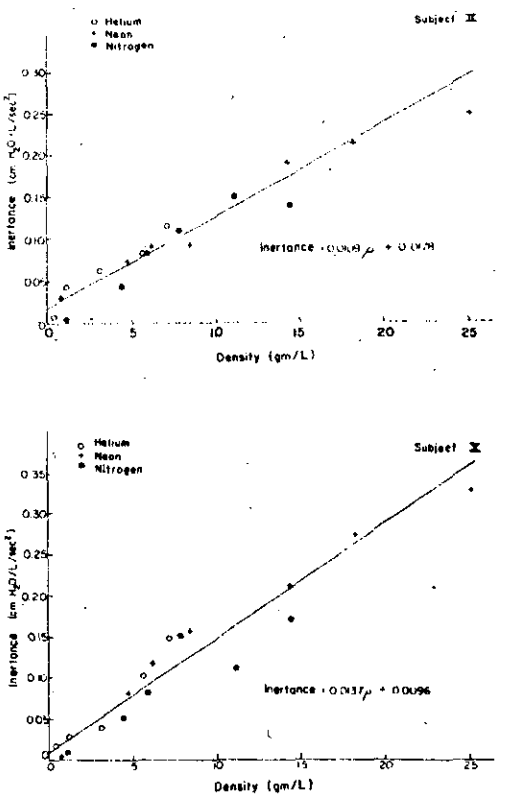


FIG. 4. Average inertance values plotted against density of the breathing gas.

resistance increased with density in a linear manner over the entire density range studied. Maximum voluntary ventilation and maximum expiratory flow decreased sharply as the density was increased from 1 gm/L to 5 gm/L, but the rate of decrement in performance declined appreciably as the density was increased above 5 gm/L. However, the magnitude of the changes measured in pulmonary mechanical function from a density of 1 gm/L to one of 25 gm/L, and the impact these changes had on exercise capacity were not as great as had been expected during planning for the study.

### Tidal Breathing–Flow Resistance

The non-elastic resistance of the subjects was similar to previous measurements in the lower density range (3, 12, 13, 23). Although non-elastic resistance increased steadily with density, there was only a threefold increase in resistance during quiet breathing over the entire range of densities. Such an increase in resistance is smaller than that required to produce symptoms of dyspnea in patients with obstructive pulmonary disease or asthma. This level of increase in resistance in acute exposures produced no measurable increase in resting $O_2$ consumption, no subjective difficulty in breathing, and no change in respiratory pattern toward slower, deeper breathing which is often seen with artificially imposed external breathing resistance.

During periods of hyperpnea, the effect of gas density became more prominent. The greater the increase in ventilation, and hence the greater the gas flow level, the greater was the influence of gas density on pulmonary mechanical function. Thus at a flow rate of 2 L/sec the rate of change of non-elastic resistance with changes in density was twice that found at a flow of 1 L/sec.

### Maximum Voluntary Ventilation

Maximum voluntary ventilation is normally performed by a subject breathing in a volume range in which the maximum expiratory flows attainable are limited by airway compression. The gas flows obtained in this maneuver correspond closely to those obtained at the same lung volumes during a forced vital capacity maneuver (15). Consequently, any factor influencing maximum gas flow should have a similar effect on maximum voluntary ventilation. This was found to be the case; a more detailed consideration of the MVV results follows.

### Forced Vital Capacity–Maximum Expiratory Flow Rates

Airway compression during expiration (1, 19, 25) may be responsible for reductions of maximum expiratory flow and maximum voluntary ventilation caused by increased gas density (1, 2, 4, 7, 10, 12, 13, 17, 18, 19, 21, 22, 24, 25, 27). Wood and Bryan (26) hypothesized that increased gas density reduced maximum flow in accordance with its effects on the factors (convective acceleration, turbulent flow and laminar flow) determining the resistance of the upstream airways. Of these, convective acceleration is the most important factor in determining the maximum flow at sea level conditions and for lung volumes above 40% of vital capacity; turbulent flow is of lesser significance in the same circumstances (11). Thus, at high lung volumes the maximum flow was expected to be proportional to density raised to a power between $-0.5$ (convective acceleration) and $-0.428$ (turbulent flow). At low lung volumes, the density exponent was expected to approach zero (laminar flow) and this was indeed found by Wood and Bryan (26) and Anthonisen et al. (1). Also, in many

cases, the density exponents calculated from maximum expiratory flow, and MVV data in the literature correspond well with the concepts for the determination of the maximum flow outlined above. However, the density exponent values for the maximum flows and maximum voluntary ventilations for subjects II and X are closer to zero than many of the other values cited or calculated from the literature. A less negative density exponent signifies less reduction in maximum voluntary ventilation or maximum expiratory flow with density increases than in cases where the density exponent has a larger absolute value. The density exponents for subjects II and X are also closer to zero than $-0.428$ and thus ventilatory capacity was greater than what would be expected for a turbulent flow-limiting circumstance.

### Influence of Duration of Exposure on the Effects of Increased Gas Density

The disagreement between these results and prior theoretical analysis (26) can be partially explained by comparing measurements of peak expiratory flows and maximum voluntary ventilations made during conditions of prolonged exposure to increased gas density (saturation conditions) with the same measurements made during short duration exposures. Schaefer et al. (21), Hamilton et al. (7) and Dougherty and Schaefer (4) have all shown that there is recovery of ventilatory ability and maximum expiratory flows during a prolonged period at one depth. Under some circumstances a very substantial part (44%) of the ventilatory impairment from increased gas density due to compression has been recovered without reduction of the density which induced the loss (21). The measurements in this study were made ½ to 2½ days after any change in pressure and all pressure changes were made slowly. Thus, they can be classified with the other measurements made after a prolonged period at one ambient pressure.

From the discussion above, it seems likely that the relationships of maximum flow and maximum voluntary ventilation to density are dependent to some extent on the circumstances of the pressure exposure. The density exponents of these relationships should be smaller (more negative) for short exposures (or for short exposures with elevated oxygen tensions) than for longer exposures. In fact, the values of the density exponents for the maximum flow- and MVV-density relationships measured during prolonged pressure exposure are nearer to zero than would have been predicted from the theoretical analysis of density effects on flow limitation (26). The importance of this finding is that maximum expiratory gas-flow and thus maximum ventilatory rates in prolonged pressure exposures are affected less by density increases than had previously been predicted.

## Conclusions

### Validity of Extrapolation

Based on the findings of this study, it is reasonable to extrapolate pulmonary mechanical function from high density-low pressure to low density-high pressure conditions. For peak expiratory flows, maximum voluntary ventilation and flow resistance there is a good correlation with density and there is no indication of separation according to the inert gas species being breathed. The significance of this finding is that experiments done at obtainable and safe pressures can be used to predict pulmonary function in circumstances unobtainable because of chamber limitations.

### Cause of Ventilatory Restriction

For the acute circumstances investigated in this pulmonary function study, ventilatory restriction followed effort-independent expiratory flow-limitation quite closely. Even though flow resistance increased linearly with density, the resistances did not become great enough to prevent high ventilatory rates from being achieved for brief periods of time. Based on the integration of the pulmonary function results with the results of the associated exercise study on the same subjects (9), we would expect extremely heavy exercise to be prevented by expiratory flow limitation at densities greater than about 5 gm/L. Brief periods of medium to heavy work, however, may never be restricted by expiratory flow limitation, even at densities far in excess of 25 gm/L. On the other hand, increased density of breathing gas and the associated increase in flow resistance may limit the duration of useful work by causing excessive fatigue of the respiratory muscles. The data do not permit quantitative description of this effect.

### Conditions Producing Failure

The pulmonary mechanical limitation imposed by the environmental conditions of this study was sufficient to restrict the work capacity of the subjects at extreme levels of exertion (9). This limitation, however, changed very little with breathing densities greater than 10 gm/L and the ventilatory capacity at the most severe condition (crude neon at 1200 fsw) was sufficient to support a work level of 900 kg·m/min for the planned short period of time. As the density of this latter condition (25 gm/L) is equivalent to the density of normoxic helium at 5000 fsw, and extrapolation based on equal density conditions appears valid, it is believed that the pulmonary mechanical function of an unencumbered man will be sufficient at depths up to 5000 fsw to support useful activity. Because of the relationships between maximum voluntary ventilation and density and between maximum expiratory flow and density, it also appears that adequate ventilation can be achieved at densities greater than 25 gm/L and therefore at depths even greater than 5000 fsw. Thus, for practical purposes, if man is given an adequate, low resistance breathing device, his pulmonary mechanical function should not limit the depth to which he can dive.

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# COMPTES RENDUS HEBDOMADAIRES

DES

# SÉANCES ET MÉMOIRES

DE LA

# SOCIÉTÉ DE BIOLOGIE

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TOME DEUXIÈME — HUITIÈME SÉRIE

ANNÉE 1885

TRENTE-SEPTIÈME DE LA COLLECTION

Avec figures

PARIS

G. MASSON, ÉDITEUR

LIBRAIRE DE L'ACADÉMIE DE MÉDECINE

120, BOULEVARD SAINT-GERMAIN

1885

## Phénomènes objectifs que l'on peut observer sur les animaux soumis aux hautes pressions, par M. P. Regnard.

En se reportant aux diverses communications que nous avons déjà faites à la Société, le lecteur verra que nous avons pu constater déjà un certain nombre de phénomènes dont les principaux sont la contracture musculaire et le coma. L'analyse microscopique que nous avons faite avec M. Vignal nous a démontré en outre que ces faits étaient dus à la pénétration de l'eau dans l'intimité des tissus qui se trouvaient détruits par elle.

Mais tout ce que nous avions étudié jusqu'à ce jour ne nous avait pas permis de voir ce qui se passait pendant la compression elle-même; en effet, nous introduisions nos animaux dans l'appareil; puis, après les avoir soumis à une pression correspondant à un fond donné, nous les retirions et nous constations l'effet produit. Tout ce qui se passait entre le début et la fin de l'expérience nous échappait.

Il en résultait que nos expériences étaient passibles d'une objection sérieuse qui nous a été faite par M. le docteur Raphaël Dubois; nous ne savions pas si les phénomènes observés résultaient de la pression même ou au contraire de la dépression consécutive.

Un seul moyen nous restait pour obtenir la vérité sur ce point, c'était de voir tout ce qui se passait pendant la compression. Pour cela, il fallait construire un vase *transparent* résistant à une pression de 600 atmosphères; c'est ce que nous avons tenté de faire avec l'aide de M. Ducretet.

Il est bien évident qu'il nous fallait absolument abandonner l'idée d'un récipient en verre; au delà d'une vingtaine d'atmosphères, tous les vases de cette nature sont brisés et cela d'une manière d'autant plus dangereuse que les changements de texture du verre se font silencieusement et que tel récipient qui a résisté à vingt atmosphères se brise subitement à sept ou huit dans une épreuve subséquente.

L'acier seul pouvait nous servir et nous avons imaginé de creuser à l'extrémité inférieure d'une culasse d'acier fondu M deux orifices en ligne droite dans lesquels nous avons essayé d'enchâsser des lames de glace de Saint-Gobain de cinq centimètres d'épaisseur.

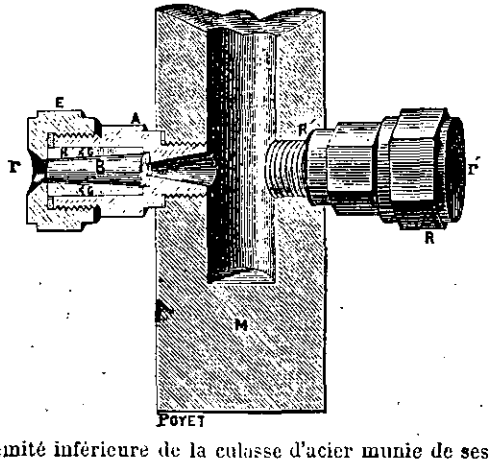


Fig. 1 — Extrémité inférieure de la culasse d'acier munie de ses deux hublots de quartz hyalin.

Nous avons, dès le début, été arrêté par ce fait que vers deux cents

atmosphères la glace la plus homogène se brisait, se poudroyait absolument, la haute pression ayant produit une trempe des plus dangereuses.

Nous avons alors essayé du quartz dont la texture cristalline est beaucoup plus homogène et nous avons réussi à faire des cônes B qui, enchâssés dans une garniture spéciale de glu marine et de gutta G et soutenus par un solide contre-écrou E, en acier fondu, ont pu résister aux essais, à une pression de plus de huit cents atmosphères.

On conçoit dès lors comment, avec une semblable disposition, il est possible de faire passer un rayon de lumière électrique à travers les deux hublots et, si les animaux en expérience se trouvent sur le trajet de ce rayon, leur image pourra être recueillie au dehors par un objectif et projeté sur un écran avec tel grossissement que l'on voudra.

C'est ce que montre la figure 2, qui représente une coupe de la totalité de notre appareil.

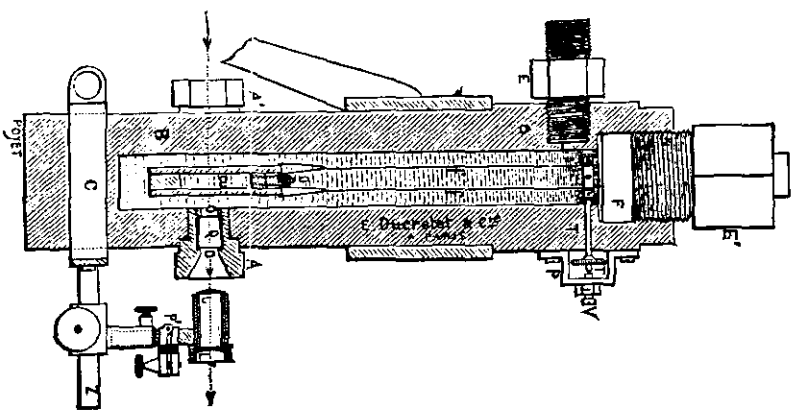

Fig. 2. — Coupe générale de l'appareil pour l'étude des animaux vivant *sous haute pression.*

B représente la coupe de la culasse d'acier, A un des hublots vu en coupe avec son ouverture O et son quartz Q qui, ici, est très peu conique. A' représente le hublot opposé vu en exécution. Le collier C et la crémaillère Z portent l'objectif achromatique L, L' que des vis et une genouillère P' permettent de placer dans toutes les situations possibles. Le rayon lumineux traverse l'appareil, suivant le sens marqué par les flèches.

Un chapeau d'acier F est solidement serré par un écrou de bronze E' sur un cuir gras et assure la fermeture du récipient dans lequel l'eau faisant pression est introduite par l'écrou à vis E mis en rapport par un tube de cuivre capillaire avec la presse Cailletet.

L'instrument présente même un perfectionnement des plus ingénieux que nous devons à notre habile constructeur M. Ducretet. En face des

hublots, en Cu, on aperçoit la cuve de glace où seront renfermés les animaux; cette cuve est suspendue par des fils de soie à un treuil en cuivre Po que l'on peut manœuvrer de l'extérieur par une poulie T. On peut donc monter ou descendre la cuve et amener devant les hublots la partie que l'on veut étudier. Chose curieuse : la perfection des joints est telle dans cet instrument que, malgré les nombreuses causes de fuites qu'il présente, la pression colossale de 600 et de 800 atmosphères s'y garde pendant des heures.

Notre figure 3 représente l'aspect général d'une expérience faite à haute pression sur des animaux vivants. A l'arrière-plan, on voit le générateur de lumière électrique lançant des rayons parallèles dans le bloc d'acier à travers les quartz. Le microscope de projection recueille l'image des animaux en expérience (cyclops) et la projette sur un écran où les observateurs peuvent la suivre. L'un de ceux-ci est occupé à maintenir le centrage des rayons lumineux, l'autre à produire la pression au moyen de la pompe Cailletet.

C'est ainsi que l'appareil est monté dans une chambre obscure au Laboratoire de la Faculté des Sciences de Paris.

Ceci dit du manuel opératoire, examinons ce qui se passe quand on met les animaux sous les pressions qui correspondent aux grands fonds de l'Océan.

Nous nous servons pour cela de cyclops, de gammarus pulex, de daphnies, etc., en un mot d'animaux assez petits pour que leur corps ne vienne pas fermer complétement les hublots de l'appareil et pour que leur transparence nous permette de suivre même les mouvements de leurs organes pendant l'expérience.

Dès les premiers coups de pompe, les animaux qui nageaient tranquillement dans le liquide sont pris d'une certaine inquiétude, ils s'agitent et cela jusqu'à ce qu'on ait atteint une profondeur d'environ 1,000 mètres (100 atm.). Mais en somme ils continuent à vivre dans les mêmes conditions qu'à la surface.

Au delà de 1,000 mètres, ils tombent lentement au fond de l'eau; leurs membres s'agitent avec rapidité, leurs appareils natatoires se raidissent et sont pris d'un tremblement très énergique. Les animaux demeurent à part cela immobiles au fond de l'eau. Ils semblent incapables de se mouvoir, ils sont tétanisés.

Si on les mène rapidement à 400 atmosphères (4,000 mètres), on les voit tomber subitement comme une pluie jusqu'au fond de la cuve où ils restent inertes, sans avoir même les mouvements de tremblement de la première période. Ils demeurent dans cet état tant que dure la pression.

Chaque fois que cette pression change brusquement, ne fût-ce que d'une vingtaine d'atmosphères, les animaux sont pris d'une secousse tétanique unique et générale, puis ils retombent dans le repos.

Si on les ramène d'un coup vers 1,000 mètres ou à la surface (100 at

0 atmosphères), ils reprennent *instantanément* leur course dans le liquide sans paraître avoir été le moins du monde incommodés.

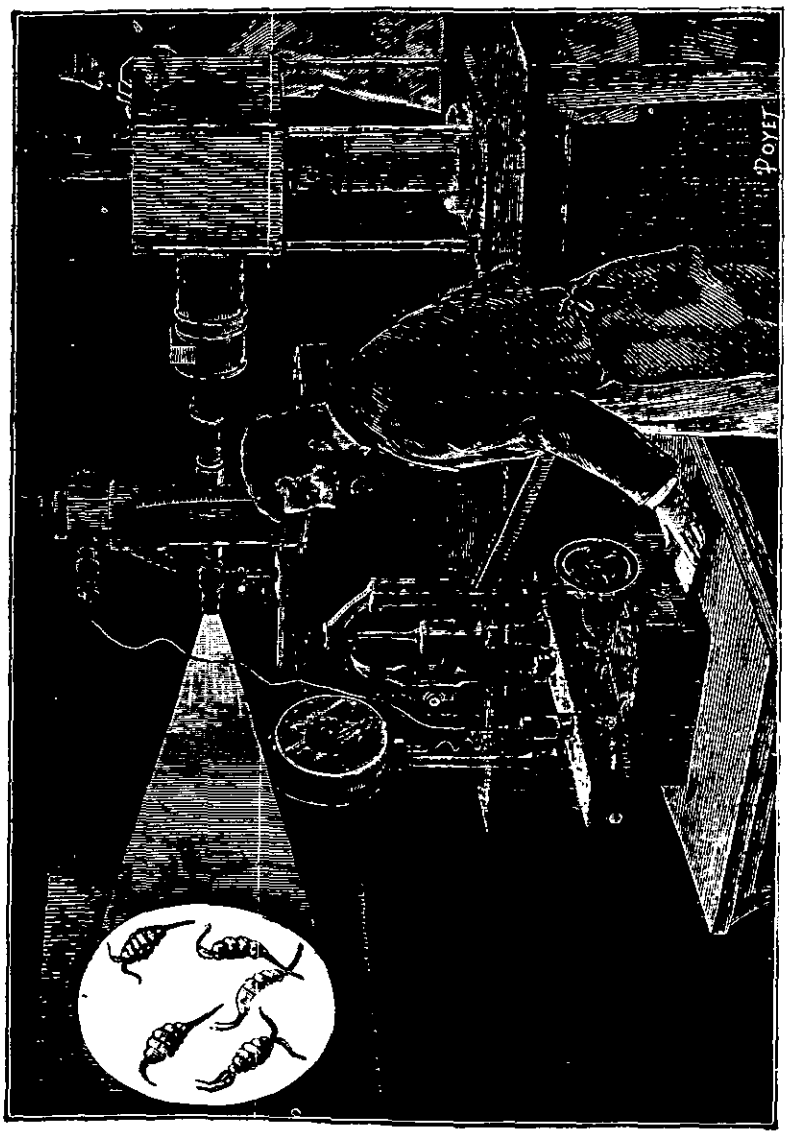


Fig. 3. — Aspect général d'une expérience à haute pression

Ceci nous démontre que les accidents que nous avons signalés sont bien des accidents de pression et non de dépression, car, dans ce dernier cas, les animaux seraient malades après la dépression, et c'est le contraire qui a lieu.

Suivant nous, la différence de compressibilité entre les substances animales et l'eau, différence très faible mais réelle, fait que, aux hautes pressions, le système nerveux, comprimé, est d'abord excité, puis inhibé (tétanisme du début, coma à 4,000 mètres). La suppression de la pression lui rend son état primitif et ses fonctions.

Si on prolonge la pression pendant longtemps, qu'arrive-t-il? Il arrive ce que nous avons autrefois décrit. Le coma persiste après la compression et l'animal met plusieurs heures à revenir à son état primitif, au lieu de ressusciter subitement.

C'est qu'alors, en vertu de la différence de compressibilité, les tissus se sont laissé imbiber lentement d'eau qui les a pénétrés (1) et il faut que cette eau ait été chassée pour que l'animal reprenne ses fonctions. Jusque-là, il demeure en état de vie latente.

En résumé, les premiers résultats des hautes pressions sur les animaux sont : l'excitation du système nerveux, puis son inhibition par compression ; les résultats consécutifs, si la pression dure, sont l'imbibition des tissus (nerveux et autres) comprimés et l'état de vie latente jusqu'à ce que, après la décompression, ils se soient débarrassés de l'excès d'eau.

Si la pression dure plus longtemps encore, les tissus ne peuvent arriver à la *restitutio ad integrum* et meurent.

1. Voir la communication que nous avons faite en commun avec M. Vignal.

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Masson et C^ie^, Éditeurs, 120 boulevard Saint-Germain, Paris.

# SOCIÉTÉ d'E.E.G. et de NEUROPHYSIOLOGIE CLINIQUE DE LANGUE FRANÇAISE

## *Séances des 5 et 6 décembre 1972*

### Évolution du tremblement au repos et pendant l'effort au cours de plongées profondes en atmosphère hélium-oxygène.

J. C. ROSTAIN et C. LEMAIRE.

*Département de Neurophysiologie appliquée* (1), *Institut de Neurophysiologie et de Psychophysiologie du C.N.R.S., 31, chemin Joseph-Aiguier, F 13274 Marseille Cedex 2 et Centre Expérimental Hyperbare de la C.O.M.E.X.* (2), *traverse de la Jarre, F 13009 Marseille*

La progression de l'homme vers les grandes profondeurs marines (au-delà de 100 m) a été rendue possible grâce à l'utilisation de mélanges respiratoires à base d'hélium. Cependant, cette progression a été ralentie par la mise en évidence de modifications physiologiques apparaissant entre 200 et 300 m, décrites sous le terme de syndrome nerveux des hautes pressions (S.N.H.P.) (BRAUER *et al.*, 1969 ; FRUCTUS *et al.*, 1969). Ce syndrome est caractérisé dans ses manifestations essentielles par l'apparition d'un tremblement, par une accentuation des activités E.E.Graphiques de fréquence thêta et par l'apparition d'une somnolence. Des symptômes analogues sont décrits chez différentes espèces animales (BRAUER *et al.*, 1970 ; Mac INNIS *et al.*, 1967 ; MILLER *et al.*, 1967 ; ROSTAIN *et al.*, 1970). Le tremblement apparaissant comme un bon critère d'étude, nous avons voulu préciser ses caractéristiques et ses conditions d'apparition au cours de plongées humaines très profondes.

#### *Méthodes*

Cette étude a été effectuée au cours d'une série de trois plongées en atmosphère hélium-oxygène à des profondeurs de 500, 520 et 610 m (400 à 420 mb d'$O_2$ ; 130 mb d'azote ; température de l'enceinte : 31° ± 1°. Le mode de compression a été différent d'une plongée à l'autre.

(1) Subventionné en partie par la D.R.M.E. (contrats n° 70-34-297-00-480-75-01 et 71-34-342-00-480-75-01).
(2) Subventionné en partie par le C.N.E.X.O.
*Tirés à part* : R. NAQUET, C.N.R.S., I.N.P. 3, 31, chemin Joseph-Aiguier, F 13274 Marseille Cedex 2.

Six sujets sains, âgés de 22 à 30 ans, ont participé à cette série de plongées. La mesure du tremblement est effectuée par accélérométrie (géophone « geo-space Hs-J » placé sur le majeur de la main droite). Les signaux sont reproduits sur papier (Elema Schönander) et enregistrés sur bandes magnétiques analogiques à partir desquelles est effectué un traitement sur ordinateur (PDP 12 digital equipment corporation). L'analyse qui porte sur trois séquences successives de 17,5 secondes de durée, consiste d'une part à déterminer l'amplitude moyenne du signal et d'autre part à établir les spectres de puissance.

L'activité électrique du biceps brachial et du long supinateur est recueillie par électrodes de surface ; elle est amplifiée (BP 700 c/s), intégrée (circuit de Miller) et reproduite sur papier (Elema Schönander).

Le tremblement est mesuré au cours de l'épreuve du serment, répétée plusieurs fois par jour à heures fixes au cours des plongées et au cours des confinements en atmosphère hélium-oxygène (10 m de profondeur) qui précèdent les expériences. Pour l'une d'entre elles (Physalie VI), le tremblement est également enregistré pendant le maintien d'une charge (épreuve du serment avec charge de 1 et 2 kg au niveau du poignet).

## Résultats.

Les mesures effectuées au cours des différents confinements ne montrent aucune modification significative. Il n'en a pas été de même des plongées.

1) *Physalie V* (520 *m*). La compression de 0 à 520 m d'une durée de 74 h 23 mn a comporté deux paliers de 15 heures à 350 et 460 m et trois phases de compression rapide à 1 m/mn (0-110 m ; 350-400 m ; 460-490 m). Le tremblement est apparu vers 300 m ; son amplitude par rapport à la valeur de contrôle effectuée en surface est de 200 p. 100. Il conserve des valeurs de 100 à 150 p. 100 jusqu'au passage à 490 m. Il atteint alors des valeurs de l'ordre de 400 à 600 p. 100 (entre 490 et 520 m). Ce tremblement régresse au cours de la décompression.

2) *Sagittaire II* (500 *m*). La compression de 0 à 500 m effectuée sans palier, avec une vitesse décroissante en fonction de la profondeur a duré 49 heures. Le tremblement apparaît vers 300 m. Il atteint à l'arrivée au fond une amplitude de 300 p. 100 par rapport à la valeur de contrôle. Pendant le séjour de 100 heures à 500 m, ce tremblement se renforce encore (400 p. 100). Il ne régresse que pendant la décompression.

3) *Physalie VI* (610 *m*). La compression a duré 177 heures. Elle a comporté un palier de 46 heures à 350 m et deux paliers de 14 heures à 535 et 565 m. Le tremblement qui apparaît toujours entre 200 et 300 m est cependant moins important à 610 m que lors des deux précédentes plongées à 500 et 520 m (200-250 p. 100). Son amplitude est plus faible le soir que le matin. Ce tremblement disparaît rapidement pendant la décompression.

Dans tous les cas, la fréquence de ce tremblement est comprise entre 8 et 12 c/s. Cette fréquence est d'autant plus stable que l'amplitude est importante.

La mesure du tremblement pendant le maintien d'une charge, effectuée au cours de la plongée à 610 m montre que l'amplitude du tremblement avec ou sans charge, par rapport à celle de la surface sans charge, augmente en fonction de la force exercée et en fonction de la profondeur.

Au cours des épreuves de maintien de charge, la fréquence est en général plus rapide que lors des épreuves sans charge, mais ses variations relatives ne sont pas constantes.

Au point de vue des activités E.M.G., avec les conditions d'enregistrement utilisées, il n'a pas été possible de mettre en évidence des activités particulières pouvant être corrélées avec le tremblement détecté par accélérométrie.

Au point de vue clinique, ce tremblement siège de préférence aux extrémités ; pour des profondeurs supérieures à 450 m, des secousses musculaires et des fasciculations peuvent compléter ce tableau. Les sujets sont peu gênés dans leurs actes professionnels. L'écriture est perturbée.

## Discussion.

Le tremblement présente toujours une augmentation sensible entre 250 et 300 m et il atteint à 350 m des valeurs à peu près analogues (200 p. 100) pour Physalie V et Sagittaire II, légèrement

inférieures pour Physalie VI (compression de 0 à 350 m plus lente). Après 350 m, les résultats sont très différents selon les plongées, l'augmentation d'amplitude étant plutôt en relation avec le mode de compression plutôt qu'avec la profondeur. Ainsi à 610 m, grâce à une courbe de compression lente à paliers, le tremblement est moins important que pour les plongées à 520 m et à 500 m. Dans ce dernier cas, le niveau de tremblement est intermédiaire entre Physalie V et VI, moins important que pour Physalie V, du fait de la suppression des compressions rapides à 1 m/mn, plus important que pour Physalie VI, du fait d'un départ plus rapide et de l'inexistence de paliers. Si la vitesse de compression est très rapide (cas de plongées à 180 m effectuées en quelques dizaines de minutes), le tremblement peut atteindre, dès 180 m, des valeurs importantes (BENNETT, 1966, 1971 ; observations personnelles). Un tremblement est également décrit chez l'animal exposé à des pressions croissantes d'hélium-oxygène. Chez le singe, l'utilisation de vitesses de compression pouvant varier de 10 m/heure à 240 m/heure ne modifie pas de manière évidente la profondeur où apparaît le tremblement (généralement entre 300 et 450 m) (BRAUER *et al.*, 1970 ; ROSTAIN *et al.*, 1970). Par contre chez la souris, MILLER *et al.* (1972) montrent que la profondeur où apparaît le tremblement peut varier dans de grandes proportions ; pour des vitesses de compression de 100 m/mn et 5 m/mn, il survient respectivement entre 350 et 500 m et entre 750 et 1100 m.

Le mode de compression joue donc un rôle important dans la potentialisation du tremblement. Cependant, la persistance de ce tremblement observée pendant le séjour de 100 heures à 500 m montre qu'à partir de certaines profondeurs, d'autres facteurs peuvent entrer en jeu.

L'hélium en tant que tel ne semble pas intervenir à pression faible ou élevée. Les divers confinements de plusieurs jours chez l'homme, à des pressions voisines de la pression atmosphérique, ne révèlent pas de modifications significatives. Par ailleurs, le remplacement de l'hélium par de l'hydrogène chez le singe (BRAUER *et al.*, 1970 ; ROSTAIN et NAQUET, 1972) ou par le néon chez la souris (MILLER *et al.*, 1972) n'empêche pas l'apparition du tremblement.

Ce tremblement qui n'influence pas le travail musculaire local, ni l'activité électromyographique chez l'homme est plus rapide que le tremblement parkinsonien ; sa fréquence est de 8 à 12 c/s. Cette fréquence est retrouvée chez le singe *Papio papio*, le tremblement étant objectivé à partir d'une certaine intensité par l'E.M.G. (ROSTAIN, 1971). Par ses caractéristiques il apparaît être une exagération du tremblement physiologique décrit par de nombreux auteurs chez l'homme et l'animal. Ce tremblement physiologique peut devenir perceptible à l'œil nu et atteindre une grande amplitude dans certains cas : effort mental, exercice physique, anxiété, douleur, hyperthyroïdisme, etc. (BINET, 1920 ; BRUMLIK, 1962 ; FRIEDLANDER, 1956).

*En conclusion*, dans nos expériences l'augmentation d'amplitude du tremblement est la première manifestation d'un syndrome en relation avec les conditions hyperbares (S.N.H.P.). Il apparaît à des profondeurs d'autant moins grandes que la vitesse de compression est rapide et, pour une vitesse donnée, son intensité croît avec la profondeur. La cause et l'origine de ce tremblement sont à déterminer.

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## ABSTRACT

### THE INITIAL MANIFESTATIONS OF HELIUM NARCOSIS *IN MAN*

(the results of neurophysiological studies)

G. L. Zaltsman

A group of human beings has been investigated for the initial outward manifestations of helium narcosis in the conditions of breathing 10—14% helium-oxygen mixtures under the pressures of 10, 12, 14, and 16 atm., and neurophysiological studies have been carried out.

The earliest and the most typical narcotic symptom is the specific «helium» tremor of the upper extremities and trunk observed under pressures of 13—16 atm., and the accompanying «low» motorial shifts — the initial indications of bradykinesia, amimia and rigidity of muscles. By a number of signs these shifts can be approached to akynetico-rigid syndrom arising in parkinsonism as a result of disturbance of the striar system function.

In studying the higher nervous activity a certain general inhibitory state of motorial and verbal reactions and a lowering of mental efficiency have been established. No qualitative disturbances of complex forms of cortical activity occurred.

Electroencephalographic shifts are in the suppression of the α-rhythm and a general shift of activity towards quick frequencies.

A conception is put forward that the striar system with a successive involvement of non-specific thalamo- and reticulo-cortical systems makes up a neurophysiological substratum of the initial narcotic shifts.

# НАЧАЛЬНЫЕ ПРОЯВЛЕНИЯ ГЕЛИЕВОГО НАРКОЗА У ЧЕЛОВЕКА

(результаты нейрофизиологических исследований)

Г. Л. Зальцман

## Внешние проявления гелиевого наркоза

Искусственные гелиокислородные дыхательные смеси стали применяться в практике подводных погружений в конце 30-х годов. Замена азота воздуха более индифферентным гелием позволила постепенно увеличить диапазон рабочих давлений до 16—20 ати, при этом явлений «глубинного опьянения» и других типичных признаков общего наркоза не отмечалось. Это породило негативное отношение многих специалистов к самой возможности наркотического действия гелия на организм человека.

Каждый, кто дышал гелиокислородной смесью при давлениях 10—16 ати и выше, отмечал резкое охлаждение организма и ритмичную дрожь верхних конечностей и туловища. Эти ощущения обычно связываются с охлаждающим действием гелиевых смесей, поскольку теплопроводность гелия более чем в 7 раз превышает воздушную.

В проведенных нами специальных наблюдениях над испытуемыми, дышавшими 10—14%-й гелиокислородной смесью под давлением 14 и 16 ати в рекомпрессионной камере (Зальцман, 1961), был констатирован ритмичный тремор с частотой 5—8 в 1 сек., распространяющийся на верхние конечности, туловище, иногда и нижнюю челюсть. Тремор был больше всего выражен в кистях. Во время выдержки при неизменном давлении размах движений уменьшался и тремор исчезал через 3—5 мин., а при давлениях 20 ати — через 5—10 мин. Одновременно отмечалась некоторая замедленность и скованность движений, а при более высоких давлениях осуществление двигательных актов было затруднено.

Волевые усилия в значительной мере подавляли тремор, однако последний мешал выполнению работ, требующих тонкой координации движений. Так, если испытуемый проводил прямые линии карандашом, последние имели волнообразные искривления. Выраженных изменений мышечной силы, как показали эргометрические определения С. Д. Куманичкина у наших испытуемых при давлении 16 ати, не наступало. Производительность физической работы не изменялась.

При применении специальной регистрации удалось установить, что групповые ритмические движения пальцев рук появляются при дыхании гелиокислородной смесью уже под давлением 4—6 ати. При давлении 8—10 ати, когда испытуемый ощущал дрожь, ритмические сокращения следо-

вали чаще и были более длительными (до 10 движений подряд). И, наконец, при давлении 12—14 ати, когда тремор мог наблюдаться через иллюминатор, регистрировались непрерывные ритмические движения. Дальнейший физиологический анализ показал, что наступление характерного гелиевого тремора у человека и у животных [1] строго связано с определенной величиной парциального давления гелия и не зависит от общей величины давления, если в дыхательную смесь входят другие компоненты. Так, одни и те же испытуемые ощущали дрожь при дыхании гелиокислородной смесью с 90%-м содержанием гелия под давлением 12 ати и выше и при дыхании воздушно-гелиевой смесью с 67%-м содержанием гелия под давлением 16 ати и выше. Парциальное давление гелия в обоих случаях было равно 11—12 ата. Таким образом, характерный тремор — это первое проявление *действия повышенных давлений гелия* и, как показали исследования на животных,[2] не случайное.

По мере дальнейшей компрессии в гелиевой среде к тремору присоединяются другие гиперкинезы и «низкие» двигательные нарушения. Что касается *корреляции тремора с охлаждающим действием* гелиевой среды, то ее установить не удалось. Наблюдения показали, что во время компрессии, когда проявляется тремор, температура в камере обычно повышается на 7—15°, а затем понижается до комнатной, когда тремор исчезает. У одних и тех же испытуемых, дышащих той же гелиокислородной смесью при равном давлении, тремор проявляется в большей мере при «сухом» спуске, а не при подводном, когда температура понижается до 5—10°. Создание гипертермических условий при компрессии животных в гелиевой среде приводило к развитию общих судорог при давлении в 30 ати. И, наконец, следует отметить, что «гелиевый» тремор наступает во время компрессии сразу в отсутствие других признаков гипотермии; последние, как правило, развиваются в более поздние сроки, когда тремор проходит.

**Результаты изучения высшей нервной деятельности**

Первые исследования умственной работоспособности человека в условиях повышенных давлений гелиокислородной среды были проведены в конце 30-х годов, когда решался вопрос о внедрении новых смесей. Применяя различные тесты, Бенке и Ярброу (Behnke a. Jarbrough, 1938) *не обнаружили в этих условиях* выраженных нарушений работоспособности у испытуемых. С тех пор мнение о сохранении нормальной работоспособности человека в условиях повышенных давлений гелиевой среды стало господствующим.

*Детальное исследование высшей нервной деятельности* в условиях начального наркотического действия гелия было проведено нами (Зальцман, 1961) на 6 испытуемых, каждый из которых последовательно в разные дни дышал 10—14%-й гелиокислородной смесью под давлением 10, 12, 14 и 16 ати. В результате применения *комплексной методики*, включающей различные приемы исследований, была выявлена следующая картина.

Безусловные двигательные рефлексы при электрокожном раздражении поверхностного сгибателя пальцев руки не менялись во всем диапазоне давлений. При применении ритмических раздражений под давлением 10 ати имел место сдвиг оптимальной частоты стимулов, вызывавших наиболее выраженную двигательную реакцию, в сторону уменьшения.

Условные двигательные реакции, выработанные посредством речевой инструкции (нажатие рукой на педаль при появлении звуковых или световых сигналов), претерпевали следующие изменения: скрытый период уве-

[1] См. нашу статью, стр. 186.
[2] См. там же.

личился лишь при давлении 16 ати на 0.16 сек., или на 38% (с вероятностью 98%). Величина ответов существенно не менялась, экстросигнальные ответы отсутствовали. При регистрации двигательных ответов на аппарате Жуковского на команды «больше» и «меньше», которые выполнялись без зрительного контроля, имело место увеличение угла отклонения конечности. Сдвиги были равными при обеих командах и прогрессировали от 5% при давлении 10 ати (с вероятностью 45—70%) до 20% при давлении 16 ати (с вероятностью 98—99%).

Своеобразные изменения наступали при проверке ранее выработанных тормозных рефлексов. При воспроизведении положительного и тормозного рефлексов на комплексный раздражитель (два 4-членных последовательных комплекса разноцветных огней, отличающихся порядком 2 средних членов) отмечались преимущественные нарушения положительного рефлекса. Однако частота нарушений убывала от 71% при давлении 10 ати до 0 при давлении 16 ати. Скрытый период запаздывающего рефлекса не изменялся при давлении 10 ати и уменьшался при более высоких давлениях максимально на 0.6—1.4 сек., или на 6—15% (с вероятностью 50—98%). Величина рефлекса повышалась при всех давлениях на 6—12% (с вероятностью 45—85%).

Течение цепного рефлекса (последовательные нажатия на клавиши разными пальцами рук) в целом не нарушалось. Отдельные случаи ошибочных движений не прогрессировали по мере увеличения давления.

Сравнивая рисунки испытуемых, сделанные до компрессии и при давлении 10—16 ати, можно было отметить как случаи уменьшения, так и некоторого увеличения размеров изображаемых предметов, а также волнообразное искривление прямых линий, менее выраженное, если линии имели сложные конфигурации. Тенденций к обеднению деталями не отмечалось.

Критическая частота различаемых световых стимулов понижалась при давлении 10 ати с 40.2 в 1 сек. до 37.4 в 1 сек. в среднем.

Наименьшие изменения были выявлены при исследовании II сигнальной системы (наступающее в гелиевой среде искажение голоса не учитывалось, как явление физического порядка). При проведении словесного (ассоциативного) эксперимента отмечалось только небольшое, на 0.07—0.18 сек., или на 5—12%, увеличение скрытого периода при давлениях 12—16 ати (с вероятностью 60—97%). При наблюдении можно было установить некоторое замедление артикуляции.

Задания различной сложности и команды выполнялись испытуемыми в условиях повышенных давлений гелиевой среды (10—16 ати) так же четко, как вне камеры.

В приведенных материалах исследований В. В. Смолина, К. М. Рапопорта и Г. А. Кучук (стр. 139 наст. сборника), применявших ряд наших тестов, а также собственные модификации, были получены сходные изменения. При давлении гелиевой среды в 20 ати скрытый период двигательного рефлекса увеличивался на 19—38%, а запаздывающего — уменьшался на 17—19%. Размер букв при письме был увеличен на 18—35%. Число слов в пробе с запоминанием уменьшалось до 40%, возрастали сроки устного решения примеров (до 21%), количественно понижалась работоспособность при применении пробы Ландольта (до 39%). Качественных нарушений не отмечалось.

### Результаты электроэнцефалографических исследований

Электроэнцефалографические исследования на людях в условиях повышенных давлений гелиевой среды 13, 16 и 20 ати приведены в статье В. В. Смолина, К. М. Рапопорта и Г. А. Кучук (аналогичных исследований

в доступной литературе найти не удалось). Авторы отметили 2 феномена: подавление α-ритма и смещение активности в сторону быстрых частот. Снятие ЭЭГ при закрытых глазах позволило определить уменьшение α-индекса от 14 до 80%, уменьшение амплитуды α-волн — от 26 до 76% и увеличение их частоты — максимально на 1.4 кол./сек. Появлялись волны с частотой 20—40 кол./сек. и амплитудой 5—10 мкв. После открывания глаз усиливалась быстрая активность. Сдвиги прогрессировали по мере повышения давления. Медленная активность не выявлялась даже при давлении гелиевой среды в 20 ати.

### О нейрофизиологических механизмах начального наркотического действия повышенных давлений

Наиболее характерный и ранний симптом начального наркотического действия гелия — тремор верхних конечностей и туловища, преходящий при давлениях 10—16 ати и более выраженный при давлениях 20 ати, есть результат нарушения нервной регуляции двигательных актов (разновременное поступление импульсов в антагонистические группы мышц). Анализ этих и других двигательных проявлений гелиевого наркоза позволяет сблизить их с акинетико-ригидным синдромом, возникающим при паркинсонизме в результате нарушения функции стриарной системы.

Как в том, так и в другом случае тремор стереотипен, ритмичен, имеет частоту 5—8 в 1 мин., распространяется на конечности, туловище, голову (больше всего выражен в кистях), уменьшается при произвольных движениях. Из других симптомов нарушения миостатических функций в условиях повышенных давлений гелиевой среды могут быть отмечены начальные проявления брадикинезии (увеличение скрытого периода двигательных реакций), амимии (отсутствие признаков двигательного возбуждения и других эмоциональных сдвигов), ригидности мышц (некоторая скованность и замедленность движений, затрудненное осуществление двигательных актов). Эти нарушения наступают при сохраненном интеллекте.

Сказанное позволяет прийти к заключению, что в условиях начального наркотического действия повышенных давлений гелия страдает функция стриарной системы — высшего подкоркового регуляторно-координационного аппарата.[3]

Результаты изучения высшей нервной деятельности показали, что в условиях начального наркотического действия повышенных давлений гелия не происходит качественных нарушений основных кортикальных функций, включая самые сложные ее формы. Выявляется лишь определенная заторможенность двигательных реакций (увеличение скрытого периода на 38% *при давлениях 16—20 ати*) и *словесных реакций* (увеличение скрытого периода на 12%) и ухудшение памяти (уменьшение числа запоминаемых слов на 25—40% при давлениях 16—20 ати). Это сказывается и при выполнении сложных видов умственной деятельности (увеличение времени решения примеров на 10—25%, уменьшение числа операций в пробе Ландольта на 12—35% при давлениях 16—20 ати). Заторможенностью реакций, осуществляющих проприоцептивный контроль, следует, по-видимому, объяснять увеличение амплитуды двигательных ответов на аппарате Жуковского (одинаковое при командах «больше» и «меньше»).

Важно отметить, что скрытый период запаздывания, характеризующий процессы внутреннего торможения, изменялся под давлением 12—16 ати

[3] Прямые электрофизиологические данные, подтверждающие эту точку зрения, были получены на животных при отведении биопотенциалов хвостатого ядра и скорлупы в условиях действия на организм повышенных давлений гелиевой среды (см. нашу статью на стр. 206).

на 6—15%, а при 20 ати — на 17—19%, т. е. значительно меньше, чем элементарные двигательные акты. Это еще раз подчеркивает примат «низких» двигательных нарушений в гелиевой среде.

Касаясь вопроса о нейрофизиологическом субстрате установленных сдвигов, следует сказать, что он вряд ли может быть решен однозначно без специального экспериментального анализа. Большинство авторов связывает понижение тонуса коры в первую очередь с изменением активности неспецифической таламо-кортикальной системы. Однако не исключается участие стволовых отделов ретикулярной формации и хвостатого ядра.

Результаты электроэнцефалографических исследований — подавление α-ритма и общий сдвиг активности в сторону быстрых частот, наступающие при давлениях гелиевой среды 13—20 ати, — позволяют заключить в соответствии с данными ряда авторов (Moruzzi a. Magoun, 1949; Schneider et al., 1951; Magoun, 1952; Arduini a. Arduini, 1954; Rossi a. Zirandoli, 1955; Schlag a. Brand, 1958, и др.), что в условиях начального наркотического действия гелия имеет место активирование ретикулярной формации среднего мозга и соответствующее активирование высших отделов.

Сопоставляя все рассмотренные проявления начального наркотического действия повышенных давлений гелия, можно прийти к заключению о заинтересованности в этом процессе ряда отделов мозга: стриарной системы, неспецифической таламо-кортикальной и ретикуло-кортикальной. Однако приоритет должен быть отдан стриарной системе, поскольку характерный тремор, возникающий в результате функциональных нарушений в этой системе, является наиболее постоянным и наиболее ранним патогномоничным симптомом гелиевого наркоза, который объективно выявляется при давлениях много ниже 10 ати.

Возникает вопрос, можно ли связать с избирательным действием гелия на стриарную систему остальные выявленные сдвиги.

Являясь центром экстрапирамидной системы, стриарная система осуществляет не только миостатическую функцию. При раздражении хвостового ядра были обнаружены эффекты пробуждения и генерализованные изменения в коре, аналогичные тем, которые возникают при стимулировании ретикулярных структур (Shimamoto, Verzeano, 1954; Stoupel, Terzuolo, 1954; Buchwald et al., 1959, и др.). Установлены и противоположные, тормозные эффекты — удлинение времени реакции нейронов больших полушарий, появление caudate-spindles и наступление сна (Деметреску и Деметреску, 1961; Buchwald et al., 1961; Crautzfeldt, Jung, 1961, и др.). Большинство авторов предполагает, что эти последние эффекты осуществляются через неспецифические ядра таламуса.

Таким образом, представленные данные позволяют связать со стриарной системой не только симптоматику начальной стадии гелиевого наркоза, но и начальные изменения высшей нервной деятельности (общая заторможенность) и электроэнцефалографические сдвиги (восходящее активирование). Последние эффекты, по всей вероятности, осуществляются через посредство неспецифических таламо- и ретикуло-кортикальных систем.

Подводя итоги обсуждения начального наркотического действия повышенных давлений гелия на организм человека, механизм этого действия можно связывать с избирательным активированием стриарной системы и последующим вовлечением в процесс неспецифической таламо- и ретикуло-кортикальной систем. С этих позиций могут быть однозначно интерпретированы низкие двигательные нарушения, изменения высшей нервной деятельности и изменения биоэлектрической активности мозга. Отметим, что предложенное представление нуждается еще в дальнейшей экспериментальной проверке.

**Заключение**

На группе испытуемых в условиях дыхания 10—14%-ми гелиокислородными смесями под давлением 10, 12, 14 и 16 ати определялись внешние проявления гелиевого наркоза и проводились нейрофизиологические исследования. Анализ полученных результатов, а также данных других авторов позволил следующим образом представить начальное наркотическое действие гелия.

Начальное наркотическое действие гелиевой среды проявляется у человека при давлениях порядка 13—16 ати и выше. Наиболее ранним и характерным наркотическим симптомом является специфический «гелиевый» тремор верхних конечностей и туловища и другие сопутствующие «низкие» двигательные сдвиги — начальные признаки брадикинезии, амимии, ригидности мышц. По целому ряду признаков эти сдвиги могут быть сближены с акинетико-ригидным синдромом, возникающим при паркинсонизме в результате нарушения функции стриарной системы.

При изучении высшей нервной деятельности показано отсутствие качественных нарушений сложных форм кортикальной деятельности (при давлениях до 20 ати). Выявлена определенная общая заторможенность двигательных и словесных реакций, некоторое снижение умственной работоспособности и ухудшение памяти. Указанные проявления понижения общего тонуса коры связываются с непосредственным изменением активности неспецифической таламо-кортикальной системы.

В электроэнцефалографических исследованиях (при действии давлений 13—20 ати) определяется феномен подавления α-активности и общий сдвиг биотоков в сторону быстрых частот, что связывается с активированием неспецифической ретикуло-кортикальной системы.

Предлагаемая точка зрения об избирательном наркотическом действии повышенных давлений гелия на стриарную систему с последующим вовлечением неспецифических таламо- и ретикуло-кортикальных систем подлежит дальнейшей экспериментальной проверке.

# DROWNING AND NEAR-DROWNING

Articles selected by Barbara B. Tabeling, M.D.
University of Florida - College of Medicine
Gainesville, Florida

# 7

# DROWNING AND NEAR-DROWNING

BARBARA B. TABELING

Many methods of resuscitation after drowning have been described over the centuries; but only recently has its pathophysiology and a rational approach to therapy come to light. Swann and his coworkers (1947) documented biochemical and physiologic events that occurred during drowning of experimental dogs in freshwater and seawater. In the decade following their report of the hypoxemia, blood volume, and electrolyte changes that occur, many clinicians believed that treating electrolyte and blood volume abnormalities was of primary importance to the care of near-drowned humans. Because there was no ready means of cardiac defibrillation at that time, there was little hope of resuscitating humans drowned in freshwater. After the advent of closed-chest cardiac massage and external cardiac defibrillation, new investigations documented major advances in management of near-drowning. In 1960, Redding, Voigt, and Safar reported the effects of positive-pressure ventilation with air and with oxygen on near-drowned experimental animals, and the beneficial effects of intravascular volume replacement after seawater aspiration. Halmagyi and Colebatch (1961) demonstrated that significant hypoxemia resulted from aspiration of even small volumes of fluid and was probably due to venous admixture. A summary by Fuller (1963) of autopsy findings of a large series of drowned humans and of clinical findings of a series of near-drowned humans differed widely from previous findings in experimental animals. Fuller made a number of recommendations for the management of near-drowned persons based on this study; most have withstood the test of later investigations. In 1966, Reidbord and Spitz used electron microscopy to document ultrastructural pulmonary changes that occur with drowning and noted that these findings were consistent with reports of clinical findings.

A series of investigations by Modell and coauthors defined the experimental animal model of near-drowning and documented the temporary nature of electrolyte and blood volume changes (Modell et al., 1966), the effect of aspirated fluid on pulmonary surfactant activity (Giammona and Modell, 1967), and the influence of volume of fluid aspiration (Modell et al., 1967). Modell and Davis (1969) then determined that drowned humans rarely aspirate enough water to cause severe electrolyte changes. In the 1970's, Modell and coauthors evaluated the effects of available modes of ventilatory support on near-drowned animals and found that continuous positive airway pressures (CPAP) and controlled mechanical ventilation with positive end-expiratory pressure (PEEP) were equally beneficial after seawater near-drowning (Modell et al., 1974), while controlled mechanical ventilation with PEEP more reliably improved pulmonary venous admixture than PAP after freshwater near-drowning (Bergquist et al., 1980).

A report by Modell et al. (1976) of a large series of near-drowned humans documented the excellent survival rate that can be achieved with current modes of therapy, while a large series reported by Conn and coauthors (1980) demonstrated a similar excellent result in general and in cerebral resuscitation with aggressive measures. A single case report by Siebke et al. (1975) of normal survival after 40 min submersion in icy water emphasizes the importance of prolonged aggressive resuscitation in such a situation.

Studies related to the causes of drowning include the report by Craig (1961) that documented hypoxemia occurring during exercise after hyperventilation. This may result in loss of consciousness and thus in drowning of competent swimmers. Keating et al. (1969) investigated effects of water temperature on thin and heavy swimmers and documented different mechanisms responsible for failure of swimming in cold water.

Dr. Martin Nemiroff has made major contributions to resuscitation following cold water submersion and abstracts of three of his many papers are included (all published in 1977).

The "diving reflex" is believed to be a protective mechanism associated with immersion that may improve ability to survive. Campbell and coauthors (1969) reported the first investigation of multiple cardiovascular responses occurring after immersion of different parts of the body, and postulated the mechanism by which the diving reflex occurs.

# DROWNING AND NEAR-DROWNING

B. B. TABELING

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# *Comparison of Ventilatory Patterns in the Treatment of Freshwater Near-drowning in Dogs*

*Robert E. Bergquist, M.D.,* Mark M. Vogelhut, M.D.,* Jerome H. Modell, M.D.,† Stacy J. Sloan,‡ Bruce C. Ruiz§*

**The authors compared controlled mechanical ventilation (CMV) plus positive end-expiratory pressure (PEEP) with continuous positive airway pressure (CPAP) when expiratory pressure was increased in 5-cm $H_2O$ increments to improve $Pa_{O_2}$ and decrease intrapulmonary physiologic shunting ($\dot{Q}_{sp}/\dot{Q}_t$) in 30 dogs that had been near-drowned with fresh water (22 ml/kg). After aspiration, significant arterial hypoxemia and increased $\dot{Q}_{sp}/\dot{Q}_t$ developed in all the animals. When $FI_{O_2}$ was increased from 0.21 to 0.4, a significant decrease in $\dot{Q}_{sp}/\dot{Q}_t$ occurred.**

**Thirty minutes after aspiration, the dogs were divided into four treatment groups. In dogs that breathed spontaneously with zero end-expiratory pressure (ZEEP), Group I, $\dot{Q}_{sp}/\dot{Q}_t$ did not change after the initial response to an increased $FI_{O_2}$. Controlled mechanical ventilation (CMV) with ZEEP, Group II, produced a further moderate decrease in $\dot{Q}_{sp}/\dot{Q}_t$. The response to spontaneous ventilation with continuous positive airway pressure (CPAP), Group III, was variable. Four dogs had decreases in $\dot{Q}_{sp}/\dot{Q}_t$ at 15 cm $H_2O$ CPAP to less than 12 per cent of cardiac output, whereas the other six dogs had pulmonary shunting that remained above 40 per cent of cardiac output. All dogs treated with CMV plus PEEP, Group IV, had significant decreases in $\dot{Q}_{sp}/\dot{Q}_t$ at 15 to 20 cm $H_2O$ PEEP. There was a transient increase in pulmonary artery-occluded pressure after aspiration, with a persistent increase in pulmonary vascular resistance. Cardiac output decreased significantly with CMV and with the application of 15 and 20 cm $H_2O$ PEEP and CPAP. It was lowest with the combination of CMV plus PEEP.**

**This study suggests that PEEP was most effective in reversing $\dot{Q}_{sp}/\dot{Q}_t$ and hypoxemia after freshwater near-drowning. This effect was most consistent in those animals receiving CMV, despite significant decrements in cardiac output. Continuous positive airway pressure alone was variably effective. (Key words: Drowning. Lung: shunting. Ventilation: continuous positive airway pressure; continuous positive-pressure breathing; positive end-expiratory pressure; shunting; zero end-expiratory pressure.)**

PREVIOUS STUDIES of dogs have shown that controlled mechanical ventilation (CMV) must be combined with positive end-expiratory pressure (PEEP) to improve arterial blood oxygen tension ($Pa_{O_2}$) after aspiration of fresh water.[1] Those studies used a fixed level of 10 cm $H_2O$ PEEP. In clinical practice, rather than being set at one level, PEEP is frequently varied to obtain optimal response in $Pa_{O_2}$, physiologic intrapulmonary shunt ($\dot{Q}_{sp}/\dot{Q}_t$), or compliance. During treatment of human victims of freshwater near-drowning, we noticed that in some patients $Pa_{O_2}$ increased and $\dot{Q}_{sp}/\dot{Q}_t$ decreased during spontaneous ventilation with varied PEEP or continuous positive airway pressure (CPAP), but others needed the addition of CMV to PEEP for optimal improvement (personal observation). In this study we compared CMV plus PEEP with CPAP when expiratory pressure was varied to improve $Pa_{O_2}$ and decrease intrapulmonary physiologic shunting in dogs near-drowned with fresh water.

## Methods

Thirty mongrel dogs weighing 21 ± 3 kg (mean ± SD) were anesthetized with sodium pentobarbital, 25 mg/kg, intravenously, and their tracheas were intubated with cuffed endotracheal tubes connected to a constant-volume ventilator (J. H. Emerson Co.) equipped with an air–oxygen blender (bird Corp.). This system allowed us to deliver CMV with zero end-expiratory pressure (ZEEP), CMV with PEEP or continuous positive-pressure ventilation (CPPV), or spontaneous ventilation with either ZEEP or CPAP. Additional 25-mg increments of sodium pentobarbital were given as needed to prevent spontaneous movement. Lactated Ringer's solution at a rate of approximately 12 ml/kg/h was given for maintenance. Femoral-artery and 5-Fr quadruple-lumen thermodilution, flow-directed pulmonary-artery catheters were placed percutaneously. Position of the pulmonary-artery catheter was verified by intravascular pressure tracing. The animals' body temperatures were maintained at 37 ± 1 C with heat lamps when necessary. Femoral arterial blood pressure (BP), mean pulmonary arterial pressure ($\overline{PAP}$). Pulmonary artery-occluded pressure ($\overline{PAOP}$), heart rate (HR), respiratory rate (f), and temperature were monitored. Cardiac output ($\dot{Q}_t$) was calculated by the thermodilution method (IL 601, Instrumentation Laboratories, Inc.), using the mean of three successive determinations during exhalation. The IL 113 electrode system was used to measure $pH_a$, $Pa_{CO_2}$, $Pa_{O_2}$, $pH_{\bar{v}}$, $P\bar{v}_{CO_2}$, and $P\bar{v}_{O_2}$; these values were corrected to body temperature. Hematocrit was measured by the microcapillary method. Right-to-left

* Fellow in Anesthesiology.
† Professor and Chairperson.
‡ Nursing Student, University of Florida College of Nursing.
§ Assistant in Anesthesiology.

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Address reprint requests to Dr. Modell: Department of Anesthesiology, University of Florida College of Medicine, Box J-254, J. Hillis Miller Health Center, Gainesville, Florida 32610.

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TABLE 1. Intrapulmonary Physiologic Shunt Fraction ($\dot{Q}_{sp}/\dot{Q}_t$) (Mean ± SD) Pre- and Post-Freshwater Aspiration and During Spontaneous Ventilation (Group I), CMV (Group II), CPAP (Group III), or CMV with PEEP (Group IV): Statistically Significant Differences ($P < 0.05$) are Marked and Defined

| Minutes after Aspiration | $F_{I_{O_2}}$ | Group I Spontaneous with ZEEP | Group II CMV with ZEEP | PEEP or CPAP (cm $H_2O$) → | Group III Spontaneous with CPAP | Group IV CMV with PEEP |
|---|---|---|---|---|---|---|
| 0 | .21 | 0.10 ± 0.04 | 0.12 ± 0.06 | 0 | 0.10 ± 0.05 | 0.11 ± 0.06 |
| 15 | .21 | 0.72 ± 0.12* | 0.78 ± 0.08* | 0 | 0.69 ± 0.12* | 0.75 ± 0.08* |
| 30 | .21 | 0.68 ± 0.08* | 0.64 ± 0.16* | 0 | 0.67 ± 0.10* | 0.67 ± 0.11* |
| 45 | .40 | 0.60 ± 0.16* | 0.53 ± 0.14* | 0 | 0.59 ± 0.13*§ | 0.48 ± 0.10* |
| 60 | .40 | 0.61 ± 0.15* | 0.42 ± 0.11* | 5 | 0.46 ± 0.13*§† | 0.29 ± 0.12*†‡ |
| 75 | .40 | 0.58 ± 0.15* | 0.44 ± 0.05*§ | 10 | 0.35 ± 0.16*†‡ | 0.22 ± 0.13*†‡ |
| 90 | .40 | 0.55 ± 0.16* | 0.41 ± 0.12*§ | 15 | 0.28 ± 0.18*†‡ | 0.19 ± 0.17†‡ |
| 105 | .40 | 0.61 ± 0.18* | 0.42 ± 0.09*§ | 20 | 0.29 ± 0.19*§†‡ | 0.13 ± 0.10†‡ |
| 120 | .40 | 0.62 ± 0.13* | 0.38 ± 0.07*‡ | 0 | 0.42 ± 0.18*†‡ | 0.40 ± 0.13*‡ |

CMV ↓ (Group II) CMV ↓ (Group IV)

* $P < 0.05$ when compared with values at zero time period for the same group.

† $P < 0.05$ when compared with values at the 45-minute time period for the same group.

‡ $P < 0.05$ when compared with Group I at the same time period.

§ $P < 0.05$ when comparing Group II or Group III with Group IV at the same time period.

intrapulmonary physiologic shunt fraction ($\dot{Q}_{sp}/\dot{Q}_t$) was calculated with the computer program of Ruiz *et al.*,[2] and oxygen availability was calculated as $Ca_{O_2} \times \dot{Q}_t \times 10$. Pulmonary vascular resistance (PVR) was calculated as

$$PVR = \frac{\overline{PAP} - \overline{PAOP}}{\dot{Q}_t} \times 79.98$$

Control data were obtained while the animals spontaneously breathed room air. To qualify for this study, $Pa_{O_2} \geq 70$ torr and $Pa_{CO_2} \leq 45$ torr were required of all dogs immediately after induction of anesthesia. All dogs aspirated distilled water, 22 ml/kg, at time zero via a gravity-flow device described previously.[3] After aspiration, the animals were allowed to breathe room air spontaneously at ZEEP, and all measurements and calculations were made 15 and 30 min later. Next, the fraction of inspired oxygen ($F_{I_{O_2}}$) was increased to 0.4. Fifteen dogs, chosen at random, were paralyzed with a continuous infusion of succinylcholine hydrochloride and CMV was instituted with a tidal volume ($V_T$) of 15 ml/kg and f 10/min. The remaining 15 animals continued to breathe spontaneously. After 15 min had elapsed, data were obtained.

The two groups were then divided into two subgroups. Each of the four resultant groups received one of four treatment modalities. Five dogs were allowed to continue breathing spontaneously at ZEEP (Group I). Another five dogs were ventilated by CMV and ZEEP ($V_T$ = 15 ml/kg; f = 10/min) (Group II). Ten dogs were allowed to breathe spontaneously and CPAP was increased by 5 cm $H_2O$ every 15 min until 20 cm $H_2O$ was reached (Group III). Ten dogs received CMV ($V_T$ = 15 ml/kg; f = 10/min) and PEEP was increased by 5 cm $H_2O$ every 15 min until 20 cm $H_2O$ was reached (Group IV). Data were obtained 15 min after establishment of the new conditions. Finally, end-expiratory pressure was decreased abruptly from 20 cm $H_2O$ to zero in Groups III and IV and data were obtained after 15 min.

The data were analyzed by use of Student *t* tests for paired and unpaired data to determine statistical significances of differences between time periods in each group and also among groups at equivalent time periods. $P < 0.05$ was regarded as significant.

## Results

Significant increase in $\dot{Q}_{sp}/\dot{Q}_t$ developed after aspiration in all the animals (table 1). When $F_{I_{O_2}}$ was increased from 0.21 to 0.40 in the 14 animals¶ that breathed spontaneously after near-drowning (Groups I and III), $\dot{Q}_{sp}/\dot{Q}_t$ decreased an average of 8 per cent of cardiac output within 15 min. The 15 dogs that had their ventilation controlled during breathing of 40 per cent oxygen (Groups II and IV) had an average decrease of shunting of 15 per cent within 15 min. The difference between the decreases in shunting of the dogs that breathed spontaneously and those treated by CMV was significant.

During the 75-min treatment period (from 30 to 105 min after aspiration), $\dot{Q}_{sp}/\dot{Q}_t$ did not change significantly in the five animals that breathed spontaneously with ZEEP (Group I) or in the five animals that had CMV with ZEEP (Group II) (table 1).

The ten animals that were treated with CPAP and spontaneous ventilation (Group III) had variable responses. The mean $\dot{Q}_{sp}/\dot{Q}_t$ decreased with each 5-cm

¶ Blood was not analyzed for one animal at this time because of technical difficulties.

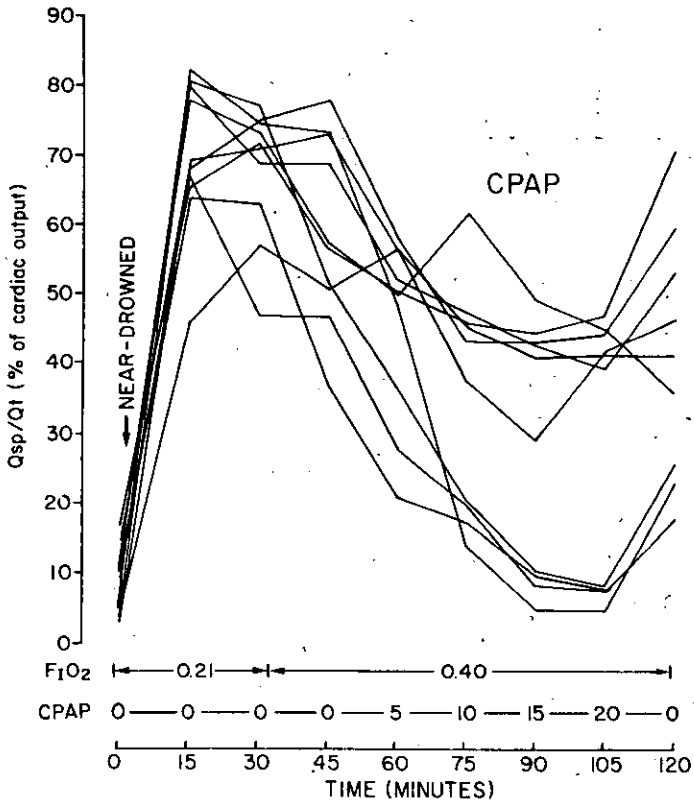


FIG. 1. Individual variations in intrapulmonary physiologic shunt fraction ($\dot{Q}_{sp}/\dot{Q}_t$) of each animal after freshwater aspiration and treatment with CPAP, which was varied from 0 to 20 cm $H_2O$. The $F_{I_{O_2}}$ was changed from 0.21 to 0.40 30 min after aspiration in all animals.

$H_2O$ increment of CPAP from 0 to 15 cm $H_2O$ CPAP (table 1). At each level of CPAP, the $\dot{Q}_{sp}/\dot{Q}_t$ was less than at ZEEP. The $\dot{Q}_{sp}/\dot{Q}_t$ also was less at 15 and 20 cm $H_2O$ CPAP than at 5 cm $H_2O$ CPAP. When examining the responses of the individual animals in this group to increasing levels of CPAP, we saw two distinctly different patterns. Four of the ten animals had marked decreases in $\dot{Q}_{sp}/\dot{Q}_t$ with 15 cm $H_2O$ CPAP to only 5 to 10 per cent of cardiac output. The remaining six animals had $\dot{Q}_{sp}/\dot{Q}_t$ greater than 40 per cent of their cardiac outputs at 20 cm $H_2O$ CPAP (fig. 1).

In the ten animals that had PEEP applied while CMV was being administered (Group IV), $\dot{Q}_{sp}/\dot{Q}_t$ decreased with each incremental increase in PEEP. The $\dot{Q}_{sp}/\dot{Q}_t$ was less at all levels of PEEP than with ZEEP. The range of $\dot{Q}_{sp}/\dot{Q}_t$ in the individual dogs at 20 cm $H_2O$ PEEP with CMV was 4 to 32 per cent of cardiac output; seven of the ten animals had shunting of 12 per cent or less at that time.

All of the animals experienced acidemia after aspiration, but the treatment groups could not be differentiated from controls for either $pH_a$ or $Pa_{CO_2}$ (table 2). Changes in $Pa_{O_2}$ followed an inverse relationship to intrapulmonary physiologic shunting (table 2).

The $\overline{PAOP}$ in the 30 dogs increased significantly from 6 ± 4 torr before near-drowning to 12 ± 7 torr 15 min after aspiration. At 30 min, it had decreased to 8 ± 6 torr, and by 45 min, it was no longer significantly increased. The $\overline{PAOP}$ increased when PEEP was applied in Groups III and IV; however, since intrapleural pressure was not measured, we were not able to calculate the effective transmural filling pressure (fig. 2).

Peripheral vascular resistance increased significantly from 183 ± 82 to 259 ± 123 dynes/sec/cm$^{-5}$, 15 min after the 30 dogs aspirated water. The values were still significantly increased 30 min and 45 min after aspiration, and for the control animals (Group I), they remained so at all time periods studied throughout the experiment (fig. 3). The two groups treated with end-expiratory pressure also had significantly increased PVR even when mean $Pa_{O_2}$ had returned to at least 99 torr.

Fifteen minutes after aspiration, cardiac output decreased from 4.4 ± 0.9 to 3.4 ± 1.0 l/min in the 30

TABLE 2. Arterial Blood $P_{O_2}$, $P_{CO_2}$, and *p*H Pre- and Post-Freshwater Aspiration and During Spontaneous Ventilation (Group I), CMV (Group II), CPAP (Group III), or CMV with PEEP (Group IV) (*Mean* ± SD)

| | Minutes after Aspiration | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 0 $F_{I_{O_2}}$ .21 | 15 $F_{I_{O_2}}$ .21 | 30 $F_{I_{O_2}}$ .21 | 45 $F_{I_{O_2}}$ .40 | 60 $F_{I_{O_2}}$ .40 | 75 $F_{I_{O_2}}$ .40 | 90 $F_{I_{O_2}}$ .40 | 105 $F_{I_{O_2}}$ .40 | 120 $F_{I_{O_2}}$ .40 |
| Group I, Spontaneous with ZEEP | | | | | | | | | |
| $P_{O_2}$ (torr) | 90 ± 7 | 29 ± 5*† | 34 ± 5*† | 50 ± 9* | 51 ± 7* | 48 ± 12* | 47 ± 10* | 46 ± 12* | 45 ± 11* |
| $P_{CO_2}$ (torr) | 38 ± 2 | 49 ± 3* | 45 ± 6* | 46 ± 9* | 42 ± 7* | 38 ± 4* | 37 ± 6 | 39 ± 9 | 39 ± 10 |
| *p*H | 7.39 ± .03 | 7.25 ± .03* | 7.24 ± .06* | 7.23 ± .07* | 7.26 ± .06* | 7.26 ± .05* | 7.31 ± .08* | 7.32 ± .10 | 7.27 ± .12* |
| Group II, CMV with ZEEP | | | | | | | | | |
| $P_{O_2}$ | 86 ± 6 | 25 ± 5*† | 30 ± 5*† | 49 ± 10* | 53 ± 6*§ | 59 ± 7*§ | 62 ± 11*‡§ | 57 ± 7*§ | 60 ± 13* |
| $P_{CO_2}$ | 35 ± 8 | 50 ± 6* | 51 ± 10* | 50 ± 15* | 44 ± 8 | 41 ± 7 | 43 ± 8 | 40 ± 7 | 41 ± 6 |
| *p*H | 7.41 ± .04 | 7.22 ± .03* | 7.18 ± .07* | 7.16 ± .11* | 7.26 ± .13* | 7.22 ± .14* | 7.24 ± .13* | 7.26 ± .13* | 7.27 ± .12* |
| PEEP or CPAP (cm $H_2O$) ↓ | 0 | 0 | 0 | 0 | 5 | 10 | 15 | 20 | 0 |
| Group III, Spontaneous with CPAP | | | | | | | | | |
| $P_{O_2}$ | 94 ± 18 | 38 ± 6*† | 35 ± 7*† | 52 ± 14* | 60 ± 17* | 78 ± 29†‡ | 99 ± 52†‡ | 101 ± 57†‡ | 65 ± 24* |
| $P_{CO_2}$ | 33 ± 5 | 45 ± 8* | 43 ± 8* | 46 ± 11* | 45 ± 10* | 44 ± 9* | 44 ± 9* | 44 ± 9* | 35 ± 11† |
| *p*H | 7.40 ± .04 | 7.26 ± .08* | 7.28 ± .11* | 7.23 ± .06* | 7.28 ± .06* | 7.29 ± .05*† | 7.25 ± .06* | 7.20 ± .06*‡ | 7.25 ± .07* |
| Group IV, CMV with PEEP | | | | | | | | | |
| $P_{O_2}$ | 85 ± 12 | 30 ± 3*† | 33 ± 6*† | 56 ± 10* | 83 ± 27†‡ | 103 ± 40†‡ | 125 ± 43†‡ | 121 ± 38†‡ | 61 ± 12*‡ |
| $P_{CO_2}$ | 38 ± 14 | 42 ± 7 | 44 ± 9 | 47 ± 7 | 42 ± 9 | 41 ± 11 | 45 ± 11 | 51 ± 10* | 43 ± 6 |
| *p*H | 7.40 ± .02 | 7.25 ± .11* | 7.29 ± .09* | 7.23 ± .06* | 7.28 ± .06* | 7.29 ± .05*‡ | 7.25 ± .06* | 7.20 ± .06*‡ | 7.25 ± .07* |

* $P < 0.05$ when compared with values at zero time period for the same group.
† $P < 0.05$ when compared with values at the 45-minute time period for the same group.
‡ $P < 0.05$ when compared with Group I at the same time period.
§ $P < 0.05$ *when comparing Group II or Group III with Group IV* at the same time period.



Anesthesiology
V 52, No 2, Feb 1980

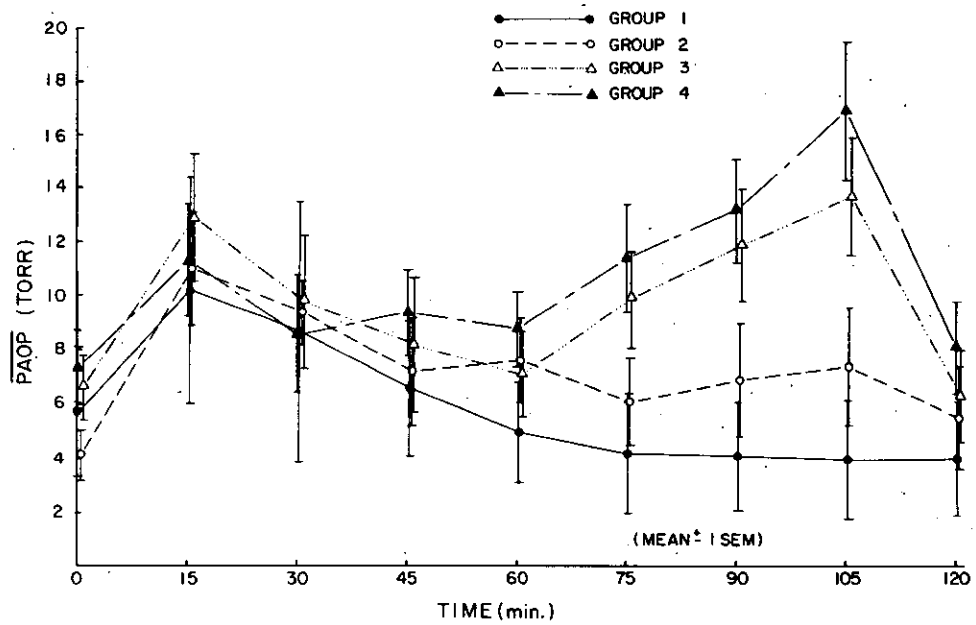


FIG. 2. Pulmonary arterial occlusion pressure ($\overline{PAOP}$) (mean ± 1 SE) before and after near-drowning in animals permitted to breathe spontaneously at ZEEP (Group I), with CMV (Group II), with CPAP (Group III), and with CPPV (Group IV). All groups had significant increases in $\overline{PAOP}$ 15 min after aspiration. $\overline{PAOP}$ then returned to pre-aspiration levels, but became significantly increased again at 75, 90, and 105 min in Groups III and IV.

dogs. However, 30 min after aspiration, cardiac output values for the dogs did not differ from those measured prior to near-drowning. Treatment with CMV alone decreased cardiac output significantly (table 3). Application of 5 and 10 cm $H_2O$ CPAP did not decrease cardiac output in spontaneously breathing dogs, nor did 5 or 10 cm $H_2O$ PEEP further decrease cardiac output in animals receiving CMV. However, application of 15 and 20 cm $H_2O$ PEEP with both spontaneous and controlled ventilation did significantly decrease cardiac output. Cardiac output was depressed more when CMV was being given simultaneously with 15 and 20 cm $H_2O$ PEEP than with spontaneous ventilation and CPAP. When the relationship between cardiac output and $\dot{Q}_{sp}/\dot{Q}_t$ in the animals receiving positive end-expiratory pressure was subjected to regression analysis, there was a significant correlation in the dogs breathing spontaneously ($n = 58$; $r = 0.55$; $P < 0.001$), but not in those whose ventilation was controlled mechanically ($n = 60$; $r = 0.19$; $P > 0.2$).

Fifteen minutes after PEEP was abruptly decreased from 20 cm $H_2O$ to zero in Groups III and IV, there were significant increases in $\dot{Q}_{sp}/\dot{Q}_t$ and cardiac output and a decrease in $Pa_{O_2}$ values (tables 1, 2, and 3).

Oxygen availability decreased significantly after near-drowning and remained depressed in all four groups. When comparing groups, we saw no difference among treated and untreated animals at any time period except during CMV with 20 cm $H_2O$ PEEP.

## Discussion

All dogs that aspirated distilled water had severe arterial hypoxemia and intrapulmonary physiologic shunting. Spontaneous breathing of 40 per cent oxygen for 15 min decreased $\dot{Q}_{sp}/\dot{Q}_t$, which suggests that, although $\dot{Q}_{sp}/\dot{Q}_t$ was caused largely by perfused areas of lung that had no ventilation, a fraction of the $\dot{Q}_{sp}/\dot{Q}_t$ can be categorized as relative shunting, or areas of low but finite ventilation-to-perfusion ratio.[4] A further decrease in $\dot{Q}_{sp}/\dot{Q}_t$ occurred when CMV was applied while the dogs breathed 40 per cent oxygen. This suggests that CMV either further recruits alveoli to participate in gas exchange or decreases cardiac output, either of which produces a secondary decrease in $\dot{Q}_{sp}/\dot{Q}_t$. However, we could not demonstrate a significant correlation between cardiac output and $\dot{Q}_{sp}/\dot{Q}_t$ in animals whose ventilation was controlled, thus suggesting that recruitment occurred.

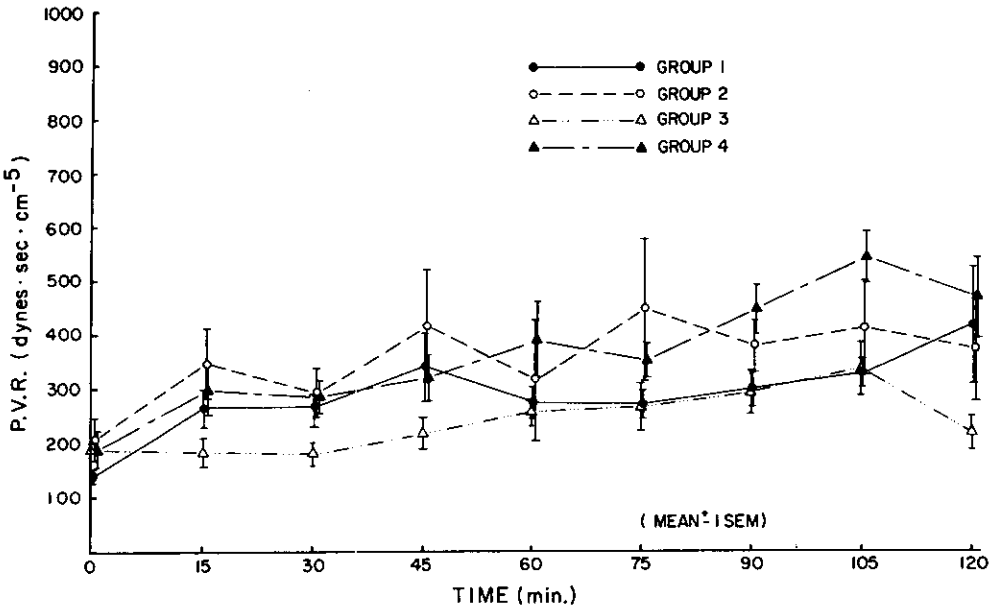


FIG. 3. Pulmonary vascular resistance (PVR) (mean ± 1 SE) before and after near-drowning in animals permitted to breathe spontaneously at ZEEP (Group I), with CMV (Group II), with CPAP (Group III), and with CPPV (Group IV). The PVR was significantly increased at at least four time periods after aspiration in all groups.

We found that CPAP significantly increased $Pa_{O_2}$ and decreased $\dot{Q}_{sp}/\dot{Q}_t$ in some animals but not others. However, every animal treated with CMV and PEEP had a significant improvement in arterial oxygenation and decrease in shunting. It has been shown that freshwater aspiration alters the surface tension properties of pulmonary surfactant and thus promotes alveolar instability and collapse.[5] It may be that some of our animals needed a greater transpulmonary pressure than they could spontaneously generate to open alveoli. Therefore, CPAP at the levels used was unable to maintain a sufficient functional residual capacity (FRC) to better match $\dot{V}_A/\dot{Q}$. By producing higher peak-inflation pressure and thereby, increased transpulmonary pressure, CMV may have effectively opened alveoli in these animals' lungs and allowed PEEP to maintain a more normal FRC.

The increase in $\overline{PAOP}$ seen immediately after as-

TABLE 3. Cardiac Output (Mean ± SD) Pre- and Post-Freshwater Aspiration and during Spontaneous Ventilation (Group I), CMV (Group II), CPAP (Group III), or CMV with PEEP (Group IV): Statistically Significant Differences ($P < 0.05$) are Marked and Defined

| Minutes after Aspiration | $F_{I_{O_2}}$ | Cardiac Output (l/min) Group I Spontaneous with ZEEP | Cardiac Output (l/min) Group II CMV with ZEEP | PEEP or CPAP (cm $H_2O$) → | Cardiac Output (l/min) Group III Spontaneous with CPAP | Cardiac Output (l/min) Group IV CMV with PEEP |
|---|---|---|---|---|---|---|
| 0 | .21 | 4.0 ± 0.5 | 4.4 ± 1.0 | 0 | 4.3 ± 0.9 | 4.6 ± 1.2 |
| 15 | .21 | 3.4 ± 0.8 | 2.9 ± 0.6* | 0 | 3.7 ± 1.1 | 3.5 ± 1.2* |
| 30 | .21 | 3.4 ± 0.8 | 4.1 ± 1.2 | 0 | 4.0 ± 1.4 | 3.9 ± 1.0† |
| 45 | .40 | 3.3 ± 1.2 | 2.5 ± 1.4* | 0 | 3.7 ± 1.1 | 2.8 ± 0.9* |
| 60 | .40 | 3.2 ± 0.6* | 2.6 ± 1.1* | 5 | 3.5 ± 0.9 | 2.6 ± 0.9* |
| 75 | .40 | 3.2 ± 0.6* | 2.4 ± 1.0* | 10 | 3.2 ± 1.1* | 2.5 ± 0.7* |
| 90 | .40 | 3.1 ± 0.5* | 2.3 ± 0.3*‡ | 15 | 2.7 ± 1.0*†§ | 1.9 ± 0.5*†‡ |
| 105 | .40 | 2.9 ± 0.3* | 2.1 ± 0.5*‡§ | 20 | 2.4 ± 0.7*†§ | 1.6 ± 0.3*†‡ |
| 120 | .40 | 3.0 ± 1.1 | 2.5 ± 0.9* | 0 | 3.7 ± 1.3§ | 2.4 ± 0.8* |

CMV (Group II) ↓ CMV (Group IV) ↓

* $P < 0.05$ when compared with values at zero time period for the same group.

† $P < 0.05$ when compared with values at the 45-minute time period for the same group.

‡ $P < 0.05$ when compared with Group I at the same time period.

§ $P < 0.05$ when comparing Group II and Group III with Group IV at the same time period.

piration was probably due to a temporary hypervolemia from rapid absorption of the distilled water. The return of $\overline{PAOP}$ to normal within 30 to 45 min is consistent with results of previous studies that have shown that the hypervolemia seen with aspiration of this quantity of fluid is transient.[6] An increase in PVR, presumably in response to hypoxia, occurred immediately after aspiration. Although this may have contributed to the decrease in cardiac output that was observed, the fact that cardiac output had increased by 30 min, while PVR was still 67 dynes/sec/cm$^{-5}$ above normal and $\overline{PAOP}$ was 2 torr above normal, suggests the heart was not capable of handling the acute increase in blood volume that resulted from water aspiration, but recovered once this fluid was redistributed and no longer caused a significant increase in $\overline{PAOP}$.

The results of this study differed from those of a previous study of the effect of PEEP therapy on near-drowned dogs breathing spontaneously reported by this laboratory.[1] In that experiment, we did not exceed 10 cm $H_2O$ PEEP. In the current study, eight of ten dogs had less $\dot{Q}_{sp}/\dot{Q}_t$ at 15 cm $H_2O$ CPAP than at 10 cm $H_2O$ CPAP, which emphasizes the importance of individualizing positive airway pressure. Also, in the previous study, inspiratory pressures were permitted to decrease below ambient whereas in the present study, CPAP was used to minimize decreases in inspiratory pressure. In clinical practice, we have observed a decrease in $\dot{Q}_{sp}/\dot{Q}_t$ and an increase in compliance when some patients are converted from PEEP to CPAP while breathing spontaneously even though the transpulmonary pressure is decreased. Perhaps this difference in pressure pattern may have helped keep lung units functional during all portions of the respiratory cycle in the dogs that had significantly decreased $\dot{Q}_{sp}/\dot{Q}_t$ when CPAP was applied during spontaneous ventilation.

In the present study, we made no attempt to augment effective circulating blood volume or cardiac output when PEEP was increased. Cardiac output was most severely affected in those animals with CMV and PEEP administered simultaneously. Thus, even though $Pa_{O_2}$ was increased and $\dot{Q}_{sp}/\dot{Q}_t$ decreased compared with untreated animals, oxygen availability was not improved. This finding prevents us from making any definitive recommendations as to the direct transfer of these animal studies to human application. We conclude that PEEP is the single most important variable in reversing the arterial hypoxemia in freshwater near-drowning. An adequate response can be produced by means of spontaneous ventilation and CPAP in some instances, but in others, it may be necessary to combine mechanical inflation of the lung with PEEP to improve arterial oxygenation significantly. When treating an individual patient, we must consider the effects of therapy on both cardiac output and $\dot{Q}_{sp}/\dot{Q}_t$. If a significant decrease in cardiac output occurs, it may be necessary to augment cardiac output to ensure more adequate oxygen delivery.

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# CARDIOVASCULAR RESPONSES TO PARTIAL AND TOTAL IMMERSION IN MAN

BY L. B. CAMPBELL,* B. A. GOODEN AND J. D. HOROWITZ*
*From the Department of Human Physiology and Pharmacology, University of Adelaide, Australia*

(*Received* 2 *December* 1968)

SUMMARY

1. Short-term cardiovascular effects of partial and total immersion of eighteen human subjects in the horizontal plane have been examined. Brachial arterial pressure, heart rate, forearm blood flow and respiratory movements were monitored simultaneously throughout the experiments. Forearm vascular resistance was calculated from the mean blood pressure and mean flow.

2. Total immersion, including the face, with breath-holding resulted in a $61 \pm 43\%$ increase in forearm vascular resistance with an associated $29 \pm 15\%$ reduction in forearm blood flow. The concurrent bradycardia was significantly different from the heart rate changes during breath-holding with the torso only immersed, or during total immersion with snorkel-breathing. Neither breath-holding in air or with only the torso immersed, nor total immersion with snorkel-breathing produced such a diving response.

3. Breath-holding, after several minutes of total immersion and snorkel-breathing, produced an attenuated diving response. It therefore appears that a full diving response can be obtained only when the apnoea commences at the moment of face immersion.

4. The present investigation supports the concept that in man face immersion is an essential predisposing factor for the diving response, and cortical inhibition of the respiratory centre is important for its initiation and maintenance.

## INTRODUCTION

Paul Bert (1870) was the first to record that in animals such as the duck a marked bradycardia occurs upon immersion in water. A similar diving bradycardia has since been observed in many other vertebrates. Irving

* Work carried out in part fulfilment of the requirements for the Honours Degree of Bachelor of Medical Science, University of Adelaide.

(1934) proposed that bradycardia is only one component of widespread reflex cardiovascular adjustments that take place upon immersion. The functional significance of such reflex adjustments, he suggested, is to conserve the limited oxygen reserve during the period of immersion, while maintaining normal perfusion through the cerebral and coronary vascular beds. To achieve this, the flow through peripheral and abdominal vessels must virtually cease. If the flow were only moderately reduced, the oxygen extraction by the tissues could correspondingly increase and no oxygen conservation would occur (Folkow, Nilsson & Yonce, 1967).

Investigation of the diving response in man has been less extensive than in animals and most studies have been concerned with changes in heart rate (Irving, Scholander & Grinnell, 1940; Scholander, Hammel, Le-Messurier, Hemmingsen & Garey, 1962; Craig, 1963; Harding, Roman & Whelan, 1965). Examination of changes in the peripheral circulation in the forearm and calf has been confined to situations where only the face has been immersed (Elsner, Garey & Scholander, 1963; Brick, 1966).

In the present investigation forearm blood flow, heart rate and blood pressure have been recorded during immersion of the whole body, with and without immersion of the face and with and without breath-holding, in an attempt to analyse the effects of these different procedures on the cardiovascular responses to immersion.

## METHODS

The subjects were eighteen healthy males aged between 18 and 25 years. Two were experienced underwater swimmers.

A 3·7 m diameter pool containing water to a depth of 1·3 m was used. Subjects lay supine on a light aluminium stretcher supported on trestles, initially in the air above the water and then immersed with the uppermost portions of the body no more than 6 in. below the surface. Only shallow immersion was attempted so that the subjects would not experience difficulty in breathing. The face was either supported above the level of the water or immersed with the rest of the body. With immersion of the face, the breath was either held or the subject continued to breathe through a mouthpiece and snorkel tube. The water temperature was maintained at $34 \pm 0{\cdot}5°$ C. The laboratory air temperature was $24 \pm 1°$ C.

*Forearm blood flow.* Blood flow was measured in the right forearm by venous occlusion plethysmography. A pneumatic cuff was inflated around the wrist, to a pressure of 200 mm Hg, to exclude hand circulation. A second cuff around the upper arm was inflated intermittently to a pressure of 60 mm Hg to occlude venous but not arterial flow. The plethysmograph was a modified Whitney mercury-in-rubber strain-gauge consisting of a small plastic block into which were sealed the ends of two insulated copper wires 2 m long. A 35 cm loop of siliconized rubber tubing of wall thickness 0·8 mm and bore 0·5 mm containing an unbroken column of mercury was attached to the ends of the wires in the block. All conductive surfaces were sealed so that the instrument was completely insulated from the water. The plastic block of the strain-gauge was placed at the point of maximum convexity of the forearm and the tubing applied around the limb. The free end of the loop was fixed in place by an adjustable clamp to a pin extending from the plastic block. The tubing was always kept

slightly taut. The strain-gauge formed one arm of a low impedence Wheatstone bridge and the output was fed to a Beckman four-channel pen recorder.

Calibration was carried out by stretching the rubber tubing by known increments in a screw gauge and measuring the deflexion of the pen recorder.

*Heart rate.* The electrocardiogram was monitored by two precordial electrodes and an earth (Hardin *et al.* 1965). The precordial electrodes were mounted on a thin rubber sheet through which the leads were sealed. These two electrodes were placed over the sixth left intercostal space, and a rubber strip wound around the chest to ensure electrical contact between the skin and the electrodes. The rubber strip did not hinder the subject's respiratory excursions. An indifferent electrode was fixed to the left upper arm.

These electrodes provided an electrocardiogram with a strong R wave component, which was directed into a Beckman cardiotachometer coupling and the heart rate recorded on one channel of the pen recorder.

*Respiration.* Respiratory excursions were followed by means of a thoraco-abdominal stethograph and recorded on one channel of the recorder. The record served simply to differentiate periods of apnoea from those of normal respiration.

*Blood pressure.* In most experiments left brachial arterial pressure was measured by auscultation, using an anaeroid manometer, both with the subject in air and under water. Korotkow sounds were sufficiently distinct to make the accuracy of the method approximately $\pm 5$ mm Hg. Blood pressure was recorded once every 30 sec during the resting phases and approximately once every 15 sec immediately before, during and after experimental procedures. The increased environmental pressure during immersion accounted for 5 mm Hg of the elevation in arterial blood pressure.

As a check on the auscultatory method, the brachial arterial pressure was recorded directly in one subject. A 21-gauge needle was inserted into the artery under local anaesthesia and connected by 60 cm sterilized, heparinized, saline-filled polyethylene tubing to a Statham pressure transducer. Since the transducer and cable could not be immersed in water, they were fixed above the pool on a 40 cm long steel post extending from the stretcher. In this way the subject's arm and the transducer remained in the same relative position independent of movement of the stretcher. The relative pressure changes produced during the various procedures were essentially the same as those obtained by auscultation.

*Procedure.* All experiments began outside the pool, where the electrocardiogram electrodes, thoraco-abdominal stethograph and pneumatic cuffs for both plethysmograph and blood pressure recording were fitted. The subject then entered the pool and lay supine on the stretcher above the surface of the water (Plate 1).

The right arm was supported by a rest in a slightly elevated position relative to the heart, and the strain-gauge applied to the forearm. The experiments which followed were divided into two series.

### *Series I*

This series consisted of twelve experiments in which the subject breathed through the nose between procedures.

*Breath-holding in air.* After a 5 min control period, during which all parameters were recorded and the subject settled, instruction was given to hold the breath in 'moderate' inspiration for 1 min. Following this procedure, recording continued for a further 5 min to allow the parameters to return to base line.

*Transfer to water.* Recording stopped and the pneumatic cuffs were deflated. The stretcher and subject were then transferred to two lower trestles so that the torso was immersed but not the face. The head was supported by an adjustable rest and the torso was held under water by weight belts laid across the pelvis and ankles.

*Breath-holding, face out.* Following the transfer to water, records were obtained over a 5 min control period. Then the subject performed a 1 min breath-hold with the face still in the air but the torso immersed.

*Breath-holding, face submerged.* After a 4 min rest period a nose clip was applied, the subject inspired, the head rest was lowered, and light pressure on the subject's forehead produced total submersion of the face without voluntary effort by the subject. The subject was now totally submerged. After 1 min the face was brought out of water and supported again on the head rest.

*Snorkel-breathing, face submerged.* Following a further 4 min rest period the subject's face was again submerged for 1 min but during this time the subject breathed continuously through a short snorkel (internal volume 32 ml). This procedure was followed by a 4 min rest period with the face in air once more and the subject breathing through the nose without snorkel.

*Transfer to air.* The subject and stretcher were then lifted out of the water and placed on the higher trestles. Recording was continued for 2 or 3 min until shivering precluded accurate data.

### *Series II*

A further five experiments were performed which were the same as Series I except that the subject breathed through the snorkel between procedures and the final snorkel-breathing, face-submerged procedure was modified. This modification was designed to test the effects of breathing with the face submerged for several minutes, followed by superadded apnoea of 1 min duration. After the 1 min of breath-holding, the subject remained totally immersed for several minutes and then the face was brought out of the water.

The base line mean for each parameter was calculated by averaging the readings during the first two of the 3 min before each procedure. The mean level of each parameter during the actual procedure was calculated from the readings taken during the last 30 sec of the procedure.

Mean blood pressure was calculated from the formula: $\frac{1}{3}$ (systolic pressure + 2 (diastolic pressure) ).

Vascular resistance was calculated by dividing mean blood pressure by mean blood flow.

## RESULTS

### *Series I*

The mean results of the twelve experiments in this series are summarized in Fig. 1.

The variation in individual base line means precluded useful analysis of the changes during procedures by the usual standard deviation test. However, differences were readily apparent when changes in the level of a parameter relative to the subject's individual base line were analysed by two tailed paired *t* test. This test was also used to compare changes in each parameter between consecutive procedures. A result referred to as 'significant' in the following text therefore means 'significant by two tailed paired *t* test' (Hill, 1966).

*Breath-holding in air.* This produced a slight rise in heart rate, blood pressure and forearm blood flow, while the forearm vascular resistance decreased slightly. The only significant change was the rise in blood pressure (Table 1).

*Transfer to water.* Immersion of the body produced a significant increase in blood flow and blood pressure. Heart rate was unaltered.

*Breath-holding, face out.* The effect of breath-holding with the body immersed but the face out of water produced similar responses to breath-holding in air, except for a significant tachycardia.

*Breath-holding, face submerged* (Fig. 2). Breath-holding with simultaneous total immersion produced a rise in blood pressure similar to that seen with the two earlier procedures, but instead of a rise in heart rate there was now a bradycardia ($-6 \pm 15$ %). This was not a significant

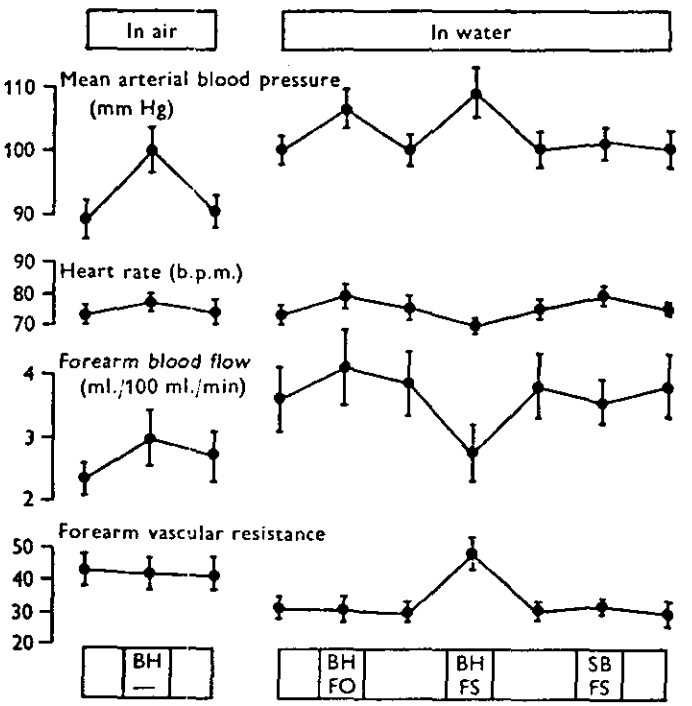


Fig. 1. Averaged results of Series I experiments. Vertical lines through each point represent the S.E. of the means.

Abbreviations: BH, breath-hold (1 min), FO, face out with torso immersed, FS, face submerged as well as torso, SB, snorkel-breathing, b.p.m., beats per minute. The increased environmental pressure during immersion accounted for 5 mm Hg of the elevation in arterial blood pressure.

change from the preceding base line, but was a significant fall when compared with the response elicited by the previous procedure. The most dramatic changes were a fall in forearm blood flow ($-29 \pm 15$ %) and an increase in vascular resistance ($61 \pm 43$ %).

*Snorkel-breathing, face submerged.* This 1 min period of total immersion and continuous snorkel-breathing produced no significant change. Moreover, the lack of response observed during this procedure was significantly different from the response obtained during breath-holding, face submerged.

Because of the inconsistent nature of the recordings following the

TABLE 1. Experiments of Series I

| | In air | | In water | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Breath-hold | | Transfer to water | | Breath-hold face out | | Breath-hold, face submerged | | Snorkel breathing, face submerged | |
| | % change with S.D. | $2P$ | % change with S.D. | $2P$ | % change with S.D. | $2P$ | % change with S.D. | $2P$ | % change with S.D. | $2P$ |
| Mean blood pressure | 12 ± 7 | < 0·001 | 11 ± 5 | < 0·001 | 7 ± 4 | < 0·001 | 9 ± 8 | 0·001 → 0·005 | 1 ± 3 | 0·60 → 0·70 |
| Heart rate | 7 ± 14 | 0·10 → 0·20 | 1 ± 10 | 1·00 | 9 ± 13 | 0·02 → 0·05 | − 6 ± 15 | 0·10 → 0·20 | 3 ± 8 | 0·20 → 0·30 |
| Forearm blood flow | 23 ± 35 | 0·05 → 0·10 | 56 ± 54 | 0·02 → 0·05 | 12 ± 23 | 0·05 → 0·10 | − 29 ± 15 | < 0·001 | − 7 ± 22 | 0·10 → 0·20 |
| Forearm vascular resistance | − 3 ± 26 | 0·60 → 0·70 | − 25 ± 22 | 0·05 → 0·10 | 2 ± 24 | 0·80 → 0·90 | 61 ± 43 | < 0·001 | 11 ± 21 | 0·40 → 0·50 |

Twelve subjects, except the final procedure in which there were ten.
$2P < 0{\cdot}05$ implies significant by two tailed paired $t$-test.
$(n-1)$ degrees of freedom where $n$ is the number of subjects.

transfer to air no statistical evaluation of the responses during this time was attempted.

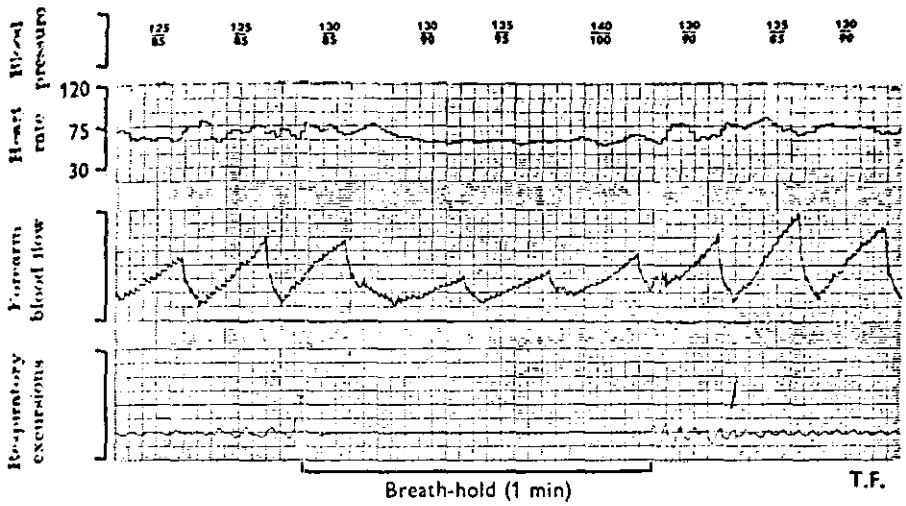


Fig. 2. Typical record obtained during breath-holding with face submersion to produce total immersion.

*Series II*

In these experiments in which the subjects breathed through a snorkel between procedures instead of through the nose, breath-holding in air produced a significant rise in blood pressure only as in Series I. The transfer to water produced a response similar to Series I, but the rise in blood pressure was not significant. Breath-holding with the face out of water evoked no significant response (Table 2).

Breath-holding with the face submerged produced significant changes in all parameters. The responses were identical with those obtained in Series I, except that now the bradycardia was significant.

Submersion of the face while respiration was continued through the snorkel caused a small but significant increase in blood pressure almost exclusively in the systolic element.

Breath-holding produced a further increase in mean blood pressure, but a reduction in heart rate. Forearm blood flow was reduced and vascular resistance increased, but none of these changes was significant. When compared with the preceding breath-hold, face submerged, the changes in blood flow and vascular resistance were significantly different. The reduction in blood flow and the rise in vascular resistance were both smaller during this final breath-hold procedure.

*Variability between subjects.* One of the subjects in Series II was an amateur competitive swimmer (J.P.). His responses were different from

TABLE 2. Experiments of Series II

| | In air Breath-hold | | Transfer to water | | In water: Breath-hold, face out | | In water: Breath-hold, face submerged | | In water: S.B., F.S./ B.H., F.S. | |
|---|---|---|---|---|---|---|---|---|---|---|
| | % change with S.D. | 2P | % change with S.D. | 2P | % change with S.D. | 2P | % change with S.D. | 2P | % change with S.D. | 2P |
| Mean blood pressure | 9±6 | 0·02→0·05 | 4±3 | 0·05→0·10 | 8±8 | 0·05→0·10 | 8±4 | 0·01→0·02 | 15±12 | 0·05→0·10 |
| Heart rate | −7±18 | 0·40→0·50 | 3±6 | 0·20→0·30 | −8±13 | 0·10→0·20 | −15±10 | 0·02→0·05 | −13±15 | 0·05→0·10 |
| Forearm blood flow | −21±33 | 0·20→0·30 | 27±12 | 0·005→0·01 | −38±28 | 0·05→0·10 | −51±11 | 0·001→0·005 | −16±40 | 0·20→0·30 |
| Forearm vascular resistance | 62±85 | 0·10→0·20 | −17±9 | 0·01→0·02 | 110±107 | 0·05→0·10 | 133±69 | 0·001→0·005 | 64±88 | 0·10→0·20 |

Same five subjects for all procedures. $2P < 0·05$ implies significant by two-tailed paired $t$ test.

any other subject tested in these experiments. Whenever he held his breath, in air or water, face under or face out of water, he showed only one response, namely, a rise in blood pressure, a fall in heart rate and forearm blood flow and a rise in forearm vascular resistance.

## DISCUSSION

The essential finding in this study was that total immersion, including the face, with breath-holding resulted in a marked diving response, i.e. a bradycardia and an increased forearm vascular resistance with an associated fall in forearm blood flow. Breath-holding either in air or with only the torso immersed did not produce such a response. Neither did total immersion with snorkel-breathing. Separation of breath-holding and face immersion by immersing the face and snorkel-breathing for several minutes before breath-holding, resulted in an attenuated diving response during the apnoeic period. It therefore appears that the full diving response can be obtained only when apnoea commences at the moment of face immersion.

### *Series I*

In both series of experiments the subjects inspired only moderately immediately before the breath-holding period to avoid a Valsalva manoeuvre. This was considered important, since Sarnoff, Hardenbergh & Whittenberger (1948) demonstrated that elevation of intrapulmonary pressure by 40 mm Hg markedly reduces the systemic arterial pressure in dogs. In the present experiments a significant increase in blood pressure occurred during the final 30 sec of the breath-holding procedures. A typical Valsalva manoeuvre is also characterized by a reduction in forearm blood flow (Roddie, Shepherd & Whelan, 1958), whereas in the current experiments no significant change in flow occurred during breath-holding in air. Thus, it appears that the subjects did not raise intrathoracic pressure sufficiently to evoke a Valsalva response.

However, the variability in the response between different subjects may have been due partly to the inability to control the degree of intrathoracic pressure. Craig (1963) showed that the tachycardia characteristic of breath-holding in air was directly proportional to the increase in intrathoracic pressure. A similar tachycardia in air was observed by Harding *et al.* 1965). In the present study there was no significant change in heart rate during breath-holding in air. This difference may be related to posture since, in the studies of Harding *et al.* and Craig the subjects stood vertically, whereas in the present experiments the subjects were horizontal.

The elevation of mean blood pressure following immersion in water may be related to two factors. First, since the rise in blood pressure was signifi-

cant in Series I, but not Series II where all subjects were repeating the experiment, an emotional factor may have been involved. Secondly, once transferred, the subject breathed with the chest immersed under one or more inches of water which was equivalent to mild negative pressure breathing. Kilburn & Sieker (1960) demonstrated a small but consistent elevation of both systolic and diastolic brachial arterial pressure during similar negative pressure breathing.

The finding of a significant increase in forearm blood flow on immersion in water can be largely ascribed to the difference in temperature of the laboratory air and the pool water.

Breath-holding, torso immersed with the face out of the water resulted in changes similar to those during breath-holding in air. Craig (1963) and Harding *et al.* (1965) found that the tachycardia during breath-holding decreases as the depth of immersion of the vertical subject is increased. In the current experiments with the subjects horizontal, there could be no facilitation of venous return by adding an external hydrostatic pressure gradient.

Breath-holding, face immersed produced a marked diving response. Elements of this diving response have been demonstrated by other authors during face immersion alone and also during total body immersion (Irving *et al.* 1940; Scholander, Hammel, Le Messurier, Hemmingsen & Garey, 1962; Craig, 1963; Harding *et al.* 1965). The present investigation appears to be the first in which several major cardiovascular parameters had been measured simultaneously during total immersion in man.

As soon as the procedure commenced, a diving response was observed, which indicates that the triggering mechanism is probably neural rather than changes in blood gas tensions.

From the investigations of Kawakami, Natelson & DuBois (1967) and Brick (1966), it was expected that, if face receptors are of importance in man, a diving response should be initiated upon snorkel breathing with the face and trunk fully immersed. However, no significant change in any parameter was observed in the present study during this procedure.

### *Series II*

During the final procedure, i.e. continuous snorkel breathing with the face submerged, there was a small but significant elevation of arterial blood pressure almost exclusively in the systolic element, probably due to the added stress of the procedure.

The measurements following the onset of voluntary apnoea showed a marked attenuation of the cardiovascular response when the immersion of the face was separated from the onset of asphyxia. This may have resulted from partial adaptation of facial receptors.

The initiation of the response still followed immediately upon apnoea, and the changes in parameters evoked by this procedure rapidly returned to pre-breath-holding levels when voluntary respiration was recommenced.

Andersen (1963), from his work with ducks, proposed that abolition of activity in the medullary respiratory centre is a determinant factor for initiation of the diving response. A similar situation apparently applies in man, although in this latter case the apnoea is voluntary instead of spontaneous.

The results of the present study support the theory that in man face immersion is an essential predisposing factor for the diving response, while cortical inhibition of respiration is important in its initiation and maintenance.

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# CEREBRAL SALVAGE IN NEAR-DROWNING FOLLOWING NEUROLOGICAL CLASSIFICATION BY TRIAGE

A.W. CONN, J.E. MONTES, G.A. BARKER AND J.F. EDMONDS

ABSTRACT

This paper describes a simple neurological classification for near-drowning victims into three main categories consisting of:

Category A (Awake)
Category B (Blunted Consciousness)
Category C (Comatose).

Category C is sub-classified into:

C.1 (Decorticate)
C.2 (Decerebrate)
C.3 (Flaccid).

This triage classification is based on the level of consciousness at a post-rescue time interval of approximately one to two hours, and functions as a guide to therapeutic management. Cerebral salvage results using this classification and comparing routine and aggressive therapy are reported in a retrospective review of 96 patients seen at The Hospital for Sick Children, Toronto, during a 10-year period (1970–1979 inclusive). Aggressive therapy for neurological purposes included continuous dehydration, controlled hyperventilation, moderate hypothermia, barbiturate coma, and continuous muscular paralysis for four days.

All patients in categories A (51 cases) and B (6 cases) recovered completely using routine medical management.

In category C (39 comatose patients) there was an overall mortality of 33.3 per cent with a cerebral morbidity of 23.9 per cent and normal recovery in 43.6 per cent. When reviewing the results of treatment, two subcategories, (C.1 and C.2) were combined for comparative purposes. Results in 14 cases using routine therapy revealed a mortality of 21.4 per cent, a morbidity of 42.8 per cent and an intact survival rate of 35.7 per cent. In comparison, 11 patients who received aggressive (H.Y.P.E.R.) therapy had no mortality, a morbidity of 9.0 per cent and a significant 90.9 per cent incidence of intact survival. In subcategory C.3 (14 patients) there were only four survivors, with one patient in each treatment group surviving intact (14.2 per cent).

Intact cerebral survival is of paramount importance. Our findings justify immediate resuscitation in all near-drowning cases regardless of the patient's initial condition or possible prognosis. The use of an early neurological triage classification seems most appropriate to facilitate therapeutic management. Aggressive treatment (H.Y.P.E.R. therapy) in decorticate cases (subcategory C.1) and decerebrate cases (subcategory C.2) has led to a significant reduction in morbidity and mortality in near-drowned patients.

TRIAGE IS DEFINED as "the sorting out and classification of casualties of war or other disaster to determine priority of need and proper place of treatment".[1] Near-Drowning[2] victims also require individual assessment and categorization of their condition to facilitate proper therapeutic management. In conjunction with Dr. Jerome H. Modell,[3] we have utilized a simple triage classification for an initial neurological assessment of these patients, in order to evaluate their subsequent course and make recommendations. This paper reports our cerebral 'salvage' results, classified by triage, in a retrospective review of 96 near-drowned children. The series includes all near-drowning patients who visited the emergency department, all admissions to the ward or intensive care unit, and all late admissions with neurological sequelae who were seen at the Hospital for Sick Children, Toronto, during 10-year period 1970 to 1979 inclusive.

A.W. Conn, M.D., F.R.C.P.(C); J.E. Montes, M.D.; G.A. Barker, M.D., F.F.A.R.A.C.S.; J.F. Edmonds, M.B., F.R.C.P.(C), The Intensive Care Unit, Hospital For Sick Children, 555 University Avenue, Toronto, Canada M5G 1X8.

## A NEUROLOGICAL CLASSIFICATION OF NEAR-DROWNING BY TRIAGE (FOLLOWING RESUSCITATION)

Following rescue, successful cardiopulmonary resuscitation and hospital admission, the clinician often faces an acute dilemma regarding future management. The selection of appropriate

TABLE I

MORBIDITY AND MORTALITY IN NEAR-DROWNING CASES

| Category | Totals | Cases | | |
|---|---|---|---|---|
| | | Died | Brain damaged | Normal |
| A (Awake) | 51 cases (53.1%) | 0 | 0 | 51 |
| B (Blunted) | 6 cases (6.2%) | 0 | 0 | 6 |
| C (Comatose) | 39 cases (40.7%) | 13 | 9 | 17 |
| Totals | 96 cases (100%) | 13 (13.5%) | 9 (9.3%) | 74 (77.0%) |

treatment may be very difficult if, for example, the duration of submersion is uncertain (unknown, erroneous or contradictory) and the asphyxial effects of a submersion time of twenty seconds versus twenty minutes are contrasted!

A suitable classification is required for therapeutic purposes which will be relevant to all cases of near-drowning, despite the many variable factors usually present. These factors, previously described, [4,12] include numerous physiological features (especially the activity of the 'diving' reflex),[35-37] immersion hypothermia,[30,38,39] submersion time,[31-33] and the efficacy of initial[40,41] and subsequent resuscitation.[4,12] Unfortunately, these variables are uncontrolled and uncontrollable, but play a major role in the patient's subsequent course. This helps to explain the lack of agreement in near-drowning regarding the course and classification of cases[16,44,45,47,50,51] and the selection of prognostic factors.[16,46,48,49,59]

Since complete cerebral recovery is of paramount importance, the most appropriate therapeutic guide is based on a clinical classification of the patient's level of consciousness. Since brain injury following submersion differs in many respects from that occurring in other situations such as cerebral trauma or Reye's Syndrome, the use of the Glasgow Coma Scale[5] or Lovejoy's Coma Stages,[6] for example, are not directly applicable. A basic triage classification is recommended jointly with Dr. J. Modell,[3] which consists of three main categories A (Awake), B (Blunted) and C (Comatose). This process establishes the therapeutic priorities which affect subsequent cerebral salvage. The patient's category is determined by the state of consciousness at a specific time interval, approximating one to two hours after rescue.[25]

Using this classification, our results are reported in Table I. It is apparent that all cerebral morbidity and all mortality occurred in category C exclusively. Therefore, the category C group of comatose patients was subdivided into three subcategories, C.1 (Decorticate), C.2 (Decerebrate), and C.3 (Flaccid), according to the progressive depth of coma (Table II).

TABLE II

A 'TRIAGE' CLASSIFICATION OF NEAR-DROWNING PATIENTS (Assessed at 1–2 hr after rescue)

| Category | Description |
|---|---|
| A (Awake) | – Alert<br>– Fully Conscious |
| B (Blunted) | – Obtunded, stuporous but rousable<br>– Purposeful response to pain<br>– Normal respirations |
| C (Comatose) | – Comatose, not rousable<br>– Abnormal response to pain<br>– Abnormal respiration |
| C Subcategories (Comatose) | |
| C.1 | – (Decorticate)<br>– Flexion response to pain<br>– Cheyne-Stokes respiration |
| C.2 | – (Decerebrate)<br>– Extensor response to pain<br>– Central (?) hyperventilation |
| C.3 | – (Flaccid)<br>– No response to pain<br>– Apneustic or "cluster" breathing |

The sex and age distribution in the series are reported in Table III and Table IV. The high incidence in male children and in the younger (1–5 yr) age groups agree with previous reports.[7,8,13,44,45] A correspondingly high incidence in category C is also evident. The annual distribution of cases is presented in Table V and reveals a sudden increase in cases since 1975. The increase occurs mainly in category C, suggesting more successful resuscitation.

The management and results in each category is reviewed and discussed in detail in the following sections.

TABLE III

SEX DISTRIBUTION OF NEAR-DROWNING PATIENTS

| | Category | | | | C Subgroups | | | |
|---|---|---|---|---|---|---|---|---|
| Sex | A | B | C | Total (%) | C.1 | C.2 | C.3 | Total |
| Male | 36 | 3 | 30 | 69 (71.9%) | 7 | 13 | 10 | 30 |
| Female | 15 | 3 | 9 | 27 (28.1%) | 2 | 3 | 4 | 9 |
| Totals | 51 | 6 | 39 | 96 | 9 | 10 | 14 | 39 |

TABLE IV

AGE DISTRIBUTION OF NEAR-DROWNING PATIENTS

| | Category | | | | C Subgroups | | | |
|---|---|---|---|---|---|---|---|---|
| Age | A | B | C | Total (%) | C.1 | C.2 | C.3 | Total |
| < 1 yr. | 5 | — | 1 | 6 (6.2%) | — | 1 | — | 1 |
| 1–5 yrs. | 27 | 1 | 28 | 56 (58.3%) | 9 | 12 | 7 | 28 |
| 6–10 yrs. | 9 | 3 | 8 | 20 (20.8%) | 3 | 2 | 3 | 8 |
| > 10 yrs. | 10 | 2 | 2 | 14 (14.6%) | — | — | 2 | 2 |
| Totals | 51 | 6 | 39 | 96 | 12 | 15 | 12 | 39 |

## DISCUSSION OF NEAR-DROWNING CASES BY CATEGORY

*Category A: (Awake)*

These patients are awake and alert with minimal asphyxial injury, but require admission to hospital. Continuous observation is needed in the event that neurological, pulmonary, or other deterioration occurs. After the usual history and physical examination, all routine laboratory tests must be done, including arterial blood gases, serum electrolytes, blood and throat cultures, and chest x-ray films. The use of antibiotics remains controversial,[9] but symptomatic therapy is all that is usually required. After 12 to 24 hours, a thorough re-examination and complete reassessment should be done before discharge home. A follow-up programme in one to two days will reveal later complications such as pulmonary infection.

There were 51 cases in category A (53.1 per cent of the total). All were discharged from the hospital as completely normal and none required re-admission. These results are contrasted with Fuller's mortality in 77 drowned patients of whom 18.2 per cent were awake on admission but subsequently died.[10] No causes of death were given, but late death from pulmonary infection has been reported in this group.[11]

TABLE V

ANNUAL DISTRIBUTION OF NEAR-DROWNING PATIENTS

| | Category | | | | "C" Subgroups | | | |
|---|---|---|---|---|---|---|---|---|
| Year | A | B | C | Total | C.1 | C.2 | C.3 | Total |
| 1970 | 2 | 0 | 3 | 5 | 2 | 1 | 0 | 3 |
| 1971 | 6 | 0 | 0 | 6 | 0 | 0 | 0 | 0 |
| 1972 | 3 | 1 | 2 | 6 | 0 | 1 | 1 | 2 |
| 1973 | 5 | 0 | 4 | 9 | 0 | 2 | 2 | 4 |
| 1974 | 4 | 0 | 3 | 7 | 2 | 0 | 1 | 3 |
| 5 yrs. | 20 | 1 | 12 | 33 | 4 | 4 | 4 | 12 |
| 1975 | 9 | 0 | 3 | 12 | 2 | 1 | 0 | 3 |
| 1976 | 5 | 0 | 1 | 6 | 0 | 1 | 0 | 1 |
| 1977 | 5 | 2 | 7 | 14 | 2 | 2 | 3 | 7 |
| 1978 | 4 | 1 | 6 | 11 | 0 | 5 | 1 | 6 |
| 1979 | 8 | 2 | 10 | 20 | 1 | 3 | 6 | 10 |
| 5 yrs. | 31 | 5 | 27 | 63 | 5 | 12 | 10 | 27 |
| 10 yrs. | 51 | 6 | 39 | 96 | 9 | 16 | 14 | 39 |

*Category B: (Blunted)*

This group of patients is semi-conscious from more serious asphyxia, but they have normal pupillary reactions and purposeful responses to pain. Close continuous observation is essential, and careful monitoring of respiratory and cir-

culatory parameters is necessary for the first 24 hours. Because the level of consciousness may change rapidly and clinical signs lag behind a rise in intracranial pressure, the normal routine followed for a head injury should be used to detect any deterioration in neurological state.

Until full consciousness returns, certain specific therapeutic measures are recommended in addition to the treatment outlined under Category A. These special measures are intended to prevent or to reduce intracranial hypertension and include initial diuresis, restriction of fluid to half of maintenance requirements, increased concentrations of inspired oxygen and maintenance of normothermia. Subsequent therapy is related to the patient's progress.

These patients will require a longer stay in the intensive care unit because of the high incidence of pulmonary aspiration,[10,14] but most will recover uneventfully. A potentially unfavourable course may be foreseen by indirect evidence of severe anoxia, such as intractable metabolic acidosis, a prolonged resuscitation, or gross pulmonary oedema. Clinical guidelines are unreliable in this group, so if these findings are accompanied by progressive neurological depression, the patient should be reclassified into category C.

There were six patients in category B (6.2 per cent) during the period 1970–1979. Since these patients suffer more severe asphyxia and are more liable to pulmonary as well as to cerebral complications, all should be admitted to hospital for 24–48 hours. All children in this group also had recovered completely at the time of discharge.

It is noted that all patients in categories A and B (57 cases) recovered completely with routine medical management. This group includes two patients in category C.1 at rescue who improved rapidly to category A during the subsequent two hours. There were also two patients in category A at rescue who deteriorated neurologically and are included in category C.1. Many others changed just one category or subcategory in the early post-rescue period.

*Category C: (Comatose)*

The group of 39 patients in category C suffered severe asphyxia and were all in a state of coma with abnormal responses to pain and abnormal patterns of respirations. The depth of coma, according to their clinical responses[53,54] was grouped into three subcategories, C.1 (decorticate), C.2 (decerebrate) and C.3 (flaccid), each with a correspondingly poorer prognosis. It is obvious that only in this comatose group can the results of treatment be compared.

The rationale for aggressive therapy to improve cerebral salvage is as follows. Any acute brain injury, including asphyxia from near-drowning, will cause abolition of neuronal function, oedema, vasomotor paralysis (hyperaemia), and tissue acidosis.[56] It is now believed that neurones which survive the primary brain insult and could recover, often die secondarily from the effects of cerebral oedema[25] or raised intracranial pressure as a result of brain swelling.[26,28] Therapeutic measures are primarily directed at the control of intracranial pressure, but a direct neuronal effect by hypothermia[26] and barbiturate coma[21,22] is possible. The onset of intracranial hypertension is variable in time, but the more severe the injury the earlier the onset. The lethal effects on the brain of a continuously high intracranial pressure are too well known for further comment. In instances of severe asphyxia, this process is predictable, often preventable, and usually controllable. Since a damaged brain is extremely susceptible to hypoxia, and pulmonary oedema with hypoxaemia is usually present,[15,16] this complication must be rigorously controlled by using diuretics, high positive end-expiratory pressure (PEEP), and high concentrations of inspired oxygen. Other complications[52] affecting cerebral recovery to a lesser extent are omitted from this paper.

## Management of Category C Patients

At the time of admission, a victim of near-drowning may appear to be dead cerebrally or show substantial evidence of brain injury. The high incidence of death or permanent brain damage in category C is confirmed in this series. Only six patients (28.5 per cent) out of 21 comatose cases in this category recovered completely with routine treatment, whereas aggressive therapy (outlined later) in patients in the same category produced an intact survival of 11 patients (61.1 per cent) in 18 cases. The incidence of brain damage also diminished from eight patients (38.1 per cent) in 21 cases to one patient (5.5 per cent) in 18 cases.

Our overall percentage figures in 39 comatose cases (Category C), can be compared with 18 comatose cases in Dr. Modell's paediatric series[3] as follows: mortality 33.3 per cent vs 39 per cent; morbidity 23.9 per cent vs 17 per cent; normal 43.6 per cent vs 44 per cent. The similarity might be explained by our 14 patients known to be in the

C.3 (Flaccid) subcategory (or deepest coma) which weighted the series. Nevertheless a comparison of the treated and untreated cases in subcategories C.1 and C.2 as presented in Table VII reveals a significant difference in our neurological results with aggressive treatment.

Therefore an assumption should be made that the brain injury is reversible and early and aggressive therapeutic measures should be initiated. The introduction of single or sequential methods of treatment is not our practice, since all measures to achieve these goals should be implemented and must take priority over the treatment of other body systems. The twin goals of cerebral salvage are to preserve those neurones that are viable, but non-functioning, and to prevent a significant rise in intracranial pressure.

Our therapeutic regimen for all category C cases was derived from personal experience, conversations with Dr. M. Spence[57] of Auckland, N.Z. and his treatment as reported by Dr. R. Trubuhovich[17] and previous reports.[43] Our regimen has been given the acronym 'H.Y.P.E.R.'[4,12] based on the usual clinical state of the comatose near-drowned patient on admission (i.e. these patients are hyper-hydrated and hyper-ventilating with hyper-pyrexia, hyper-excitability and hyper-rigidity). These five findings suggest the corresponding therapeutic measures for critical cerebral care. This treatment has evolved continuously since first reported in 1976[18] and may be considered therapeutic "overkill", but seems justified by the results. The measures, as currently applied, are summarized as follows.

*Hyper-hydration*

This problem[4,27] is best controlled by commencing treatment as soon as the circulation is completely stable. Initial treatment consists of the immediate administration of furosemide 0.5 to 1.0 $mg \cdot kg^{-1}$ intravenously, repeated until adequate diuresis occurs. Later, fluid restriction to one third of the maintenance requirements is instituted and continued until cerebral compliance returns to normal, consciousness is regained, or clinical or laboratory evidence of dehydration is detected. It is essential that fluid balance be accurately controlled, and that continuous direct measurement of electrocardiogram, central venous pressure, blood pressure, and possibly pulmonary capillary wedge pressure be made. When available, daily cardiac index and blood volume measurements may confirm other clinical findings.

*Hyper-ventilation*

After global asphyxia, cerebral shunts or steals from alterations in autoregulation cannot be determined. Therefore, the $Pa_{CO_2}$ is arbitrarily maintained at 4 kPa (30 mm Hg). This level is controversial and represents a compromise between hypocapnia with possible excessive cerebral vasoconstriction, and normocapnia or hypercapnia with excessive cerebral blood flow and raised intracranial pressure. Nevertheless, if an abrupt rise of intracranial pressure occurs, hyperventilation can be increased temporarily to deal with such an emergency.

The high concentration of inspired oxygen is maintained as required, and the risk of pulmonary toxicity is accepted. A high arterial oxygen tension (> 20 kPa [150 torr]) theoretically favours diffusion of oxygen through oedematous pericapillary areas of the brain. A PEEP of 0.67 to 1.33 kPa (5–10 mm Hg)[58] provides adequate oxygenation in most cases, prevents pulmonary micro-atelectasis, and avoids a possible rise of cerebral venous pressure (intracranial pressure). Nevertheless, prolonged continuous paralysis can lead to major $\dot{V}/Q$ abnormalities[60] and routine changes of position are recommended to prevent this.

*Hyper-pyrexia*

Using a cooling mattress and relaxants, body temperature should be rapidly reduced and maintained at 30 ± 1° C. This level achieves a satisfactory reduction in both cerebral oxygen requirements[29] and intracranial pressure and is above the upper level for spontaneous ventricular fibrillation (approximately 28° C). Obviously rectal or other core temperatures must be monitored continuously.

Hypothermia suppresses normal immune response so that daily bacterial cultures from blood, trachea and bladder are essential. In addition white cell counts and platelet counts may provide additional evidence of infection. The prophylactic use of antibiotics remains controversial.

*Hyper-excitability*

Barbiturates have been used recently in large doses to protect the brain.[19–21] Their mode of action includes reduction of intracranial pressure from cerebral vasoconstriction and a probably direct beneficial effect on neurones, although the exact mechanism remains controversial. The summation of beneficial metabolic effects of barbiturate treatment when combined with

TABLE VI

RESULTS OF TREATMENT IN CATEGORY C PATIENTS (1970–1979)

| Category | Total | Treatment | Results (Cases) (%) Dead | Damaged | Normal |
|---|---|---|---|---|---|
| C.1 Comatose (Decorticate) | 9 cases | (−) 4 cases | 0 | 2 | 2 |
| | | (∓) 4 cases | 1 | 0 | 3 |
| | | (+) 1 case | 0 | 0 | 1 |
| | Totals | 9 cases | 1 (11.1%) | 2 (22.2%) | 6 (66.0%) |
| C.2 Comatose (*Decerebrate*) | 16 cases | (−) 5 cases | 2 | 3 | 0 |
| | | (∓) 1 case | 0 | 1 | 0 |
| | | (+) 10 cases | 0 | 1 | 9 |
| | Totals | 16 cases | 2 (12.5%) | 5 (31.2%) | 9 (56.2%) |
| C.3 Comatose (Flaccid) | 14 cases | (−) 6 cases | 4 | 1 | 1 |
| | | (∓) 1 case | 0 | 1 | 0 |
| | | (+) 7 cases | 6 | 0 | 1 |
| | *Totals* | 14 cases | 10 (71.4%) | 2 (14.2%) | 2 (14.2%) |
| Combined Totals | 39 cases | 39 cases | 13 (33.3%) | 9 (23.9%) | 17 (43.6%) |

(−) indicates routine supportive treatments.
(∓) indicates that one or two of the H.Y.P.E.R. measures were used.
(+) indicates H.Y.P.E.R. therapy.

hypothermia has been reported[20] and refuted.[22] Steroids are ineffective in the treatment of the pulmonary lesion in fresh-water drowning[23] but are known to prevent a rise in intracranial pressure[24,26] and to improve cerebral compliance. Currently, recommended doses are:

1. Phenobarbitone 50 $mg \cdot kg^{-1}$ on the first day, given slowly intravenously in three divided doses, and 25 $mg \cdot kg^{-1}$ in three divided doses on the second, third, and fourth days of treatment. Daily determinations of barbiturate blood level are necessary to achieve the optimal therapeutic goal of 75 to 100 mg per litre. In some patients we have observed that the spinal fluid barbiturate levels are approximately half the blood levels, and that barbiturate levels may rise for 24 hours after therapy is discontinued. A long-acting barbiturate (40 hours using phenobarbitone) is preferred to other barbiturates because circulatory depression is minimal and treatment can be promptly reinstituted if intracranial pressure rises unexpectedly.

2. Dexamethasone, loading dose 0.2 $mg \cdot kg^{-1}$: maintenance 0.1 $mg \cdot kg^{-1}$ every six hours. Start treatment within six hours.

*Hyper-rigidity*

Decorticate or decerebrate rigidity is an obvious clinical cause of raised intracranial pressure. However, simple nursing procedures such as lowering the head or tracheal suctioning may precipitate a rise in intracranial pressure of 30 minutes duration. For these reasons, as well as for the need to control ventilation, which lowers intracranial pressure, complete muscle paralysis is maintained continuously. For this purpose, we use intravenous d-tubocurare 0.5 to 1.0 $mg \cdot kg^{-1}$, or intravenous pancuronium 0.1 $mg \cdot kg^{-1}$ either hourly or as needed, to prevent all movement. Later, when all relaxant therapy is discontinued and weaning from the respirator is commenced, a nerve stimulator should be employed to test for residual curarization (up to three days).

It is obvious that any emergency department can initiate H.Y.P.E.R. therapy following cardiopulmonary resuscitation of a near-drowning victim. It is recommended that subsequently the patient be safely transported for continued treatment to a regional critical care unit where personnel and extensive monitoring facilities are continuously available.

The value of each individual treatment in this regimen is uncertain, and the optimal drug dosages have not yet been verified. Theoretically, each therapeutic measure should facilitate cerebral recovery but their qualitative and quantitative effects await prolonged and careful clinical study. Nevertheless, it has been possible in our institution to make a significant improvement in cerebral salvage[4,12] (see Table VI and Table VII).

TABLE VII

RESULTS COMPARING TREATMENT IN CATEGORY C PATIENTS

| Category | Total | Treatment | Results (Cases) (%) | | |
|---|---|---|---|---|---|
| | | | Dead | Damaged | Normal |
| C.1 Comatose (Decorticate) | 8 cases | Routine (−) (∓) | 1 (12.5%) | 2 (25%) | 5 (62.5%) |
| | 1 case | H.Y.P.E.R. (+) | 0 | 0 | 1 (100%) |
| | 9 cases | | 1 | 2 | 6 |
| C.2 Comatose (Decerebrate) | 6 cases | Routine (−) (∓) | 2 (33.3%) | 4 (66.6%) | 0 |
| | 10 cases | H.Y.P.E.R. (+) | 0 | 1 (10%) | 9 (90%) |
| | 16 cases | | 2 | 5 | 9 |
| C.3 Comatose (Flaccid) | 7 cases | Routine (−) (∓) | 4 (57.1%) | 2 (28.4%) | 1 (14.2%) |
| | 7 cases | H.Y.P.E.R. (+) | 6 (85.7%) | 0 | 1 (14.2%) |
| | 14 cases | | 10 | 2 | 2 |
| Combined C.1 and C.2 | 14 cases | Routine (−) (∓) | 3 (21.4%) | 6 (42.8%) | 5 (35.7%) |
| | 11 cases | H.Y.P.E.R. (+) | 0 | 1 (9.0%) | 10 (90.9%) |
| | 25 cases | | 3 | 7 | 15 ($P < 0.02$)* |

(−) indicates routine supportive treatment.
(∓) indicates that one or two of the H.Y.P.E.R. measures were used.
(+) indicates H.Y.P.E.R. therapy.
*The results of routine and H.Y.P.E.R. therapy in the combined C.1 and C.2 sub-groups were compared by Fisher's exact probability test.

When using H.Y.P.E.R. therapy, cerebral monitoring is limited to a few measures which become of paramount importance. The sole clinical evidence of cerebral change is obtained by observing changes in pupillary size or reactions. The monitoring of intracranial pressure is mandatory with direct continuous measurement by means of a Richmond screw or ventricular drain. A daily electroencephalogram (EEG) is valuable, as it will reveal abnormalities and barbiturate effect and, hopefully, will show progressive improvement.[1] After 12 to 24 hours the electroencephalogram is not flat at 30° C and levels of phenobarbitone of 75 to 100 mg per litre, unless cerebral death has occurred. A cerebral function monitor may provide additional help and is presently under investigation.

Based on experience, it is recommended that a minimum of four days treatment is necessary to control cerebral swelling effectively and to prevent relapses. Any major rise in intracranial pressure spontaneously, or from mild stimulation, indicates that the brain is still damaged and swollen and will require an additional two days of therapy. If intermittent rises of intracranial pressure (≥ 2.66 to 3.33 kPa [20 to 25 mm Hg]) occur, treatment consists of vigorous hyperventilation until 3 to 5 $mg \cdot kg^{-1}$ of thiopentone can be administered intravenously. These measures can be supplemented by administration of mannitol when necessary. A computerized tomography scan is recommended to rule out a space-occupying lesion when intracranial pressure rises unexpectedly or repeatedly.

When the decision to discontinue therapy is made, phenobarbitone and relaxants are stopped and the patient is allowed to rewarm passively over a 24-hour period and to regain consciousness, which usually takes one to four days. Reinstitution of treatment is easily undertaken if required, but has not been required in any of our near-drowned patients.

### RESULTS IN CATEGORY C PATIENTS

Immediate resuscitation is recommended in all cases of near-drowning despite a report to the contrary.[16] A number of factors can delay the onset of brain death, especially in cold water drowning,[30–34] and justify extensive resuscitation efforts regardless of the victim's initial condition.[42] As a result of this policy, there has been an increase in the number of patients admitted in a comatose state including subcategory C.3 (Flaccid). This group of 14 patients might formerly have been termed and treated as deceased but there were two patients (14.2 per cent), one in each treatment group, who survived intact and who justify our policy.[42]

There were 25 patients in the C.1 and C.2 categories, with a more hopeful prognosis, which have been combined in Table VII for a comparison of routine and H.Y.P.E.R. therapy. A significant statistical difference exists ($P < 0.02$) between the incidence of complete cerebral recovery in the partially treated group (35.7 per cent) and the fully treated (H.Y.P.E.R.) group (90.9 per cent).[55] Fortunately, the fear that a reduction in mortality by aggressive therapy might be associated with an increase in morbidity[43] has not been confirmed (42.8 per cent reduced to 9.0 per cent).

In conclusion, the use of all H.Y.P.E.R. measures simultaneously for cerebral salvage appears justified in all near-drowning patients in category C. The success of these H.Y.P.E.R. measures has implications for the management of other conditions involving brain injury.

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## RÉSUMÉ

Ce travail décrit une classification neurologique simple pour les victimes de noyade. Trois catégories sont proposées:

Catégorie A (conscience)
Catégorie B (décébration)
Catégorie C (coma).

La catégorie C est subdivisée en trois classes:

C1 (décortication)
C2 (décébration)
C3 (flaccidité).

Cette classification est basée sur le niveau de conscience évalué une à deux heures après le sauvetage et sert de guide pour la mise en marche du traitment. Les résultats de récupération cérébrale chez 96 patients du Hospital for Sick Children de Toronto obtenus d'après cette classification sont rapportés en retrospective pour la période de 10 années allant de 1970 à 1979 inclusivement. Une thérapeutique neurologique agressive signifiait l'hydratation continue, l'hyperventilation contrôlée, l'hypothermie, le coma barbiturique et une curarisation continue pendant quatre jours.

Tous les patients des classes A (51 cas) et B (6 cas) ont récupéré complètement avec le traitement médical usuel.

Dans la catégorie C (39 comateux), la mortalité totale a été de 33.3 pour cent avec une morbidité cérébrale de 23.9 pour cent et une récupération à la normalité de 43.6 pour cent. Lors de la révision du résultat thérapeutique, deux sous-catégories C1 et C2 ont été formées dans un but de comparaison. Chez 14 patients chez qui on avait employé le traitement usuel,

on a trouvé une mortalité de 21.4 pour cent, une morbidité de 42.8 pour cent et une survie avec récupération totale de 35.7 pour cent. En comparaison, chez 11 patients traités de façon aggressive, il n'y a pas eu de mortalité, la morbidité a été de 9.0 pour cent et un taux significatif de 90.9 pour cent de survie sans séquelles a pu être constaté. Dans la sous-catégorie C3, (14 patients), il n'y a eu que quatre survivants dont un patient par groupe qui a récupéré complètement (14.2 pour cent).

Une survie avec une fonction cérébrale intacte est extrèmement importante. Nos données justifient une réanimation immédiate de toutes les victimes de noyade indépendemment de leur condition initiale ou du pronostic. L'emploi d'une classification neurologique précoce semble appropriée à la mise en marche du traitement qui doit être aggressif en cas de décortication (sous-catégorie C1) et de décérébration (sous-catégorie C2), dans le but de produire une réduction importante de la morbidité et de la mortalité chez les victimes de noyade.

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# THE 1962 WELLCOME PRIZE ESSAY

## Drowning and the Postimmersion Syndrome
## A Clinicopathologic Study

*By*

CAPTAIN ROGER H. FULLER, MC, USN*

DROWNING is a common killer. In the United States 7 per cent of accidental deaths are by drowning, accounting for over 7,000 lives each year. In wartime the toll is much heavier. Peacetime rates are increasing, paralleling the increase in popularity of water sports and recreation.

Death by drowning differs from most other forms of asphyxial death in that the anoxia, hypercapnia, and acidosis are complicated by physical and chemical changes that result from the introduction of the surrounding water, with its contained solids and solutes, into the gastrointestinal tract and into the circulatory system by way of the respiratory tract. In experimental animals the physical and chemical alterations vary with the electrolyte content of the drowning fluid.[1] Thus, dogs drowned in fluids hypotonic to the blood show an increase in blood volume and a dilution of the blood elements. Ventricular fibrillation is a frequent occurrence. Those drowned in sea water, on the other hand, do not fibrillate; they have reduced blood volumes resulting from transfer of water from the blood to the lung alveoli; and they absorb electrolytes from the sea water. This interchange of water and electrolytes can be followed by using radioactive tracers. In the human victim of immediately fatal submersion similar transfers can in a majority of cases be demonstrated by physical and biochemical differences in blood from the left and right sides of the heart.[2]

Forensic pathologists have for many years collected data on physical and chemical changes in the blood from left and right heart of drowning victims as well as from individuals dead of other causes. It has been well established that these changes (Tables 1 and 2) do indicate concentration or dilution of elements of the blood by the entry of drowning fluid or solutes in the same manner as is seen under experimental conditions. Similar changes in electrolytes, however, are known to occur following death from causes other than drowning;

TABLE 1

ELEVEN SIMULTANEOUS DEATHS. FRESH WATER TRAINING ACCIDENT CHLORIDES AS MG NaCl/100 CC PLASMA (NORMAL 570 TO 620 MG%)

| Rt. Heart Chloride | Lt. Heart Chloride | Chloride Difference | Diatoms in Lung Sections |
|---|---|---|---|
| 560 | 550 | −10 | + |
| 520 | 520 | 0 | + |
| 470 | 390 | −80 | + |
| 440 | 400 | −40 | + |
| 500 | 420 | −80 | + |
| 520 | 560 | +40 | + |
| 500 | 530 | +30 | + |
| 520 | 500 | −20 | − |
| 430 | 320 | −110 | − |
| 510 | 480 | −30 | − |
| 520 | 440 | −80 | − |

TABLE 2

SIX SIMULTANEOUS DEATHS. SEA WATER TRAINING ACCIDENT CHLORIDES AS MG NaCl/100 CC BLOOD (NORMAL 450 TO 500 MG%)

| Rt. Heart Chloride | Lt. Heart Chloride | Chloride Difference | Diatoms in Lung Sections |
|---|---|---|---|
| 590 | 800 | +210 | + |
| 500 | 980 | +480 | + |
| 480 | 820 | +340 | + |
| 500 | 800 | +300 | + |
| 480 | 920 | +440 | + |
| 500 | 900 | +400 | + |

* Deputy Director, Armed Forces Institute of Pathology, Washington 25, D.C.

the rates at which they occur may be different in the left and right sides of the heart; and the magnitudes of the changes may exceed those commonly seen in drowning.[3] Because of these postmortem changes resulting from diffusion and autolysis, it is only in the minority of instances that a definite determination of drowning can be made solely on the basis of a measurement of such levels as protein, chloride or sodium concentration, freezing point, electrical conductivity, or specific gravity of plasma from the left and right sides of the heart. These determinations are of much more significance when they are made within a few hours of death and/or when the drowning has occurred in sea water. In the latter instance the magnitude of the chloride and magnesium differential usually far exceeds what might be expected from postmortem diffusion.

Diatoms present in most natural waters serve as tracers of the drowning fluid; and they can be shown to reach the circulatory system, presumably through ruptured pulmonary capillaries. Whether or not ventricular fibrillation commonly occurs in human fresh-water drowning is not known.

The asphyxia of human accidental drowning is frequently further complicated by the aspiration of vomitus into the lung. During the drowning process vomiting under water is induced by the swallowing of large amounts of fluid and by the stimulus of the first stage of asphyxia. If the victim is rescued, vomiting during and after resuscitation is common.

### Acute Drowning Deaths

The protocols of 3,000 autopsies of drowning victims have been reviewed and the microscopic sections of 500 examined.

The usual gross postmortem findings that have been described as more or less characteristic of drowning[4] were commonly noted in these cases. A stiff, lathery, white, or pinkish foam in the mouth and respiratory passages was frequently present in bodies examined within a day or two of death. With the onset of putrefaction and the percolation of gases through the respiratory tract, this fine foam was replaced by a bubbly, sanguinous fluid. Before the onset of putrefaction the characteristic watery emphysema of the lungs was usually present. The organs were overexpanded; and they retained their shape and size when the thoracic cavities were opened and when they were removed. They were heavy (usually 1,000 to 2,000 grams), wet, and showed varying degrees of punctate hemorrhage into the pleura and parenchyma. Inspection of the larynx, trachea, and bronchi often revealed aspirated vomitus, mud, sand, or particles of aquatic vegetation within the lumen. The stomach was frequently distended—sometimes by gas forced into it during attempts at resuscitation, and sometimes by water swallowed during the drowning process.

On microscopic examination of the lungs there was characteristically distention of the alveoli, alveolar ducts, and terminal bronchioles; and some alveolar walls appeared to have ruptured. Varying amounts of hemorrhage and edema, evidenced by a protein precipitate in the alveoli, were usually present. Blood vessels were congested; and saccular dilatation of alveolar capillaries was seen. Erythrocytes within the capillaries and alveoli frequently were hemolyzed in cases of either fresh or salt water drowning. Distention with occlusion of capillaries by masses of agglutinated platelets was a frequent finding when autopsy was done within a few hours of death; but fibrin thrombi were not usually seen. Masses of agglutinated platelets were frequently seen in larger blood vessels in the lung sections and less frequently in the vessels of other organs. The relationship of these agglutinative platelet thrombi, apparently agonal, to the fact that clotting of blood postmortem is usually not seen in drowning is speculative. Fluidity of postmortem blood in drowning has been attributed to the release of fibrinolysins resulting from asphyxia.

Autolytic changes in the lung, advanced to a degree out of proportion to those seen in other organs such as liver and kidney, were frequently present in the cases re-

viewed. Furthermore, lobules of lung apparently inundated by drowning fluid and/or vomitus showed autolysis and hemolysis considerably more advanced than in immediately adjacent lobules. This spotty lobular distribution of advanced autolysis of lung, if present, seems to be characteristic of aspiration.

Particulate matter presumably aspirated with the drowning fluid was seen in the lung sections of 70 per cent of the drowning cases reviewed. Forensic pathologists have studied the significance of foreign bodies in the lungs of the drowned for years. It is known that a certain amount of microscopic foreign material can enter the bronchi and central portions of the lungs of bodies that have been immersed after death, especially if the body has sunk to a considerable depth or has been buffeted about by water turbulence. The finding of significant amounts of microscopic aquatic zora and fauna widely dispersed in the lung periphery is, however, considered to be good evidence of drowning; and their recovery is attempted by means of digestion and sedimentation technics as a part of the medical investigation of bodies recovered from water.

The foreign materials noted in the lung sections of our cases were aspirated vomitus in 24 per cent; mud, sand, or fragments of aquatic vegetation, frequently recognized by their birefringence, in 60 per cent; and diatoms, green algae, or dinoflagellates in 33 per cent. They were most apt to be found in portions of the lung sections showing the most advanced autolysis.

Individuals who drown in shallow water such as lakes, ponds, and rivers are most likely to aspirate particulate matter. If the victim has sunk to the bottom and has exerted a violent agonal struggle or had asphyxial convulsions before respirations cease, sediments are stirred up and suspended in the water aspirated with the terminal gasps.

Diatoms are the most commonly encountered aquatic microorganisms in the lungs of the drowned. They are microscopic unicellular or colonial algae having distinctive cell walls impregnated with silica and containing chlorophyll and diatomin, a brown pigment. Over 10,000 species ranging in size from a few micra to a few hundred micra have been described universally distributed in fresh and salt water wherever there is a combination of light and moisture. Living fairly close to the surface and constituting a major portion of the plankton, their skeletons accumulate on the bottom where those from past ages have formed large deposits of diatomaceous earth or kieselguhr. This is used commercially as a mild abrasive, as an ingredient of insulating and absorbent materials, and in the fabrication of fine filters. Present in toothpastes and powders, in some paints, and in building plasters, diatom skeletons may reach the lungs by methods other than the aspiration of water.[5]

Diatom fragments up to 30 micra in diameter have been shown to enter the pulmonary veins during drowning and gain access to the organs of the major circulatory system in small numbers. Being transparent and resistant to corrosive chemicals, they are best recovered from blood by hemolysis, and from tissue by chemical digestion followed by centrifugation or sedimentation and microscopic examination. By virtue of the distinctive sculpturing of their cell walls, they can be recognized without any detailed knowledge of marine biology.[6]

Many of the drowning deaths in our series were incidental to a vehicular accident into water; and many were associated with a variety of mechanical injuries. In this group, fat and marrow emboli to the lungs were frequently seen. In a few instances with these findings either there was no history of injury or the autopsy protocol failed to mention it. It is speculated that the release of fat and marrow emboli might be produced by an asphyxial convulsion in water during the drowning process. Fat embolization is known to result from convulsions under other circumstances. Organs other than the lungs showed the changes seen in other forms of asphyxia.

### Delayed-Drowning Deaths

Some authors have reported signs and symptoms in cases of near drowning that

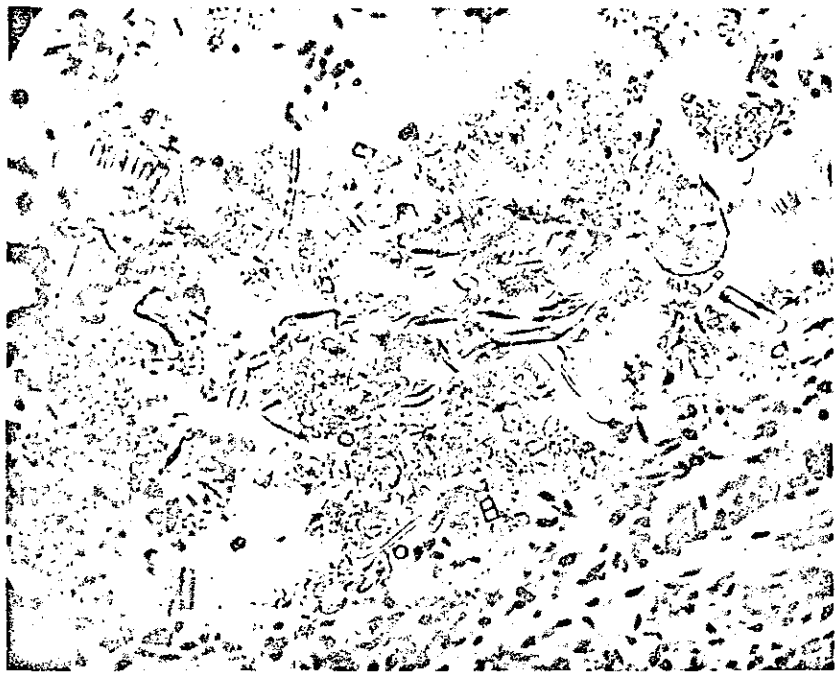

FIG. 1. Section of lung to show diatom skeletons within a small bronchus. Drowning in a fresh-water lake. AFIP Neg. 61-5578. ×265.

they have attributed to the effects of asphyxia.[7-9] Part of the syndrome is a diffuse or nodular hazy opacification of the lung fields seen on radiographic examination of the chest, which has been ascribed to pulmonary edema unrelated to aspiration. Other authors have stated that if resuscitation from drowning is successful, recovery is usually complete without significant residual damage.[10,11] The following cases are reported as examples of the fatal post-immersion syndrome. There has been very little documentation of such cases, probably because they are relatively rare and occur only infrequently, or not at all, in the experience of any one physician. It can be expected that with the newer technics of resuscitation such as mouth-to-mouth rescue breathing,[12] closed chest cardiac massage, cardiac defibrillation and pacemakers, and intermittent positive-pressure breathing, together with a greater exposure to the hazards of swimming pools, boating, skin diving, etc., there will be increased numbers of near-drowning victims. Rational treatment of these individuals should be based not only on their symptomatology and on information obtained from animal experiments, but also on the pathologic findings at autopsy of the fatal cases.

Autopsy material from 18 delayed-drowning deaths has been studied. Each of the victims was rescued from water in an unconscious and apneic state. Artificial respiration—mouth-to-mouth, manual, or mechanical—was applied in each instance, with return of spontaneous respiration in all but three. Two of these died within a few minutes; and one was maintained on artificial respiration for 12 hours before death ensued. Survival time ranged from a few minutes to 19 days. Drowning was in fresh water in 11 instances, in sea water in 7. Survival time, symptomatology, and pathologic findings were not related to the salinity of the drowning fluid except in one victim of drowning in the Great Salt Lake, which is approximately 28 per cent saline. In this instance, consciousness and spontaneous respiration were restored; and the victim survived for 11½ hours. There was extensive chemical corrosion of the mucosa of the stomach, duodenum, trachea, and bronchi, with massive pulmonary and gas-

tric hemorrhage. This patient also had gross hemoglobinuria with pigment casts in the renal tubules, probably derived from absorption of extravasated hemolyzed blood rather than intravascular hemolysis.

Thirteen of the 18 regained consciousness. Five remained comatose for periods ranging from a few minutes to 19 days.

As would be expected, signs and symptoms related to injury of the respiratory and central nervous systems were most prominent. Vomiting, ascribed to cerebral hypoxia and gastric distention by swallowed water and by air forced into the stomach during resuscitation, were frequent, and added the hazard of further aspiration.

Temperature was recorded in six cases and was elevated in all, ranging up to 106°F. White blood cell counts, recorded in five cases, ranged from 12,200 to 38,000 per cubic millimeter. In a case surviving 3¼ hours after submersion in sea water, hematocrit was 55 and hemoglobin 19.8 gm%. In another case, however, surviving 3 days after submersion in fresh water hematocrit on the day of the accident was 61, hemoglobin 21 gm%, and total blood volume was reduced, mainly because of a plasma deficit of 1,440 cc. Both cases had massive pulmonary edema and pneumonitis with escape of large amounts of plasma into the lungs. The inference drawn from these two cases is that following both sea water and fresh water drowning, hemo-concentration may be expected; and if it occurs plasma replacement is indicated.

Hemoglobinuria occurred in the Great Salt Lake case already mentioned. In another case surviving fresh water drowning for 3 days, the urine was scanty, grossly bloody on the second and third day, and the BUN rose to 132 mg%. Acute tubular necrosis of the kidneys with pigmented tubular casts was found at autopsy. This lesion was probably due to a prolonged period of hypotension on the first day rather than intravascular hemolysis, since laboratory tests on the first day indicated hemoconcentration rather than hemodilution, which would be operative if the latter were the case.

Tachycardia, gallop rhythm, and hypotension to shock levels were the main cardiovascular signs. Open cardiac massage for cardiac arrest was done in one instance with initial success, followed by a recurrence of asystole, which was unresponsive to additional massage. In another case, closed-chest cardiac massage and cardiac pacemaker were of no avail in restoring systole to a heart that stopped 7¾ hours after rescue.

Morphologic evidence of pulmonary parenchymal damage was present in all cases, varying from an early hemorrhagic desquamative and exudative vital reaction, in cases surviving for only a few minutes, through increasing degrees of severity of pneumonitis to severe bronchopneumonia, multiple abscesses, and bilateral empyema in a case surviving for 19 days. Desquamation of alveolar epithelial and septal cells into the alveolar lumen exposes alveolar capillaries to the drowning fluid, altering permeability and allowing the escape of plasma. Further injury of a mechanical nature inflicted by the violent respiratory action against resistance during the drowning struggle is increased by heroic resuscitative efforts producing hemorrhage. Further chemical injury results from the aspiration of vomitus, debris, and particulate matter that may be in the drowning fluid. Within a surprisingly short time a polymorphonuclear exudate dominates the picture. Hyaline material applied to the walls of injured respiratory bronchioles, alveolar ducts, and alveoli is seen from 12 hours through the third day. Foreign body reaction to aspirated particles is well developed by the third day. These foreign particles may be silt, sand, and vegetable material, especially diatoms, as well as meat and vegetable fibers in aspirated vomitus. One case, dying on the nineteenth day of central nervous system lesions, showed a resolving bronchopneumonia with lymphocytes and plasma cells predominant in the exudate.

Several of the brains were edematous. In two patients who remained comatose until their deaths, both on the nineteenth day, there was laminar necrosis of the deep layers of the cerebral and cerebellar cortex, as well as minor softening in other elements of

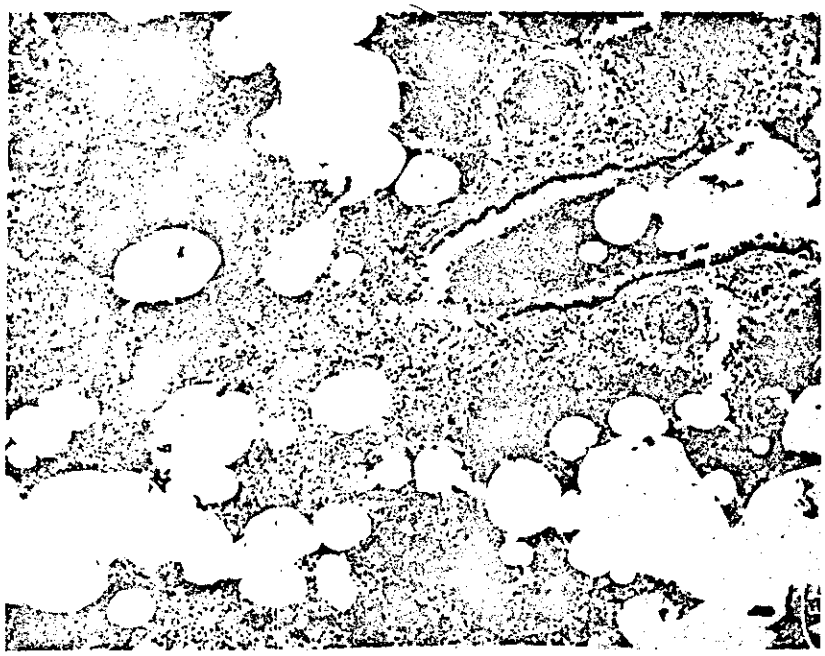

FIG. 2. Case 1. Died several minutes after rescue from fresh-water. Section of lung to show edema, hemorrhage, and early desquamative and exudative pneumonitis. AFIP Neg. 61-5598. ×70.

the cerebral gray matter. The neuropathologic features of one of these cases have been reported by Courville.[13] In the other case the necrotic lesions appeared to be of different ages, suggesting progression of the injury beyond the acute anoxic episode.

The two cases with benzidine-positive pigmented renal casts have been mentioned. Submersion was in fresh water in one case and in salt water in the other. I am not convinced that intravascular osmotic hemolysis is the explanation for this finding, since in one instance the medium was hypertonic; while in the other, laboratory data do not support the theory of hemodilution.

## CASE REPORTS

*Case 1.* AFIP Acc. 194146. Survival several minutes. A 20-year-old Caucasian male was seen to sink while swimming in a fresh water creek. He was recovered in an estimated 10 minutes and was apneic and comatose. Pulse was present for "some time" after rescue. Manual and mechanical artificial respiration were administered for about an hour. At autopsy the lungs weighed 1,240 grams. Diatoms were present. Edema, hemorrhage, and early pneumonitis were observed.

*Case 2.* AFIP Acc. 182658. Survival 2½ hours. An 18-year-old Negro male was rescued unconscious and apneic from a fresh water swimming pool. Artificial respiration was given, and consciousness and spontaneous respiration returned in a few minutes. He was hospitalized 30 minutes after the accident. Pulse 84, regular; respirations, 26. There were cough productive of pink frothy sputum and bilateral rales. Two hours postsubmersion, pulse 140, respirations 48, bloody sputum. Patient was complaining of back pain. Morphine sulfate, ¼ gr., was given. He died 2½ hours postsubmersion. Autopsy was done 10 hours postmortem. The lungs weighed 1,800 grams. There was edematous pneumonitis. Right heart, whole blood was 420 mg % NaCl. Brain weight, 1,500 grams.

*Case 3.* AFIP Acc. 1028511. Two and one-half hour survival. A 24-year-old male epileptic was rescued from fresh water, comatose and apneic. He was intubated and resuscitated, but died 2¼ hours after submersion. Autopsy: Pulmonary edema with hemorrhagic pneumonitis.

*Case 4.* AFIP Acc. 727332. Survival 3 hours. A 19-year-old Negro male nonswimmer was removed apneic and comatose from the bottom of a swimming pool. Artificial respiration was given and resulted in return of spontaneous breathing and consciousness. Cough produced frothy hemorrhagic sputum. He suddenly vomited a large amount of material and expired 3 hours after submersion. Autopsy: Lungs weighed 1,740 grams. Edematous pneumonitis with aspirated vomitus and diatoms in lung sections.

*Case 5.* AFIP Acc. 948583. Survival 3¼ hours. A 22-year-old Caucasian male was submerged several minutes in a helicopter sinking in sea water. He was comatose and apneic when recovered. Artificial respiration was given, with return of spontaneous res-

piration and consciousness. There were dyspnea, cyanosis, frothy sputum, tachycardia, bilateral rales, and opacification of lung fields on x-ray examination. Blood pressure was 90/70, white blood count 14,500, hemoglobin 19.8 gm/100 cc, hematocrit 55. Bilateral rupture of tympanic membranes. Water (760 cc) was removed from stomach; there was fecal incontinence. Coma and depression of respiratory rate occurred, with death 3¼ hours postsubmersion. Autopsy: Brain weight, 1,500 grams; cerebral swelling without necrosis. Lungs, 2,700 grams. Early hemorrhagic pneumonitis.

*Case 6.* AFIP Acc. 187618. Survival 3½ hours. No clinical history was available, other than that this 52-year-old Caucasian male was rescued from salt water and died 3½ hours later. Autopsy: Brain weight, 1,200 grams; cerebral swelling with herniation. Lungs weighed 2,850 grams. Edema and pneumonitis.

*Case 7.* AFIP Acc. 851078. Survival 5½ hours. A 9-year-old male was removed apneic and comatose from the bottom of a swimming pool. Tracheotomy was done and 100 per cent $O_2$ given under pressure. Thoracotomy was performed and the heart found in asystole. Cardiac massage was done for 2 hours, with restoration of sinus rhythm and pulse to 90. No return of spontaneous respiration. He was placed in a Drinker respirator but died 5½ hours after submersion. Autopsy: Lungs weighed 600 grams. Pulmonary hemorrhage, edema, and early pneumonitis. Brain weight, 1,400 grams; brain swollen.

*Case 8.* AFIP Acc. 649850. Survival 5 hours. A 22-year-old Negro male dove into fresh water pool from diving board and failed to surface. Removed comatose and apneic. Respiration restored after about the seventh prone-pressure cycle. Hospitalized; dyspnea and bilateral rales were noted. No cyanosis. Blood pressure 118/80; pulse 86; respiration 30. Chest x-ray film showed bilateral diffuse haziness of lung fields, most marked in the hilar regions. Treated with nasal oxygen and penicillin, but became quite restless and apprehensive. Sodium luminal, 2 gr, were given. He suddenly began vomiting and coughing up bloody fluid; blood pressure fell; and he expired 5 hours after submersion. At autopsy lungs weighed 2,100 grams and were the seat of a widespread edematous and hemorrhagic pneumonitis. Diatoms and aspirated vomitus were seen in the sections.

*Case 9.* AFIP Acc. 1010272. Survival 7¾ hours. An 11-year-old Caucasian female dove into a deep fresh water pool and failed to surface. She was rescued, after an estimated 4 to 5 minutes of submersion, by a lifeguard, who administered mouth-to-mouth rescue breathing. Spontaneous respiration was restored by means of a mechanical respirator. The victim was hospitalized, comatose, in severe respiratory distress, and cyanotic, with pulse 140, respiration 64, blood pressure 130/50. Bilateral moist rales, absent tendon reflexes. Abdomen distended and tympanitic. Tracheotomy was performed. X-ray of chest showed diffuse hazy opacification of both lung fields. She was treated with oxygen, Levin tube, tracheal suction and penicillin, but heart action ceased prior to respiratory arrest. Cardiac pacemaker and external cardiac massage were of no avail, death occurring 7¾ hours postsubmersion. Autopsy: Weight 102 lb, height 5 feet, 1 inch. Brain findings: weight 1,460 grams, swollen, pale, no necrosis. Lungs weighed 1,600 grams. Severe pneumonitis with early hyaline membrane formation and aspirated vomitus.

*Case 10.* AFIP Acc. 149218. Survival 11½ hours. A 20-year-old Caucasian male was submerged in Great Salt Lake (28% saline). Hospitalized 2½ hours later in shock, cyanotic, vomiting, and coughing bloody fluid. Blood pressure 110/82; pulse 105; temperature 102°; white blood cell count 38,000; hemoglobin 14.5 gm/100 cc. Treated with oxygen tent, caffeine sodium benzoate, morphine sulphate (⅙ gr), penicillin, 10% glucose in water followed by a unit of plasma intravenously, but continued in shock, with a terminal temperature of 106°. Died 11½ hours postsubmersion. Autopsy: Necrosis of mucosa of trachea, bronchi, bronchioles, stomach, and duodenum. Lungs weighed 1,200 grams and showed edema, hemorrhage, and minimal exudative pneumonitis and venous thrombi. Massive gastric hemorrhage. Bladder distended with port wine-colored benzidine-positive urine. Benzidine-positive casts in renal medullary tubules. Brain weight, 1,200 grams.

*Case 11.* AFIP Acc. 733075. Survival 12 hours. A 20-year-old Caucasian male was recovered comatose and apneic after an estimated 5 minutes of submersion in fresh water. Pulse full and regular. Artificial respiration with good pulse, blood pressure, and color until cardiac arrest, unresponsive to open-chest cardiac massage 12 hours after submersion. Autopsy: lungs weighed 1,960 grams; hemorrhagic and edematous pneumonitis with fat and bone marrow emboli (attributed to thoracotomy). No renal glomerular fat emboli. Brain weighed 1,380 grams.

*Case 12.* AFIP Acc. 169611. Survival 12 hours. A 23-year-old Japanese female rescued from suicide attempt in salt water bay. Artificial respiration, resulting in revival. Found dead in bed next morning, approximately 12 hours after submersion. Autopsy: Lungs weighed 1,380 grams. Severe pneumonitis with hyaline membranes. Diatoms in lung sections. Brain weighed 1,400 grams.

*Case 13.* AFIP Acc. 795969. Survival 17 hours. A 20-year-old Caucasian male rescued comatose after falling into sea. Artificial respiration, with return of spontaneous respiration and consciousness but confused and blurred vision. Sixteen hours later comatose, and oral temperature 107°. Death 17 hours after rescue. Autopsy: Lungs weighed 1,800 grams; hemorrhage, edema, minimal pneumonitis.

*Case 14.* AFIP Acc. 814155. Survival 19 hours. A 20-year-old Negro male. Found on sandy bottom of fresh water lake, estimated 3 to 5 minutes after he disappeared while swimming. Comatose and apneic.

FIG. 3. Lung section from Case 10, who survived in coma for 7¼ hours after rescue, to show exudative pneumonitis with early hyaline membrane formation. AFIP Neg. 61-5581. ×70.

Respiration resumed after several minutes of artificial respiration. Admitted cyanotic and comatose to hospital. Regained consciousness, but condition precarious. Treated with tourniquets, positive-pressure oxygen, and Levin tube, but died 19 hours postsubmersion. Autopsy: Severe pneumonitis with formation of hyaline membranes. Crystalline debris and many diatoms in bronchioles and alveoli.

*Case 15.* AFIP Acc. 995062. *Survival 3 days.* A 16-year-old Negro male. Stomach cramps while swimming in pool. Removed from bottom comatose and apneic. Mouth-to-mouth and mechanical resuscitation, with recovery. Admitted to hospital alert, cooperative, not cyanotic. Temperature 98°, pulse 104, respiration 60, blood pressure 140/0, complaining of epigastric pain. Vomited repeatedly and be-

FIG. 4. Case 14. Death 19 hours after rescue. Section of lung to show severe aspiration pneumonia and hyaline membrane formation. AFIP Neg. 61-5592. ×165.

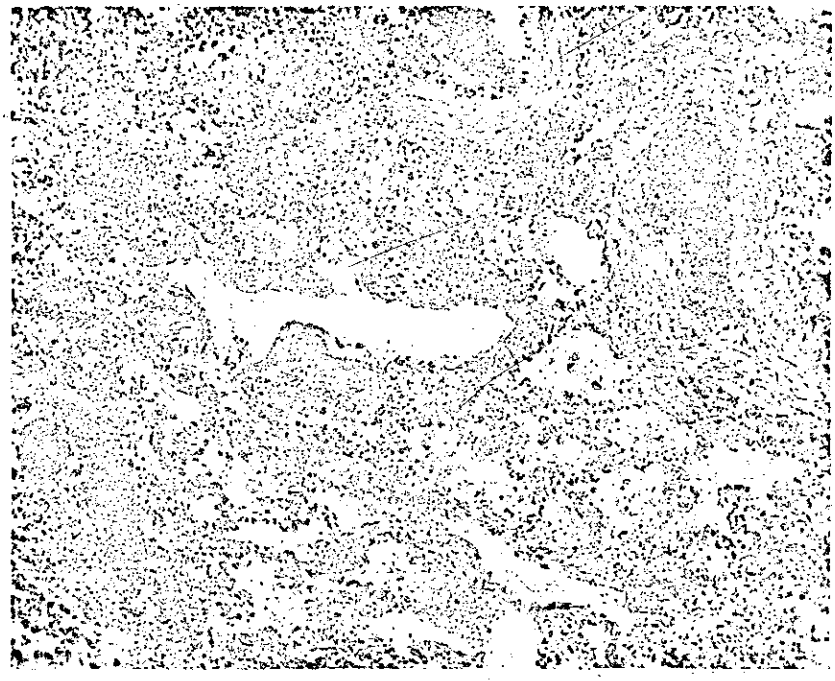

FIG. 5. Case 15. Death 3 days after rescue. Section of lung to show pneumonitis with hyaline membrane formation. AFIP Neg. 61-5596. ×90.

came quite dyspneic and cyanotic. Endotracheal tube inserted and positive-pressure oxygen at 20 mm, Hg begun. Chest x-rays showed bilateral nodular densities. Blood volume studies with $Cr^{51}$ showed a plasma deficit of 1,441 cc. Hematocrit 65, white blood cell count 4,000, hemoglobin 21 grams. Urine amber, acid, with specific gravity of 1.017, 50 mg% alb., gross blood in sediment. On positive-pressure breathing for 12 hours, during which time respiratory symptoms were controlled, but he remained hypotensive. Next day temperature 102°, pulse 150, respiration 60, hematocrit 46, hemoglobin 14.5 gm, white blood cell count 14,200, blood urea nitrogen 73 mg%, sodium 130, potassium 5.6, chloride 88:5 mEq/L, and $CO_2$ content 42 volume %. Oliguria; and rise of BUN to 132 mg% and blood pressure to 150/118. White count rose to 30,000, with 94 per cent granulocytes. Death on third day. Autopsy: Severe bronchopneumonia with formation of hyaline membranes and foreign body reaction to aspirated vomitus. Acute tubular necrosis of kidneys, with benzidine-positive casts in cortical and medullary tubules. Focal necrosis of spleen.

*Case 16.* AFIP Acc. 995063. Three-day survival. A 38-year-old Negro male was seized with cramps while swimming in salt water and submerged. Rescued and revived by lifeguard but refused hospitalization. At home with dyspnea, cough, and wheezing. Collapsed, became comatose and died on third day. Autopsy: Confluent bronchopneumonia involving all lobes. Diatoms and vomitus in lung sections.

*Case 17.* AFIL Acc. 1023219. Survival 19 days. A 21-year-old Caucasian male. Practicing holding his breath and remaining submerged as long as possible in private pool. Found on bottom by wife. Artificial respiration, with return of spontaneous respiration; but patient remained hospitalized in a comatose, decorticate state until death on nineteenth day. Temperature first day was 108.8°F. Autopsy: Bilateral bronchopneumonia, lung abscesses, and empyema. Brain weight, 1,500 grams. Laminar necrosis of middle layers of cerebral cortex. Softening and severe cell change in lenticular nuclei.

*Case 18.* AFIP Acc. 627596. Survival 19 days. A 29-year-old Filipino male using a homemade diving apparatus in sea water was found unconscious in 10 feet of water and brought to shore apneic. Artificial respiration, with restoration of spontaneous respiration and convulsive movements in a few moments. Hospitalized. Bilateral pulmonary rales. Repeated brief convulsions. Blood pressure 120/80, pulse 88, respiration 34. X-ray examination of chest negative. Electrocardiogram normal. $HCO_3$ 4 mEq/L, 4 hours later 21.1 mEq/L, BUN 22 mg%, chlorides 127 mEq/L, hematocrit 44. Following day, sodium potassium and chlorides normal. White blood cell count 23,000, hematocrit 45. Survived for 19 days in decorticate state with hyperpyrexia. Treatment included oxygen tent constantly, penicillin, and streptomycin. Autopsy: Resolving bronchopneumonia, purulent tracheo bronchitis. Fresh brain weight 1,277 grams. Grossly visible, widespread laminar necrosis of cerebral cortex, most marked in parietal and occipital areas. Focal malacia of hippocampus and basal ganglia. Purkinje cell loss in cerebellum. The necrotic lesions appeared to be of varying ages.

### Comments

Pulmonary edema and hemorrhage are common autopsy findings in victims of obstructive asphyxia; and undoubtedly this mechanism plays a role in the pulmonary pathologic features of the postimmersion syndrome. In the preceding cases, however, an inflammatory component was invariably present, even in those with very short survival. The pneumonitis varied from an early vital reaction through various stages of aspiration pneumonia, occasionally with hyaline membrane formation, to lung abscesses and empyema. It frequently was associated with the aspiration of vomitus and sedimentary debris. Heroic and prolonged artificial respiration probably was injurious to the lung in some cases. Prolonged breathing of pure oxygen under pressure may possibly have had an irritant effect on the lung in some instances.

An apparently favorable clinical situation after rescue and resuscitation may be reversed with dramatic suddenness. The rapid development of pneumonitis and/or the onset of vomiting and further aspiration appear to be responsible for this turn of events and should be anticipated in the clinical management of the survivor of submersion. Case 18, with severe anoxic cerebral necrosis, survived in coma for 19 days. The necrotic lesions appeared to be of various ages, as though there had been a progression of damage after the acute anoxic episode. Such progression of injury might occur if the cerebral circulation were reduced by brain swelling and edema in the postimmersion period. Therapeutic measures aimed at the reduction of cerebral edema should be emphasized to minimize this additional injury.

### Nonfatal Submersion

Because of the discrepancies between the findings in experimental animals drowned under artificial conditions and autopsy findings in humans, it was decided to collect and review the clinical records and lung radiographs of individuals treated in hospitals of the United States Navy and having a diagnosis of nonfatal submersion. Only those cases have been included who required resuscitation. To date the records of 50 cases have been reviewed. Except for

Fig. 6. Case 15. Three-day survival. Section of lung to show aspiration pneumonia. AFIP Neg. 61-5594. ×50.

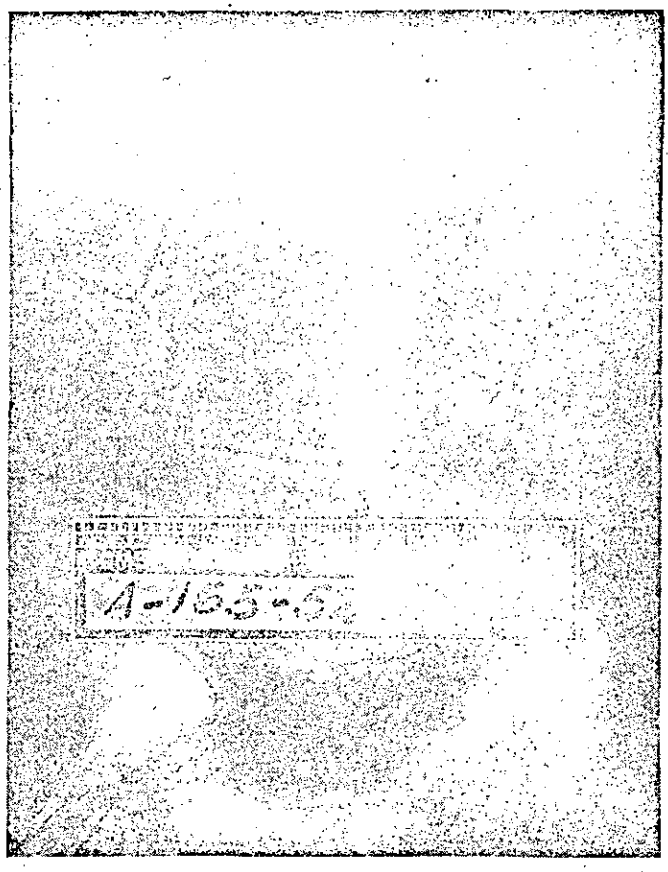

FIG. 7. Case 18. Survival in coma for 19 days after rescue. Gross section of fixed brain to show laminar cerebral cortical necrosis. Tripler General Hospital Neg. 6047.

two female infant victims of near drowning in bathtubs, the patients were all males, ranging in age from 17 to 73 years, with the majority in the late teens or early twenties. Thirty-four of the submersions were in sea water, the remaining 16 in fresh water.

The clinical signs and symptoms of this group, together with those of the 18 fatal cases, are listed in Table 3. The results of hemoglobin and hematocrit determinations, as well as the specific gravities of the first specimen of urine obtained after rescue, are tabulated also, since these data (Table 4) would reflect hemodilution or hemoconcentration if they occurred in human nonfatal cases, as they do in experimental animals whose lungs have been artificially inundated.

The fresh-water near-drowning cases did not show evidence of hemodilution by these criteria. Hemoconcentration was detected in victims of near-drowning in both fresh- and sea-water. Transudation of plasma into the lung would explain the minor degrees of hemoconcentration encountered, since clinically these patients had pulmonary edema.

Significant elevations of serum sodium and chloride were recorded in some of the cases of salt water near-drowning, indicating absorption of these electrolytes from lung or gastrointestinal tract, or both. The levels of these electrolytes recorded in fresh-water cases were lower than those for salt water, but within the range of normal. The number of cases with these data was disappointingly small (Table 5).

Case 17 of the fatal group and an additional nine cases in the nonfatal group illustrate the hazard of a common maneuver in water.[14,15] These individuals were strong swimmers who attempted an endurance underwater swim after hyperventilating. Without any prior distress they "blacked out" under water, sank to the bottom, and

TABLE 3

CLINICAL SIGNS AND SYMPTOMS OF THE POSTIMMERSION SYNDROME

*Central Nervous System*
Coma—variable duration after rescue
Convulsions—common during resuscitation
Trismus
Visual disturbances—occasional complaint first 1 to 2 days
Amnesia
Abnormal reflexes—usually transient
Cephalalgia
Delirium

*Cardiovascular System*
Cardiac arrhythmias—revert with oxygenation
Cardiac arrest—ventricular fibrillation not recorded
Tachycardia
Hypotension—occasional hypertension during asphyxial phase

*Blood*
Hemoconcentration—both fresh and salt water
Hemoglobinemia—rare, transient, fresh water
Leukocytosis

*Respiratory System*
Tachypnea
Dyspnea
Cough
Bloody, frothy sputum
Chest pain
Laryngospasm
Pulmonary rales
Distant breath sounds
Abnormal lung radiograph—common, usually clears in a few days
Cyanosis

*Gastrointestinal System*
Vomiting—common during and after resuscitation
Abdominal distention—swallowed water and air forced into stomach during resuscitation
Intense thirst—sea water

*Genitourinary System*
Albuminuria
Hemoglobinuria—rare

*General*
Fever
Rigor
Acidosis—transient
Hyperchloremia (sea water)—transient
Hypochloremia (fresh water)—transient
Hyperglycemia (asphyxial)
Azotemia

TABLE 4

HEMOGLOBIN, HEMATOCRIT, AND URINE SPECIFIC GRAVITY DETERMINATIONS IN HUMAN NEAR-DROWNING CASES

| Hemoglobin gm/100 cc | | | | Specific Gravity First Urine Specimen | |
|---|---|---|---|---|---|
| Fresh Water Cases | Sea Water Cases | Fresh Water Cases | Sea Water Cases | Fresh Water Cases | Sea Water Cases |
| 12.5 | 13.5 | 50 | 44 | 1.025 | 1.026 |
| 15 | 14.5 | 55 | 43 | 1.022 | 1.017 |
| 18.6 | 14 | 46 | 43 | 1.011 | 1.025 |
| 13 | 14.5 | 53 | 47 | 1.022 | 1.022 |
| 14 | 14 | 55 | 45 | 1.008 | 1.030 |
| 13 | 14.5 | 54 | 49 | 1.023 | 1.007 |
| 12 | 14 | 44 | 47 | 1.021 | 1.024 |
| 13 | 16 | 46 | 52 | 1.032 | 1.017 |
| 14.5 | 14.3 | 65 | 43 | 1.024 | 1.028 |
| 15.9 | 13 | 48 | 40 | 1.008 | 1.008 |
| 21 | 13.3 | 45 | 40 | | 1.011 |
| 15 | 15.5 | | 42 | | 1.020 |
| 15.4 | 15.1 | | 55 | | 1.025 |
| | 13.5 | | 43 | | 1.026 |
| | 12.5 | | 44 | | 1.015 |
| | 14 | | 44 | | 1.026 |
| | 19.8 | | 41 | | 1.022 |
| | 14.5 | | 45 | | 1.029 |
| | 14.5 | | 51 | | 1.020 |
| | 15.3 | | 48 | | 1.007 |
| | 17 | | 45 | | 1.013 |
| | 15.5 | | 41 | | 1.025 |
| | 16.6 | | 45 | | 1.005 |
| | 16.2 | | 47 | | |
| | 14.4 | | 45 | | |

TABLE 5

SERUM ELECTROLYTE DETERMINATIONS IN MILLIEQUIVALENT/LITER IN SEA AND FRESH WATER HUMAN NEAR-DROWNING CASES

| Sodium | | Potassium | | Bicarbonate | | Chloride | |
|---|---|---|---|---|---|---|---|
| Normal = 137–147 mEq/L | | Normal = 4.1–5.6 mEq/L | | Normal = 23–31 mEq/L | | Normal = 96–102 mEq/L | |
| Fresh Water Cases | Sea Water Cases | Fresh Water Cases | Sea Water Cases | Fresh Water Cases | Sea Water Cases | Fresh Water Cases | Sea Water Cases |
| 136 | 142 | 4.3 | 4.3 | 21 | 25 | 103 | 96 |
| 141 | 150 | 6.2 | 4.9 | 26 | 11.5 | 99 | 124 |
| 141 | 158 | 4.7 | 4.9 | 23 | | 105 | 112 |
| 130 | 151 | 5 | 4.5 | 19 | 24.7 | 95 | 127 |
| | 150 | | 3.5 | | 13.8 | 109 | 98 |
| | | | | | | 107 | 108 |
| | | | | | | 102 | 121 |

were rescued by a lifeguard or companion. Those who were successfully resuscitated were able to recount their experience but could give no explanation for the blackout. They were not epileptics nor easily subject to syncope. For want of a better explanation, it is assumed that during hyperventilation they blow off carbon dioxide and during the underwater swim become hypoxic to the point of syncope before sufficient carbon dioxide has accumulated to warn them of the need to oxygenate. This group constitutes 20 per cent of the nonfatal submersion cases studied; and the number of fatal drownings of this type can only be estimated. Instructors and swimmers should be more aware of the danger in this type of activity.

Radiographic abnormalities of the lungs were common, being recorded in 30 of this group of 50 near-drowning cases. Compatible with pulmonary edema and usually of brief duration, they persisted for longer than 2 days, accompanied by fever and leukocytosis, in 22 of the cases. In one instance the lung fields were not clear until the fortieth day. The presence of fever and leukocytosis and the inferences drawn from the fatal cases lead one to conclude that the early pulmonary edema is overlaid by a pneumonitis of variable severity and duration.

Twelve of the cases had a transient albuminuria and/or cylinduria probably resulting from an episode of renal hypoxia. One of these was associated with a rise of BUN to 55 mg% on the fifth day, followed by a fall to normal levels within a few days. There was one instance of what has been called drowning hemoglobinuria.[16]

*Case 19.* An 18-year-old Caucasian male blacked out while swimming in an indoor fresh-water pool with a snorkel mask and was removed from the bottom comatose and apneic, but with feeble heart action. Mouth-to-mouth rescue breathing was administered, and after a few minutes spontaneous breathing began accompanied by partial return of consciousness. He was hospitalized in a hyperactive, delirious, cyanotic, and tachypneic state, coughing up large amounts of bloody, frothy sputum. Blood pressure was unobtainable; temperature 100°, pulse 110, respirations 40. Hematocrit 54, white blood cell count 27,750; blood serum and urine contained hemoglobin. Urine specific gravity 1.023, 2+ protein, positive guaiac. Serum sodium 136, potassium 3.4, chloride 102, $HCO_3$ 21 mEq/L. With positive-pressure administration of oxygen and intravenous administration of aminophylline, vasopressor, sodium bicarbonate (88 mEq), and sodium chloride (200 mEq), there was considerable improvement. The victim gave no history of epilepsy. There were transient lateral deviation of the right eye, bilateral pulmonary rales, and diminished breath sounds; abdomen was distended and tympanitic, and there was a transient positive Babinski sign on the right. Radiograph of chest showed opacities consistent with pulmonary edema. Penicillin was administered. The day following submersion he was still febrile but no longer cyanotic or icteric, he excreted a normal volume of urine negative to analysis, and had a white blood cell count of 21,700. Hematocrit 43. Serum sodium 142, potassium 4.1, bicarbonate 29 mEq/L. The radiograph showed considerable clearing of the lung fields, which was more marked 3 days later. The victim was then afebrile, and he was discharged to his home for an additional 5 days of bed rest.

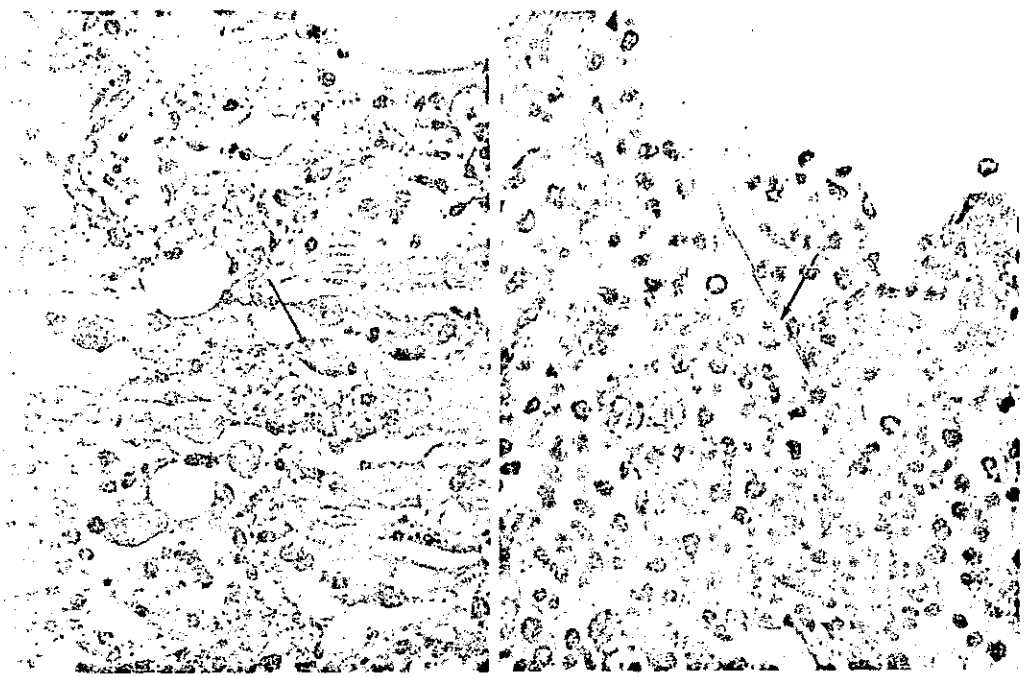

FIG. 8. Case 12 (left) and Case 7 (right). Lung sections from cases of delayed drowning death to show aspirated diatoms. In the left hand figure the small pennate diatom is within an alveolar macrophage. AFIP Negs. 61-5593 and 61-5586. ×440 (left). ×575 (right).

The transient hemolysis in this case was probably caused by absorption of water in the lungs, which was not of sufficient volume to affect the blood volume appreciably or to produce anemia. The slight degree of hemoconcentration (hematocrit 54) resulted from shock and plasma loss into the lungs.

### Treatment of the Rescued

Promising technics of resuscitation have been developed in recent years. The necessity for immediate inflation of the lungs often during the process of rescue has been stressed. Sufficient gaseous exchange to sustain life is possible when only a small amount of lung tissue remains functional. Further inundation of the lungs by aspiration of vomitus and spread of pulmonary edema are the main immediate hazards of the successfully resuscitated. A reversal of the clinical course in these cases may occur unexpectedly and with dramatic suddenness. Therefore, continuous observation in the emergency or recovery-room environment is highly desirable during the first 24 hours of the postresuscitation state. Intermittent positive-pressure breathing with oxygen and a bland antifoaming agent, and tracheal intubation or tracheotomy with suction under local anesthesia if necessary tend to reverse the flow of plasma into the lungs, reduce dead air space, and facilitate tracheobronchial toilet. Because positive-pressure breathing tends to lower the systemic blood pressure and pure oxygen may be a pulmonary irritant, pressure and oxygen concentration should be reduced as oxygen saturation of the blood and degree of pulmonary moisture permit. Adrenal cortical steroids support the patient through a stressful period and tend to depress the inflammatory reaction in the lungs. Broad-spectrum antibiotics should be used because of the likelihood of bacterial contamination of the lungs. Emptying the stomach of air and fluid removes the electrolytes of sea water and reduces the risk of aspirating vomitus and the respiratory and abdominal distress incident to gastric dilatation. Muscle relaxants and passive respiration may be necessary in the face of laryngospasm, trismus, or convulsions. Alkali therapy is indicated if hemolysis has occurred.

Cases have been cited indicating that in both salt-water and fresh-water near-drowning, hemoconcentration due to plasma deficit is seen. Plasma replacement aids in the maintenance of an adequate circulation. Electrolyte therapy will depend on the results of laboratory examinations. Electrolyte changes resulting from asphyxia and aspiration appear to be rapidly corrected if respiratory and cardiac functions are adequate. Osmotic therapy directed toward the reduction of cerebral edema may halt progression of brain damage in comatose cases.

## Conclusions

This study of approximately 3,000 autopsy protocols of drowning victims, with review of the microscopic sections from 500, combined with a study of the clinical records of 50 resuscitated and hospitalized victims of near-drowning, has led the author to the following conclusions:

(1) As in the case of the experimental drowned animal, there is in the acutely fatal human drowning case an interchange of water and electrolytes between the alveoli and the blood; and there is an escape of plasma into the lung.

(2) An additional event of considerable importance in the clinical managemen of the rescued and resuscitated is the frequent aspiration during drowning of mineral debris, aquatic flora and fauna, and vomitus into the lung.

(3) The acute pulmonary edema of the resuscitated victim of near-drowning is accompanied by a pneumonitis of rapid onset, which usually resolves but may progress to lung abscess and empyema.

(4) Anoxic cerebral necrosis following near-drowning occurs rarely.

(5) In the revivable near-drowning victim profound blood volume changes and electrolyte imbalances are not a great problem; though hemoconcentration caused by pulmonary edema is seen in both fresh- and sea-water cases. Transient cardiac irregularities and asystole are encountered; but ventricular fibrillation, though it may occur, has not been noted.

(6) Hemoglobinuria may be associated with near-drowning in fluids both hypertonic and hypotonic to the blood.

(7) Transient or fatal renal dysfunction may occur after submersion in fresh and salt water. The lesion at autopsy is an acute tubular necrosis similar to that seen in shock and other types of renal hypoxia.

(8) The swimmer who hyperventilates before attempting an endurance underwater swim runs the risk of syncope and drowning.

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# Drowning by Total Immersion

## Effects on Pulmonary Surfactant of Distilled Water, Isotonic Saline, and Sea Water

*Samuel T. Giammona, MD, and Jerome H. Modell, MD, Miami, Fla*

DEATH by drowning is one of the major causes of childhood mortality. Studies of the mechanisms of drowning have demonstrated that two types of death may occur.[1] Asphyxia without fluid aspiration is responsible for less than 10% of drowning deaths, but fluid aspiration occurs in about 80% to 90% of drowning victims.[2]

The pathophysiological changes which occur during drowning with fluid aspiration depend upon both the composition and volume of fluid aspirated.[3-5] The most consistent finding in studies of drowning by aspiration of fluid is acute asphyxia with persistent arterial hypoxemia.[3-7] This suggests that alveolar capillary membrane derangement occurs. This study was designed to see the effects of drowning by total immersion in distilled water, distilled water with chlorine, isotonic saline, and sea water on extracts of the alveolar lining layer (pulmonary surfactant).

### Methods

Twenty mongrel dogs weighing 16 to 29 kg and in good physical condition were divided into groups of five according to the type of fluid aspirated.

**Group 1.**—These were given isotonic saline (NS) solution (0.9%).

**Group 2.**—These were given distilled water (DW).

**Group 3.**—These were given chlorinated distilled water (DWC), distilled water to which five parts per million of chlorine (tri-chloro-s-triazinetrione) was added on the day of the experiment.

**Group 4.**—These were given sea water (SW), obtained from the Atlantic and containing sodium 509 mEq/liter and chloride 561 mEq/liter.

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From the departments of pediatrics and anesthesiology, University of Miami School of Medicine, and Jackson Memorial Hospital, Miami, Fla.
Reprint requests to PO Box 875, Biscayne Annex, Miami, Fla 33152 (Dr. Giammona).

The animals were anesthetized with 50 mg increments of 2.5% sodium thiopental given intravenously to produce basal narcosis (cessation of spontaneous movement, respiration, and lid reflex remaining active). Lead 2 of the electrocardiogram was monitored continually. A surgical cut down was performed on the left femoral artery and a siliconized polyethylene catheter (0.066 inches, diameter) was threaded into the mid-abdominal aorta. The catheter was connected to a pressure transducer and a direct writing recorder and aortic pressure was monitored throughout the experiment. The trachea was intubated under direct vision; the endotracheal tube cuff was inflated; and the animals permitted to breathe spontaneously. The endotracheal tube was connected via a Y adapter to a reservoir containing a measured quantity of water and to a breathing bypass, as described previously.[7] At zero time the bypass was occluded and each dog was allowed to spontaneously aspirate unlimited quantities of fluid. The animals remained under fluid continuously until death occurred as indicated by cessation of aortic pulsation recorded by the aortic catheter pressure system. At death, the reservoir was clamped and the fluid in the trachea was allowed to drain spontaneously with the dog in a supine position. The total volume of fluid aspirated minus the volume of the tracheal drainage was considered the total immersion volume. Autopsy was performed on animals and lungs were removed and weighed.

Pulmonary surfactant was extracted within two hours after death by the modified foam fractionation method.[8] Ten milligrams of the dried foam from the lung extracts were placed in 200 ml of saline and allowed to age one hour to form a stable surface film at room temperature (22 C) prior to measurement. The surface tensions of pulmonary surfactant present in the tracheal drainage fluid were measured separately. Fifty milliliters of the tracheal drainage fluid was added to 150 ml of saline in a teflon lined tray and allowed to age one hour prior to surface tension measurements. All measurements were performed on a modified Wilhelmy Balance as the surface area was compressed from 100 sq cm to 20 sq cm at a frequency of 1 cycle every 90 seconds. The surface

area-surface tension loop was recorded on a direct writing XY recorder.

A surfactant activity index (SAI) was calculated for each of the extracts and tracheal fluid samples according to the equation suggested by Clements and co-workers,

$$SAI = 2\ (ST\ maximum - ST\ minimum)/ST\ maximum + ST\ minimum.$$

The maximum surface tension was that observed on expansion of the surface film to 100 $cm^2$ and the minimum tension was that observed on compressing the film to 20 $cm^2$. The range of possible values for SAI is from 0 to 2. Lung extracts with normal surfactant activity have an SAI greater than 1.25 and lung extracts with loss of surface activity have a low SAI.[9] The SAI thus serves as an index of surface compressibility with high values indicating that alveolar lining layers are capable of maintaining a stable surface tension-surface area relationship promoting alveolar stability.

## Results

Apnea occurred within 10 seconds of fluid aspiration in all animals and persisted from 10 to 40 seconds. This was followed in the NS and SW groups by a marked hyperventilation of the fluid which quickly became a foamy froth. In the DW and DWC groups the fluid appeared blood-tinged in eight of the dogs and the amount of froth was not as marked.

Ventricular fibrillation developed in eight of the animals (four DW, three DWC, and one SW). The time from onset of aspiration to death for each of the four groups was: $5 \pm 3$ min DW, $5 \pm 2$ min DWC, $9 \pm 2$ min NS, and $8 \pm 3$ min SW.

**Isotonic Saline (Group 1).**—The mean quantity of fluid absorbed or retained was $17.2 + 4.0$ ml/kg. At autopsy the lungs were heavy and appeared edematous with purplish red colored dependent portions. The mean ratio of lung weight to body weight was $21.0 \pm 3.6$ gm/kg. The lungs grossly did not appear to contain air in the dependent portions, however, during the course of foam fractionation, these areas of the lungs did inflate and deflate evenly. Surface tensions of lung extracts were normal ($9 \pm 3$ dynes/cm minimum, $56 \pm 7$ dynes/cm maximum). Tracheal fluid also had normal surface tensions ($5 \pm 3$ dynes/cm minimum, $63 \pm 7$ dynes/cm maximum). The SAI of lung extracts was $1.45 \pm 0.10$; SAI tracheal drainage fluid, $1.69 \pm 0.14$ (Table 1).

**Distilled Water (Group 2).**—The mean quantity of fluid absorbed or retained was $35.1 \pm 5.3$ ml/kg. Multiple small areas of collapsed lung and petechial hemorrhage were found in the upper lobes, in addition to the type of pathological findings described in the dependent portions of the lungs in group 1. The mean ratio of lung weight to body weight was $34.9 \pm 5.3$ gm/kg. Some areas of the lungs were difficult to inflate during foam fractionation and collapsed prematurely during deflation. The surface tension of the foamed extract was $21 \pm 6$ dynes/cm minimum, $58 \pm 9$ dynes/cm maximum. The surface tension of the tracheal fluid was $30 \pm 3$ dynes/cm minimum and $54 \pm 5$ dynes/cm maximum. The SAI of the lung extract was $1.00 \pm 0.30$; SAI of tracheal drainage fluid, $0.57 \pm 0.16$ (Table 2).

**Chlorinated Distilled Water (Group 3).**—The mean quantity of fluid absorbed or retained was $25.5 \pm 4.4$ ml/kg. Multiple areas of collapsed lung and petechial hemorrhages were observed and the lungs appeared similar to those in the distilled water group. There was difficulty on inflation and premature collapse during deflation. The mean ratio of the lung weight to body weight was $38.7 \pm 4.7$ gm/kg. The surface tension of the lung extract was $19 \pm 4$ dynes/cm minimum and $49 \pm 4$ dynes/cm maximum. The surface tension of the tracheal drainage fluid was $27 \pm 4$ dynes/cm minimum and $58 \pm 3$ dynes/cm maximum. The SAI of the lung extract was $0.89 \pm 0.22$. The SAI of the tracheal fluid was $0.75 \pm 0.13$ (Table 3).

**Sea Water (Group 4).**—The mean quantity absorbed or retained was $6.4 \pm 4.8$ ml/kg. The lungs of the animals in the sea water group were very similar in appearance to those of the saline group, except they were heavier and of deeper color. The mean ratio of lung weight to body weight was $35.4 \pm 3.6$ gm/kg. Surface tension of lung extract was $7 \pm 4$ dynes/cm minimum, $45 \pm 9$ dynes/cm

**Table 1.—Drownings With Isotonic Saline**

| Dog | Body Wt (kg) | Lung Wt/ Body Wt (gm/kg) | Vol Aspirated (ml/kg) | Time to Death (min) | Surface Tension: Lung Extracts (dynes/cm) Min | Surface Tension: Lung Extracts (dynes/cm) Max | Surface Tension: Tracheal Fluid (dynes/cm) Min | Surface Tension: Tracheal Fluid (dynes/cm) Max | Surface Activity Index: Lung Extract | Surface Activity Index: Tracheal Fluid |
|---|---|---|---|---|---|---|---|---|---|---|
| 100 | 25.0 | 22.0 | 21.3 | 9.0 | 10 | 50 | 2 | 59 | 1.33 | 1.87 |
| 101 | 20.5 | 26.8 | 19.2 | 10.5 | 9 | 51 | 10 | 65 | 1.40 | 1.47 |
| 102 | 25.5 | 17.9 | 13.7 | 8.5 | 8 | 66 | 4 | 53 | 1.57 | 1.72 |
| 103 | 18.6 | 19.6 | 12.1 | 9.5 | 9 | 56 | 6 | 70 | 1.45 | 1.68 |
| 104 | 19.1 | 18.8 | 19.5 | 9.0 | 8 | 59 | 5 | 70 | 1.52 | 1.73 |
| Mean | 21.7 | 21.0 | 17.2 | 9.3 | 9.0 | 56.0 | 5.0 | 63.0 | 1.45 | 1.69 |
| SD | ±3.3 | ±3.6 | ±4.0 | ±1.5 | ±3.0 | ±7.0 | ±3.0 | ±7.0 | ±0.10 | ±0.14 |

**Table 2.—Drownings With Distilled Water**

| Dog | Body Wt (kg) | Lung Wt/ Body Wt (gm/kg) | Vol Aspirated (ml/kg) | Time to Death (min) | Surface Tension: Lung Extracts (dynes/cm) Min | Surface Tension: Lung Extracts (dynes/cm) Max | Surface Tension: Tracheal Fluid (dynes/cm) Min | Surface Tension: Tracheal Fluid (dynes/cm) Max | Surface Activity Index: Lung Extract | Surface Activity Index: Tracheal Fluid |
|---|---|---|---|---|---|---|---|---|---|---|
| 105 | 16.4 | 27.7 | 37.2 | 2.5 | 23 | 47 | 26 | 62 | 0.69 | 0.82 |
| 110 | 23.6 | 35.0 | 42.9 | 8.0 | 13 | 65 | 31 | 52 | 1.33 | 0.51 |
| 111 | 19.5 | 33.2 | 34.6 | 8.1 | 21 | 69 | 35 | 51 | 1.07 | 0.37 |
| 112 | 22.7 | 42.4 | 30.6 | 3.3 | 30 | 56 | 30 | 55 | 0.61 | 0.59 |
| 113 | 20.5 | 36.4 | 30.0 | 2.3 | 17 | 55 | 30 | 52 | 1.05 | 0.54 |
| Mean | 20.5 | 34.9 | 35.1 | 4.8 | 21.0 | 58.0 | 30.0 | 54.0 | 1.00 | 0.57 |
| SD | ±2.8 | ±5.3 | ±5.3 | ±3.0 | ±6.0 | ±9.0 | ±3.0 | ±5.0 | ±0.30 | ±0.16 |

**Table 3.—Drownings With Distilled Water (Chlorine)**

| Dog | Body Wt (kg) | Lung Wt/ Body Wt (gm/kg) | Vol Aspirated (ml/kg) | Time to Death (min) | Surface Tension: Lung Extracts (dynes/cm) Min | Surface Tension: Lung Extracts (dynes/cm) Max | Surface Tension: Tracheal Fluid (dynes/cm) Min | Surface Tension: Tracheal Fluid (dynes/cm) Max | Surface Activity Index: Lung Extract | Surface Activity Index: Tracheal Fluid |
|---|---|---|---|---|---|---|---|---|---|---|
| 106 | 21.6 | 42.2 | 30.7 | 3.4 | 21 | 44 | 28 | 60 | 0.71 | 0.73 |
| 107 | 21.6 | 45.2 | 25.5 | 6.3 | 21 | 49 | 26 | 62 | 0.80 | 0.82 |
| 108 | 26.8 | 35.0 | 20.3 | 4.0 | 21 | 50 | 25 | 56 | 0.82 | 0.77 |
| 109 | 19.1 | 36.0 | 22.1 | 7.7 | 12 | 55 | 21 | 55 | 1.28 | 0.90 |
| 114 | 21.6 | 35.0 | 29.0 | 1.5 | 20 | 49 | 33 | 57 | 0.84 | 0.53 |
| Mean | 21.1 | 38.7 | 25.5 | 4.5 | 19.0 | 49.0 | 27.0 | 58.0 | 0.89 | 0.75 |
| SD | ±2.8 | ±4.7 | ±4.4 | ±2.4 | ±4.0 | ±4.0 | ±4.0 | ±3.0 | ±0.22 | ±0.13 |

**Table 4.—Drownings With Sea Water**

| Dog | Body Wt (kg) | Lung Wt/ Body Wt (gm/kg) | Vol Aspirated (ml/kg) | Time to Death (min) | Surface Tension: Lung Extracts (dynes/cm) Min | Surface Tension: Lung Extracts (dynes/cm) Max | Surface Tension: Tracheal Fluid (dynes/cm) Min | Surface Tension: Tracheal Fluid (dynes/cm) Max | Surface Activity Index: Lung Extract | Surface Activity Index: Tracheal Fluid |
|---|---|---|---|---|---|---|---|---|---|---|
| 115 | 19.5 | 38.5 | 7.8 | 10.0 | 7 | 40 | 2 | 41 | 1.40 | 1.81 |
| 116 | 21.8 | 34.4 | 13.5 | 2.3 | 9 | 38 | 5 | 37 | 1.23 | 1.52 |
| 117 | 27.3 | 39.2 | 1.2 | 10.0 | 10 | 42 | 10 | 46 | 1.23 | 1.29 |
| 118 | 28.6 | 30.3 | 2.7 | 8.3 | 7 | 60 | 10 | 61 | 1.58 | 1.44 |
| 119 | 22.7 | 34.8 | 6.8 | 9.4 | 1 | 45 | 8 | 45 | 1.91 | 1.40 |
| Mean | 24 | 35.4 | 6.4 | 8.0 | 7.0 | 45.0 | 7.0 | 46.0 | 1.47 | 1.49 |
| SD | ±3.8 | ±3.6 | ±4.8 | ±3.3 | ±4.0 | ±9.0 | ±4.0 | ±9.0 | ±0.30 | ±0.20 |

maximum. Surface tension of tracheal drainage fluid was 7 ± 4 dynes/cm minimum, 46 ± 9 dynes/cm maximum; SAI of lung extract was 1.47 ± 0.30 and of tracheal fluid was 1.49 ± 0.20 (Table 4).

## Comment

The effects of drowning in hypotonic and hypertonic fluids on serum electrolyte concentrations have been studied by many.[2-7] Swann et al reported the effects of drowning by total immersion in sea water in dogs to be quite different from those following aspiration of fresh water. While sea water caused fulminating pulmonary edema, death after total immersion in fresh water was most frequently due to ventricular fibrillation from electrolyte changes superimposed on hypoxia.[10,11] Fuller, in a review of case reports in humans who suffered fresh water drowning, found the main pathological finding to be pulmonary edema rather than intravascular complications of water absorption.[6]

The extensive changes in serum electrolytes reported during experimental drowning by total immersion are due to movement of fluid and electrolytes across the alveolar capillary interphase. The difference in the ratio of lung weight to body weight in the four groups in this study reflect some of the fluid changes that occur. The lung weights of the animals in the saline group were significantly less ($P < 0.001$) than the other three groups, since the isotonic fluid is quickly equilibrated with plasma. In the sea water group, the lung/body weight ratio is greater since the hypertonic fluid draws fluid into the lungs from the plasma. Since more distilled water was absorbed than saline or sea water, the fact that the lungs of the animals in groups 2 and 3 were heavier than those in group 1 appears inconsistent. This apparent discrepancy can be explained. Death occurred too rapidly for fluid to be completely removed from interstitial spaces of the lung. This accounts for increased weight.

Karpovich in studying rats, guinea pigs, and cats subjected to total immersion, observed that the tracheobronchial tree was filled with water and froth.[12] By using a colored solution he was able to demonstrate the presence of the solution throughout the alveolar surfaces of the lungs. Upon attempting to reinflate the lungs, full inflation could not be accomplished even under high pressure. He assumed this was due to the resistance of the air bubbles found in the froth and mucus blocking the respiratory passages. Huber and Finley in 1964, demonstrated that a single lobe of the dog's lung can be lavaged with isotonic saline solution without deleterious effects to the animal after resuscitation except for the presence of atelectasis in the lobe following repeated washings.[13] In the present study, isotonic saline and sea water were able to wash out intact pulmonary surfactant, as the tracheal drainage fluid demonstrated normal surface activity. This washing out was not complete as normal surface activity was present in the foam removed from the intact lung after death. Distilled water groups (2 and 3), however, showed abnormal surface activity in both the tracheal fluid that was passively drained and the foamed extract from the lung. Thus there is marked alteration in the surface tension properties of lung extracts from dogs after total immersion in distilled water with or without chlorine.

Bondurant and Clements have demonstrated that distilled water in vitro inactivates normal pulmonary surfactant.[14,15] These changes have been ascribed to interference with the ionic subphase of the surface film resulting in abnormal surfactant activity by Scarpelli et al[16] who in their studies demonstrated that a minimum concentration of sodium and chloride (0.15 to 0.2N) was essential for normal surface tension measurements. The results of the present study may be best explained by alterations in the ionic contents of the subphase of the alveolar lining layer in the DW and DWC groups.

The alterations found in the foamed ex-

tracts in which distilled water was used suggests that there was direct damage to the pulmonary surfactant lining the alveolar cell wall or that there was some alteration in the extractibility of the pulmonary surfactant following exposure to distilled water. The changes found in the pulmonary surfactant would be conducive to developing uninflatable lungs in the animals exposed to distilled water. This would be consistent with the findings observed at autopsy in these animals.

The majority of animals which aspirated DW and DWC (seven of ten) died rapidly with ventricular fibrillation. The blood-tinged frothy fluid present in the tracheal bronchial tree of these animals probably represented pulmonary edema. It has been demonstrated experimentally that loss of surface activity in lung extracts is frequently associated with lesions resulting in pulmonary edema.[17,18] In this study, fluid from animals did not demonstrate normal surface activity, but tracheal fluid drained from the normal saline and sea water aspiration groups had normal surface tensions. Since death occurred rapidly in these animals, these findings are consistent with the thesis that following aspiration of distilled water, pulmonary edema may result from a physical or chemical change in the pulmonary surfactant as well as from circulatory overload.

The exact mechanisms for the alteration of pulmonary surfactant following distilled water aspiration are not known. Although total immersion drowning may exaggerate the pathophysiological changes found, in near-drownings there may also be similar mechanisms affecting the pulmonary surfactant activity in areas directly exposed to distilled water. Studies of these mechanisms may have bearing on therapy used for drowning victims.

## Summary

The effect of drowning by total immersion with distilled water (with and without chlorine), isotonic saline, and sea water on the surface activity of pulmonary surfactant was studied in dogs. Distilled water was found to alter the surface tension measurements of lung extracts. While surfactant was washed out of the lungs with isotonic saline and sea water aspiration, the compression characteristics of surfactant were not altered.

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# Ventilation and circulation after fluid aspiration[1]

DENIS F. J. HALMAGYI[2] AND H. J. H. COLEBATCH[3]
*Department of Medicine, University of Sydney, Sydney, New South Wales, Australia*

HALMAGYI, D. F. J. AND H. J. H. COLEBATCH. *Ventilation and circulation after fluid aspiration.* J. Appl. Physiol. 16(1): 35–40. 1961.—Ventilated volumes, arterial oxygen content and carbon dioxide tension, cardiac output, 'effective' pulmonary capillary flow, systemic arterial, pulmonary arterial and pulmonary arterial wedge pressures were determined before and after the intratracheal administration of 1–3 ml/kg body weight of fresh and sea water in 23 intact and 14 vagotomized sheep in light thiopentone anesthesia. Five untreated animals served as controls. A precipitous fall and a prolonged depression of arterial oxygen saturation was observed, largely independent of the amount of fluid inhaled. Hypoxemia was due to a gross increase in venous admixture resulting from the perfusion of large unventilated portions of the lungs. Fluid aspiration was also followed by a significant degree of pulmonary hypertension caused by arteriolar constriction in the lungs. Pulmonary hypertension was found to be unrelated to hypoxia.

SUBMERGED ANIMALS or animals whose lungs were literally flooded with large quantities (70–200 ml/kg) of fresh or sea water have been used by previous workers to study the effect of aspiration of fluid into the lungs (1–6). Death in these experiments occurred within a few minutes and was due to airway obstruction and/or to ventricular fibrillation induced by electrolyte changes.

Under natural conditions fluid aspiration into the airways is bound to precipitate laryngospasm in the conscious man or animal. In the unconscious subject the amount of material available for inhalation at one time may be limited. It therefore appears likely that in many cases only small amounts of fluid enter the respiratory tract. The effects of this type of aspiration have hitherto not been investigated.

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[2] Adolph Basser Research Fellow of the Royal Australasian College of Physicians.
[3] Joint Coal Board Research Fellow.

It is the purpose of this paper to describe some of the cardiopulmonary consequences of inhaling limited quantities of fresh and sea water in lightly anesthetized sheep.

## METHODS

Sixty-two experiments performed on thirty-seven sheep weighing 30–54 kg are included in this study. The fasting, supine animals were anesthetized with 10–15 mg/kg of thiopentone intravenously. This dose was followed by a continuous intravenous saline drip of 2.0–2.5 ml/min. containing 0.20–0.25 mg/kg/min. Thiopentone and 0.15 mg/kg/min. heparin. A cuffed Magill tube (no. 10-12) was used for intubation of the trachea. A no. 7 cardiac catheter was passed via the femoral vein into the pulmonary artery. A cannula was inserted into the femoral artery and a thermometer into the rectum.

After a control period, a thin polythene tube attached to a syringe was passed to just beyond the distal end of the endotracheal tube. In five animals (*group A*) the polythene tube was then withdrawn and no fluid was administered. These animals served as controls. Fresh water (1 ml/kg) was injected into the trachea of 10 sheep (*group B*) and sea water (1 ml/kg) into the trachea of 8 (*group C*). Measurements were carried out 5 and 30 minutes after the fluid injection. Forty minutes later, six animals of *group B* (small, fresh) were given 3 ml/kg fresh water (*group D*) and six animals of *group C* (small, sea), 2.5 ml/kg sea water (*group E*).

A catheter was introduced into the bronchus of the left or right lower lobe through a bronchoscope in six additional animals. The catheter was firmly wedged into the bronchus in order to prevent regurgitation. The bronchoscope was then removed and the endotracheal tube inserted. Fresh water (1 ml/kg) was injected through the catheter (*group F*). Measurements in *groups D, E* and *F* were repeated only at 5 minutes.

Bilateral cervical vagotomy was performed in 14 sheep. In six of these, 1 ml/kg fresh water was injected into the trachea (*group G*); in seven others, 1 ml/kg sea water (*group H*). Fresh water (3 ml/kg) was administered to

TABLE 1. *Mean Changes in Ventilation and Circulation in Intact and Vagotomized Sheep Following Intratracheal Administration of Fresh and Sea Water*

| Group | Min. After Inhalation | A (5) | B (10) | C (8) | D (5) | E (6) | F (6) | G (6) | H (7) | I (5) | J (8) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $Sa_{O_2}$, % | 0 | 81.3 | 85.4 | 83.8 | 80.7 | 60.9 | 86.7 | 88.1 | 89.2 | 87.7 | 72.8 |
| | 5 | 82.7 | 67.1† | 58.4† | 50.2* | 32.4* | 87.7 | 76.6* | 73.2* | 52.6† | 55.2† |
| | 30 | 81.4 | 68.8† | 61.2† | | | | 80.1† | 78.4† | | |
| $\dot{V}_E$, l/min. m² BSA, BTPS | 0 | 6.36 | 7.26 | 6.37 | 7.49 | 10.30 | 7.81 | 8.73 | 7.53 | 10.03 | 9.90 |
| | 5 | 6.26 | 10.04 | 10.48* | 15.87* | 13.23 | 8.39 | 14.95 | 9.50* | 11.55 | 11.34 |
| | 30 | 6.43 | 8.35 | 7.56 | | | | 9.90 | 9.54* | | |
| $\dot{V}_A$, l/min/m² BSA, BTPS | 0 | 2.74 | 2.71 | 2.37 | 3.11 | 3.16 | 2.35 | 2.59 | 2.42 | 2.86 | 2.75 |
| | 5 | 2.64 | 3.75* | 3.38 | 4.38 | 2.83 | 2.58 | 3.46 | 2.90 | 2.64 | 2.31 |
| | 30 | 2.55 | 3.00 | 2.55 | | | | 2.74 | 2.85 | | |
| $Pa_{CO_2}$, mm Hg | 0 | 38.8 | 40.4 | 42.3 | 36.2 | 41.9 | 38.8 | 38.5 | 40.6 | 38.4 | 40.2 |
| | 5 | 39.8 | 38.0 | 42.5 | 36.3 | 48.8 | 36.9 | 38.5 | 37.9 | 48.4* | 43.1 |
| | 30 | 41.1 | 38.9 | 41.9 | | | | 38.5 | 37.7 | | |
| $\dot{Q}p.a.$, l/min/m² BSA | 0 | 3.10 | 3.65 | 3.69 | 2.75 | 3.89 | 3.02 | 2.91 | 3.33 | 2.65 | 3.36 |
| | 5 | 3.20 | 3.66 | 3.61 | 4.01† | 5.05 | 3.01 | 3.27 | 3.77 | 3.47 | 3.56 |
| | 30 | 2.94 | 3.57 | 3.63 | | | | 2.75 | 3.57 | | |
| $\dot{Q}s$, % of $\dot{Q}p.a.$ | 0 | 30 | 21 | 24 | 30 | 51 | 18 | 17 | 13 | 16 | 39 |
| | 5 | 28 | 48† | 52† | 62* | 75* | 18 | 34* | 39† | 57† | 56† |
| | 30 | 30 | 46† | 52† | | | | 29* | 35† | | |
| $\bar{P}p.a.$, mm Hg | 0 | 9 | 13 | 12 | 15 | 14 | 15 | 13 | 11 | 15 | 13 |
| | 5 | 8 | 21† | 18† | 22† | 19† | 18 | 19† | 12 | 25* | 16† |
| | 30 | 8 | 16† | 14 | | | | 15 | 12 | | |
| $R_{pulm}$, dynes sec. cm$^{-5}$/m² BSA | 0 | 232 | 286 | 291 | 441 | 326 | 391 | 370 | 270 | 454 | 316 |
| | 5 | 200 | 453† | 436* | 464 | 343 | 484 | 490* | 285 | 591 | 391 |
| | 30 | 218 | 391† | 340 | | | | 452 | 290 | | |

*Groups A–F:* intact animals. *A* = untreated controls; *B* = 1 ml/kg fresh water intratracheally; *C* = 1 ml/kg sea water intratracheally; *D* = 3 ml/kg fresh water intratracheally; *E* = 2.5 ml/kg sea water intratracheally; *F* = 1 ml/kg fresh water into lower lobe. *Groups G–J:* vagotomized animals. *G* = 1 ml/kg fresh water intratracheally; *H* = 1 ml/kg sea water intratracheally; *I* = 3 ml/kg fresh water intratracheally; *J* = 2.5 ml/kg sea water intratracheally. Numbers in parentheses indicate no. of animals. $\dot{Q}p.a.$ = pulmonary arterial blood flow; $\dot{Q}s$ = venous admixture; $\bar{P}p.a.$ = mean pulmonary arterial pressure; $R_{pulm}$ = total pulmonary arterial resistance. 0 = control measurement. *† Significance of difference between values at 0 and 5, 0 and 30 min. (* < *P* .05; † < *P* .01).

five animals of *group G* (vagotomized, small, fresh) 40 minutes after the small dose (*group I*); to all animals of *group H* (vagotomized, small, sea) and to still another one, 2.5 ml/kg sea water was injected into the trachea 40 minutes following the small dose (*group J*).

Oxygen content of the blood was determined by Gordy and Drabkin's method (7), using a Unicam S.P. 600 spectrophotometer. The method was recalibrated for sheep blood. Blood carbon dioxide content was determined manometrically (8); blood pH was measured by using a Stadie cell with a glass electrode and a Cambridge meter as reported previously from this laboratory (9). $Pa_{CO_2}$ was read from the nomogram of Singer and Hastings (10). Expired air was collected for 1½–2½ minutes in Douglas bags; their contents were measured and analyzed by the Haldane method.

Pressures were measured by Southern capacitance manometers and amplifiers and recorded on a four-channel Both pen-recorder. The reference level was a point 4 inches above the back of the supine animal. Pulmonary arterial pressure (Pp.a.) was measured in all experiments. In some cases pulmonary arterial wedge pressure (Pp.a.w.) and femoral arterial pressure (Pf.a.) were determined in addition. Pressures were measured preceding and following the determination of cardiac output; the arithmetical mean of these two measurements was expressed in mm Hg and used for further calculations. In only one stage of these experiments (immediately following fluid administration) were these two readings found to differ.

Blood samples were taken in the mid-period of ventilation measurements. The Fick principle was used to calculate pulmonary arterial blood flow ($\dot{Q}p.a.$). The shunt equation ($Cc_{O_2} - Ca_{O_2}/Cc_{O_2} - C\bar{v}_{O_2}$) was used to calculate venous admixture ($\dot{Q}s$) as percentage of $\dot{Q}p.a.$ $Cc_{O_2}$ ($O_2$ content of pulmonary capillary blood)

was estimated by converting $PA_{O_2}$ into saturation with the aid of Bartels' and Harms' nomogram for the sheep (11). $PA_{O_2}$ was obtained by the alveolar air equation (12).

Total pulmonary ($R_{pulm}$), pulmonary vascular (Rp.v.) and systemic ($R_{syst}$) resistances were calculated by the usual formulas and expressed in dynes sec. $cm^{-5}$. Blood flows, ventilated volumes and resistances are expressed on basis of 1 $m^2$ BSA. The latter was calculated by using the following formula: $BSA(cm^2) = 8.3\sqrt[3]{w^2}$ where w = body weight in grams (12). Symbols not explained here correspond to the recommendations of Pappenheimer *et al.* (13).

## RESULTS

Most of the results are summarized in table 1.

### *Mortality Rate*

The intratracheal administration of 1–3 ml/kg fresh or sea water proved fatal in 8–48 experiments. (At a later stage effective measures were found to prevent death. These will be described in a subsequent paper.) In only one instance was death due to instillation of fresh water; a mechanical obstruction of the airways occurred. Sea water was responsible for death in 4–8 intact and 3–13 vagotomized sheep. Death in these cases followed on respiratory arrest. The electrocardiogram and pressure tracings in the femoral and pulmonary arteries were obtainable for a period occasionally exceeding 15 minutes following the onset of apnea.

### *Arterial Hypoxemia*

*Intact animals.* An immediate drop in $Sa_{O_2}$ occurred after both fresh and sea water. The extent of the drop was not markedly different after the administration of sea or fresh water, small or large amounts. In the large quantity groups (*D* and *E*), however, the starting values of $Sa_{O_2}$ were considerably lower than those in the small quantity groups (*B* and *C*). Hypoxemia was still present at 30 minutes following small amounts of fresh (*group B*) and sea (*group C*) water. No hypoxemia occurred following the injection of 1 ml/kg fresh water into the lower lobe (*group F*). The speed of recovery of $Sa_{O_2}$ is shown in table 2.

*Vagotomized animals.* A significant drop in $Sa_{O_2}$ occurred in all groups though the resulting hypoxemia was less severe than in the intact animals. Hypoxemia at 5 minutes was not significantly different in *groups B* (intact, small, fresh) and *G* (vagotomized, small, fresh) or in *groups C* (intact, small, sea) and *H* (vagotomized, small, sea). At 30 minutes $Sa_{O_2}$ was significantly higher in *group G* (vagotomized, small, fresh) than in *group B* (intact, small, fresh) ($P = .02$), and in *group H* (vagotomized, small, sea) than in *group C* (intact, small, sea) ($P = .05$).

TABLE 2. *Speed of Recovery of Hypoxemia Following Intratracheal Administration of 1 ml/kg of Fresh and Sea Water*

| Time, min. | Arterial $O_2$ Saturation, % | |
|---|---|---|
| | Fresh water | Sea water |
| 0 | 77.1 | 82.8 |
| 5 | 62.5 | 48.9 |
| 30 | 65.5 | 54.1 |
| 60 | 72.2 | 68.3 |
| 90 | 74.9 | 72.3 |

Mean changes derived from 4 experiments.

### *Ventilation*

*Intact animals.* $\dot{V}_E$ increased significantly at 5 minutes in *groups C* (small, sea) and *D* (large, fresh). In the other groups the rise was not statistically significant.

*Vagotomized animals.* The changes in *groups G* (small, fresh) and *H* (small, sea) were essentially similar to those seen in their intact counterparts (*groups B* and *C*). Contrary to the finding in *group D* (intact, large, fresh), no change occurred in *group I* (vagotomized, large, fresh). The difference between the ventilatory response of the two latter groups was statistically significant ($P = .05$).

### *Alveolar Ventilation*

*Intact animals.* An increase occurred in all groups except *E* (large, sea). The rise, however, was significant only at 5 minutes in *group B* (small, fresh).

*Vagotomized animals.* None of the changes was statistically significant.

### *Arterial $P_{CO_2}$*

*Intact animals.* No significant changes occurred.

*Vagotomized animals.* A significant increase in *group I* (large, fresh) only.

### *Pulmonary Arterial Blood Flow*

$\dot{Q}$p.a. remained unaffected by small quantities of inhaled fluid in both the intact and the vagotomized animals. The intratracheal injection of large amounts of fluid was followed by a rise in $\dot{Q}$p.a. in both categories.

### *Venous Admixture*

No change occurred in *groups A* (controls) and *F* (fluid into one lobe). In all other groups and throughout all periods Qs increased significantly.

### *Pulmonary Arterial Pressure*

*Intact animals.* At 5 minutes the rise was significant in all groups but *F* (fluid into one lobe). If, however, pressure changes occurring between 0 and 5 minutes were compared in *groups A* (controls) and *F* (fluid into one

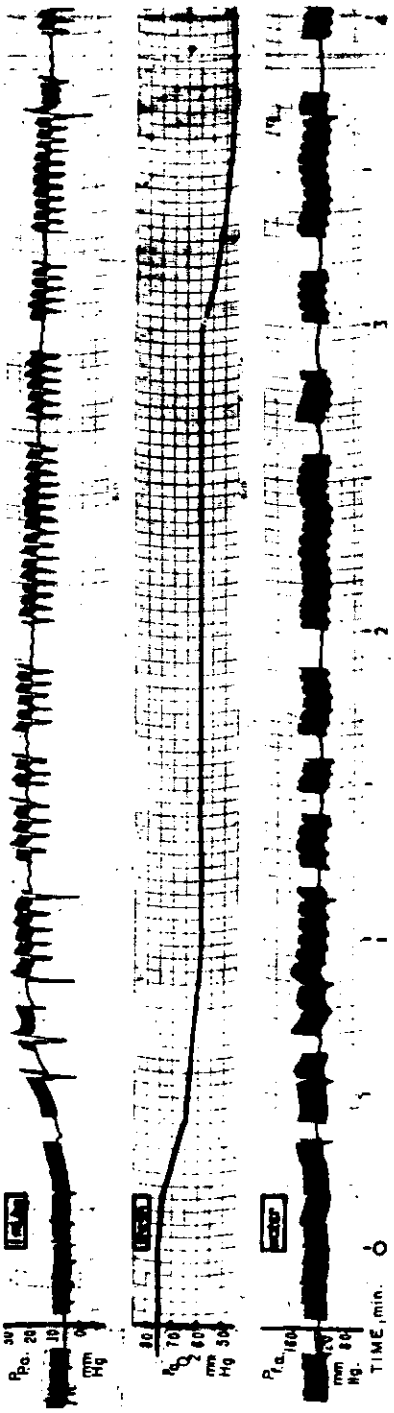


FIG. 1. Continuous records of pulmonary (Pp.a.) and femoral (Pf.a.) arterial pressures in an intact sheep during intratracheal administration of 1 ml/kg fresh water. The continuous record of an intra-arterial $O_2$ electrode was replotted in order to demonstrate simultaneous changes in $Pa_{O_2}$. Allowance was made for the 15-sec. delay in response of the electrode. Continuous segments in pressure records are electrical means.

lobe), the difference turned out to be significant ($.02 < P < .05$). At 30 minutes $\bar{P}$p.a. remained significantly elevated in *group B* (small, fresh) only.

*Vagotomized animals.* At 5 minutes $\bar{P}$p.a. was increased in all groups but *H* (small, sea). At 30 minutes $\bar{P}$p.a. was not significantly different from that at 0.

The rate of increase of $\bar{P}$p.a. following intratracheal fluid administration is shown in figure 1. In addition to the pulmonary and femoral arterial traces, the continuous record of an intra-arterial $O_2$ electrode[4] was replotted on the figure. In general, the maximum increase in Pp.a. was achieved within 1 minute and was followed by a much slower decrease.

### *Total Pulmonary Resistance*

*Intact animals.* A significant rise only occurred following the administration of small quantities of fluid (*groups B* and *C*). In *group F* (fluid into one lobe) the rise in $R_{pulm}$ was in itself not statistically significant. When compared with changes occurring between 0 and 5 minutes in *group A* (controls) the difference was significant ($P = .05$).

*Vagotomized animals.* Only the injection of a small amount of fresh water (*group G*) resulted in a significant increase.

### *Pulmonary Arterial Wedge Pressure*

This was measured in five animals at 0 and 5 minutes following the intratracheal administration of 1 ml/kg fresh water. The average increase in $\bar{P}$p.a. in these animals was from 13 to 20 mm Hg.$\bar{P}$p.a.w. in the same time changed from 7 to 8 mm Hg.

### *Pulmonary Vascular Resistance*

This parameter was measured in five sheep before and 5 minutes following the administration of 1 ml/kg fresh water. Its average value increased from 159 to 303 dynes sec. $cm^{-5}/m^2$ BSA.

### *Systemic Arterial Pressure and Resistance*

This was measured in about half of our animals. A slight decrease was observed following the administration of large quantities of fluid.

### *Right Ventricular Work*

This was calculated by multiplying $\dot{Q}$p.a. by $\bar{P}$p.a. The result is regarded as a rough approximation. The injection of small quantities of fluid was accompanied by an increase amounting to 30–35%; the increase following the injection of large amounts of fluid averaged 90–100%.

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[4] $O_2$ electrode was designed and operated by G. Charlton, M.D.S., from the Dept. of Bacteriology of the University of Sydney. Details of this instrument will be published elsewhere. His interest and cooperation are gratefully acknowledged.

DISCUSSION

It has long been suspected that rapid death due to respiratory arrest might occur on immersion (14). In these experiments fresh water appeared to be fatal only by volume, causing mechanical obstruction of the airways. Respiratory arrest following the intratracheal administration of sea water occurred independently of the quantity inhaled. Vagotomy did not reduce the incidence of respiratory arrest.

In those animals in which respiratory arrest subsequently developed, the lowest levels of $Sa_{O_2}$ were found following the fluid, at a time when rate and depth of breathing appeared to be comparable to those which maintained respiration. It is suggested that in some animals hypoxia was so severe as to cause central respiratory failure.

The penetration of fluids into the airways depends mainly on their viscosity and on gravitational forces. Oily materials will not immediately penetrate beyond the bronchioles, though water will reach the alveoli instantly (15). By assuming that hypoxemia was a consequence of alveolar flooding, the following correlations should be observed: *a*) a decrease in $Sa_{O_2}$ dependent on the amount of fluid introduced and *b*) a speed of recovery determined by the rate of reabsorption of the fluid. These correlations were not found to occur. Hypoxemia resulting from the intratracheal injection of 1 ml/kg fluid was somewhat less severe in the vagotomized animals than in the intact sheep. Furthermore, no hypoxemia followed the introduction of fluid into one lobe only. One milliliter per kilogram of fresh water is absorbed within 2–3 minutes from the lungs; the same amount of sea water increases its volume and remains in the lungs for several hours (16). $Sa_{O_2}$ in animals given 1 ml/kg fresh water was still low at 30 minutes and the rate of recovery of $Sa_{O_2}$ was not markedly different after fresh or sea water injection. These observations suggest that flooding of the alveoli does not in itself account for the precipitous fall and prolonged depression of $Sa_{O_2}$ in these experiments.

Calculated $Pa_{O_2}$ in some of our animals decreased to a value of 25–30 mm Hg. It has been demonstrated that consciousness is lost and abnormal cortical activity starts at a cerebral $Pv_{O_2}$ level of 15–25 mm Hg (17). Histological evidence of hypoxic brain damage was reported in a case of delayed death due to drowning (18). Hypoxemia produced by small amounts of fluid in some of our experiments was near to or beyond this limit of tolerance for the conscious state. This has obvious implications in appreciating the potential hazards of fluid aspiration in human beings.

Changes in ventilation could not account for the hypoxemia. The fluid-induced rise in $\dot{V}_E$ was apparently not dependent on the integrity of the vagus nerve.

A gross increase in $\dot{Q}s$ was found to be responsible for the fall in $Sa_{O_2}$. This increase in $\dot{Q}s$ was the result of continued perfusion of large, nonventilated areas of the lung produced by aspiration of fluid. Since the magnitude of $\dot{Q}s$ was not directly related to the volume of inhaled fluid, it is suggested that the closure of entire populations of alveoli was caused by the surface tension effect of water. This mechanism will be dealt with in detail in a subsequent paper (Colebatch and Halmagyi, in preparation).

The somewhat high values of $\dot{Q}s$ during the control periods were due to uneven ventilation and to some degree of lung collapse caused by the supine position and the anesthesia. Its presence tended to minimize the effect of fluid aspiration by the distribution of fluid to areas that were already poorly ventilated.

Pulmonary hypertension following the administration of small quantities of fluid was accompanied by an increase in $R_{pulm}$ and, in the cases where it was measured, an unchanged $\bar{P}p.a.w.$ This was suggestive of pulmonary arteriolar constriction. The effect of inhaling small amounts of fresh water was more marked and more sustained than that of small quantities of sea water. Vagotomy shortened the duration of the effect of the former and abolished that of the latter. One wonders if this discrepancy could be regarded as indicative of a difference in the genesis of pulmonary hypertension induced by the aspiration of small quantities of fresh and sea water.

The increase in $\bar{P}p.a.$ following the inhalation of large amounts of fluid was accompanied by a rise in $\dot{Q}p.a.$ in both the intact and the vagotomized sheep. As a result, $R_{pulm}$ increased only slightly. Under normal conditions, a similar increase in flow is unlikely to affect $\bar{P}p.a.$ We suggest, therefore, that an increase in pulmonary arteriolar tone has occurred.

The increase in right ventricular work was especially marked following the inhalation of large amounts of fluid. This increase in cardiac performance during severe hypoxemia provides a further burden for the myocardium.

$P_{A_{O_2}}$ remained normal in nearly all of these experiments. No relationship could be obtained between the pulmonary vasoconstrictor response and changes in $Sa_{O_2}$ or $S\bar{v}_{O_2}$. The administration of fluid into one lobe was followed by a mild increase in $\bar{P}p.a.$ despite the absence of hypoxemia. On the other hand, Pp.a. remained practically unchanged after the administration of 1 ml/kg sea water in vagotomized animals despite a significant hypoxemia. It appears, therefore, fairly safe to eliminate hypoxia as a possible cause of fluid-aspiration-induced pulmonary hypertension.

The increase in $\bar{P}p.a.$ in these experiments is believed to be due to the penetration of fluid into the terminal airways, causing pulmonary arteriolar constriction by a mechanism at present unknown. It might offer a satisfactory explanation as to why the right ventricle is found dilated in victims of drowning as opposed to the left ventricular dilatation characteristic of suffocation (3, 19).

Fluid aspiration may occur during anesthesia, prolonged unconsciousness, bulbar paralysis and a number of other clinical conditions. Perhaps more important than drowning, these experiments are an indication of the physiological consequences of fluid aspiration in general which have previously received little attention.

Many parts of this work depended on the cooperation of the members of the technical staff of the department. It is with great pleasure that we acknowledge the work of P. Donelly, D. Fahey, T. Miller, W. Green and Miss Maureen Woodward. Our thanks are also due to the Department of Illustrations. It was also a privilege to enjoy Prof. C. R. B. Blackburn's interest and support throughout the completion of this work.

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# Sudden Failure of Swimming in Cold Water

W. R. KEATINGE,* M.A., M.B., PH.D. ; C. PRYS-ROBERTS,† M.B., PH.D., F.F.A. R.C.S.
K. E. COOPER,‡ M.A., M.B., M.SC. ; A. J. HONOUR,§ M.A., D.PHIL. ; J. HAIGHT,|| B.A.

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**Summary: To investigate the effect of cold water on swimming four men who declared themselves good swimmers were immersed fully clothed on separate days in water at 23·7° and 4·7° C. The time that they were able to swim in the cold water was much shorter than in the warm. The two shortest swims ended after 1·5 and 7·6 minutes, before rectal temperature fell, when the men suddenly floundered after developing respiratory distress with breathing rates of 56–60/min. The other cold swims, by the two fattest men, ended less abruptly with signs of general and peripheral hypothermia.**

**It is concluded that swimming in cold water was stopped partly by respiratory reflexes in the thin men and hypothermia in the fat, and partly by the cold water's high viscosity. The longer swimming times of the fat men are attributed largely to their greater buoyancy enabling them to keep their heads above water during the early hyperventilation.**

**The findings explain some reports of sudden death in cold water. It is clearly highly dangerous to attempt to swim short distances to shore without a life-jacket in water near 0° C.**

## Introduction

Most deaths after shipwreck result from immersion hypothermia (Molnar, 1946 ; McCance *et al.*, 1956 ; Keatinge, 1965), but most deaths in inland waters are too rapid for this. For example, a good swimmer aged 20 recently disappeared within five minutes while he was trying to swim 50 yards (46 metres) to shore from an overturned dinghy in the calm water of a reservoir at 10–11° C. (Keatinge, 1969). Such accidents are often ascribed to cramp. However, sudden cooling of the skin causes breathlessness, which is accompanied by severe and often uncontrollable reflex hyperventilation (Keatinge and Nadel, 1965). This does not normally harm healthy people supported in cold water, but it seemed possible that it might prevent them from swimming.

The present experiments were designed to see whether good swimmers with clothes of a type worn by small-boat sailors could swim as far in water near 0° C. as in warmer water, and to see what eventually stopped them. Respiratory and temperature measurements were made by means that interfered as little as possible with respiration and with swimming.

* Now Reader in Physiology London Hospital, London E.1.
† First Assistant, Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford.
‡ Assistant Director, M.R.C. Body Temperature Research Unit, Radcliffe Infirmary, Oxford.
§ Research Officer, Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford.
|| Medical Research Council Scholar, Radcliffe Infirmary, Oxford.

## Procedure and Methods

The subjects were four men aged 24 to 36 who declared themselves to be good swimmers. Subjects 1 and 4 were physiologists involved in the experiments, subject 3 was a student, and subject 2 an amateur dinghy sailor. Medical examination showed all of them to be free of cardiovascular or respiratory disease. Heights and weights were recorded and skinfold thicknesses were measured by callipers (John Bull British Indicators Ltd.) at four standard sites: biceps mid-way between acromion process and medial epicondyle of the elbow, subscapular over the lower corner of the scapula, abdominal 5 cm. below and lateral to the umbilicus, and subcostal at the lower border of the ribs below the mid-point of the clavicle.

Each man was immersed twice, first in an indoor swimming pool (water temperature 23·7° C., air 20·3° C.) and three weeks later (in March) in an outdoor pool (water temperature 4·7° C.,

air 11·0° C.). They wore a woollen shirt, jacket with zip fastener, trousers, underpants, socks, gloves, and gym shoes. A rope was tied round the waist and held by an observer so that the subject could be pulled from the water at once if necessary. Subject 4 swam without recording leads to avoid any encumbrance from these. With the other subjects a thermocouple was attached to the chest over the centre of the sternum, its junction touching the skin but not covered by sticking plaster, and another was used to measure rectal temperature at a depth of 6 cm. Ventilation was measured with a heated screen pneumotachograph (Godart CP1) recording outflow only. The flow signal was integrated electrically breath-by-breath to give tidal volumes. The subject wore a nose clip and breathed into a mouthpiece (internal cross-section 1·8 sq. cm.) and valve assembly; the outflow valve led via flexible tubing to the pneumotachograph head mounted on a metal boom carried by one of the observers. The boom also carried leads from the subject to stationary recording apparatus. E.C.G. leads were attached to forehead and chest (sternum), but artifacts allowed satisfactory E.C.G. records to be made in the water for only short periods. The flow and volume signals from the tachograph and the output of the E.C.G. were displayed on a Devices four-channel recorder. The output of the thermocouples was read from galvanometers (Ellab and Sçalamp).

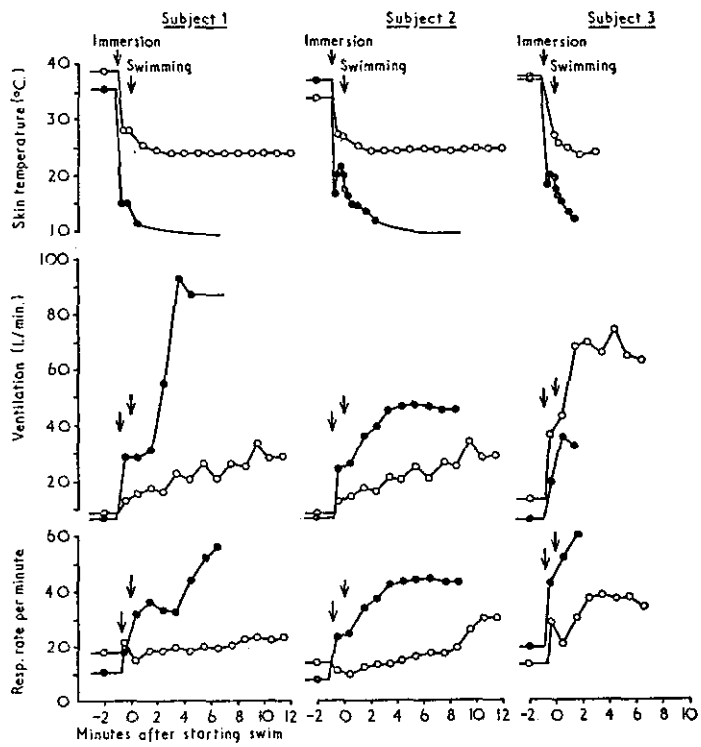
In each experiment the subject sat quietly in air for five minutes while resting temperature, air flow, tidal volume, and E.C.G. were recorded. He then climbed quickly down a ladder into the water, kept still holding the side for 45 seconds, and was then told to swim just as he would if he were trying to reach a distant shore after a boat accident. He swam within a few feet of the edge of the pool, turning every 18 metres to keep within the range of the recording leads. All were told that the experimenters would end the immersion at 12 minutes or (except for Subject 4) when the subject cooled to an extent that presented any danger. They were told that they should otherwise keep swimming until they found it impossible to swim further.

## Results

### Control Immersions

In the control immersions (23·7° C.) three of the four men swam without discomfort for the full 12 minutes, and said that they could have continued much longer if asked to do so. The other, the thinnest (Subject 3, Table I), was not able to swim so long. From the start he was seen to have to swim more energetically than the fatter men to keep his head above water, and in the eighth minute he became too exhausted to continue and grabbed the side of the pool.

Readings were obtained from Subjects 1 to 3. Their skin temperatures dropped to 24–25° C. within two minutes of the start of the swim and remained at that level thereafter (see Chart). Pulmonary ventilation in Subjects 1 and 2 rose to about 30 l./min. as they swam, with almost proportionate increases in rate of breathing. In Subject 3 both ventilation and rate rose more rapidly, reached 60–80 l./min. and 30–40 breaths/min. in the third minute, and remained at these levels until he gave up from exhaustion in the eighth minute.




Skin temperature, ventilation, and rate of breathing before and during swims. ○ - - - ○ warm water (23·7° C.). ● - - - ● cold water (4·7° C.).

TABLE I.—*Details of Subjects*

| Subject | Age in Years | Height (cm.) | Weight (kg.) | Skinfold Thicknesses (mm.) | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Biceps | Subscapular | Abdominal | Subcostal | Mean |
| 1 | 24 | 185 | 74 | 3·4 | 10·2 | 6·8 | 8·5 | 7·2 |
| 2 | 29 | 183 | 77 | 6·7 | 11·3 | 10·5 | 10·2 | 9·7 |
| 3 | 24 | 173 | 71 | 3·6 | 9·2 | 7·1 | 7·7 | 6·9 |
| 4 | 36 | 185 | 83 | 7·6 | 13·0 | 13·5 | 14·8 | 12·2 |

### Cold Immersions

In the cold immersions (4·7° C.) all subjects experienced discomfort and difficulty in breathing as soon as they entered the water. During the 45 seconds that they kept still these sensations decreased as the water under their clothing warmed; skin temperatures, which fell to 15–18° C. immediately after immersion, usually rose a few degrees during this 45-second period. When they started to swim the skin temperatures fell again and were always below 12° C. by the end of the third minute.

None of the men was able to swim in the cold water for the full 12 minutes. At the start they swam higher in the water and with more energetic and uneven movements than in the control swims. They then slowed down and sank progressively lower in the water so that mean swimming speeds were virtually the same as in the control immersions (Table II).

In the two shortest swims in cold water the end was abrupt. Subject 1 spat out his mouthpiece after swimming for just over five minutes, in order to ease his breathing, and after swimming

for a further two and a half minutes with increasing difficulty he inhaled a little water, floundered, grabbed at the side of the pool, and was pulled ashore. The end of Subject 3's swim was even more sudden. After swimming for only one and a half minutes he floundered and sank without managing to reach the side of the pool, which was about 1 metre from his head, and had to be pulled ashore. Within one minute of leaving the water both of these subjects were alert, cheerful, and shivering very little. Both said that shortness of breath and general fatigue had prevented them from swimming further. The records showed that their respiration was very rapid by the time they stopped swimming. Subject 1's rate of breathing had risen to 56/min. and his pulmonary ventilation to 93 l./min. by the end of the swim. Subject 3's rate of breathing had risen as high as 60/min.; his ventilation was lower than the high values reached at the end of his control swim, probably because tidal volume near the end of the cold swim was limited by his very high rate of breathing and by reflex inhibition of expiration due to stimulation of cutaneous cold receptors (Keatinge and Nadel, 1965). Neither subject suffered a fall in rectal temperature during these short swims; Subject 1's rectal temperature was 37·4° C. and Subject 3's was 36·8° C. both before and at the end of their swims.

TABLE II.—*Swimming Time, Distance, and Speed*

| Subject | 23·7° C. Immersions | | | 4·7° C. Immersions | | |
|---|---|---|---|---|---|---|
| | Swimming Time (min.) | Distance Covered (m.) | Mean Speed (m./min.) | Swimming Time (min.) | Distance Covered (m.) | Mean Speed (m./min.) |
| 1 | >12 | 261 | 21·8 | 7·58 | 144 | 19·0 |
| 2 | >12 | 225 | 18·8 | 9·83 | 224 | 22·7 |
| 3 | 7·5 | 135 | 18·0 | 1·50 | 29 | 19·3 |
| 4 | >12 | 198 | 16·5 | 11·42 | 176 | 15·4 |
| Mean | | 205 | 18·8 | | 143 | 19·1 |

The two fatter subjects (Nos. 2 and 4) swam for longer in cold water but had to stop after 9·83 and 11·42 minutes respectively. Both reported that inability to control their breathing in time with their swimming movements had made it difficult to swim during the first few minutes in cold water. Within about seven minutes breathing had started to become easier and the initial sensations of cold and tingling in the limbs had declined, presumably because of adaptation of sense organs, but these sensations were then replaced by increasing shivering and by heaviness and clumsiness of the limbs. These increased until the men felt unable to continue, swam slowly to the ladder, and climbed out. The airflow records from Subject 2 show that his rate of breathing and ventilation rose to moderately high but not extreme levels during the first five minutes of the swim and then declined a little so that by the time he left the water they were not much higher than they had been at the end of his control swim. His rectal temperature fell from 37·1 ° C. before immersion to 35·0° C. 10 minutes after he left the water; the thermocouple was displaced at the time he left the water. Subject 4, swimming without recording leads, probably suffered similar respiratory and temperature changes, since he was seen to be breathing with difficulty when he started to swim and to be shivering hard after leaving the water.

## Discussion

The times for which the men could swim in water at 4·7° C. were not only short compared with the times for which they could swim in water at 23·7° C. but were also short compared with the times for which they could have been expected to survive with support in water at 4·7° C. For example, in one earlier series of experiments none of a group of five volunteers suffered large enough falls in body temperature to threaten life, or serious after-effects of any kind, as a result of repeated 20-minute immersions in water at 5° C., whether or not they exercised or were protected by clothing (Keatinge, 1969).

The respiratory distress that halted the two shortest cold swims can be explained largely by reflexes from cutaneous cold receptors. The breathing rates of 56–60/min. recorded just before the end of these cold swims contrast with rates of only 20–30/min. at a similar stage in the warmer swims. Showers at near 0° C. cause not only reflex hyperventilation with an inspiratory shift in respiration, but a sensation of breathlessness and inability to control breathing voluntarily (Keatinge and Nadel, 1965). It is easy to understand that such reflexes might induce intolerable respiratory distress during hard physical work. The work required to swim in water at 4·7° C. will in any case be somewhat greater than in water at 23·7° C. because of the higher viscosity of the colder water, 1·5 centipoise (cp.) compared with 0·9 cp. This disadvantage of cold water can only be counteracted to a slight extent by its greater density of 1·000 g./ml. compared with 0·995 g./ml. for water at 23·7° C., which would make it marginally easier for a swimmer to float. There is evidence that reflexly induced cardiac arrhythmias may occasionally cause sudden death of healthy young men in cold water (Keatinge and Evans, 1961; Keatinge *et al.*, 1964), but only on rare occasions. The present experiments suggest that the reflex respiratory response to cold is a much more frequent hazard to life in cold water.

The two fattest men were presumably able to swim through their initial respiratory difficulty in cold water because their lower specific gravity enabled them to float with less physical exertion. The heaviness of the limbs and progressive shivering that ultimately stopped them must have resulted from local and general hypothermia. Moderate cooling of forearm muscle produced by immersing the arm in water at 18° C. for 30 minutes slows contraction and relaxation, though it increases the endurance time for sustained contraction (Nukada, 1955; Lind, 1959). Neuromuscular conduction in the rat tail fails when local temperature falls to 4–5° C. (Li, 1958), but such failure is unlikely to have occurred in the present brief experiments, since volunteers were earlier found to be able to maintain almost as high rates of energy expenditure when they exercised as hard as possible for 20 minutes in water at 5° C. as in water at 15° C. (see Keatinge, 1969). It appears that slowing of muscle contraction and malfunction of muscular and cutaneous sense organs due to local cooling, combined with impaired cerebral function due to general hypothermia, were sufficient to end the longer swims.

From the practical point of view the most striking finding was that none of four fit people who thought themselves to be good swimmers could cover 250 metres in water at 4·7° C., while one of them failed to cover 30 metres. This was in spite of the water being calm and the risk of panic being minimized by their knowledge that rescue facilities were at hand. Since the early respiratory disturbance prevented all of the men from controlling their breathing soon after they started the cold swim it seems inevitable that waves breaking in their faces at this time would have put them into severe difficulty within seconds. Glaser and Hervey (1951) reported a swim lasting nine minutes in water at about 2° C., which was ended by the experimenters. Critchley (1943) quoted a remarkable wartime report of a shipwreck survivor said to have swum for 9 to 14 hours wearing indoor clothing and an overcoat in sea-water at −1° C. Swimming endurances of this kind by very fat men present no theoretical difficulty, but are clearly exceptional.

Surgeon Commander Rawlins has brought to our notice the recent drowning of all of nine Servicemen aboard a training canoe that overturned in "icy" water of the Potomac River on 6 March 1968; it was stated at the court of inquiry that "nothing explains why the canoe could have capsized and why all nine men drowned." The present results, obtained at almost the same time as that accident, show that swimming time in such water is usually remarkably short. No further comments seem to be necessary to emphasize the need for the occu-

pants of small boats to wear a life-jacket capable of keeping the face above water, and the danger in trying to swim even short distances to shore in cold water without one.

We are indebted to Mr. B. Cobern for his skilled technical assistance.

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# *Effects of Ventilatory Patterns on Arterial Oxygenation after Near-drowning in Sea Water*

*Jerome H. Modell, M.D.,* Hugh W. Calderwood, V.M.D.,† Bruce C. Ruiz,‡ John B. Downs, M.D.,§ Roy Chapman, Jr., M.D.§*

**Forty-three dogs were anesthetized and subjected to aspiration of 22 ml/kg of sea water. After 5 minutes, fluid was drained from the lungs by gravity; 33.1 ± 5.9 ml/kg were recovered. Thirty-four dogs were apneic at this time and were treated with intermittent positive-pressure ventilation with a self-inflating bag. Forty-five minutes later, the 40 animals that survived were divided into four equal groups; one group breathed spontaneously and served as a control, the second was treated with IPPV, the third breathed spontaneously against 10 cm $H_2O$ PEEP, and the fourth received IPPV plus PEEP (*i.e.*, CPPV). Arterial oxygen tensions of the animals in both groups with PEEP significantly increased during the 75-minute treatment period. By 48 hours two more dogs had died; however, $Pa_{O_2}$'s had returned to normal in the 38 that survived, regardless of the mode of treatment. It is concluded that gravity drainage and immediate mechanical ventilation of victims who aspirate large quantities of sea water are important, since 40 of the 43 animals were resuscitated after being submerged for 5–10 minutes. Blood-gas data showed that positive end-expiratory pressure, with or without mechanical ventilation, significantly increased $Pa_{O_2}$ after aspiration of sea water, suggesting that it is indicated in the treatment of sea-water near-drowning victims. Two case reports of human victims of near-drowning in sea water which support the animal studies are presented. (Key words: Complications, aspiration: sea water; Ventilation, positive end-expiratory: aspiration; Ventilation, intermittent positive-pressure: aspiration.)**

IT IS WELL KNOWN that pulmonary edema and hypoxemia occur after aspiration of sea water.[1,2] The hypoxemia is largely secondary to true or absolute intrapulmonary shunting.[3] Recently, increasing functional residual capacity (FRC) by combining intermittent positive-pressure ventilation (IPPV) with positive end-expiratory pressure (PEEP), *i.e.*, continuous positive-pressure ventilation (CPPV), has been shown to increase $Pa_{O_2}$ in some patients with severe respiratory insufficiency.[4] Furthermore, Cheney and Martin have shown that this mode of ventilatory support will significantly decrease shunt and increase $Pa_{O_2}$ in animal models of pulmonary edema, so long as PEEP is applied.[5] The above suggest that this treatment also might be beneficial in treating victims of near-drowning. Therefore, the following experiment was designed to determine whether PEEP alone, or in combination with mechanical ventilation, can improve arterial oxygenation during treatment of near-drowning in sea water in dogs.

## Methods

Forty-three dogs (33 mongrels and ten beagles) weighing 12.5 ± 2.2 kg were anesthetized with sodium pentobarbitol, 25 mg/kg, intravenously. The trachea of each dog was intubated with a cuffed endotracheal tube, a catheter was placed in the femoral artery, and an esophageal thermistor was inserted. The animals breathed 100 per cent oxygen via a

* Professor and Chairman of Anesthesiology.
† Instructor in Anesthesiology and Comparative Medicine.
‡ Laboratory Technologist II, Anesthesiology.
§ NIH Research Fellow in Anesthesiology.

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nonrebreathing system for 15–20 minutes and arterial blood was analyzed for $pH$, $P_{CO_2}$ and $P_{O_2}$ with appropriate electrodes. The animals then breathed room air for 15–20 minutes before a second blood sample was drawn for analysis. All values were corrected for body temperature. Following completion of the baseline studies, the animals aspirated 22 ml/kg of sea water¶ through a chamber described previously.[6] At the end of 5 minutes, the animals were placed in a head-down position and fluid was permitted to drain by gravity. If the animal was apneic at this time, resuscitation was attempted by use of IPPV with a self-inflating bag containing air. $Pa_{O_2}$, $Pa_{CO_2}$, and $pH_a$ were determined 15 and 30 minutes after aspiration. The dogs then breathed 100 per cent oxygen for 15 minutes and a third postaspiration blood gas sample was drawn. Three dogs died during this 45-minute interval. The 40 animals that survived were divided into four equal groups and treated for the next 75 minutes as follows.

Group I served as the control. Ten dogs breathed 100 per cent oxygen spontaneously for 1 hour through a nonrebreathing system, and then breathed room air for 15 minutes.

Group II received PEEP only. Ten animals breathed spontaneously through a nonrebreathing system. The exhalation valve was connected to 10 cm $H_2O$ positive end-expiratory pressure (PEEP). $F_{I_{O_2}} = 1.0$ for 60 minutes and 0.21 for 15 minutes.

Group III received respirator therapy only (IPPV). Each of the ten animals was paralyzed with succinylcholine and its ventilation controlled with a volume-limited respirator (Emerson Post-Operative Ventilator) with a tidal volume of 15 ml/kg. The rate was adjusted to maintain $Pa_{CO_2}$ between 35 and 45 torr. $F_{I_{O_2}} = 1.0$ for 60 minutes and 0.21 for 15 minutes. After 75 minutes of mechanical ventilation, the dogs were permitted to breathe spontaneously.

Group IV received respirator therapy and PEEP (*i.e.*, CPPV). These ten dogs were treated like Group III, except that the exhalation port of the ventilator was connected to a system which produced 10 cm $H_2O$ PEEP.

Additional blood gas tensions and $pH$ values were determined at intervals over the next 3 hours at both $F_{I_{O_2}} = 0.21$ and $F_{I_{O_2}} = 1.0$. The arterial catheter then was removed and the incision closed. All surviving animals were placed in an oxygen tent containing approximately 40 per cent oxygen for at least 24 hours or until a $Pa_{O_2}$ above 70 torr was maintained during breathing of room air. At 24, 48, 72, and 168 hours blood samples were obtained from the femoral artery while the dogs breathed room air and analyzed for $pH$, $P_{CO_2}$ and $P_{O_2}$. The temperature of each animal was taken and its head was inserted into a polyethylene bag into which 100 per cent oxygen flowed at a rate of 25–35 l/min. Holes made in the bag permitted the excess oxygen and carbon dioxide to escape freely. After 15–20 minutes another sample of arterial blood was obtained and analyzed.

## Results

Of the 43 animals subjected to aspiration of 22 ml/kg of sea water, 42 were still under water 5 minutes later. We drained 33.1 ± 5.9 ml/kg of fluid from the 43 dogs by gravity. Nine dogs made ventilatory efforts, but only five appeared to move any air at this time. The remaining 34 dogs were apneic. When intermittent positive-pressure ventilation with a self-inflating bag containing air was applied, 33 of the latter dogs regained spontaneous ventilation; however, two died within 27 minutes. One of the survivors required closed-chest cardiac massage in addition to IPPV. All dogs still alive 45 minutes after aspiration, when the different modes of treatment were initiated, had severe arterial hypoxemia (tables 1 and 2). Hypercarbia and acidosis also were observed after aspiration (tables 3 and 4).

During the 75-minute experimental treatment period, $Pa_{O_2}$'s increased slightly in the control animals. $Pa_{O_2}$'s of the animals ventilated mechanically without PEEP were not significantly different from these values (tables 1 and 2). The animals treated with mechanical ventilation plus PEEP (CPPV) had the highest mean $Pa_{O_2}$'s during the treatment period (fig. 1). Within 15 minutes of initiation of treatment,

¶ Obtained from the Atlantic Ocean, 5 miles east of Jacksonville, Florida. Electrolyte concentrations were: sodium 484 mEq/l, potassium 10.2 mEq/l, chloride 578 mEq/l, magnesium 109 mEq/l, and calcium 21.2 mEq/l.

TABLE 1. Arterial Oxygen Tension (torr) before and after Aspiration of 22 ml/kg Sea Water at $F_{IO_2}$ = 1.0 (Mean ± SD)

| | Preaspiration 0 | ¾ Hour | Hours after Aspiration: Treatment 1 | 1¼ | 1½ | 1¾ | Posttreatment 3¼ | 4¼ | 24 | 48 | 72 | 168 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Group I, spontaneous ventilation | 574 ±47 | 115* ± 98 | 125* ±116 | 136* ±105 | 159* ±117 | 177* ±132 | 216* ±185 | 270* ±197 | 477 ±154 | 477 ±154 | 492 ±100 | 518 ±66 |
| Group II, spontaneous ventilation and 10 cm $H_2O$ PEEP | 562 ±67 | 182* ±110 | 491† ±126 | 473† ±140 | 510† ± 80 | 521† ± 71 | 310* ±197 | 333* ±188 | 521 ± 57 | 526 ± 31 | 553 ± 42 | 543 ±48 |
| Group III, IPPV (15 ml/kg) tidal volume | 561 ±42 | 164* ±118 | 161* ± 85 | 181* ±113 | 200* ±132 | 205* ±123 | 294* ±178 | 284* ±190 | 410* ±147 | 464 ±146 | 487 ±102 | 517 ±29 |
| Group IV, CPPV (15 ml/kg) and 10 cm $H_2O$ PEEP | 551 ±31 | 141* ±121 | 555† ± 77 | 552† ± 86 | 534† ± 90 | 537† ± 87 | 356* ±191 | 387 ±188 | 496 ±110 | 518 ± 64 | 522 ± 81 | 536 ±46 |

* Compared with zero time for the group, $P < 0.01$.
† Significantly higher than Group I value, $P < 0.001$.

TABLE 2. Arterial Oxygen Tension (torr) before and after Aspiration of 22 ml/kg Sea Water at $F_{IO_2}$ = 0.21 (Mean ± SD)

| | Preaspiration 0 | Hours after Aspiration: Treatment ¼ | ½ | 2 | Posttreatment 2½ | 3 | 4 | 24 | 48 | 72 | 168 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Group I, spontaneous ventilation | 93 ±14 | 41* ±18 | 40* ± 7 | 52* ±15 | 52* ±13 | 54* ±16 | 55* ±16 | 85 ±17 | 92 ±18 | 96 ±14 | 97 ±7 |
| Group II, spontaneous ventilation and 10 cm $H_2O$ PEEP | 98 ±10 | 32* ± 8 | 41* ± 8 | 81*† ± 7 | 65* ±18 | 60* ±21 | 70* ±23 | 95 ±14 | 96 ±11 | 101 ± 9 | 98 ±8 |
| Group III, IPPV (15 ml/kg) tidal volume | 94 ±15 | 37* ±14 | 42* ±11 | 59* ±19 | 55* ±23 | 53* ±26 | 63* ±25 | 79 ±21 | 83 ±25 | 90 ±16 | 89 ±9 |
| Group IV, CPPV (15 ml/kg) and 10 cm $H_2O$ PEEP | 89 ±11 | 37* ± 9 | 44* ± 8 | 88† ±14 | 68* ±20 | 67* ±19 | 65* ±16 | 92 ±10 | 93 ± 6 | 97 ± 9 | 99 ±8 |

* Compared with zero time for the group, $P < 0.01$.
† Significantly higher than Group I value, $P < 0.001$.

TABLE 3. Arterial pH (Mean ± SD) before and after Aspiration of 22 ml/kg Sea Water at $F_{I_{O_2}} = 0.21$

| | Preaspiration 0 | Hours after Aspiration | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Treatment | | | Posttreatment | | | | | |
| | | ¼ | ½ | ¾* | 1* | 1½* | 2 | 3 | 4 | 24 | 48 | 72 | 168 |
| Group I, spontaneous ventilation | 7.46 ±0.09 | 7.22‡ ±0.05 | 7.25‡ ±0.05 | 7.24‡ ±0.08 | 7.30‡ ±0.05 | 7.35‡ ±0.05 | 7.41 ±0.04 | 7.43 ±0.05 | 7.45 ±0.05 | 7.36‡ ±0.05 | 7.42 ±0.04 | 7.42 ±0.02 | 7.42 ±0.04 |
| Group II, spontaneous ventilation and 10 cm $H_2O$ PEEP | 7.40 ±0.05 | 7.20‡ ±0.06 | 7.19‡ ±0.06 | 7.18‡ ±0.08 | 7.18‡ ±0.10 | 7.22‡ ±0.04 | 7.27‡ ±0.04 | 7.39 ±0.05 | 7.39 ±0.06 | 7.38 ±0.04 | 7.41 ±0.04 | 7.42 ±0.04 | 7.42 ±0.03 |
| Group III, IPPV, (15 ml/kg) tidal volume | 7.37 ±0.14 | 7.21† ±0.13 | 7.26† ±0.06 | 7.29 ±0.09 | 7.29 ±0.09 | 7.35 ±0.06 | 7.39 ±0.06 | 7.43 ±0.08 | 7.41 ±0.03 | 7.38 ±0.16 | 7.36 ±0.06 | 7.38 ±0.05 | 7.42 ±0.03 |
| Group IV, CPPV, (15 ml/kg) and 10 cm $H_2O$ PEEP | 7.42 ±0.12 | 7.21‡ ±0.06 | 7.25‡ ±0.05 | 7.27‡ ±0.08 | 7.26‡ ±0.11 | 7.30‡ ±0.06 | 7.32† ±0.04 | 7.40 ±0.09 | 7.44 ±0.08 | 7.38 ±0.04 | 7.43 ±0.03 | 7.42 ±0.03 | 7.41 ±0.04 |

* $F_{I_{O_2}} = 1.0$.
† Compared with zero time for the group, $P < 0.05$.
‡ Compared with zero time for the group, $P < 0.01$.

TABLE 4. Arterial Carbon Dioxide Tension (torr) before and after Aspiration of 22 ml/kg Sea Water at $F_{I_{O_2}} = 0.21$ (Mean ± SD)

| | Preaspiration 0 | Hours after Aspiration | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Treatment | | | Posttreatment | | | | | |
| | | ¼ | ½ | ¾* | 1* | 1½* | 2 | 3 | 4 | 24 | 28 | 72 | 168 |
| Group I, spontaneous ventilation | 33 ± 9 | 47‡ ± 8 | 44‡ ± 7 | 49‡ ± 7 | 42† ± 8 | 41† ± 6 | 37 ± 6 | 34 ±5 | 33 ±7 | 38 ±5 | 36 ±6 | 37 ±1 | 38 ±2 |
| Group II, spontaneous ventilation and 10 cm $H_2O$ PEEP | 40 ± 8 | 53‡ ±10 | 53‡ ± 9 | 53‡ ±13 | 55‡ ±13 | 50‡ ± 6 | 47 ±13 | 35 ±4 | 36 ±4 | 37 ±5 | 35 ±4 | 37 ±3 | 36 ±5 |
| Group III, IPPV (15 ml/kg) tidal volume | 41 ±12 | 49 ±11 | 43 ±10 | 48 ± 9 | 45 ±16 | 40 ± 6 | 36 ± 5 | 33 ±9 | 35 ±5 | 37 ±3 | 39 ±5 | 37 ±5 | 36 ±6 |
| Group IV, CPPV (15 ml/kg) and 10 cm $H_2O$ PEEP | 35 ±12 | 47† ± 8 | 41 ± 6 | 44 ± 9 | 44 ±13 | 41 ± 6 | 40 ± 4 | 34 ±6 | 30 ±6 | 38 ±4 | 35 ±2 | 36 ±3 | 36 ±3 |

* $F_{I_{O_2}} = 1.0$.
† Compared with zero time for the group, $P < 0.05$.
‡ Compared with zero time for the group, $P < 0.01$.

Anesthesiology V 40, No 4, Apr 1974

their $Pa_{O_2}$'s increased from 141 ± 121 torr to 555 ± 77 torr at $F_{I_{O_2}} = 1.0$. At the completion of treatment, mean $Pa_{O_2}$ at $F_{I_{O_2}} = 0.21$ was 88 ± 14 torr, compared with a preaspiration value of 89 ± 11 torr (table 2). $Pa_{O_2}$'s at all times tested during treatment were significantly higher in this group than in either the control group or animals ventilated without PEEP ($P < 0.001$). In the dogs that breathed spontaneously with PEEP, $Pa_{O_2}$'s also increased significantly, and by the end of the treatment period mean $Pa_{O_2}$ at $F_{I_{O_2}} = 1.0$ was 521 ± 71 torr. Mean $Pa_{O_2}$ while breathing room air at this time was 81 ± 7 torr, compared with a preaspiration value of 98 ± 10 torr. These values are higher than those in either the control group or the animals ventilated without PEEP ($P < 0.001$). There was no significant difference between the values for animals breathing spontaneously with PEEP and those being ventilated mechanically with PEEP at any time.

When treatment with PEEP or CPPV was discontinued 120 minutes following aspiration, $Pa_{O_2}$ decreased. Mean $Pa_{O_2}$'s in these groups remained above that of the control group for the remainder of the experiment; however, they were not significantly different (tables 1 and 2). Within 24 hours of near-drowning, $Pa_{O_2}$'s of all but four animals returned to values similar to those before near-drowning, and after a week all survivors had $Pa_{O_2}$'s of at least 75 torr while breathing room air. $Pa_{CO_2}$'s and $pH_a$'s also returned to normal in all groups. During the week that the animals were observed, two more dogs died.

## Discussion

Previously, we demonstrated that when dogs aspirated 11 ml/kg of sea water and no attempt was made to drain the fluid and/or to resuscitate the animal, 80 per cent succumbed within approximately 10 minutes.[3] In contrast, during the present study, of the 43 animals that aspirated twice that volume of sea water and were treated with gravity drainage and IPPV, 40 survived for at least 24 hours. The procedure of draining fluid from the lungs and initiating IPPV employed with these animals occurred between 5 and 10 minutes of the onset of aspiration. The fact that these animals remained under water for at least 5 minutes, and were then resuscitated from the acute hypoxia, hypercarbia, and acidosis that occurred, is indeed encouraging. This leads one to question how long an interval between onset of immersion and resuscitation is possible if survival is to occur. It also lends greater credibility to reports in the literature of patients who have been successfully resuscitated 10 minutes,[7] 17 minutes,[8] and even 22 minutes[9] after onset of immersion.

Previously, we have shown that although sea water washes out some material with surface activity, it does not alter the surface tension characteristics of the pulmonary surfactant that remains behind.[10] In this regard, aspiration of sea water differs from aspiration of fresh water, which significantly elevates the minimum surface tension values of pulmonary surfactant seen on maximum film compression.[10] This suggests that the pathophysiologic process causing hypoxemia after aspiration of sea water is different than that caused by fresh water near-drowning. The primary problem after aspiration of sea water is that of fluid-filled, but perfused, alveoli, accounting for the large absolute or true intrapulmonary shunt.[3]

The dramatic increase in arterial oxygen tension in the animals that had positive end-expiratory pressure applied to their airways, with or without mechanical ventilation, suggests that increased ventilation to the perfused areas occurred. This, in turn, decreased the magnitude of the intrapulmonary shunt. A similar increase in $Pa_{O_2}$ occurred in an earlier study after aspiration of fresh water, when mechanical ventilation was combined with PEEP.[11] However, it did not occur when PEEP was used in spontaneously breathing dogs. We attribute the difference between the results observed in spontaneously breathing animals with PEEP in the two studies to the fact that the animals that aspirated fresh water suffered a change in the surface tension properties of pulmonary surfactant, while those that aspirated sea water did not.[10] It seems reasonable that if the surface tension properties of pulmonary surfactant were normal, merely placing positive pressure on end exhalation would tend to prevent airway closure at end-expiration and promote

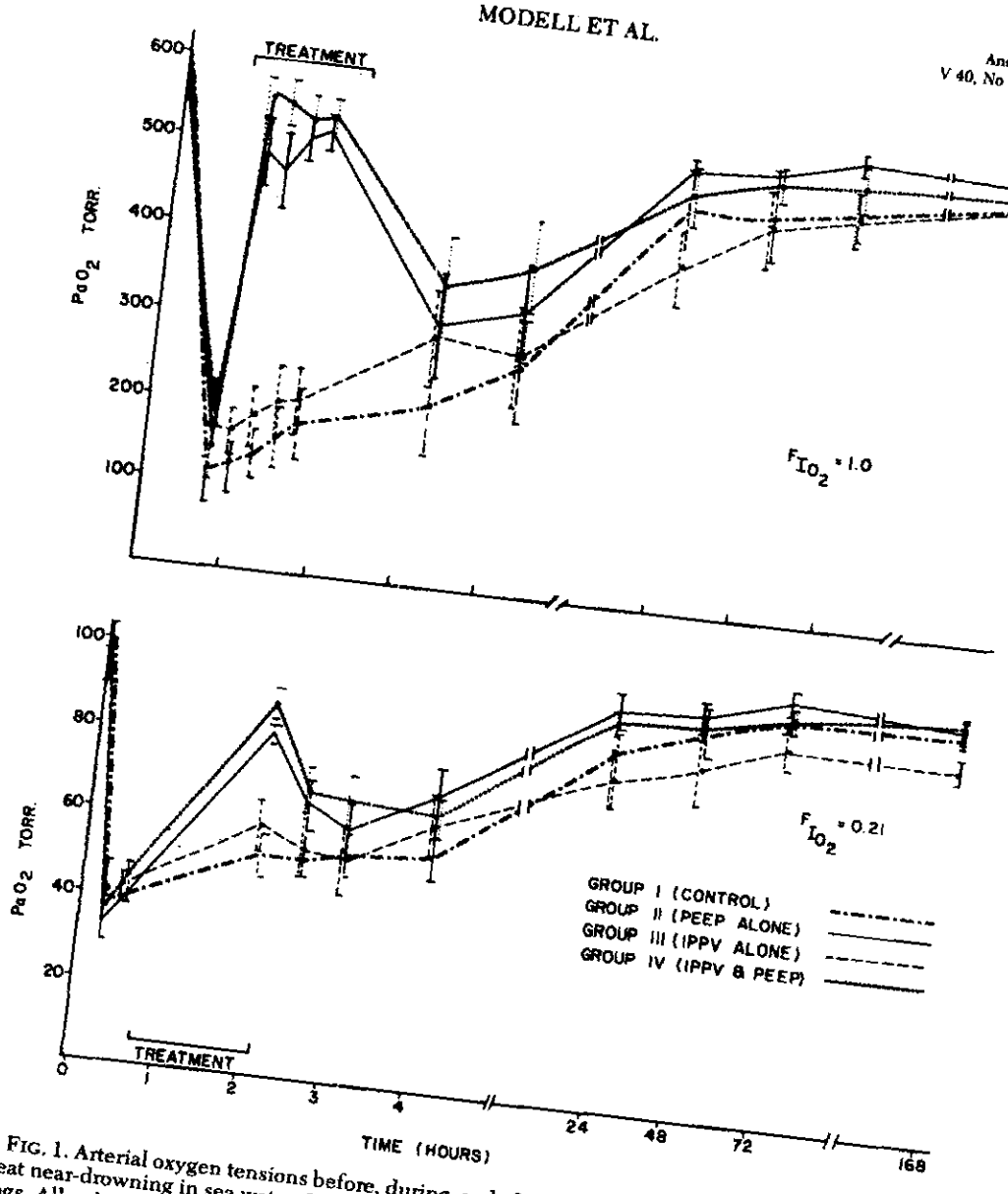


FIG. 1. Arterial oxygen tensions before, during, and after three ventilatory patterns were used to treat near-drowning in sea water. Values for these groups are compared with those for nontreated dogs. All values represent means ± SD.

maintenance of a greater functional residual capacity. On the other hand, if the surfactant were altered or destroyed, the alveoli would tend to collapse and require greater opening pressures than are usually obtained in the anesthetized, spontaneously breathing dog. In this case, if the alveolus were opened forcibly by the peak end-inspiratory pressure achieved during mechanical ventilation, it would stand a better chance of remaining open with PEEP. However, if the alveoli were partially opened with each breath with intermittent positive-pressure ventilation, but PEEP was not applied, the alveoli, being deficient in normal surfactant properties, would tend to recollapse.

An alternative explanation for the increased $Pa_{O_2}$ observed in the dogs that aspirated sea

water and were treated with either CPPV or PEEP could be that a diminution of oxygen consumption and a significant change in cardiac output occurred. Neither oxygen consumption nor cardiac output was measured in our studies. However, if this were the dominant mechanism for the improvement in arterial oxygenation, we would expect identical results after aspiration of fresh water; yet PEEP did not improve $Pa_{O_2}$ in spontaneously breathing animals after aspiration of fresh water.[11]

The arterial oxygen tensions of most animals had returned to near normal by 24 hours, regardless of treatment, and $Pa_{O_2}$'s by 48 hours were not significantly different from preaspiration values in any group. This could be compared with our earlier fresh-water study, where significant hypoxemia was still present after 48 hours, and it took 3 to 7 days for the animals to regain normal $Pa_{O_2}$'s.[11] This, again, can be explained by the fact that, with normal surfactant activity in the animals that aspirated sea water, a much more rapid return to normal $\dot{V}_A/\dot{Q}$ would be expected, whereas after aspiration of fresh water regeneration of normal surfactant would be necessary before one would expect $Pa_{O_2}$ to stabilize.

In conclusion, this study gives additional, albeit indirect, evidence for our earlier observations that one of the major differences between the effects on the lung of aspiration of fresh water and aspiration of sea water is that the surface tension properties of pulmonary surfactant are altered with fresh water but not with sea water. We also demonstrated that gravity drainage and immediate mechanical ventilation of the victim who aspirates large quantities of sea water are important, since they significantly increase the survival rate. The blood-gas data obtained in this experiment suggest that positive end-expiratory pressure, with or without mechanical ventilation, is indicated in the treatment of sea-water near-drowning victims to improve arterial oxygenation. One would expect that if this therapy were continued for the first 24 hours after aspiration, the decrease in $Pa_{O_2}$ that occurred between the time therapy was discontinued and the time the 24-hour blood samples were obtained could be avoided.

While this manuscript was being written, we had the opportunity to apply the above-described principles in treating two patients. The following case reports illustrate that PEEP can cause a dramatic increase in $Pa_{O_2}$ in patients who have aspirated sea water. Early use of PEEP resulted in complete resolution of the pulmonary damage in these two patients within 48 hours.

## Report of Two Cases

*Patient 1.* A 27-year-old Caucasian man was wading in approximately 3 feet of sea water, and dove head-first onto a sandbar. He recalls lying on the ocean floor, unable to move his extremities, and holding his breath for as long as he can remember. An observer estimates that he was submerged face-down for approximately 4 minutes before he was carried, apneic and pulseless, to the beach. Mouth-to-mouth resuscitation and external cardiac massage were performed for approximately 2 minutes. Spontaneous respirations and pulses then returned. The patient was transported by ambulance and was conscious upon arrival at the hospital at 5:05 P.M.; however, he was in severe respiratory distress. Respiratory rate was 40/min, with marked intercostal retractions and cyanosis. The pulse was rapid and thready, and systolic blood pressure was 68 torr. Cyanosis persisted, in spite of administration of 100 per cent oxygen by mask, and analysis of arterial blood revealed severe hypoxemia with mixed respiratory and metabolic acidosis ($Pa_{O_2}$ 51 torr, $Pa_{CO_2}$ 48 torr, $pH_a$ 7.27). There was some improvement in the respiratory status of the patient following placement of a nasotracheal tube, intermittent positive-pressure ventilation (IPPV**), and administration of sodium bicarbonate, 7.5 g iv, ($Pa_{O_2}$ 104 torr, $Pa_{CO_2}$ 27 torr, $pH_a$ 7.44 at $F_{I_{O_2}} = 0.6$). A roentgenogram of the chest, taken prior to insertion of the endotracheal tube, showed bilateral infiltrates, which decreased following initiation of IPPV. Physical examination and roentgenograms of the cervical spine confirmed that the patient had a spinal cord compression at the level of C5–C6 secondary to a compression fracture of the fifth cervical vertebra. Following intravenous infusion of an unknown amount of 5 per cent dextrose in 0.50 physiologic saline solution blood pressure increased to 96 torr systolic and pulse rate decreased to 92 beats/min. The ventilator was changed to a Bird Mark VII and the patient was transferred to the Gainesville Veterans Administration Hospital at 8 P.M.

Upon admission to that hospital blood urea nitrogen was 20 mg/100 ml, sodium 140 mEq/l, potassium 3.6 mEq/l, and chloride 100 mEq/l. The leukocyte count was $5.4 \times 10^3$ /cu mm, and hematocrit was 43.5 per cent, with no free hemoglobin present.

** MA-1 Ventilator; Puritan-Bennett Company, Kansas City, Mo.

Shortly after arrival in the Emergency Room, during spontaneous breathing of 100 per cent $O_2$, $Pa_{O_2}$ was 61 torr. The endotracheal tube was connected to an Emerson Post-Operative IMV†† Ventilator set to deliver 12 breaths/min and 10 torr positive end-expiratory pressure (PEEP). Analysis of arterial blood showed a marked improvement in oxygenation, but metabolic acidosis persisted ($Pa_{O_2}$ 160 torr, $Pa_{CO_2}$ 22 torr, $pH_a$ 7.25, at $F_{I_{O_2}} = 0.36$). The patient was given sodium bicarbonate, 7.5 g, and the rate of the ventilator was decreased from 12 to 8 breaths/min. Soon the patient began to breathe spontaneously between the intermittent mandatory ventilation (IMV), yet $Pa_{O_2}$ was 454 torr with $F_{I_{O_2}} = 1.0$ ($Pa_{CO_2}$ 39 torr, $pH_a$ 7.37) and $Pa_{O_2}$ was 132 torr with $F_{I_{O_2}} = 0.30$ ($Pa_{CO_2}$ 38 torr, $pH_a$ 7.37). The ventilator IMV rate and $F_{I_{O_2}}$ were gradually decreased over the ensuing 6 hours with no significant deterioration in arterial blood-gas values. Sixteen hours after aspiration of salt water, mechanical ventilation was discontinued, and the patient breathed spontaneously with 10 torr PEEP without difficulty ($Pa_{O_2}$ 97 torr, $Pa_{CO_2}$ 42 torr, $pH_a$ 7.40 at $F_{I_{O_2}} = 0.30$). Arterial blood-gas analysis following a gradual decrease in PEEP to 2 torr revealed no deterioration, and the trachea was extubated. Analysis of arterial blood 15 minutes later (20 hours after aspiration) showed $Pa_{O_2}$ 72 torr, $Pa_{CO_2}$ 35 torr, and $pH_a$ 7.44 while the patient breathed room air spontaneously. $Pa_{O_2}$ continued to increase to 87 torr 45 hours after aspiration and to 92 torr at 70 hours.

In addition to the above therapy, the patient was given 4 mg dexamethasone 8 hours after near-drowning. An aspirate of the endotracheal tube was cultured and revealed no growth. No antibiotic therapy was instituted. Despite the complete resolution of his pulmonary damage, the patient remains quadriplegic at this time.

*Patient 2.* A 33-year-old Caucasian man was found floating face-down in a salt-water tidal pool. He had been drinking heavily and had been severely beaten before falling into the water. Upon examination in the emergency room of the local hospital, he breathed spontaneously but was deeply cyanotic and responded only to pain. He had numerous bruises about his face and body, as well as a fractured left seventh rib. Blood pressure and pulse rate were normal, but rales were audible throughout both lung fields. The trachea was intubated and the patient was permitted to breathe spontaneously through a Briggs T-tube adapter through which 60 per cent $O_2$ was delivered. Arterial blood drawn under these conditions had a $P_{O_2}$ of 68 torr, $P_{CO_2}$ 40 torr, and pH 7.45. The hematocrit of venous blood was 43 vol per cent; serum electrolyte concentrations were sodium 144 mEq/l, potassium 3.5 mEq/l, and chloride 106 mEq/l.

The patient was transferred via ambulance approximately 60 miles to the William A. Shands Teaching Hospital. During transit he became apneic and was treated by intermittent positive-pressure ventilation with a self-inflating AMBU bag containing an oxygen reservoir to permit administration of 100 per cent $O_2$. This ventilatory support was continued en route and upon arrival at the emergency room of the hospital. During ventilation with the self-inflating bag and 100 per cent $O_2$, arterial pH was 7.36, $Pa_{CO_2}$ 33 torr, and $Pa_{O_2}$ 72 torr. Then, the endotracheal tube was connected to a Bird Mark VI-14 ventilator at an IMV rate of 12/min and 6 cm $H_2O$ PEEP was added. $Pa_{O_2}$ increased to 348 torr, $pH_a$ was 7.38, and $Pa_{CO_2}$ was 30 torr. Intrapulmonary shunt was calculated at 21.5 per cent, and arterial-venous oxygen content difference was 3.96 vol per cent.

A roentgenogram of the chest taken on admission to the hospital showed bilateral fluffy infiltrates suggestive of pulmonary edema and a fractured seventh rib. Two teeth in the digestive tract were also noted.

PEEP was increased to 10 cm $H_2O$, which raised $Pa_{O_2}$ to 459 torr on an $F_{I_{O_2}}$ of 1.0. An increase of PEEP to 12 cm $H_2O$ produced no further improvement. $F_{I_{O_2}}$ was then gradually decreased to 0.3 and the IMV rate decreased to 8/min. PEEP was maintained at 10 cm $H_2O$ overnight. Under these conditions $Pa_{O_2}$ remained in the range of 86 to 110 torr. A roentgenogram of the chest taken six hours after admission to Shands Teaching Hospital showed marked clearing of the infiltrates. The only therapy the patient received, other than intensive pulmonary care described above, was intravenous administration of fluids. He received no antibiotic or steroid.

Since the patient had a rubber endotracheal tube with a high-pressure cuff in place, we elected to exchange it for a tube with a low-pressure cuff that had been implant-tested. Some difficulty was encountered in reintubation and the patient had to be ventilated with a self-inflating bag and mask without PEEP for approximately 15 minutes. Despite apparently adequate ventilation, pink frothy fluid was noted exuding from the larynx, and copious amounts of this fluid were suctioned after reintubation. A roentgenogram of the chest taken immediately after reintubation showed the reappearance of bilateral pulmonary edema; however, after reinstitution of PEEP at 8 cm $H_2O$, $Pa_{O_2}$ rose to 439 torr at $F_{I_{O_2}} = 1.0$. Roentgenograms of the chest again showed marked clearing.

The patient's condition remained stable, and $F_{I_{O_2}}$ was decreased. The IMV rate was progressively decreased to 2/min and the patient was maintained on 8 cm $H_2O$ PEEP until the following day. PEEP was then reduced by 1 cm $H_2O$/hr with no deterioration of $Pa_{O_2}$. Immediately prior to extubation at PEEP 2 cm $H_2O$ and $F_{I_{O_2}}$ 1.0, $Pa_{O_2}$ was 530 torr. The trachea was extubated. The lungs remained clear, and $Pa_{O_2}$ was 82 torr during breathing of room air. The patient recovered uneventfully.

†† Intermittent mandatory ventilation (IMV) mechanically hyperinflates the patient's lungs at a preset rate, but allows spontaneous ventilation to occur between mechanical hyperinflations.[12]

These case histories illustrate that prompt respiratory therapy with PEEP can readily reverse the arterial hypoxemia resulting from aspiration of sea water. The transition from controlled to spontaneous ventilation should be accomplished gradually by employing IMV. The length of time necessary to maintain PEEP varies somewhat from patient to patient. In our first patient, pulmonary stability was achieved after 20 hours, but approximately 48 hours were required before our second patient could be weaned successfully from PEEP. The courses of our patients support the findings in our animal studies demonstrating the effectiveness of positive end-expiratory pressure in treatment of near-drowning in sea water.

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# *Electrolyte Changes in Human Drowning Victims*

*Jerome H. Modell, M.D.,* and Joseph H. Davis, M.D.†*

**The sera of 118 consecutive drowning victims and 24 persons who died of other causes were drawn from both sides of the heart at autopsy and analyzed for electrolyte concentration and specific gravity. The data from humans correlate well with previous animal studies and indicate that approximately 85 per cent of both fresh- and sea-water drowning victims aspirate 10 ml of fluid or less per pound body weight. It is unlikely, therefore, that most drowning victims die acutely of electrolyte imbalance and/or ventricular fibrillation. Death is more likely to be secondary to asphyxia. Results of the study also indicate that neither the chloride test nor the specific gravity of serum can be relied upon to establish a diagnosis of death by drowning.**

IN 1921, Gettler described the chloride test for diagnosis of death by drowning.[1] Since then, others have investigated the changes which occur in serum electrolyte concentrations during drowning by total immersion.[2] In these studies profound electrolyte changes have been reported. Studies in which controlled quantities of fluid were aspirated [3, 4, 5] and experience in treating human near-drowning victims [6-9] suggest that such profound changes are rare and seldom are the primary cause of death. This study was designed to document the magnitude and incidence of electrolyte changes in human drowning victims.

## Methods

One hundred eighteen consecutive recent drowning victims were studied. Excluded from this study were victims who had been in the water for an indeterminate time and whose bodies showed signs of decomposition. Also excluded were victims with severe coronary artery disease such that the question of an initiating or concomitant heart attack could be raised. The diagnosis of drowning was based on a combination of the circumstances surrounding the terminal episode with autopsy findings of variable amounts of froth in the airway, pulmonary congestion and edema, and water in the stomach and sphenoid sinus.

The following were recorded: age, interval between drowning and the time the body was delivered to the Medical Examiner's Office and refrigerated, and the time between drowning and autopsy. At autopsy, blood was drawn from the right and left ventricles using individual sterile 13-gauge needles and 50-ml syringes. The blood was centrifuged immediately, the serum removed, and serum specific gravity determined. The sample was then frozen for future serum electrolyte analyses. Although electrolyte concentrations of all samples were determined, specific gravities of sera of persons whose blood was grossly hemolyzed are not reported.

The serum was defrosted and analyzed for sodium, potassium and chloride. Sodium and potassium were determined on a Coleman flame photometer using a commercial preparation as a standard. Chloride concentration was determined with the Buchler-Cotlove chloridometer. Differences between the left and right heart samples (L-R) were calculated. Chloride values were converted to mg/100 ml of sodium chloride in order to apply Gettler's test, which assumes that if the concentration of sodium chloride is at least 25 mg/100 ml (4.3 mEq/l) greater in whole blood from the left heart than in whole blood from the right heart, the victim drowned in sea water; if at least 25 mg/100 ml less in the left he drowned in fresh water; if there is less than a 25 mg/100 ml difference between samples from the

* Associate Professor of Anesthesiology.
† Professor of Legal Medicine.
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left and right ventricles the patient did not drown.[1] * These studies were also performed on a control group of 24 persons who died acutely of causes other than drowning with no evidence of chronic illness.

Data were entered on IBM data cards. Means and standard deviations were calculated. Tests for significance of differences between comparable data of the three groups were sought by Student's *t* test with the aid of a digital computer.[11].

## Results

A total of 74 victims who drowned in fresh water pools, rock pits or canals (FW), 44 seawater victims (SW) retrieved from Atlantic Ocean beaches, and 24 persons who died of causes other than drowning (C) were studied. Although there was no difference between the average ages of the controls and the SW drowning victims (45.5 ± SE 5.2 years and 48.9 ± SE 4.2 years, respectively), the average age of FW victims was significantly less than the other groups (27.7 ± SE 2.9 years) ($P < 0.01$). The average intervals between drowning, or death, and refrigeration were 263 ± SE 39 minutes, 238 ± SE 49 minutes, and 160 ± SE 21 minutes for the FW, SW and control groups, respectively. The average intervals between death and autopsy were: FW, 858 ± SE 55 minutes; SW, 741 ± SE 91 minutes; C, 585 ± SE 92 minutes.

Electrolyte and specific gravity data are shown in table 1 (C), table 2 (SW), and table 3 (FW). The mean values for serum chloride, sodium, potassium and specific gravity of samples taken from the left ventricle are listed and compared for significant differences between groups in table 4.

Specific gravity of serum from the left ventricle was lower than that from the right in most patients, regardless of the cause of death. In the control group, specific gravity was lower in the left ventricle than in the right in 16 victims, higher in one, and equal on both sides in five. In the SW group, specific gravity was lower in the left ventricle than in the right in 30 victims, higher in seven, and both sides were equal in one. Victims of FW drowning had lower specific gravity in the left ventricle in 54 cases, higher values in four, and equal values in both ventricles in one.

When differences in chloride concentrations of sera taken from the left and right ventricles were compared according to Gettler's criteria, errors in diagnosis were found in 42 per cent of controls, 16 per cent of SW victims, and 90 per cent of FW victims (table 5).

A frequency distribution of serum chloride and sodium concentrations found in the left and right ventricles is listed in table 6. A serum chloride concentration of 100–105 mEq/l was assumed to be normal. The incidences of values within 20 mEq/l of normal, at least 20 mEq/l less than normal, and two groups greater than normal (20–30 mEq/l and >30 mEq/l) are listed for correlation with previous studies in animals. A value of 140 mEq/l sodium was arbitrarily set as normal and the incidences of values in ranges comparable to those reported for chloride are listed.

Regressions of both the serum chloride concentration in the left ventricle and the difference in serum chloride concentration between the left and right ventricles were made on the computer, based on patient age, time from death to refrigeration, and time from death to autopsy, for correlation between factors.[12] The only significant regressions found were those of the concentration of serum chloride in the left ventricle on length of time from death to autopsy in the control group ($r = -0.627$; $P = 0.0001$) and in the SW group ($r = -0.340$; $P < 0.05$); but not in the FW group ($r = -0.174$; $P > 0.10$). These negative regressions would allow for a postmortem fall of left ventricular chloride concentration of 1.7 mEq/l per hour in the control group and 0.15 mEq/l per hour in the SW group.

## Discussion

Heretofore, electrolyte changes secondary to aspiration of hypo- or hypertonic fluid have been emphasized as a major cause of death from drowning.[2, 13] In addition, diagnostic tests based on serum chloride concentrations[1, 13] and specific gravity[14, 15] have been proposed. The results of this study together

* Since erythrocyte chloride concentration ($Cl^-$) is normally 80 per cent of serum levels,[10] whole blood $Cl^-$ is less than serum $Cl^-$. Gettler's criterion of a 25 mg/100 ml deviation in whole blood becomes 29 mg/100 ml when serum is used.

TABLE 1. Serum Electrolyte and Specific Gravity Data from 24 Persons Who Died Acutely of Causes Other Than Drowning*

| | Sample Size | Mean | SD | SE | Minimum | Maximum |
|---|---|---|---|---|---|---|
| Cl,mEq/l | | | | | | |
| (L) | 24 | 93.0 | 8.7 | 1.8 | 79.0 | 119.0 |
| (R) | 24 | 88.6 | 7.8 | 1.6 | 74.0 | 111.0 |
| (L-R) | 24 | 4.4 | 4.1 | 0.8 | −4.0 | 10.0 |
| Na,mEq/l | | | | | | |
| (L) | 24 | 135.2 | 9.9 | 2.0 | 111.0 | 149.0 |
| (R) | 24 | 133.2 | 10.7 | 2.2 | 108.0 | 148.0 |
| (L-R) | 24 | 2.0 | 7.2 | 1.5 | −20.0 | 18.0 |
| K,mEq/l | | | | | | |
| (L) | 24 | 18.6 | 9.1 | 1.9 | 7.5 | 36.2 |
| (R) | 24 | 21.3 | 9.1 | 1.9 | 5.3 | 39.5 |
| (L-R) | 24 | −2.8 | 3.8 | 0.8 | −12.7 | 2.5 |
| Specific gravity | | | | | | |
| (L) | 22 | 1.0309 | 0.0046 | 0.0010 | 1.0229 | 1.0395 |
| (R) | 22 | 1.0327 | 0.0039 | 0.0008 | 1.0272 | 1.0395 |
| (L-R) | 22 | −0.0017 | 0.0018 | 0.0004 | −0.0058 | 0.0002 |

* Samples were drawn from the left ventricle (L) and right ventricle (R). Differences in electrolyte concentration and specific gravity between the two sides of the heart are listed (L-R).

TABLE 2. Serum Electrolyte and Specific Gravity Data from 44 Persons Who Died of SW Drowning*

| | Sample Size | Mean | SD | SE | Minimum | Maximum |
|---|---|---|---|---|---|---|
| Cl,mEq/l | | | | | | |
| (L) | 44 | 120.5 | 16.8 | 2.5 | 86.0 | 171.0 |
| (R) | 44 | 103.6 | 10.8 | 1.6 | 79.0 | 137.0 |
| (L-R) | 44 | 16.5 | 13.8 | 2.1 | −20.0 | 55.0 |
| Na,mEq/l | | | | | | |
| (L) | 44 | 149.8 | 12.5 | 1.9 | 121.0 | 198.0 |
| (R) | 44 | 143.9 | 10.3 | 1.6 | 106.9 | 163.0 |
| (L-R) | 44 | 5.8 | 9.2 | 1.4 | −15.0 | 37.0 |
| K,mEq/l | | | | | | |
| (L) | 44 | 16.1 | 6.6 | 1.0 | 7.0 | 29.6 |
| (R) | 44 | 18.6 | 6.8 | 1.0 | 9.3 | 37.0 |
| (L-R) | 44 | −2.5 | 3.6 | 0.5 | −11.6 | 7.8 |
| Specific gravity | | | | | | |
| (L) | 39 | 1.0307 | 0.0037 | 0.0006 | 1.0225 | 1.0375 |
| (R) | 39 | 1.0336 | 0.0038 | 0.0006 | 1.0230 | 1.0422 |
| (L-R) | 39 | −0.0029 | 0.0042 | 0.0007 | −0.0187 | 0.0050 |

* Samples were drawn from the left ventricle (L) and right ventricle (R). Differences in electrolyte concentration and specific gravity between the two sides of the heart are listed (L-R).

with prior results from this laboratory [3, 5, 7] suggest that profound changes in serum sodium and chloride concentrations are rare in drowning victims. These results also shed considerable doubt on the reliability of diagnostic tests based on electrolyte changes.

## ELECTROLYTE CHANGES IN FW DROWNING VICTIMS

While the mean concentration of serum sodium in the left ventricle was significantly less in the FW drowning victims than in the con-

TABLE 3. Serum Electrolyte and Specific Gravity Data from 74 Persons Who Died of FW Drowning*

| | Sample Size | Mean | SD | SE | Minimum | Maximum |
|---|---|---|---|---|---|---|
| Cl,mEq/l | | | | | | |
| (L) | 74 | 89.0 | 11.4 | 1.3 | 48.0 | 131.0 |
| (R) | 74 | 86.2 | 8.3 | 1.0 | 65.0 | 103.0 |
| (L-R) | 74 | 2.8 | 8.1 | 0.9 | −40.0 | 31.0 |
| Na,mEq/l | | | | | | |
| (L) | 74 | 127.5 | 11.5 | 1.3 | 97.0 | 162.0 |
| (R) | 74 | 129.2 | 9.6 | 1.1 | 89.0 | 157.0 |
| (L-R) | 74 | −1.7 | 8.4 | 1.0 | −40.0 | 16.0 |
| K,mEq/l | | | | | | |
| (L) | 73 | 18.2 | 7.4 | 0.9 | 5.0 | 53.0 |
| (R) | 74 | 21.6 | 8.2 | 1.0 | 8.3 | 62.9 |
| (L-R) | 73 | −3.5 | 4.2 | 0.5 | −17.6 | 5.3 |
| Specific gravity | | | | | | |
| (L) | 59 | 1.0280 | 0.0040 | 0.0005 | 1.0205 | 1.0370 |
| (R) | 59 | 1.0314 | 0.0043 | 0.0006 | 1.0219 | 1.0438 |
| (L-R) | 59 | −0.0032 | 0.0032 | 0.0004 | −0.0185 | 0.0045 |

* Samples were drawn from the left ventricle (L) and right ventricle (R). Differences in electrolyte concentration and specific gravity between the two sides of the heart are listed (L-R).

trols, mean chloride and potassium concentrations in the two groups were not different. In only ten of 74 FW drowning victims (14 per cent) were the concentrations of serum chloride in the left ventricle less than 80 mEq/l; in only 12 (16 per cent) were the serum sodium concentrations less than 120 mEq/l. These values may be correlated with experimental data from animals in which aspiration of 10 ml per pound or less of FW produced sodium and chloride values less than 20 mEq/l below normal three minutes after aspiration, and aspiration of 20 ml per pound produced values more than 20 mEq/l below normal.[4] While the sodium and potassium concentrations of dog and human erythrocytes are different, the concentrations of chloride are similar in the two species. Serum concentrations of all three electrolytes in the dog are almost identical to values in humans.[10] It is reasonable, therefore, to use the chloride values for the most reliable comparison. Of further note is that sodium changes after aspiration of 10 ml of FW per pound body weight in rabbits are comparable to those found in dogs.[16] Since erythrocytes of rabbits and hu-

TABLE 4. Means and Standard Deviations of Serum Electrolyte Concentrations and Specific Gravities of Samples Obtained from the Left Ventricles of Victims of FW Drowning, SW Drowning, or Other Causes (Control)

| | Fresh Water Victims (74) | FW *vs.* Control *P* value | Controls (24) | Control *vs.* SW *P* value | Sea Water Victims (44) | FW *vs.* SW *P* value |
|---|---|---|---|---|---|---|
| Cl,mEq/l | 89 ± 11.4 | * | 93 ± 8.7 | <0.001 | 120 ± 16.8 | <0.001 |
| Na,mEq/l | 128 ± 11.5 | <0.01 | 135 ± 9.9 | <0.001 | 150 ± 12.5 | <0.001 |
| K,mEq/l | 18.2 ± 7.4 | * | 18.6 ± 9.1 | * | 16.1 ± 6.6 | * |
| Specific gravity | 1.0280 ± 0.0040 | <0.01 | 1.0309 ± 0.0046 | * | 1.0307 ± 0.0037 | <0.01 |

* No significant difference between groups, $P > 0.10$.

TABLE 5. Differences in Concentrations of Serum Chloride in the Left and Right Ventricles Calculated as mg/100 ml NaCl*

| | Total Number of Victims | Diagnosis Predicted by Gettler's Criteria | | |
|---|---|---|---|---|
| | | Fresh-water Drowning | Not Drowned | Sea-water Drowning |
| Group 1 Controls | 24 | 0 | 14 | 10 |
| Group 2 Sea-water victims | 44 | 2 | 5 | 37 |
| Group 3 Fresh-water victims | 74 | 7 | 37 | 30 |

* Cause of death compared with the expected cause of death according to Gettler's criteria.

mans have similar levels of sodium and potassium,[10] this further supports the rationale for comparison.

When dogs aspirate 10 ml or less of distilled water per pound body weight they do not die of ventricular fibrillation.[3, 4, 17] When at least 20 ml of fluid per pound is aspirated, however, fibrillation occurs in 80 per cent of animals, at a mean time of 3.25 minutes following aspiration.[4] If the animal data can be extrapolated to humans, approximately 85 per cent of human FW drowning victims aspirate less than 10 ml of fluid per pound and, therefore, probably do not die acutely of electrolyte imbalance and/or ventricular fibrillation. A more likely cause of death is asphyxia.[3, 4, 7] If these victims had been rescued and resuscitated, it is unlikely that abnormal electrolyte values would have been demonstrable, since electrolyte homeostasis is reached rapidly in both humans and animals that survive FW near-drowning.[3, 7]

There are two reasons for selecting left ventricular blood for comparison between animals and humans. First, in the animal experiments, samples were drawn from the arch of the aorta, thus reflecting electrolyte changes distal to the lung. Second, if there is a rapid transfer of fluid and electrolytes across the alveolar–capillary membrane, the resultant changes probably would have appeared distal rather than proximal to the lungs. We have compared the electrolyte values at autopsy in humans with those seen three minutes after aspiration in dogs. In dogs after drowning in FW the concentration of serum chloride progressively decreases with time.[13] If this also occurs in humans, it would exaggerate the electrolyte changes found and further strengthen the conclusion that less than 15 per cent of victims aspirated 20 ml or more of FW per pound.

## ELECTROLYTE CHANGES IN SW DROWNING VICTIMS

The mean concentrations of serum chloride and sodium in the left ventricles of sea-water drowning victims were significantly higher than those of either the controls or the fresh-water victims. Potassium concentrations were

TABLE 6. Frequency Distribution of Concentration of Serum Sodium and Chloride from the Left (LV) and Right (RV) Ventricles of FW and SW Drowning Victims and Persons Who Died from Other Causes

| | Total No. Victims | | Serum Chloride, mEq/l | | | | Serum Sodium, mEq/l | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | ≤79 | 80–125 | 126–135 | >135 | ≤119 | 120–160 | 161–170 | >170 |
| Group 1 Controls | 24 | LV | 1 | 23 | 0 | 0 | 1 | 23 | 0 | 0 |
| | | RV | 4 | 20 | 0 | 0 | 3 | 21 | 0 | 0 |
| Group 2 Sea-water victims | 44 | LV | 0 | 26 | 11 | 7 | 0 | 39 | 4 | 1 |
| | | RV | 1 | 42 | 0 | 1 | 1 | 41 | 2 | 0 |
| Group 3 Fresh-water victims | 74 | LV | 10 | 63 | 1* | 0 | 12 | 61 | 1* | 0 |
| | | RV | 16 | 58 | 0 | 0 | 12 | 62 | 0 | 0 |

* Body recovered from canal near entrance to bay; position of tide unknown.

comparable in all groups, however. When the frequency distribution of serum chloride samples from the left ventricle were analyzed, 59 per cent of victims had chloride values within 20 mEq/l of normal. An additional 25 per cent had values between 21 and 30 mEq/l above normal. These data can be compared with results of animal experiments in which three minutes after aspiration of 5 ml of sea water per pound body weight the average increase in serum chloride concentration in the aorta was less than 20 mEq/l. When 10 ml per pound of SW was aspirated, the mean increase was less than 30 mEq/l. From these data, it appears that 59 per cent of SW drowning victims aspirate 5 ml or less of SW per pound body weight, an additional 25 per cent aspirate between 5 and 10 ml of SW per pound body weight, and only 16 per cent aspirate more than 10 ml of SW per pound body weight.

These data compare well with the findings in the FW drowning victims where, based on chloride determinations in the left ventricle, 14 per cent were estimated to have aspirated more than 10 ml of water per pound body weight. The serum sodium data in the SW drowning victims indicate that the majority of patients aspirated less than 5 ml of water per pound body weight. It has been shown previously in both animal experiments and observations in human near-drowning victims, however, that following SW drowning changes in serum chloride persist longer than changes in sodium.[5, 7] It seems reasonable, therefore, to assume that the serum chloride levels would be more reliable in this situation.

### Diagnostic Tests for Drowning

The figures in table 5 emphasize the poor reliability of Gettler's chloride test for death by drowning. While his criteria would have resulted in only 16 per cent wrong diagnoses in this series of SW drowning victims, 42 per cent of controls and 90 per cent of FW victims would have been diagnosed incorrectly. Gettler proposed his test on the basis of findings in only three FW drowning victims (only two of them had been suspected to have died from drowning) and 16 SW victims.[1] Moritz questioned the reliability of this test more than 20 years ago, and emphasized the importance of performing an autopsy early, because the chloride concentrations in left and right heart blood changed with time, thus making differences more difficult to detect.[13] In the present study a negative correlation between increasing time from death to autopsy and concentration of serum chloride in the left ventricle was found in persons who had died from causes other than drowning and in SW drowning victims; however, the correlation in the FW drowning victims was not significant. If the chloride test were consistently reliable in diagnosing FW drowning when autopsy was performed immediately after death, we would expect to see a correlation between the chloride concentration of either the left heart blood or the difference between left and right heart blood and time. Such a correlation was not seen. Similar conclusions regarding the unreliability of this test have been drawn by other authors.[14]

In 1953, Durlacher, Freimuth and Swann suggested that a more accurate test for drowning could be obtained by measuring specific gravity of plasma in the right and left sides of the heart. They reported that if the specific gravity is lower in the left heart than the right, the cause of death is drowning, either FW or SW, and if the specific gravity is greater in the left than in the right, the patient died of some other cause.[14] Subsequently, however, they found 45 per cent of non-drowning victims had lower specific gravities on the left than on the right.[15] In our study the specific gravity of plasma was less in the left ventricle than in the right in 91 per cent of FW drowning victims, 79 per cent of SW drowning victims, and 75 per cent of persons who died of other causes. Thus, it is not possible to separate the drowning victims from the controls by this criterion. An important difference between their second study and ours was that they corrected the specific gravity for hemolysis. This was not done by us; however, the specific gravity was not determined for persons with gross hemolysis.

From the results of this study it may be concluded that if human and animal data can be compared, the majority of human drowning victims (approximately 85 per cent) aspirate

10 ml or less of fluid per pound body weight. It is unlikely, therefore, that most drowning victims die acutely of electrolyte imbalance and/or ventricular fibrillation. More likely, their deaths are due to acute asphyxia, and, if rescued, promptly resuscitated, and given intensive pulmonary therapy, they would stand a reasonable chance for survival. Diagnosis of death by drowning based on differences in specific gravity or chloride concentration of serum samples taken from the left and right ventricles at autopsy is not reliable.

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# *Physiologic Effects of Near Drowning with Chlorinated Fresh Water, Distilled Water and Isotonic Saline*

*Jerome H. Modell, M.D.,* Margaret Gaub, M.D.,† Frank Moya, M.D.,‡ Betty Vestal, M.S.,§ Herbert Swarz, M.D.¶*

(WITH THE TECHNICAL ASSISTANCE OF ALFREDO JALOWAYSKI AND INELDA SMITH)

**The clinical picture and biochemical changes reported in human victims of near-drowning is considerably different from those reported in dogs subsequent to total immersion in fresh water. To gain further insight into this apparent discrepancy and to study the differences in the pathophysiological response of animals to drowning in chlorinated fresh water compared to unchlorinated fresh water and isotonic saline solution, a group of experiments was undertaken.**

**The changes in cardiovascular dynamics, blood constituents and serum electrolytes observed in this study were transient, frequently limited to the arterial samples; these spontaneously reverted to normal in the thirteen animals who survived the experiment. Ten to sixty minutes post-immersion the three groups studied were indistinguishable. Conversely, acute asphyxia with arterial hypoxemia and metabolic acidosis which persisted throughout the experiment was seen in all animals. The presence of chlorine in distilled water did not significantly alter the response to aspiration.**

DEATH from drowning usually results from a combination of respiratory and circulatory disturbances secondary to the aspiration of water. In 1947, Swann and his associates[1] published the first of a series of reports on the biochemical changes in dogs following total immersion in fresh and sea water. After fresh water aspiration, the dogs developed acidosis, hypoxia, hypercarbia, a decreased hemoglobin content, and a rapid hypervolemia as measured by blood specific gravity. In addition, these investigators observed hyponatremia, hypochloremia, hyperkalemia and a transient hypertension, followed by profound hypotension and frequently ventricular fibrillation within moments of immersion.[2] In 1961, Redding *et al.*,[3] found it difficult to resuscitate dogs who aspirated fresh water since ventricular fibrillation occurred within three minutes of instituting artificial ventilation. Closed-chest cardiac massage and electrical defibrillation were followed by resumption of a spontaneous heartbeat and blood pressure. Intermittent positive pressure ventilation was discontinued after one hour and all animals died within a 24-hour period, with evidence of massive hemolysis and myocardial failure. It would appear from these experiments that the consequences of rapid absorption of water into the circulatory system and resultant changes in blood constitutents and electrolytes are of primary importance in death from fresh water drowning and the respiratory difficulties of secondary importance.

Following these excellent experiments, other investigators applied the results obtained in animals to man and have advocated methods of resuscitation stressing the circulatory problems.[4, 5, 6]

In a review of case reports compiled by Fuller,[7] however, the course of human beings who have suffered a fresh water near-drowning episode does not follow that predicted by Swann's laboratory data. The major finding in these patients is pulmonary edema rather than intravascular complications. Most fre-

* Assistant Professor of Anesthesiology and the Director of the Inhalation Therapy Service.
† Resident in Anesthesiology.
‡ Professor and Chairman of Anesthesiology.
§ Instructor in Anesthesiology.
¶ Medical Student in the Department of Anesthesiology, University of Miami School of Medicine and Jackson Memorial Hospital, Miami, Florida (present address: Public Health Hospital, Staten Island, New York).

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quently people who aspirate fresh water show normal serum electrolyte concentrations and frequently demonstrate a high hemoglobin and high hematocrit rather than the low hemoglobin, low hematocrit, and abnormal serum electrolytes as predicted from animal data. Assuming that species variation is not a factor, these differences may be related to the chlorine in fresh water pools or the debris in lakes which may alter the rate of fluid absorption.[8] Other more likely possibilities are: (1) human near-drowning victims aspirate smaller quantities of water than obtain in total immersion animal studies; or (2) the changes in concentration of blood elements and serum electrolytes secondary to fresh water aspiration rapidly revert to normal during recovery.

To gain further understanding of this apparent discrepancy between dog and man, and to study the differences in the response of animals to near-drowning in chlorinated fresh water compared to unchlorinated fresh water, the following experiments were undertaken.

## Procedure

Fifteen mongrel dogs weighing 25 to 50 pounds and in apparent good physical condition were divided into groups of five according to the type of water aspirated.

Group I: Chlorinated. Distilled water to which five parts per million of chlorine (trichloro-s-triazinetrione) was added on the day of the experiment.

Group II: Distilled. Unchlorinated distilled water.

Group III: Saline Control. Isotonic saline solution (0.9 *N*).

After a 15 gauge Rochester needle was inserted into a vein of the foreleg, 50 mg. increments of 2½ per cent sodium thiopental were given intravenously to produce basal narcosis (*i.e.*, cessation of spontaneous movement; respiration and lid reflex remained active). The trachea was intubated under direct vision, the endotracheal tube cuff inflated and the animal permitted to breathe spontaneously.

Both femoral arteries and veins were cannulated with siliconized polyethylene tubing (inside diameter, 0.066 inch). The arterial catheters were threaded to the proximal portion of the descending aorta and the venous catheters into the inferior vena cava near the right atrium. Position of catheters was subsequently confirmed at autopsy. The catheters on the left side were connected via Statham strain gauges to a multichannel photographic recorder for monitoring of arterial and venous pressures. The catheters on the right were connected to a triple stopcock assembly for sampling of blood. Lead 2 of the electrocardiogram was recorded continuously.

Twenty minutes prior to immersion, radioactive iodinated serum albumin (RISA) was injected intravenously and the needle flushed with 5 per cent dextrose in water. Five to ten minutes preimmersion, respiratory minute volume was measured in triplicate with a Wright Ventilometer connected to the endotracheal tube. Respiratory rate was counted and the average tidal volume calculated.

Four minutes prior to immersion, arterial blood samples were drawn anaerobically into heparinized, greased syringes and the *p*H measured in the AME-1 Astrup Micro Apparatus. The $P_{CO_2}$ and base excess were calculated from the Siggaard-Andersen nomogram.[9] Arterial $P_{O_2}$ was also measured on the Astrup Apparatus using a direct reading Clark type oxygen electrode.[10] Arterial and venous bloods were drawn simultaneously at this time and transferred immediately to sets of heparinized test tubes for whole blood studies and clean test tubes for clot formation for serum analysis. Care was taken to avoid stasis of blood in catheters by removing 5 ml. of blood and discarding immediately before samples were withdrawn and to avoid hemolysis. Heparinized blood was analyzed for total hemoglobin by the cyanmethemoglobin method and for hematocrit using the Guest-Weichselbaum micro-capillary centrifuge. The blood was then centrifuged, the plasma removed and analyzed for hemoglobin by a modified version of the Bing and Baker technique.[11] Serum studies included determination of sodium, potassium and calcium on the Coleman flame photometer using a commercial serum preparation as a control standard. Serum chloride analysis was performed on the Buchler-Cotlove Chloridometer. Venous blood was used for blood volume studies utilizing the RISA technique with a Picker Hemoliter Counter.

Thirty seconds prior to immersion the endotracheal tube was connected via a Y-adapter

to a water reservoir and breathing bypass (fig. 1). At zero time the bypass was occluded and each dog allowed to aspirate 10 ml. of water per pound of body weight. After aspiration the animal was again allowed to breathe room air through the emptied water reservoir. As soon as water cleared, the reservoir was disconnected from the endotracheal tube and ventilatory studies were performed. One, 3, 5, 10, 30, and 60 minutes after the onset of immersion, arterial and venous blood determinations were repeated. When the 60-minute postimmersion determinations were completed, all surviving animals were sacrificed with an over-dose of intravenous sodium thiopental and autopsy performed. Gross pathology of the tracheobronchial tree, lungs, and heart was noted.

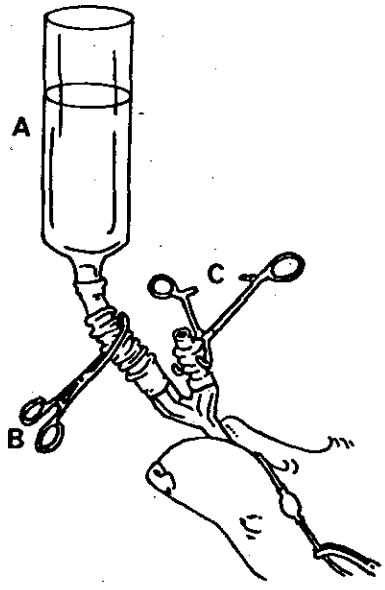


FIG. 1. Water reservoir and breathing bypass. The animal is connected to the water reservoir and breathing bypass via a cuffed endotracheal tube. At "0" time the bypass is occluded by clamping hemostat "C" and the animal allowed to aspirate fluid from the reservoir "A" by release of hemostat "B."

## Results

All data reported represent average values for each group of 5 animals. When an animal expired prior to the termination of the experiment data were included until time of death. Average control values of weight, tidal volume, total volume of fluid aspirated, and fluid/tidal volume ratio for each group are shown in table 1. Thirteen of the 15 animals survived the 60-minute experiment. One dog died five minutes after chlorinated water aspiration and one seven minutes after saline aspiration. In both, the immediate cause of death appeared to be apnea.

*Cardiovascular Changes.* A decline in systolic blood pressure was seen within 14 seconds of immersion in all 15 animals studied. This was immediately followed by hypertension before the blood pressure returned to normal levels (table 2). Both the degree and duration of hypotension were more severe in the combined fresh water group than in the saline control ($P = < 0.05$)*; however, the duration of hypertension that followed was equivalent in both groups ($P = > 0.9$). A significant difference in the degree of hypotension was also noted between groups I and II ($P = < 0.05$).

Venous pressure rose in all animals immediately following aspiration and gradually returned to normal when the arterial pressure stabilized. A transient decrease in pulse rate below 100 per minute was noted within 15 seconds of immersion in all animals who aspirated fresh water and in one after saline aspiration. A similar decrease was seen within

* Two sample Student's *t* test.

TABLE 1. Pre-aspiration Control Data

| Group | Number of Animals | Average Weight (lbs.) | Volume Fluid Aspirated (ml.) | Control Tidal Volume (ml.) | Fluid/Tidal Volume ratio |
|---|---|---|---|---|---|
| I Chlorinated | 5 | 36 | 360 | 182 | 1.98 |
| II Distilled | 5 | 43 | 430 | 186 | 2.31 |
| III Saline | 5 | 37 | 370 | 209 | 1.77 |
| All groups combined | 15 | 39 | 390 | 192 | 2.03 |

TABLE 2. Systolic Blood Pressure Changes Subsequent to Aspiration of Chlorinated Distilled Water, Unchlorinated Distilled Water, and Physiological Saline Solution (10 ml./pound)

| Group | Maximum Decline in Systolic Blood Pressure In mm. Hg | | Duration of Hypotension In Seconds | | Duration of Hypertension In Seconds | |
|---|---|---|---|---|---|---|
| | Average | Range | Average | Range | Average | Range |
| I Chlorinated | 43* | 30–56 | 22 | 12–30 | 226 | 80–600 |
| II Distilled | 77* | 32–96 | 45 | 18–85 | 173 | 76–250 |
| III Saline | 31* | 25–40 | 5* | 3–9 | 203 | 100–450 |

* $P = <0.05$

one minute in three additional animals in the saline group. Bigeminy appeared in 9 of 15 (group I, 3; group II, 2; group III, 4). An elevated T wave appeared in three of the five animals in both of the distilled water groups (with and without chlorine).

*Ventilatory Response.* Apnea occurred within nine seconds of aspiration (mean 4 seconds) in 14 of the 15 animals studied and persisted for 10 to 39 seconds. Average duration of the initial apneic episode was 25 seconds in group I, 22 seconds in group II, and 19 seconds in group III. Although all surviving animals were hyperventilating at the conclusion of the experiment, this was most marked in the saline controls ($P = < 0.05$) (table 3).

*Blood Gas and Acid-Base Studies.* The average values for arterial *p*H, $Po_2$, $Pco_2$, and base excess for each of the three groups studied are shown in figure 2. All groups show the same trends. The *p*H reached its lowest value five minutes after onset of immersion and although a gradual return toward normal was seen, the average *p*H for the three groups was still 7.30 at the end of the 60-minute test period. The $Po_2$ dropped sharply to a mean of approximately 40 mm. of mercury one minute following aspiration in all groups and remained below 50 mm. of mercury throughout the remainder of the experiment. Base excess reached its lowest value 10 minutes after onset of immersion. There was an immediate but transient rise in $Pco_2$ in all groups which reached a peak five minute postimmersion.

*Hemoglobin, Hematocrit, and Blood Volume.* Except for a transient fall in arterial hemoglobin concentration one minute after onset of immersion in both distilled water groups, the average hemoglobin values for all three groups remained essentially normal and indistinguishable (range 12.3 to 14.0 g./100 ml.). Venous hemoglobin determinations did not demonstrate this initial decline in groups I and II but rather, remained normal to moderately elevated throughout the experiment. Presumably this was because of the rapid entry of water into the arterial system which is subsequently redistributed before venous return. The hematocrit remained normal to

TABLE 3. Summary of Respiratory Response Prior to and Sixty Minutes Following Onset of Immersion

| Time | Group | Respiratory Rate per Minute | | Minute Volume (liters/minute) | | Tidal Volume (ml.) | |
|---|---|---|---|---|---|---|---|
| | | Range | Average | Range | Average | Range | Average |
| Prior to immersion | I | 20–35 | 25 | 2.6– 6.3 | 4.4 | 124–222 | 182 |
| | II | 23–87 | 42 | 4.5–11.5 | 7.0 | 131–247 | 186 |
| | III | 17–40 | 26 | 2.5– 8.6 | 5.6 | 147–233 | 209 |
| 60 min. post-immersion | I | 47–104 | 74 | 9.2–16.4 | 11.7 | 88–234 | 174 |
| | II | 64–128 | 90 | 10.0–23.2 | 17.3 | 131–257 | 189 |
| | III | 118–160 | 137* | 17.2–30.2 | 21.7 | 111–242 | 164 |

* $P = <0.05$.

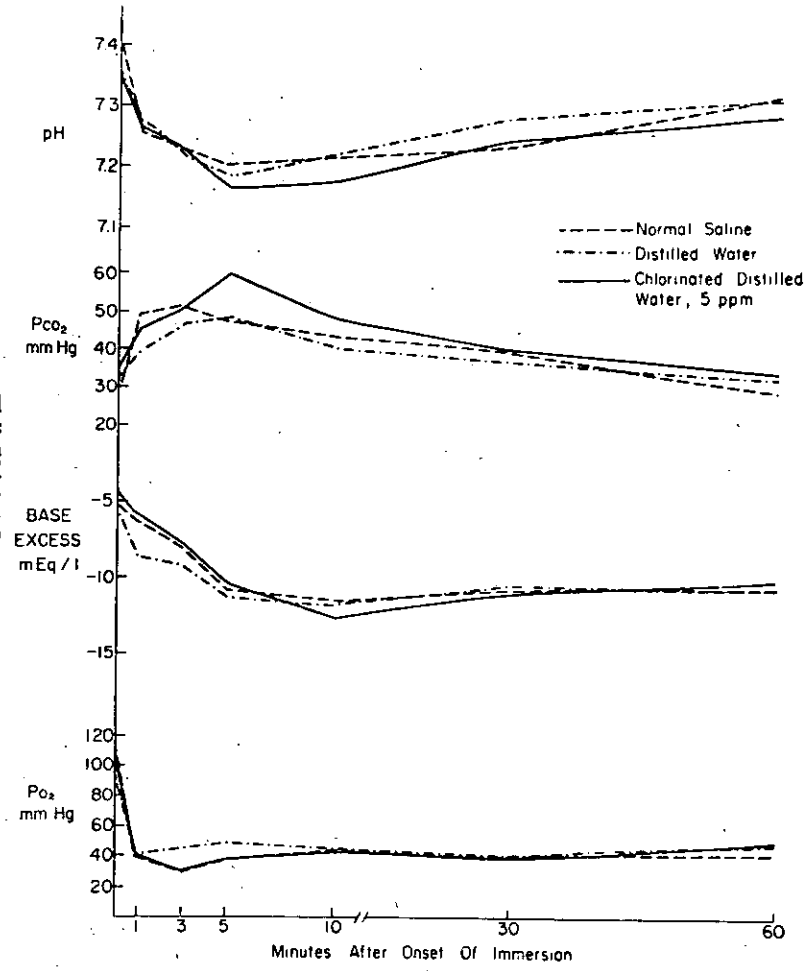


FIG. 2. Arterial blood gas and acid base changes subsequent to aspiration of chlorinated distilled water, unchlorinated distilled water, and physiological saline solution (10 ml. per pound).

slightly elevated in all three groups (range 37 to 45 volumes per cent). The blood volume demonstrated an initial sharp rise to 125 and 132 per cent of the pre-aspiration volume three minutes postimmersion in the chlorinated and unchlorinated distilled groups, respectively. These figures are not significantly different ($P = > 0.2$). The saline controls, however, showed a more gradual rise in blood volume approaching the other groups toward the end of the experiment ($P = < 0.05$ at one, three, and five minutes). Sixty minutes postimmersion, blood volumes were 129, 128, and 124 per cent of their pre-aspiration value in groups I, II, and III, respectively (fig. 3).

Gross hemolysis was observed in all animals that aspirated unchlorinated distilled water, four of five animals in the chlorinated group, and in none of the saline controls. The average plasma free hemoglobin values found in the distilled water animals were approximately twice those found in the chlorinated group. This difference was primarily the result of exceptionally high values in only two of the five animals in group II. The individual range of the peak arterial plasma hemoglobin concentration three minutes following aspiration was considerable.

*Serum Electrolytes.* The changes in arterial serum electrolytes are shown in figure 4. Serum sodium and serum chloride showed moderate decreases at one, three, and five minutes postimmersion in the animals that aspirated unchlorinated distilled water. The lowest average values were observed at one minute. These changes first appeared and

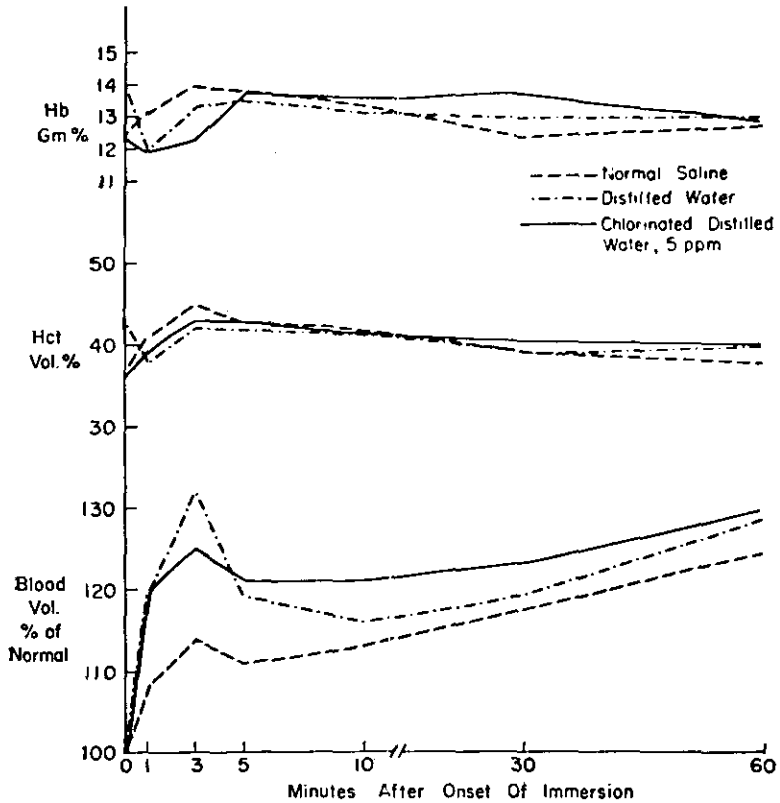


FIG. 3. Arterial hemoglobin and hematocrit and venous blood volume changes subsequent to aspiration of chlorinated distilled water, unchlorinated distilled water, and physiological saline solution (10 ml. per pound).

were most noticeable in arterial blood (sodium 118 mEq./liter; chloride 88 mEq./liter). The lowest average sodium and chloride found in venous blood were 132 mEq./liter and 97 mEq./liter, respectively, in the three-minute samples. Ten minutes post-immersion the arterial and venous electrolyte concentrations were indistinguishable. All values returned to essentially normal levels at the completion of the experiment. The chlorinated group showed a similar pattern but a less severe decline in the one minute arterial samples. The differences observed between the chlorinated and unchlorinated distilled water groups were not significant ($P = > 0.05$). Unlike the animals who aspirated distilled water, the serum sodium and serum chloride remained unchanged in the saline controls ($P = < 0.05$). Serum potassium concentration increased in all of the chlorinated and in four of the animals in the unchlorinated distilled water group; reaching a peak at three minutes and rapidly returning to normal. A transient rise in potassium was also noted in three of five saline control animals. A significant difference between the combined groups I and II *vs.* group III was seen only in the one minute samples ($P = < 0.05$). Calcium levels remained essentially normal in all three groups.

*Postmortem Findings.* The heart was of normal size in all 15 animals. Clear foam was seen in the trachea and major airways of 2 dogs, pink frothy foam in 2 and no evidence of foam or water in the remaining animals; in each of the chlorinated and unchlorinated distilled water groups. Major airways of all animals subjected to normal saline aspiration contained copious amounts of clear white foam and clear free fluid poured out of the airways.

The superior portions of the lungs of all animals were clear and contained air. The four survivors in group I showed scattered areas of hemorrhagic discoloration and atelectasis in the dependant lobes. The dependant portions of the lungs of the dog who succumbed to immersion were heavy, boggy and water logged.

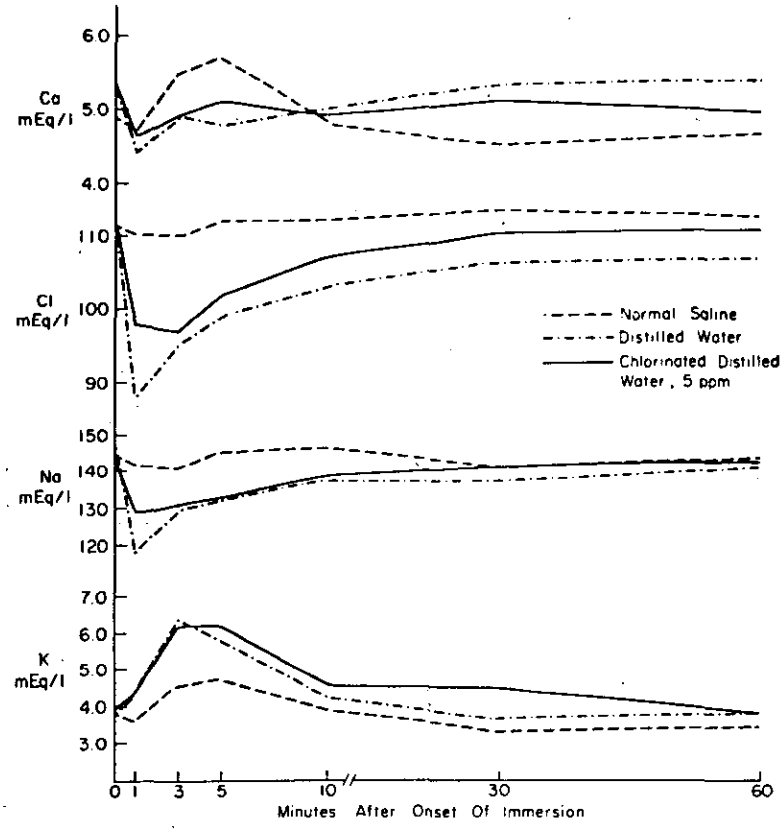


FIG. 4. Arterial serum electrolyte changes subsequent to aspiration of chlorinated distilled water, unchlorinated distilled water, and physiological saline solution (10 ml. per pound).

Spotty hemorrhagic and atelectatic areas were also seen in the dependent lobes of 4 animals in group II and in the fifth these areas were boggy and almost confluently hemorrhagic. The dependent lung fields in all of the saline controls were solid, water logged, and consisted of massively confluent, purplish, hemorrhagic areas.

Blood tinged fluid was found in the alimentary tract of some animals after chlorinated and unchlorinated distilled water aspiration.

## Discussion

In this study, two major deviations from previous experiments were employed: (1) the volume of fluid aspirated was chosen at 10 ml. per pound of body weight, or approximately two times the normal measured tidal volume of the animals; and, (2) all animals were allowed the opportunity to breathe air following immersion. Conceivably these conditions may resemble more closely the situation in the human near-drowning victim who is rescued shortly after onset of immersion than does the technique of prolonged total immersion.

In these studies blood removed for sampling was not replaced by transfusion. It is possible that acute death from primary hypervolemia [12] may have been prevented in the animals by intermittent blood sampling. In subsequent studies performed to determine the effect of aspirating various volumes of chlorinated distilled water, the same experimental protocol was followed but fewer samples were drawn so that blood loss was not major (less than 5 per cent of blood volume). Although there was a slightly greater delay in return to normal of serum electrolytes, the overall trends observed in animals aspirating 10 ml. of water per pound body weight were similar to those reported here.[13]

Although slight differences were noted in the absolute average values for blood constituents, serum electrolytes, and blood volume subsequent to aspiration between the chlorinated and unchlorinated distilled water groups

these differences were not significant. This would tend to negate the hypothesis that chlorine in fresh water significantly alters the rate of passage of fluid from the lungs into the circulatory system.

Although the serum sodium, chloride, and potassium showed transient changes in the arterial blood of the dogs immersed in distilled water with and without chlorine, all these values rapidly returned to normal. If only venous samples were obtained these changes would not have been detected. In addition, all animals showed essentially normal values for hemoglobin, hematocrit, and serum calcium. If one observes all the above values sixty minutes following immersion, the interpretation is one of normal levels. Thus, if a species variation does not exist, we may speculate that the reason the transient changes observed in this study are not seen in human near-drowning victims is that arterial blood is not sampled within the critical first few minutes after onset of immersion. Subsequently, there is a shift of the absorbed fluid and body electrolytes so that blood constituent and serum electrolyte concentrations rapidly return to normal levels despite a persistent elevation in the blood volume. Although these experiments were not designed to study the exact nature of the shifts, there is some indirect evidence that the gastrointestinal tract may receive much of the fluid because blood tinged fluid was found in the alimentary tract of some animals at autopsy.

Ventricular fibrillation has been reported frequently to be the terminating episode in death from experimental fresh water drowning, but its occurrence in man has been confirmed only twice, one a victim of fresh water [14] and the other a victim of sea water aspiration.[15] Ventricular fibrillation did not occur in this study in spite of severe hypoxemia, acidosis, and hyperkalemia (the highest transient serum potassium level observed was 9.7 *mEq./liter*). Electrocardiographic changes were primarily limited to bradycardia, bigeminy, dropped beats, and elevated T waves, all of which can be attributed to hypoxia and, in some animals, hyperkalemia.

Since the hypotensive episode observed immediately after immersion coincided approximately with the period of apnea (or breath holding), it may have been reflex in origin or secondary to a reduced venous return produced by an increased intrathoracic pressure. On the other hand, the more profound hypotension seen in the fresh water groups suggests it may be secondary to acute cardiac insufficiency resulting from rapid influx of hypotonic solution. If so, larger quantities of aspirated hypotonic water may increase the severity, and further prolong the duration, or both. The hypertensive episode which followed may be attributed to the increased blood volume and the release of catecholamines secondary to acute asphyxia.

Although significant transient changes in blood constituents, electrolytes, and the cardiovascular system were more frequently observed in groups I and II than in the saline controls, the differences were slight after the first ten minutes; subsequently the nature of the aspirated fluid did not appear to be an important factor. It would appear, therefore, that the derangement of the cardiovascular system and blood constituents was not a serious problem in these animals. Kylstra,[16] on the other hand, recently found that the nature of the aspirated fluid does severely alter the cardiovascular changes observed in animals subjected to total immersion.

The arterial blood gas and acid-base studies of all three groups studied are indistinguishable. These data indicate a common respiratroy problem regardless of the type of fluid aspirated, *i.e.*, acute asphyxia with persistent severe arterial hypoxemia and metabolic acidosis. The more severe hyperventilation noted in the saline control animals sixty minutes postimmersion was probably related to the slower rate of absorption of fluid from the lungs compared to the chlorinated and unchlorinated distilled water groups. The larger quantity of fluid remaining in the lungs at autopsy and the slower rate of increase in blood volume in this group lend support to this hypothesis.

Interestingly enough, 14 of the 15 animals studied became apneic (or breath-held) within nine seconds of aspiration; however respiratory efforts reappeared spontaneously 14 to 45 seconds following onset of immersion. These data should not be interpreted as implying that drowning or near-drowning victims will resume respiration spontaneously. They do

emphasize, however, that apnea in itself does not necessarily signify permanent cessation of respiration in the drowning victim, nor does the reappearance of spontaneous respiratory movements indicate that recovery is inevitable.

It should be emphasized that the saline group was introduced in this study as an isotonic control (0.9 *N*) and changes subsequent to its aspiration are not to be confused with those following aspiration of hypertonic sea water (3.5 *N*).

To further define the relative severity of the respiratory and cardiovascular abnormalities when different quantities of fresh water are aspirated, studies with graduated volumes of water are now in progress. It is anticipated that the relative severity of the cardiovascular and blood constituent problems will increase proportionately with an increase in volume. At lesser volumes the problem requiring therapy will be primarily respiratory.[18]

## Summary and Conclusions

The changes in serum electrolytes and blood constituents reported subsequent to fresh water aspiration in human near-drowning victims have appeared to conflict with studies on drowning in the dog. Mongrel dogs were exposed to aspiration of 10 ml. per pound of chlorinated distilled water, unchlorinated distilled water, or physiological saline solution. In all three types of aspiration an identical picture was observed of acute asphyxia with hypoxemia, hypercapnia and acidosis. Although significant deviation from normal was observed acutely following fresh water aspiration, ten to sixty minutes postimmersion all three groups were indistinguishable and demonstrated essentially normal blood constituents and electrolyte values, except for persistent arterial hypoxemia and metabolic acidosis.

Thus the dog shows physiological changes similar to those of man following near-drowning in fresh water. There is a rapid redistribution of absorbed fluid and, provided that the animal survives the initial asphyxia, serum electrolytes and blood constituents rapidly return to normal. The presence of chlorine in distilled water does not significantly alter the respiratory, biochemical, or cardiovascular response to aspiration. Physiological saline solution in the pulmonary tree is not innocuous, and aspiration or instillation of large volumes into the trachea may have serious respiratory consequences.

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# Clinical Course of 91 Consecutive Near-Drowning Victims*

*Jerome H. Modell, M.D., F.C.C.P.;** Shirley A. Graves, M.D.;† and Alan Ketover, M.D.‡*

**Hospital records of 91 consecutive near-drowning victims were studied retrospectively. Eighty-one (89 percent) of these patients survived. Patients who were alert on arrival at the emergency room survived, but those who were comatose and had fixed dilated pupils died. Other states of consciousness were unreliable predictors of survival. All patients with a normal chest roentgenogram on admission survived; however, values for arterial oxygen tension ($PaO_2$) did not necessarily correlate with the chest roentgenograms. Values for arterial blood gas tensions and pH varied widely, as follows: $PaO_2$, 25 to 465 mm Hg; arterial carbon dioxide tension ($PaCO_2$), 17 to 100 mm Hg; pH, 6.77 to 7.50; and arterial bicarbonate level, 6.6 to 29.7 mEq/L. The ratio of $PaO_2$ to the fractional concentration of oxygen in the inspired gas ($FIo_2$), which was calculated to standardize $PaO_2$ data for varying concentrations of inspired oxygen, ranged from 30 to 585 mm Hg. Only one patient with a ratio of $PaO_2/FIo_2$ greater than 150 mm Hg on admission subsequently died; this was a neurologic rather than a pulmonary death. Serum electrolytic concentrations and values for hemoglobin level and hematocrit reading neither predicted survival nor indicated that a threat to life existed. Steroid and prophylactic antibiotic therapy did not appear to increase the chance of survival. Observations on these patients are discussed in light of previous experiments in animals, and an approach to therapy is suggested.**

Previously studies by Modell et al[1-9] have reported the pathophysiologic changes that occur in dogs after aspiration of both fresh and sea water. To determine whether similar changes occur in humans, we reviewed the charts of 91 consecutive patients treated for near-drowning from 1963 to 1974 at Jackson Memorial Hospital in Miami, Fla, and at Shands Teaching Hospital and the Veterans Administration Hospital in Gainesville, Fla, from 1969 to 1974. Thirty-six of these cases have been reported in previous publications.[9-12] We correlated survival and the clinical course with sex, type of water aspirated, method of resuscitation, results of hematologic and blood chemistry studies, blood gas tensions, pH, chest roentgenographic findings, neurologic status, and method of treatment. Because the study was retrospective, not all data were available on all patients. The number of patients analyzed for each factor is either stated or designated as "(n = )."

*From the Departments of Anesthesiology, University of Florida College of Medicine, J. Hillis Miller Health Center, Gainesville, Fla; the Veterans Administration Hospital, Gainesville, Fla; and the University of Miami School of Medicine, Miami, Fla.

**Professor and Chairperson, Department of Anesthesiology, University of Florida.

†Associate Professor of Anesthesiology and Pediatrics, University of Florida.

‡Resident in Anesthesiology, University of Miami.

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*Reprint requests: Ms. Snider, Anesthesiology, University of Florida J. Hillis Miller Health Center, Gainesville 32610*

## Results

The charts of 70 male and 21 female patients were studied. Sixty-one patients suffered near-drowning in fresh water, 27 in sea water, and three in brackish water. Eighty-one patients (89 percent) survived, seven died after aspirating fresh water, and three died after aspirating sea water. The average age of the survivors was 19 years (range, 1 to 79 years). The average age of those who died was 16 years (range, 1 to 56 years).

### *Method of Resuscitation*

Initial resuscitative efforts at the scene of the accident were described in 68 charts. Six of these charts stated that the method of resuscitation was unknown; 15 patients required no resuscitation; 43 received mouth-to-mouth ventilation; five were ventilated with mechanical devices; three were resuscitated by the back-pressure method; and two had external cardiac massage, but no reference to type of ventilation was made. Of those patients who had artificial ventilation, 14 also received external cardiac massage, as noted in their charts. Twenty-three charts contained no data on initial resuscitative efforts.

### *Neurologic Status (n = 89)*

All 46 patients who were alert on arrival at the emergency room survived, although some required

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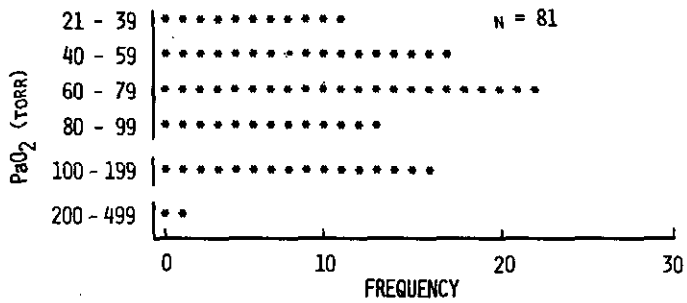


FIGURE 1. Values for $PaO_2$ on admission to hospital; $FIO_2$ ranged from 0.2 to 1.0. Each point represents one patient.

extensive therapy. Of the ten patients who died, one was described as combative but responsive to pain, one was lethargic, one was semicomatose, four were comatose, and an additional three were comatose with fixed dilated pupils. Seven patients were brought to the emergency room without a spontaneous heart beat; three lived, and four died. Of the three survivors, two had residual neurologic damage.

*Arterial Blood Gas Levels and pH*

Since many of the patients exhibited severe respiratory insufficiency on arrival at the emergency room, it was not always possible to draw arterial blood samples for determining baseline values before therapy was started. Some of the patients breathed room air spontaneously, and others received supplemental oxygen, many in combination with mechanical support of their ventilation. The values for arterial oxygen tension ($PaO_2$) on admission to the hospital ranged from 25 to 465 mm Hg (Fig 1; n = 81), with a fractional concentration of oxygen in the inspired gas ($FIO_2$) ranging from 0.2 to 1.0. A determination of $PaO_2$ made while the patient spontaneously breathed room air was available from 40 charts; the mean value (± SD) was 67 ± 21 mm Hg. The lowest $PaO_2$ in this group was 26 mm Hg, and ten patients had a $PaO_2$ of at least 80 mm Hg.

Both $PaO_2$ and $FIO_2$ were recorded in the charts of 58 patients. In an attempt to standardize the data and compare oxygenation in these patients, we calculated the $PaO_2/FIO_2$ ratio, as suggested by Moore.[13] The $PaO_2/FIO_2$ ratio ranged from 30 to 585 mm Hg (Fig 2). The lowest $PaO_2/FIO_2$ ratio observed on admission to the hospital in a patient that survived was 64 mm Hg. Only one patient with a $PaO_2/FIO_2$ ratio exceeding 150 mm Hg on admission subsequently died. This patient had suffered cardiopulmonary arrest, and although circulation returned and the $PaO_2/FIO_2$ ratio was 323 mm Hg, the patient was judged neurologically unsalvageable. Therefore, respiratory support was withdrawn.

Reported values for arterial carbon dioxide tension ($PaCO_2$) on admission ranged from 17 to 100 mm Hg, with a mean of 40 ± 16.8 mm Hg (Fig 3; n = 78). The mean pH in 78 patients was 7.26 ± 0.18, with a range of 6.77 to 7.50 (Fig 4). Values for the arterial bicarbonate level ranged from 6.6 to 29.7 mEq/L, with a mean of 17.2 ± 5.1 mEq/L (Fig 5; n = 76).

*Chest Roentgenograms (n = 90)*

The initial chest roentgenograms of 20 patients, all of whom survived, were reported as normal. Although some of these patients had normal values for $PaO_2$, others had arterial hypoxemia. The lowest $PaO_2$ in this group was 52 mm Hg at an $FIO_2$ of 0.21. Only one of these patients had an endotracheal tube inserted. Chest roentgenograms of the remaining

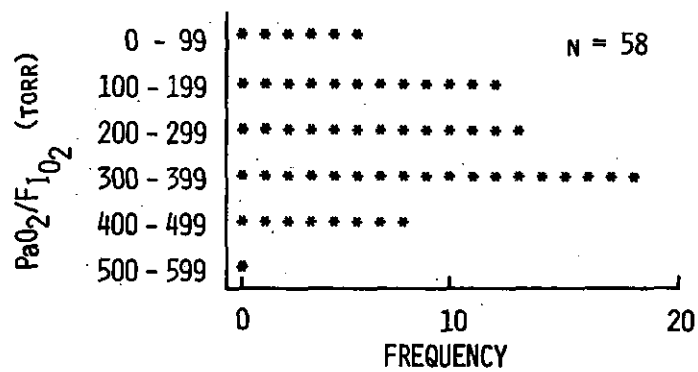


FIGURE 2. Ratio of $PaO_2/FIO_2$ on admission to hospital after near-drowning. Each point represents one patient.

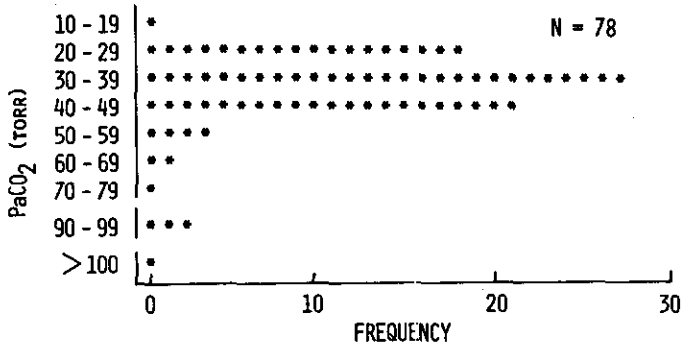


FIGURE 3. *Values for $PaCO_2$ on admission to* hospital after near-drowning. Each point represents one patient.

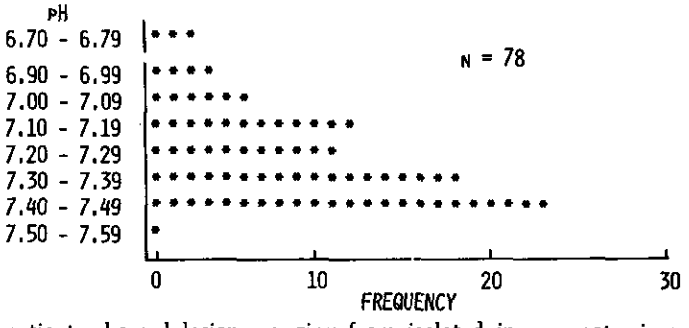


FIGURE 4. Arterial pH on admission to hospital after near-drowning. Each point represents one patient.

patients showed lesions ranging from isolated infiltrates to massive bilateral pulmonary edema. Of the 70 patients with significant abnormal roentgenologic findings, 32 had endotracheal intubation.

*Endotracheal Intubation and Mechanical Ventilation (n = 91)*

The 33 patients who were intubated all received some type of mechanical ventilatory therapy. Eleven received controlled ventilation, seven received assisted ventilation, and 15 received intermittent mandatory ventilation (IMV). The remaining 58 patients breathed spontaneously without endotracheal intubation, although many received supplemental oxygen or therapy with intermittent positive-pressure breathing at frequent intervals, or both. Twenty-four patients exhaled against positive end-expiratory pressure (PEEP).

*Serum Electrolytic Level*

Serum concentrations of sodium, chloride, and potassium were measured on admission in 83 patients. Serum sodium concentrations ranged from 126 to 160 mEq/L, serum chloride levels ranged from 86 to 126 mEq/L, and serum potassium levels ranged from 2.4 mEq/L to 6.3 mEq/L (Fig 6).

*Hemogram*

Values for the hemoglobin level and hematocrit reading of venous blood were available on admission for 83 patients. There was no difference in the mean concentration of hemoglobin or the hematocrit reading among the groups of patients who aspirated the three different types of water (Fig 7).

*Corticosteroid and Prophylactic Antibiotic Therapy (n = 90)*

Corticosteroid therapy was given to 52 patients; 44 lived, and eight died. The corticosteroid preparations administered included dexamethasone, methylprednisolone, prednisone, and hydrocortisone in doses ranging from therapeutic to pharmacologic.

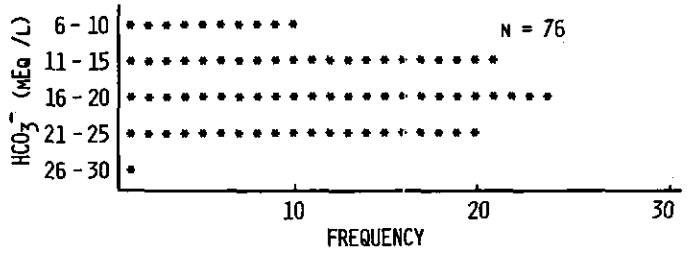


FIGURE 5. Arterial levels of bicarbonate ($HCO_3$) on admission to hospital after near-drowning. Each point represents one patient.

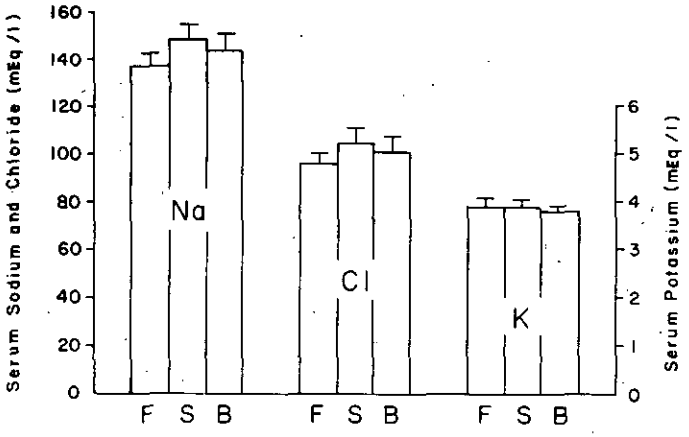


FIGURE 6. Serum concentrations (mean ± SD) of sodium, chloride, and potassium in patients who suffered near-drowning in fresh (F), sea (S), or brackish (B) water.

Of the 38 patients who did not receive steroid therapy, 36 survived. Fifty-four patients received prophylactic therapy with broad-spectrum antibiotics; 47 lived, and seven died. Of the 36 patients who did not receive antibiotic therapy prophylactically, 34 survived.

## DISCUSSION

Retrospective studies have inherent problems because the extent of disease is not constant, nor are measurements and therapy uniform. Animal studies have shown that the pathophysiologic changes which occur are related to both the type and volume of water aspirated.[1-3,13] Since human near-drowning victims aspirate variable quantities and types of fluid, the resulting pathophysiologic changes are variable. In spite of these limitations, a number of points in this series are worth considering.

Eighty-nine percent (81) of our 91 patients survived. The age of the patients was not an important factor in determining survival. Whether or not the patient had a spontaneous heart beat on arrival at the emergency room was important, since four of the ten patients that died had no spontaneous heart beat, and of the three in whom spontaneous cardiac action was restarted in the hospital, two had residual neurologic damage. These were the only two patients in our series of 81 survivors who had residual neurologic damage. This low rate (2/81, or 2 percent) of neurologic complications in survivors suggests that the fear of resuscitating a patient who will not be neurologically intact is perhaps overestimated and that extensive resuscitative efforts are advisable in all instances of near-drowning. Unfortunately, we were not able to determine accurately the length of time from the onset of immersion to rescue and resuscitation in our patients; however, there are reports of people having been successfully resuscitated after being submerged for ten,[14] 17,[15] 22,[16] and even 40 minutes.[17] These case reports cast considerable doubt on one's ability to fix an exact time of physiologic death after an anoxic episode.

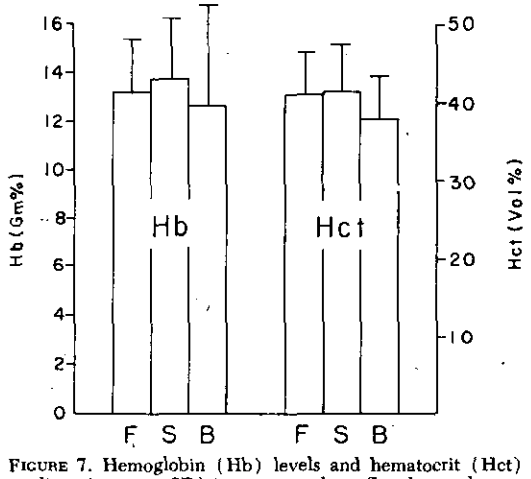


FIGURE 7. Hemoglobin (Hb) levels and hematocrit (Hct) readings (mean ± SD) in patients who suffered near-drowning in fresh (F), sea (S), or brackish (B) water.

Neurologic status was an important predictor of survival in our patients. Those who were alert on arrival at the emergency room survived; those who were comatose with fixed dilated pupils died. Other states of consciousness did not predict survival. We did not find evidence of deterioration of neurologic status after admission to the hospital unless preceded by progressive deterioration of pulmonary status. This is in contrast to earlier case reports by Courville.[18,19] Since Courville's[18,19] cases were reported in 1955 and 1960, prior to the routine clinical use of apparatus for analyzing blood gas levels, one could presume that progressive hypoxia may have played an important part in the clinical course of his patients.

The arterial blood gas tensions and pH varied

considerably in our patients. We confirmed previous findings that metabolic acidosis frequently accompanies near-drowning and that $PaCO_2$ can vary considerably.[1-4,10,12,20] When animals aspirate as little as 2.2 ml of fresh water per kilogram of body weight, the $PaO_2$ drops to approximately 60 mm Hg within three minutes.[2] Dogs that aspirate a similar quantity of sea water show an even lower $PaO_2$, approximately 40 mm Hg.[3] Since ten of our patients had a normal $PaO_2$ ($\geq$ 80 mm Hg) while spontaneously breathing room air on admission to the hospital, these patients probably aspirated little, if any, water. This number (12 percent of the 81 patients having $PaO_2$ reported) corresponds to that in Cot's[21] report, in which 10 percent of drowning victims examined at autopsy did not have evidence of water aspiration in their lungs.

If water is aspirated, a severe intrapulmonary lesion can result, as evidenced by the patient who had a $PaO_2/FIo_2$ ratio of only 30 mm Hg. Controlled studies in dogs have shown that if resuscitated, the animals can spontaneously increase their minute ventilation and effectively eliminate carbon dioxide. On the other hand, metabolic acidosis and arterial hypoxemia persist unless therapy is instituted.[1-4,8,9]

After aspiration of sea water, arterial hypoxemia is due primarily to fluid-filled but perfused alveoli.[9] After aspiration of fresh water, the fluid is absorbed rapidly; however, the surface-tension properties of pulmonary surfactant extracted after drowning in fresh water show an elevation in the minimal surface tension generated on film compression.[5] This suggests that alveolar instability leads to atelectasis. In either case the result is a large intrapulmonary right-to-left shunt.[4,5,9] The metabolic acidosis observed in these experiments is felt to be secondary to tissue hypoxia.

Application of PEEP, with or without mechanical ventilation, will significantly increase the $PaO_2$ after experimental near-drowning in sea water.[9] After near-drowning in fresh water, the combination of PEEP and mechanical ventilation produces similar results.[8] In both of these studies, the PEEP was kept constant at 10 cm $H_2O$ in all animals, and no attempt was made to manipulate intravascular fluid volume or cardiac output. Had the amount of PEEP been adjusted in each animal to produce the optimum overall ventilation/perfusion ratio, it may have resulted in an increased $PaO_2$ even without mechanical ventilatory support in dogs that aspirated fresh water. Improvement of $PaO_2$ with the application of PEEP also has been documented in human near-drowning victims.[9]

Although the chest roentgenogram did not necessarily correlate with $PaO_2$ in our study, all patients who had normal chest roentgenograms on admission survived, and only one required endotracheal intubation. This suggests that a patient with a normal chest roentgenogram on admission may be treated conservatively if he is evaluated at frequent intervals for deterioration of pulmonary status.

Fuller,[22] Cahill,[23] Modell,[12] and Hasan et al[20] have reported that electrolytic changes in near-drowning victims are usually in a range which is compatible with life. This was confirmed by our study; no patient required emergency corrective electrolytic therapy. It is doubtful that electrolytic changes played a significant role in determining survival. Studies in dogs have shown that the degree of change in serum levels of sodium and chloride is proportional to the volume of fluid aspirated.[2,3] These studies, interpreted in the light of our human observations, suggest that humans who are victims of near-drowning probably aspirate 22 ml or less of water per kilogram of body weight.[24] Also, autopsies show that only 15 percent of those who die in the water probably aspirate more than this quantity.[25]

Values for the hemoglobin level and hematocrit reading could not be used as indicators of the type of water aspirated nor of the severity of the immersion. The lowest hemoglobin level in our study was 7.6 gm/100 ml, with a hematocrit reading of 24 percent. This patient suffered near-drowning in sea water when she fell, struck her head, and received scalp lacerations. The highest values pertained to a patient who suffered near-drowning in fresh water while scuba diving. His hemoglobin level was 21.5 gm/100 ml, with a hematocrit reading of 56 percent. These figures refute the concept that those who aspirate fresh water must have a decrease in hemoglobin level and hematocrit reading and those who aspirate sea water must have an increase in hemoglobin level and hematocrit reading. On the other hand, animal studies show that fresh water, being hypotonic, is rapidly absorbed into the circulation.[2,26] Sea water, being hypertonic, draws plasma into the lung and produces hypovolemia.[3,26] The amount of change is proportional to the quantity of water aspirated.[2,3] Data from our patients suggest that massive quantities of water are seldom aspirated by humans who arrive at a hospital alive. Furthermore, even though fluid shifts can be documented in dogs within one to three minutes of aspiration, the fluid is rapidly redistributed.[2,3,7] Therefore, although a patient may have absorbed a significant quantity of water, it may not be evident at the time when blood is drawn for analysis.

The use of corticosteroid and prophylactic anti-

biotic therapy for patients who suffer near-drowning was first suggested by Modell et al[10] in a report in 1968 dealing with 12 patients, all of whom received these medications. Use of these two drugs was suggested on the basis that near-drowning is a form of aspiration pneumonitis. At that time the literature suggested that pneumonitis secondary to aspiration of gastric contents responded favorably to corticosteroid and antibiotic therapy.[27] Since there was no group of patients who had therapy with corticosteroids and antibiotics withheld, that study[10] did not establish the effectiveness of, but merely reported on, the use of such therapy.

Since then, the effectiveness of corticosteroid therapy for aspiration of acid has been challenged in controlled experiments in dogs.[28-30] Therefore, Calderwood and associates[31] studied the effect of corticosteroid therapy on survival and blood gas exchange in dogs after aspiration of fresh water. Both the steroid-treated and control groups were identical. No beneficial effect of corticosteroid therapy was documented.[31]

In the current study of 91 consecutive near-drowning victims, more patients died who received corticosteroid therapy than those who did not. Since this was a retrospective study and no attempt had been made to control who received steroid therapy, it is not possible to determine whether the degree of illness would have been identical in both groups. It is possible that those who received the steroid therapy had more serious lesions. On the other hand, when we attempted to correlate administration of corticosteroid therapy with initial values for $PaO_2$, we found no significant relationships. This suggests that patients can recover from near-drowning without complications or residua if steroid therapy is withheld pending indications for its use. Similarly, more patients died who received prophylactic antibiotic therapy than did those from whom such therapy was withheld until gram staining, culture, and clinical course suggested the presence of active infection. This observation supports those who criticize the prophylactic use of antibiotic therapy.

Of the ten patients who died in our series, four had no spontaneous heart beat upon arrival at the hospital. This indicates that initial resuscitative efforts were inadequate and that the condition of these patients may have been irreversible on admission to the hospital. Of the six remaining patients who died, two had fixed dilated pupils on admission to the hospital and did not improve neurologically. Two died between 1963 and 1966; during these years, the effectiveness of PEEP in decreasing the degree of intrapulmonary shunting after near-drowning was not appreciated. Analysis of these deaths shows that one patient was treated conservatively because he never lost consciousness completely. This was prior to the time of routine determinations of arterial blood gas levels. This child deteriorated during the first night in the hospital and died the following morning. A second patient apparently aspirated massive quantities of water, as evidenced by the complete opacification on her chest roentgenogram, a $PaO_2$ of 40 mm Hg while receiving mechanical ventilation with 100 percent oxygen, and a plasma hemoglobin concentration of 500 mg/100 ml. This patient was treated prior to the use of PEEP and required high concentrations of inspired oxygen (approximately 100 percent) throughout her course. She died 84 hours later. A fifth patient was treated in 1971 when we limited PEEP to 10 cm $H_2O$. His pulmonary status progressively deteriorated with mechanical ventilation and PEEP; he died 13 days later. The sixth patient died of bilateral staphylococcal pneumonia six days after near-drowning. The organism was suggested on gram stained preparations and later confirmed by culture. Antibiotic therapy was started within six hours of admission. This patient also developed pulmonary barotrauma during therapy with high levels of PEEP.

*Suggested Therapy*

We had hoped that this study would provide us with criteria for determining when patients require maximal ventilatory support or when they can be treated conservatively. Although definitive criteria were not produced by this study, correlating what is known from animal models with observations of these patients permits speculation about a rational method of treatment.

The importance of effective cardiopulmonary resuscitation at the scene of the accident is emphasized by the fact that 93 percent (78) of the 84 patients who had a spontaneous heart beat on admission to the hospital survived without residua. On the other hand, of the seven patients who did not have an effective heart beat reestablished by the time they were admitted to the emergency room, four died, and two were left with residual neurologic damage. This is an effective survival rate of only 14 percent (one patient).

Since one cannot accurately determine the state of a patient's arterial oxygenation by inspection alone, and since significant arterial hypoxemia can be present even though the patient is alert, the highest possible concentration of supplemental oxygen should be administered en route to the hospital, whenever possible, to all near-drowning victims. Arterial blood samples can then be analyzed immedi-

ately for $PaO_2$, $PaCO_2$, and pH to establish the extent of pulmonary insufficiency and acid-base derangement and to guide therapy. If the patient arrives at the hospital with a normal $PaO_2$ while breathing room air, he probably suffered near-drowning without aspiration and will require no further therapy. Such patients should be observed overnight, and arterial blood gas tensions and pH should be determined again to attempt to ensure that no deterioration occurs before discharge from the hospital.

When a patient is admitted with a normal chest roentgenogram, he probably can be treated without endotracheal intubation and mechanical support of his ventilation, even if he has aspirated fluid. For these patients, determine arterial blood gas tensions and pH. Treat metabolic acidosis with intravenous administration of sodium bicarbonate, and treat hypoxia with supplemental oxygen therapy. The patient should be encouraged to breathe deeply and to cough, thereby helping to reexpand alveoli. If arterial oxygenation improves after serial determinations of arterial blood gas tensions and pH, one should continue conservative therapy. On the other hand, if the $PaO_2$ deteriorates consistently, intervention with endotracheal intubation and mechanical support of ventilation is indicated.

If the patient shows obvious signs of respiratory distress, requires an inhaled oxygen concentration in excess of 40 percent to maintain an acceptable $PaO_2$, or has extensive interstitial or frank pulmonary edema, more aggressive therapy is indicated. In such patients, we recommend endotracheal intubation and PEEP. The amount of PEEP used should be that which produces the highest $PaO_2$ at the lowest possible inspired oxygen concentration without depression of cardiac output. This will be achieved when the minimum intrapulmonary shunt is reached by "optimizing" PEEP to improve the ventilation/perfusion ratio.[32,33] Although all of the patients in this series who required PEEP had endotracheal intubation, during the past year we also have used a tightly fitting mask designed for application of PEEP§ with some success in patients who were alert. Whether the patient requires mechanical ventilatory support in addition to PEEP will depend on his ability to ventilate spontaneously and to eliminate carbon dioxide. If mechanical ventilatory support must be added, we prefer to use IMV with PEEP, rather than continuous positive-pressure ventilation (CPPV). Therapy with IMV allows higher levels of PEEP with less effect on cardiovascular function,[33] because the mean intrapleural pressure and the alteration of intramural vascular filling pressure are less with IMV than with CPPV. If the patient requires mechanical support of his ventilation or PEEP after aspirating either fresh or sea water, he also may require intravenous administration of fluids to keep the effective circulating blood volume and cardiac output at a normal level. As the patient's intrapulmonary shunt improves, the level of PEEP can be reduced gradually. Frequently the patient can be extubated when the rate of IMV is reduced to zero and PEEP is reduced to 4 mm Hg or less.

Because one cannot easily distinguish the pulmonary component from the cardiovascular component, it is important to monitor both systems. In patients who require high levels of PEEP, the intrapulmonary shunt, cardiac output, and effective circulating blood volume can be monitored by utilizing a pulmonary arterial catheter. This permits measurement of pulmonary capillary wedge pressure and provides access to pulmonary arterial blood (mixed venous), which can be analyzed to calculate the degree of intrapulmonary shunt. In addition, the arterial-venous oxygen content difference gives an approximation of cardiac output. Similar approximations can be achieved from blood drawn through a catheter placed in the superior vena cava; however, this does not allow one to separate differential function of the right and left ventricles. If thermistor-tipped pulmonary arterial catheters are used, cardiac output can be determined directly with a thermodilution computerized technique.[34]

Often there is a temptation to withdraw therapy with PEEP too rapidly. Particularly after aspiration of fresh water, it is important to permit the patient's lung to stabilize before withdrawing support. We recently treated a patient (admitted subsequent to this analysis) whose $PaO_2/FIo_2$ ratio was 44 mm Hg after aspiration of fresh water. The patient had an endotracheal tube and was receiving a high level of PEEP (26 mm Hg) and IMV. Approximately 48 hours after his near-drowning, we attempted to wean him from PEEP. His intrapulmonary shunt increased from 6 percent to 38 percent when PEEP was lowered to 6 mm Hg. Therapy with PEEP was reinstituted at 14 mm Hg to obtain optimization. After maintaining the patient at constant levels of PEEP for an additional 24 hours, he was weaned within 12 hours without difficulty.

Obviously, attention must be paid to other details. Adequate renal function must be assured. Although our data suggest that changes in fluid, electrolytic levels, and the hemogram neither are predictable nor pose an immediate threat to life, their status should be evaluated, and appropriate fluid and electrolytic therapy should be administered when indi-

§ bird Corp., Palm Springs, Calif.

cated. We were not able to establish that corticosteroid and prophylactic antibiotic therapy was beneficial; however, samples of sputum should be examined and cultured regularly for identification of organisms that may cause secondary infection and require specific antibiotic therapy.

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# The Effects of Fluid Volume in Seawater Drowning

JEROME H. MODELL, M.D., FRANK MOYA, M.D., EARLENE J. NEWBY, BRUCE C. RUIZ, and APRIL V. SHOWERS, R.N.

*Miami, Florida*

THE EFFECT OF DROWNING by total immersion in seawater on the serum electrolytes, blood constituents, and cardiovascular system of dogs was reported by Swann and Spafford (*1*). In their experiments they reported severe abnormalities in these parameters. The limited data available on human near-drowning victims, although showing trends similar to Swann and Spafford's data, do not show changes of the same magnitude (2). In general, the degree of abnormality of these values in human near-drowning victims would not be considered life-threatening.

In a previous study it was found that the severity of immediate cardiovascular and electrolyte changes secondary to chlorinated freshwater aspiration was directly dependent on the quantity of fluid aspirated; however, within 1 hr of aspiration the serum electrolytes returned to normal in all surviving animals (3). It would appear reasonable that in seawater near-drowning and drowning the changes in blood constituents and serum electrolytes might also be directly dependent on the quantity of fluid aspirated. To examine this possibility and, therefore, gain further insight into the emergency therapy necessary for seawater near-drowning victims, the following studies were undertaken.

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From the Department of Anesthesiology, University of Miami School of Medicine and Jackson Memorial Hospital, Miami, Fla.

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Requests for reprints should be addressed to Jerome H. Modell, M.D., Department of Anesthesiology, University of Miami School of Medicine and Jackson Memorial Hospital, Miami, Fla. 33136.

## METHODS

Twenty mongrel dogs weighing 30 to 59 lb and in apparent good physical condition were divided into four equal groups.

After a 15-gauge plastic needle was inserted into a vein of the foreleg, 50-mg increments of 2½% thiopental sodium were given intravenously to produce basal narcosis (that is, cessation of spontaneous movement; respiration and lid reflex remained active). The trachea was intubated under direct vision, the endotracheal tube cuff was inflated, and the animal was permitted to breathe spontaneously.

Both femoral arteries and the left femoral vein were cannulated with siliconized polyethylene tubing (inside diameter, 0.066 in.). The arterial catheters were threaded to the level of the aortic arch and the venous catheter, to the inferior vena cava near the right atrium. The position of the catheters was verified at autopsy in all animals not surviving the experiment. The catheters on the left were connected via Statham strain gauges to a multichannel direct-writing recorder for monitoring of the arterial and the central venous blood pressures. The catheter on the right was connected to a triple stopcock assembly for sampling of blood. Lead II of the electrocardiogram was recorded continuously.

Twenty minutes before aspiration blood samples were drawn for background count, and radioactive iodinated serum albumin (RISA-$^{131}$I) was injected intravenously. The needle was then flushed with approximately 15 to 20 ml of 5% dextrose in water. Five to 10 min preaspiration a Wright Ventilometer was connected to the endotracheal tube, and the respiratory minute volume was measured in

triplicate. Respiratory rate was counted and the average tidal volume calculated. Four minutes before aspiration an arterial blood sample was drawn anaerobically into a heparinized, greased syringe, and the pH, $P_{CO_2}$, and $P_{O_2}$ were determined using direct-reading electrodes in an Instrumentation Laboratories 113-SI blood gas analyzing system. Buffer base was calculated and corrected for oxygen unsaturation according to the Singer-Hastings nomogram (4).

Arterial blood was also drawn at this time into a second heparinized syringe for whole blood studies and into a dry siliconized syringe and transferred immediately to a clean test tube for clot formation for serum analysis. Care was taken to avoid stasis of blood in the catheter by removing 5 ml of blood and discarding it immediately before these and subsequent samples were withdrawn. The heparinized blood was analyzed for total hemoglobin by the cyanmethemoglobin method and for hematocrit using the Guest-Weichselbaum microcapillary centrifuge. Blood volume studies were done using the RISA dilution technique; radioactivity was counted and blood volume calculated with a Picker Hemoliter Counter.* Serum studies included determination of sodium and potassium with the Coleman flame photometer using a commercial serum preparation as a control standard. Serum chloride was determined on the Buchler-Cotlove Chloridometer. Serum calcium analysis was performed by the semimicro modification of the Ferro-Ham method (5).

Thirty seconds before aspiration the endotracheal tube was connected via a Y-adapter to the water reservoir and breathing bypass as described previously (6). At zero time the bypass was occluded, and the dog was allowed to spontaneously aspirate 1, 5, or 10 ml of seawater/lb body weight according to its group. On completion of aspiration, the animal was allowed to breathe room air through the emptied reservoir. When all the water had cleared from the tubing, the animal was permanently disconnected from the reservoir to minimize dead space.

The remaining five animals were subjected to total immersion as follows: At zero time the bypass was occluded and the water reservoir opened; all animals remained underwater continuously until an arterial pulse pressure could no longer be detected on the recorder. At that time the reservoir was clamped and the remaining fluid subtracted from the total. The residual volume in the dog and in the endotracheal tube was considered the total immersion volume (average, 29 ml/lb; range, 19 to 38 ml/lb). It should be noted that additional fluid could be drained passively from the lungs and the endotracheal tube after the death of these animals. In some the total volume of fluid recovered postmortem was greater than that which was originally instilled into the trachea.

One, 3, 10, 30, and 60 min after the onset of aspiration all preaspiration determinations were repeated in viable dogs. Background counts were taken on arterial blood 45 min postaspiration in all surviving animals, and they were then reinjected with RISA 15 min before drawing of the 60-min samples. After the experiments were completed, all surviving animals had their cutdowns repaired, their endotracheal tubes removed, and were returned to their cages to be followed for 14 days for survival.

An additional four animals were prepared as above and subjected to total immersion after having been injected simultaneously with $^{51}Cr$-tagged red cells and $^{125}I$-labeled serum albumin. Blood studies were limited to determination of blood volume and red cell indexes before and 1, 3, and 10 min after aspiration. The radioactivity of the blood samples obtained was counted on a differential counter at 0.035 gamma through a 20-v window for the $^{125}I$ and at 323 gamma through a 50-v window for the $^{51}Cr$. The blood volumes were then calculated for each tracer element (7). The radioactivity of drainage fluid from the trachea and the pleural fluid collected at autopsy was also determined.

For purposes of statistical analysis, the assumption was made that the severity of the changes in parameters measured in the animals would be proportional to the quantity of fluid aspirated. The change from preaspiration normal levels in each animal for blood volume, hemoglobin, hematocrit, serum sodium, serum chloride, serum potassium, serum calcium, arterial $P_{O_2}$, $P_{CO_2}$, and pH was tabulated. The data were then analyzed for simple linear correlation between corresponding changes in factors on a digital computer. With 18 deg of freedom, correlation factors ($r$) of 0.444, 0.561, and 0.679 correspond to probability values ($P$) of 0.05, 0.01, and 0.001, respectively. In addition, individual parameters were compared to preaspiration levels by one-sample $t$ tests. In

* Picker Nuclear Division of Picker X-ray Corp., White Plains, N. Y.

TABLE 1. Number of Surviving Dogs in Each Group 1 hr and 24 hr After Seawater Aspiration

| Group | Number of Dogs in Group | 1 hr Post-aspiration | 24 hr Post-aspiration |
|---|---|---|---|
| | ← | *no.* | → |
| 1 ml/lb body wt | 5 | 5 | 5 |
| 5 ml/lb body wt | 5 | 3 | 2 |
| 10 ml/lb body wt | 5 | 1 | 0 |
| Total immersion | 5 | 0 | 0 |

order to provide better correlation with previous studies (3), the data obtained 3 min postaspiration were selected for graphic presentation.

The seawater used in these experiments was obtained from the Atlantic Ocean 3 miles due east of Miami, Fla., at a depth of 2 ft below the surface. Measured electrolyte content of this water was sodium, 509 mEq/liter; calcium, 15.4 mEq/liter; chloride, 561 mEq/liter; and potassium, 11.3 mEq/liter.

## RESULTS

All data subsequent to aspiration are reported as changes from preaspiration levels for each individual animal. In this manner each animal served as his own control. The average preaspiration control values for the 20 animals were as follows: weight, 41 lb; tidal volume, 249 ml; tidal volume per pound, 6.06 ml; blood volume (radioactive iodinated serum albumin ($^{131}$RISA)), 1.88 liters; hemoglobin, 14.4 g/100 ml; hematocrit, 39%; pH, 7.48; $Pco_2$, 22 mm Hg; $Po_2$, 95 mm Hg; serum chloride, 110 mEq/liter; serum calcium, 5.0 mEq/liter; serum sodium, 145 mEq/liter; and serum potassium, 3.2 mEq/liter. The results reported as 10-min samples for animals 223, 224, and 214 were actually obtained at 8, 8, and 9 min postimmersion, respectively, due to the early deaths of these animals.

TABLE 2. Time of Death and Intra-aortic Systolic Blood Pressure Changes After Seawater Aspiration

| Group | Dog Number | Time of Death | Pressure Drop Time of Onset | Maximum Initial Pressure Drop |
|---|---|---|---|---|
| | | *min* | *sec* | *mm Hg* |
| | 207 | — | — | — |
| | 215 | — | — | — |
| 1 ml/lb body wt | 217 | — | — | — |
| | 219 | — | — | — |
| | 222 | — | — | — |
| 5 ml/lb body wt | 206 | 34 | 2 | 50 |
| | 209 | — | — | — |
| | 213 | <24 hr | 32 | 25 |
| | 218 | — | — | — |
| | 223 | 8 | 4 | 35 |
| 10 ml/lb body wt | 204 | 11 | 4 | 100 |
| | 208 | 10 | 4 | 110 |
| | 212 | 10 | 8 | 125 |
| | 220 | 107 | 4 | 90 |
| | 224 | 8 | 4 | 130 |
| Total immersion | 210 | 10½ | 6 | 55 |
| | 214 | 9½ | 6 | 150 |
| | 216 | 10½ | 2 | 100 |
| | 221 | 16½ | 6 | 150 |
| | 225 | 12½ | 4 | 135 |

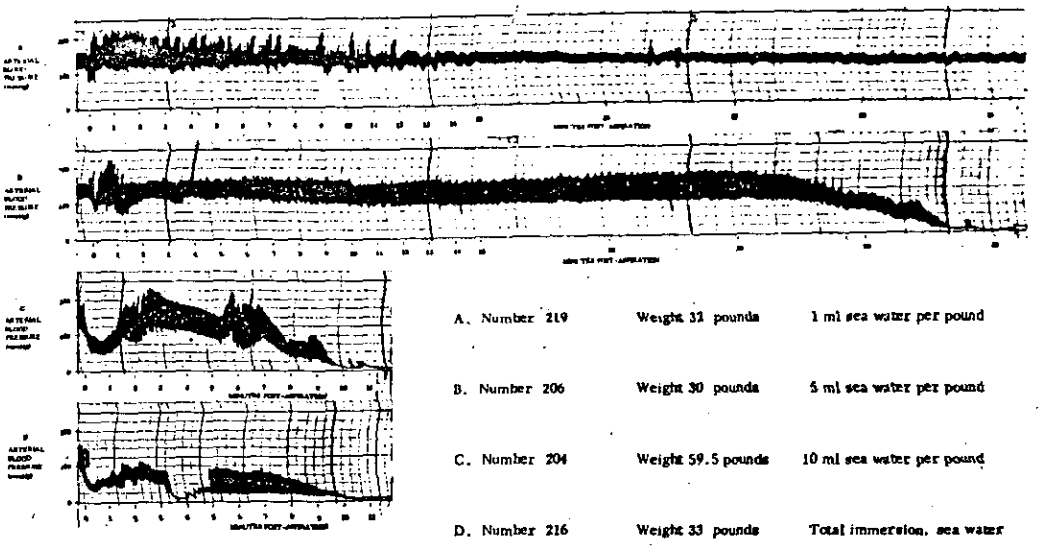


FIGURE 1. Arterial blood pressure tracings after aspiration of seawater. All measurements are taken from a polyethylene catheter at the arch of the aorta.

SURVIVAL DATA

It can be seen in Table 1 that both the 1-hr and the 24-hr survival rates were inversely proportional to the quantity of water aspirated. The exact time of delayed death in the animal in the 5-ml/lb group is not known because he was found dead in his cage on the morning after the experiment. The animal with the delayed death in the 10-ml/lb group died 107 min postaspiration (Table 2). There were no instances of fatality beyond the first 24 hr.

CARDIAC AND VASCULAR CHANGES

A decline in intra-aortic systolic blood pressure of at least 25 mm Hg below control values was observed within 8 sec of aspiration in two of the five animals who aspirated 5 ml of fluid/lb and in all animals who aspirated 10 ml or more of fluid/lb of body weight. One additional animal in the 5-ml/lb group had a decline in blood pressure 32 sec postaspiration. The magnitude of this drop in blood pressure is shown in Table 2. In nine of the ten animals who aspirated at least 10 ml of fluid/lb, the systolic blood pressure dropped to below 100 mm Hg within 30 sec of aspiration. In all but one the pressure increased spontaneously before later showing a progressive decline terminating in the death of the animal. Typical pressure tracings are seen in Figure 1. No change in blood pressure was observed after aspiration in the remaining animals in the 5-ml/lb group nor in any of the animals in the 1-ml/ lb group.

The central venous pressure increased in 18 of the 20 animals immediately after aspiration. This increased venous pressure coincided with the period of maximum respiratory efforts by the animal. In all cases the venous pressure spontaneously returned to normal regardless of whether the animals survived the experiment.

The most frequent electrocardiographic change observed after aspiration was bradycardia (less than 100 beats/min). This was seen within 3 min of aspiration in one animal in the 5-ml group and in three animals in each of the 10-ml and total immersion groups. In addition, all animals who succumbed to the experiment showed evidence of progressive hypoxia on the electrocardiogram.

BLOOD VOLUME

The blood volume ($^{131}$RISA) showed no significant change after aspiration of 1 ml of seawater/lb body weight in the samples taken 1, 3, and 10 min postaspiration. Sixty minutes later, however, after reinjection of tracer, the blood volume was lower in all animals in this group than it had been before aspiration (average blood volume, 89% of normal; range, 76 to 96%) ($P < 0.05$). The blood volume was observed to decrease 1 min postaspiration in all animals aspirating at least 5 ml of seawater/lb of body weight ($P < 0.01$). Although a decreased blood volume was still evident in 14 of 15 of these animals at 3 min, by 10 min the values obtained with $^{131}$I approached normal in the 5-ml and 10-ml groups and exceeded preaspiration levels in the total immersion group (Figure 2).

Blood volumes obtained 10 min postaspiration in the four animals subjected to total immersion after injection with $^{51}$Cr-tagged red cells and $^{125}$I-labeled serum albumin are compared to preaspiration volumes in Table 3. It is noted that, although the $^{51}$Cr blood volumes suggest a persistent hypovolemia, the $^{125}$I volumes are not consistent with this impression. To visualize the apparent increase in blood volume observed after injection with albumin tracers, the change in blood volume as measured with $^{125}$I or $^{131}$I for each of the

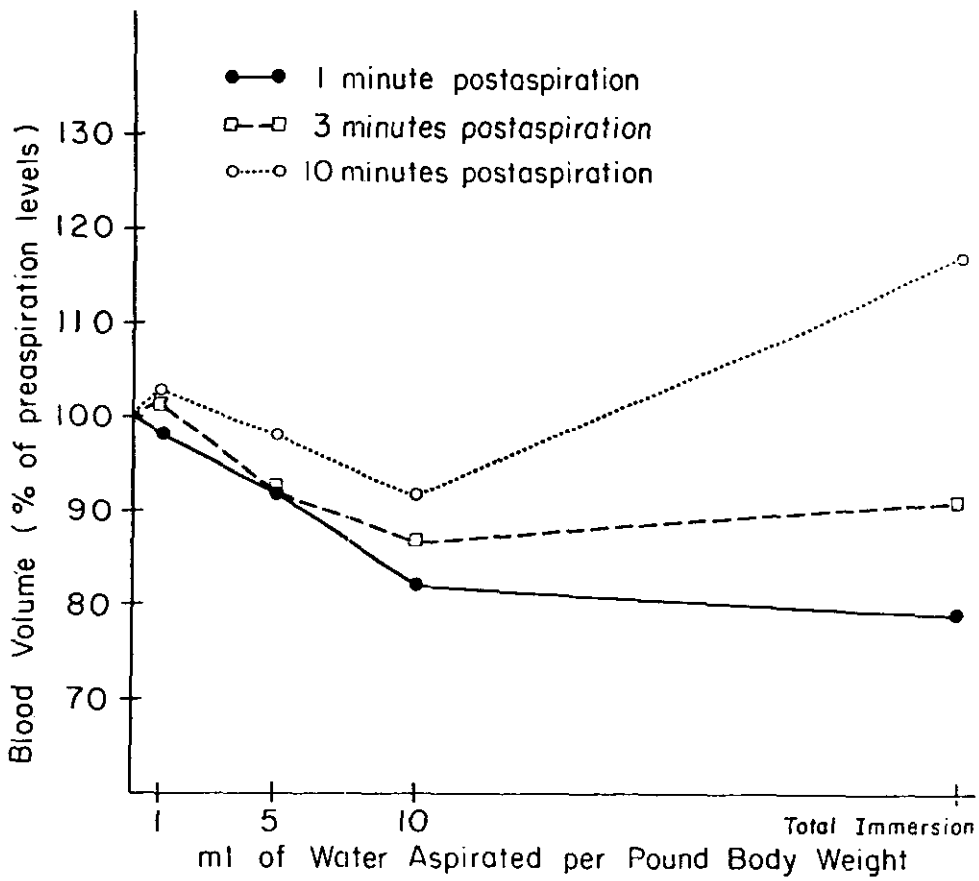


FIGURE 2. Changes in blood volume 1, 3, and 10 min after seawater aspiration as measured with radioactive iodinated serum albumin ($^{131}$I). Each point represents the median value of five animals. All values postaspiration are reported as percent of preaspiration blood volume.

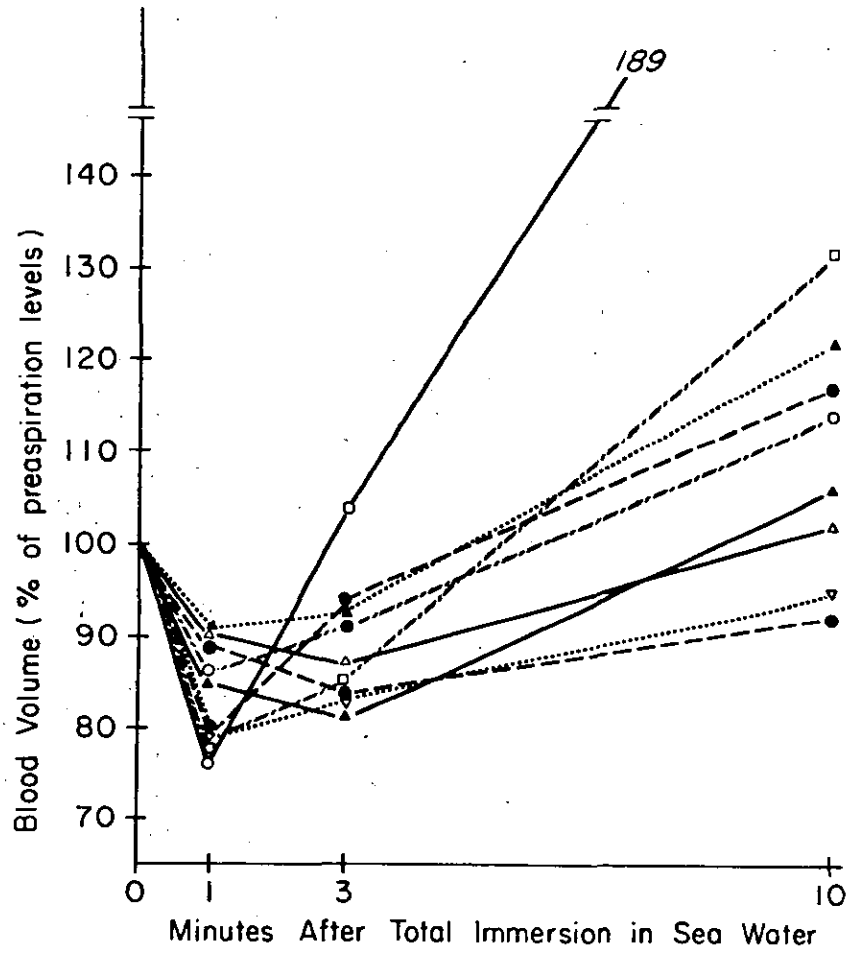


FIGURE 3. Changes in blood volume after total immersion in seawater as measured with radioactive iodinated serum albumin ($^{125}I$ or $^{131}I$). Each line represents one individual animal. All values subsequent to aspiration are reported as percent of preaspiration blood volume.

nine animals subjected to total immersion is plotted as a function of time in Figure 3.

The presence of $^{125}I$ was confirmed in the drainage fluid from the trachea of all four animals. The $^{125}I$ count of this fluid averaged 7% (range, 4 to 12%) of that contained in an equal volume of blood before immersion. Radioactivity was also found in pleural fluid at autopsy in these animals, the $^{125}I$ count averaging 4% (range, 2 to 9%) of that contained in an equal volume of blood before immersion. Cell indexes showed a decrease in mean corpuscular volume (MCV) 10 min after aspiration in three

TABLE 3. Blood Volume Changes 10 min After Total Immersion in Seawater*

| Animal Number | $^{51}Cr$ | $^{125}I$ |
|---|---|---|
| | % | |
| 229 | 61 | 95 |
| 230 | 83 | 106 |
| 231 | 67 | 92 |
| 232 | 86 | 122 |
| Average | 74 | 104 |

* These determinations were done simultaneously with $^{51}Cr$ and $^{125}I$ on the same blood samples. All results are reported as percent of preaspiration blood volume for each individual animal.

of the four animals tested (average decrease, 10 $\mu^3$).

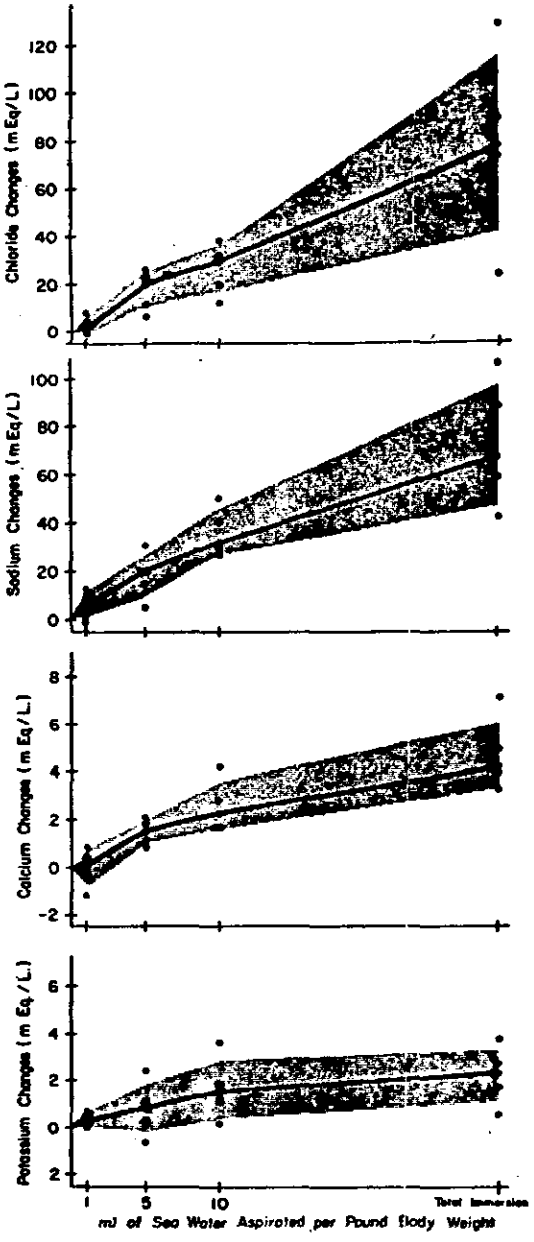


FIGURE 4. Serum electrolyte changes 3 min after seawater aspiration. All values are plotted as change from preaspiration levels in milliequivalents per liter versus volume of water aspirated for each individual animal. The median for each group is drawn, and the standard deviation is shaded. Average base line values for the 20 dogs were sodium, 145 mEq/liter; chloride, 110 mEq/liter; calcium, 5.0 mEq/liter; and potassium, 3.2 mEq/liter.

SERUM ELECTROLYTES

There was a significant increase in serum electrolyte concentration 1, 3, and 10 min postaspiration in all animals in the 5-ml, 10-ml, and total immersion groups. The changes at 3 min are plotted as a function of the quantity of water aspirated (Figure 4). A statistically significant positive correlation existed between the increased concentration of serum sodium ($r = 0.869$), calcium ($r = 0.946$), chloride ($r = 0.903$), and potassium ($r = 0.513$) and the volume of water the animals aspirated. Sixty minutes after aspiration the serum calcium and the serum potassium had returned to normal in all survivors in the 5-ml and 10-ml/lb groups. Serum sodium had returned to normal levels in two of the three survivors in the 5-ml group and in the lone survivor of the 10-ml group. The serum chloride, however, was still elevated 60 min postaspiration in these animals (mean increase, 9 mEq/liter; range, 5 to 14 mEq/liter) ($P < 0.05$).

WHOLE BLOOD HEMOGLOBIN AND HEMATOCRIT

The hemoglobin and hematocrit values in the animals who aspirated 1 ml of water/lb did not show a significant deviation from normal in any of the time periods tested. Scattergraphs of the changes in whole blood hemoglobin and hematocrit 3 min postaspiration are seen in Figure 5. A significant increase in hemoglobin and hematocrit concentrations was observed both 3 and 10 min postaspiration in the 5-ml and 10-ml groups ($P < 0.05$). After drowning by total immersion the changes in hemoglobin and hematocrit concentrations were not consistent. The correlation factors between the volume of fluid aspirated and the hemoglobin and hematocrit were not found to be significant ($r = 0.131$ and $r = 0.424$, respectively). There was, however, a strong correlation between the hemoglobin and the hematocrit themselves ($r = 0.790$). The hemoglobin and the hematocrit values returned to normal spontane-

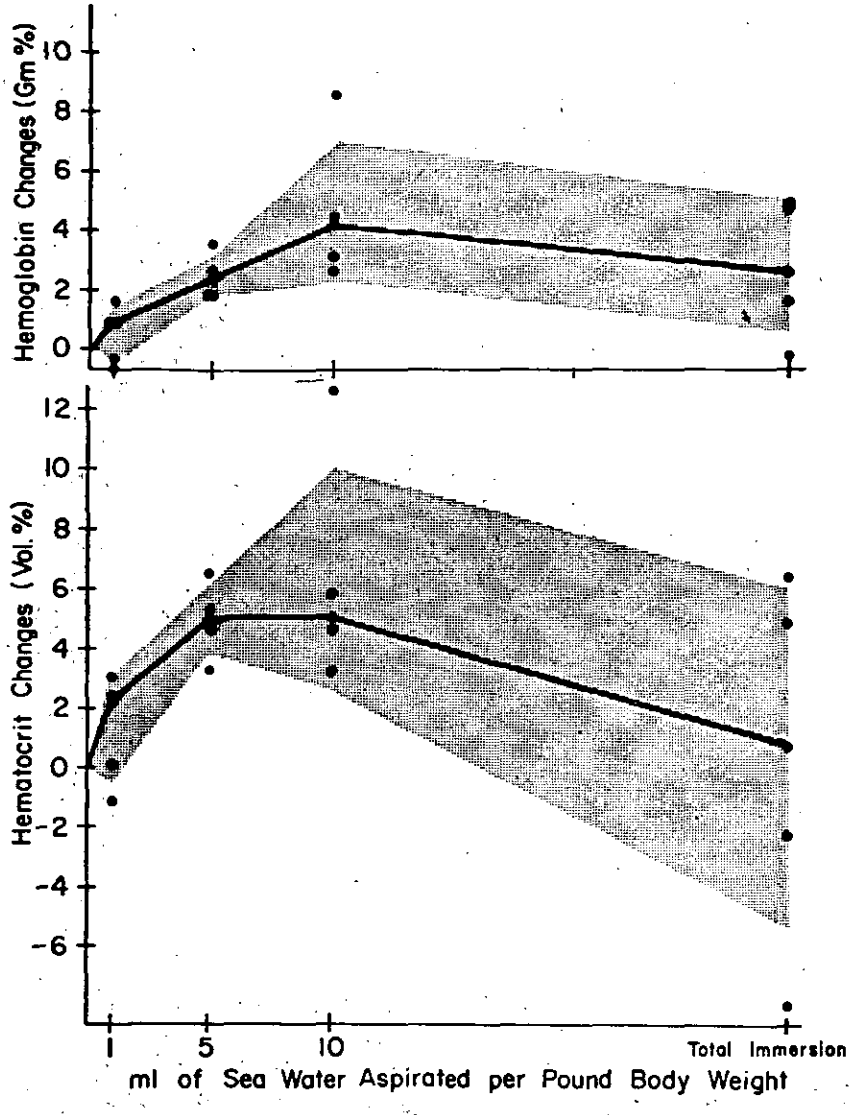


FIGURE 5. Hemoglobin and hematocrit values 3 min after seawater aspiration. All values are plotted as change from preaspiration value for each individual animal. The median is drawn, and the standard deviation is shaded. The average preaspiration normal values for the 20 animals were hemoglobin, 14.4 g/100 ml, and hematocrit, 30 vol/100 ml.

ously, and no significant differences were seen in the survivors between the control values and the 60-min samples.

#### BLOOD GAS AND ACID-BASE CHANGES

There was an immediate decrease in arterial $Po_2$ in all animals subjected to the experiment regardless of the quantity of water aspirated. These changes were analyzed for statistical significance at 3 and 10 min postaspiration. In all groups these hypoxic changes were significant ($P < 0.01$). In Figure 6 the magnitude of these changes 3 min postaspiration is plotted as a function of the quantity of water aspirated. Although significant decreases in arterial $Po_2$ are present in all animals, the severity of the hypoxia at 3 min was not dependent on

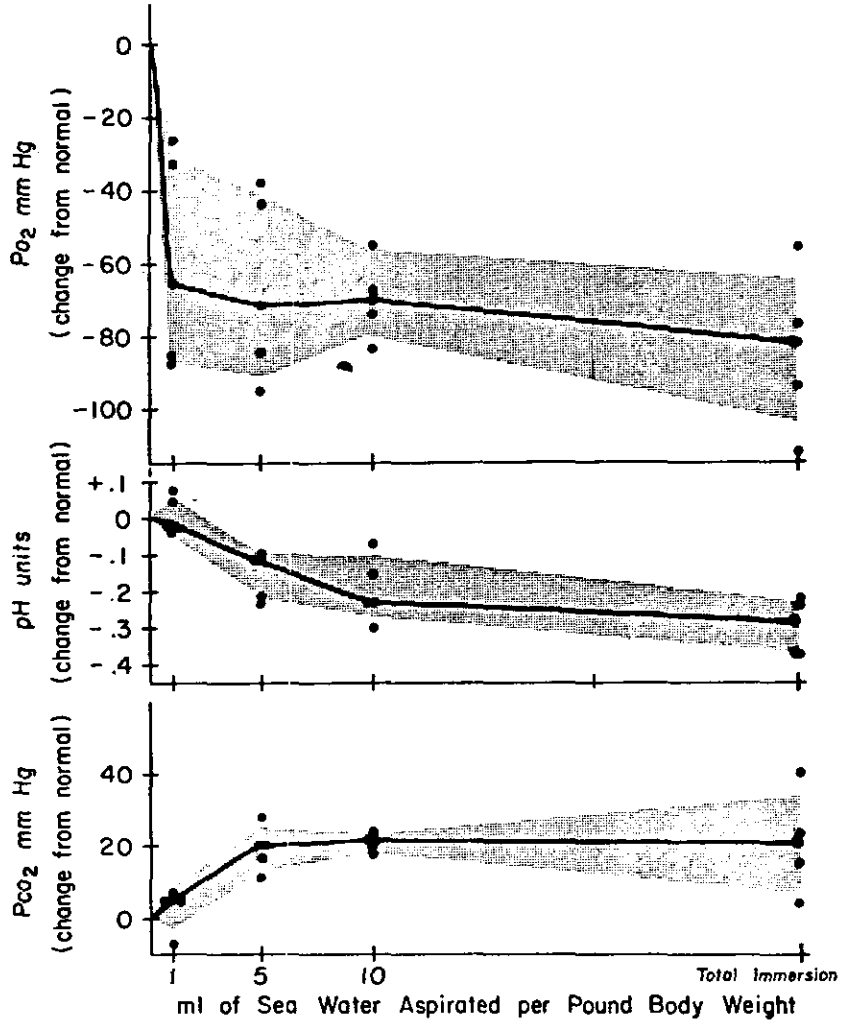


FIGURE 6. Blood gas and acid-base changes. Arterial pH, $Po_2$, and $Pco_2$ changes 3 min after aspiration are plotted as a function of the quantity of water aspirated. All values are plotted as change from preaspiration levels for each individual animal. The median is drawn, and the standard deviation is shaded for each group. Average base line values for the 20 dogs were pH, 7.48; $Po_2$, 95 mm Hg; and $Pco_2$, 22 mm Hg.

the volume of fluid aspirated ($r = -0.300$). There was a negative correlation between the changes in arterial $Po_2$ and $Pco_2$ ($r = -0.557$). At 10 min the mean arterial $Po_2$ of the animals who were to succumb to drowning within the hour was only 9 mm Hg (range, 1 to 22 mm Hg), while those who were to survive averaged 42 mm Hg (range, 30 to 60 mm Hg). Sixty minutes postaspiration a significant reduction in arterial $Po_2$ was still present in all surviving animals ($P < 0.01$). The mean preaspiration $Po_2$ for these dogs was 95 mm Hg, whereas 60 min postaspiration the mean $Po_2$ was 56 mm Hg, 40 mm Hg, and 37 mm Hg for the surviving animals in the 1-ml, 5-ml, and 10-ml groups, respectively.

The changes in pH in the 1-ml/lb group were slight. However, a significant reduction in pH was seen 3 min after aspiration

in all animals aspirating at least 5 ml of fluid/lb body weight ($P < 0.01$) (Figure 6). Three minutes postaspiration a significant negative correlation was found between the arterial pH change and the volume of fluid aspirated ($r = -0.772$) and $P_{CO_2}$ ($r = -0.532$). Ten minutes postaspiration the mean pH was $7.38 \pm 0.06$, $7.17 \pm 0.11$, $7.05 \pm 0.05$, and $7.00 \pm 0.11$ for the animals in the 1-ml, 5-ml, 10-ml, and total immersion groups, respectively.

The arterial $P_{CO_2}$ showed no significant change in animals aspirating 1 ml of seawater/lb body weight. However, there was a significant increase in $P_{CO_2}$ 3 min and 10 min postaspiration in all animals aspirating at least 5 ml of water/lb ($P < 0.05$). The change in $P_{CO_2}$ was not dependent upon a change in fluid volume ($r = -0.245$).

By 60 min postaspiration there was a return toward the preaspiration values; however, the pH was still below and the $P_{CO_2}$ slightly above these values in all but one of the survivors.

There was no significant change in the corrected buffer base concentration 1 or 3 min postaspiration in any of the four groups tested. Although the animals in the 1-ml group remained stable at 10 min, a significant decrease in buffer base concentration was seen in all animals aspirating at least 5 ml of seawater/lb body weight. The mean decrease from preaspiration values was 7.5 mEq/liter $\pm 4.0$ SD ($P = 0.05$), 12.8 mEq/liter $\pm 1.3$ SD ($P = 0.001$), and 18.4 mEq/liter $\pm 5.2$ SD ($P = 0.05$) in the animals in the 5-ml, 10-ml, and total immersion groups, respectively.

There was also a significant negative correlation between the change in buffer base concentration 10 min postaspiration and the volume of water aspirated ($r = -0.802$).

## Discussion

All the average control values were within normal limits except for the low mean arterial $P_{CO_2}$ of 22 mm Hg and the resulting borderline pH of 7.48. This can be attributed to hyperventilation from the stimulus of the endotracheal tube in lightly anesthetized animals.

It is apparent that the spontaneous survival rate after seawater aspiration is inversely proportional to the quantity of fluid aspirated. Under identical conditions of aspiration, seawater was found to be approximately twice as lethal, volume for volume, as freshwater. In this study only one out of five animals was alive 60 min after aspiration of 10 ml/lb of seawater, whereas, in a previous study of chlorinated freshwater, a minimum of 20 ml/lb was necessary to produce similar mortality statistics (3).

The onset of arterial hypotension immediately after seawater aspiration was a poor prognostic sign for spontaneous survival. Interestingly enough, in all but one of the animals aspirating at least 10 ml of fluid/lb, although the systolic blood pressure dropped below 100 mm Hg within 30 sec of aspiration, it spontaneously rose before showing a progressive decline terminating in the death of the animal.

Ventricular fibrillation, which occurs frequently after aspiration of at least 20 ml of freshwater/lb of body weight (3), was not observed in this study. The absence of ventricular fibrillation after seawater aspiration is consistent with the data reported by others (8).

Swann and Spafford (1) and Redding, Voight, and Safar (9), using different methodology, have reported that a rapid decrease in circulating blood volume occurs after drowning in seawater. In this study it was found that, when small quantities of seawater (1 ml/lb) are aspirated, changes in blood volume may be delayed. In spite of the limitations of the method employed in detecting rapid changes, animals aspirating at least 5 ml of seawater/lb body weight did show significant decreases in blood volume within 1 min of aspiration. A decrease in blood volume could not be confirmed, however, 10 min postaspiration

in the animals studied with iodine-tagged albumin.

Since blood volume data obtained with chromium-tagged red blood cells did not confirm the apparent increasing blood volume found at 10 min with $^{131}I$ and $^{125}I$ in total immersion animals, an explanation for this discrepancy is in order. The presence of $^{125}I$ in the tracheal drainage fluid confirms the fact that plasma, containing albumin, is lost from the circulating blood volume into the lungs during seawater drowning. It is also reasonable to assume that capillary permeability is altered in general and albumin is lost into the extravascular space, as evidenced by the $^{125}I$ in the pleural cavity. The apparent increase in blood volume from 1 to 10 min postimmersion is, then, a reflection of this increased permeability and combined albumin loss. The rate of this albumin loss can be correlated with the change in blood volume as measured with $^{125}I$ or $^{131}I$ as shown in Figure 3. This would then explain the inability to confirm a persistent hypovolemia after seawater drowning when albumin tagged with radioactive tracer elements is employed as the method of measuring blood volume. Although blood volume measured by $^{51}Cr$-tagged red blood cells did demonstrate hypovolemia 10 min after total immersion in seawater, even this technique is somewhat inaccurate since changes in the size of red cells (MCV) resulting from the hypertonic seawater would alter these calculations as well.

The increase in concentration of serum electrolytes was found to vary directly with the quantity of water aspirated. It is interesting to note that, with the exception of serum chloride, electrolyte values spontaneously returned to normal in all animals surviving 60 min postaspiration. Even the chloride values were not markedly elevated after 60 min. In these animals, therefore, emergency therapy would not have to be directed toward correction of electrolyte disturbances. The animals that immediately succumbed to the experiment, however, showed severe disturbances in electrolytes that may well have required therapy if resuscitation was to result in survival. This was especially true in those dying after total immersion.

As was true with experimental near-drowning and drowning in chlorinated freshwater (3), the hemoglobin and the hematocrit determinations were not found to be reliable indicators of the severity of physiological insult after seawater aspiration. Although with the aspiration of small volumes of seawater the hemoglobin and the hematocrit suggested hemoconcentration, values obtained after total immersion were widely dispersed and showed no obvious pattern.

The most significant finding of this study was the fact that regardless of the quantity of water aspirated (in some cases as little as a total of 30 ml) arterial hypoxemia was evident almost immediately. This decrease in arterial $Po_2$ persisted for at least the 60 min during which the determinations were made. A similar finding—that is, of severe prolonged hypoxia—has also been reported after aspiration of small volumes of freshwater (3). Since the persistent hypoxia is not associated with significant hypercapnia or severe acidosis in animals aspirating small quantities of water (1 ml/lb), it suggests that, although minute ventilation may be adequate, ventilation—perfusion ratios may well be disturbed. This can be due to either the presence of the fluid itself or the reaction to its presence, that is, pulmonary edema or aspiration pneumonitis or both.

This finding may explain why patients who have aspirated small quantities of water can present with severe dyspnea and hypoxia but yet show normal hemoglobin, hematocrit, and serum electrolyte values. This is frequently more persistent in patients who have aspirated small quantities of seawater because of the hypertonicity of this fluid that, by removing plasma from

the circulating blood volume, increases the total amount of fluid in the lung itself. On the other hand, with freshwater aspiration the fluid is absorbed rapidly into the circulation (3), and the residual pulmonary defect results primarily from the reaction to aspiration or chemical pneumonitis or both.

It is reasonable to suggest, therefore, that all near-drowning victims, regardless of the type or the quantity of water they aspirate, should be hospitalized and treated for hypoxia. Therapy should be continued at least until arterial blood samples can be drawn and normal $Po_2$ values demonstrated.

When larger quantities of seawater are aspirated (at least 5 ml/lb), there is also an increase in $Pco_2$ and a decrease in pH and buffer base shortly after aspiration. Although it was not the purpose of this study to investigate resuscitation techniques, it seems likely that best results might be obtained by treating this metabolic and respiratory acidosis in addition to the hypoxia per se. When doing so, it should be remembered that these animals are suffering from acute hypovolemia, and the true deficit in total-body buffer base will be greater than that reflected by the concentration in the plasma. In addition, Redding and associates (9) have also demonstrated, under experimental conditions of resuscitation after total immersion in seawater, that administration of plasma is essential to improve survival rate. Obviously, drug, fluid, and electrolyte therapy should not be neglected but should be administrated as indicated in the individual patient.

## Summary

Cardiovascular and biochemical changes were studied in 24 mongrel dogs who aspirated from 1 ml to 29 ml (total immersion) of seawater/lb body weight. The survival rate after aspiration was inversely proportional to the quantity of fluid aspirated. Volume for volume, seawater was found to be approximately twice as lethal as freshwater.

The principal cardiovascular changes observed in all animals that failed to survive the experiment were a progressive hypotension and electrocardiographic evidence of progressive hypoxia. Three minutes after aspiration, the changes in serum electrolytes were found to be dependent upon the quantity of water aspirated. By 1 hr post-aspiration, however, the serum potassium, calcium, and sodium had returned to normal in all surviving animals. Asphyxia, as evidenced by an increase in $Pco_2$ and decrease in pH and $Po_2$, developed immediately, and a significant arterial hypoxemia was still present at the conclusion of the experiment in all surviving animals. Therefore, all near-drowning victims, regardless of the type or the quantity of water they aspirate, should be hospitalized and treated for hypoxia. Therapy should be continued at least until normal arterial $Po_2$ values can be demonstrated. While attempts are being made to restore normal oxygenation and ventilation-perfusion relationships, the need for supportive drug, fluid, and electrolyte therapy can be evaluated and correction be instituted where indicated.

## Acknowledgments

The authors wish to acknowledge the advice and assistance of Drs. Albert J. Gilson, Frank Gollan, and Joel B. Mann and to thank Iris Kiem, Janet Cassady, and Richard Sandifer for statistical evaluation of the data.

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## ABSTRACT

NEMIROFF, M.J.

Resuscitation following cold-water near-drowning.

In: Proceedings of the Ninth International Conference on Underwater Education, p. 168. Colton, Calif., National Association of Underwater Instructors, 1977.

Following submersion and cessation of breathing, permanent brain damage has been thought to occur in 4 minutes. An apparent exception to this concept is the victim of cold-water near-drowning. In water temperatures below 70°F (20°C) the protective effects of hypothermia and the mammalian diving reflex may make survival possible. Such victims appear blue, pulseless, and without respirations. Sixteen patients are presented where submersion times ranged 1-40 minutes (mean 13.1 minutes) and survival was possible. Resuscitation should include rewarming and electrocardiographic monitoring. Survivability depends on aggressive, prolonged resuscitation, correct techniques, and careful medical examination.

## ABSTRACT

NEMIROFF, M.J.

Accidental cold-water immersion and survival characteristics.

In: Program and abstracts. Undersea Medical Society annual scientific meeting, May 13–16, 1977, Toronto, Canada, p. A56. Undersea Biomed. Res. 4, May. 1977. Appendix A.

The diving reflex has been considered a protective mechanism in cold water human immersion accidents. Twelve patients were selected from a series of 47 near-drowning survivors to demonstrate this reflex and its influence on survival. Eight patients are alive and normal despite the following initial clinical findings; 8 comatose, 6 with fixed dilated pupils, and 10 apneic. All were cyanotic and 11 of the 12 were hypothermic (rectal temperatures 90-96°F). The underwater times ranged from 1-38 minutes, with 2 patients submerged 4 minutes, 3 patients submerged 5 minutes, 4 patients submerged 10 minutes, and one of 15 minutes and another 38 minutes. The two fatalities in this series occurred after short immersions. The role of the diving reflex was noted because of the apnea, bradycardia, and cyanosis present in these patients. Preventive measures for hypothermia in people working near water colder than 70°F (20°C) are presented including thermal flotation gear.

ABSTRACT

NEMIROFF, M. J., G.R. Saltz and J.C. Weg.

Survival after cold-water near-drowning: the protective effect of the diving reflex.

Amer. Rev. Resp. Dis. 115 (4,Pt. 2): 145; 1977.

The fate of 11 near drowned individuals retrieved from cold water (20°C or <) after prolonged immersion (> 4 min) seen between 1967-1976 was studied. Eight survived without any neurologic deficit: 2 had residual chronic anoxic brain damage; one died. The age range was 1-42 years with 10 being 18 years or less. Documented submersion time was 4-38 minutes. At the time of recovery from the water 10 were apneic; 4 were pulseless; 10 were cyanotic; 6 had fixed dilated pupils; 4 were comatose, 2 decerebrate and 2 decorticate. At admission to the hospital recorded body temperature was 94.3° ± 2.5; all but one were hypoxemic or had a widened A-$aO_2$ gradient; $PaCO_2$ 51.7 ± 23.4 mm Hg; and all had a metabolic acidosis pH7.09 ± .13. Significant electrolyte disturbances or hemolysis did not occur. Five required intubation and mechanical ventilation for 7-16 days. Three were treated with Positive End Expiratory Pressure ranging from 10-20 cm. $H_2O$. Survival is attributed to the diving reflex which redistributes blood flow from skin muscle and gut to heart and brain and the protective effect of hypothermia. Patients with this reflex, usually children, have cyanosis, apnea, diminished or absent pulses, fixed dilated pupils and coma. If these protective mechanisms in cold water near drowning are recognized, resuscitation beginning at the water's edge, continued with oxygen supplementation en route to the hospital, and followed with necessary ventilatory support and correction of metabolic acidosis will often lead to complete recovery. The survivors include a 42 y.o. physician returned to a busy practice (10 min immersion) and an 18 y.o. college student doing "A" work (38 min immersion). The prognosis in near drowning in cold water is distinctly better than that reported in warm water.

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# Treatment of sea-water aspiration[1]

JOSEPH S. REDDING, G. CARL VOIGT AND PETER SAFAR
*Department of Anesthesiology, Baltimore City Hospitals, Baltimore, Maryland*

REDDING, JOSEPH S., G. CARL VOIGT AND PETER SAFAR. *Treatment of sea-water aspiration.* J. Appl. Physiol. 15(6): 1113–1116. 1960.—Lightly anesthetized dogs were subjected to obstructive asphyxia (simulating laryngospasm). When spontaneous breathing efforts ceased, the lungs were flooded with sea water for 30 seconds, according to a standardized experiment described previously. Five dogs were treated with intermittent positive pressure artificial respiration with 100% oxygen (IPPB/$O_2$) for 3 hours. Five additional dogs were treated identically except for the addition of an intravenous infusion of dog plasma 50 ml/kg body weight, 10 minutes after the start of artificial respiration. All the dogs treated only with IPPB/$O_2$ for 3 hours were more completely reoxygenated than were those ventilated with IPPB/air for 10 minutes in the earlier experiment. However, death with pulmonary edema followed the cessation of IPPB/$O_2$ as well as IPPB/air. When the hemoconcentration and hypovolemia, caused by flooding of the lungs with sea water, were corrected by plasma infusion in addition to IPPB/$O_2$, four of the five dogs survived.

IN A PREVIOUS STUDY (1) we devised a standardized experiment in dogs to simulate three types of near-drowning in human beings. Obstructive asphyxia (simulating laryngospasm) to the cessation of spontaneous breathing efforts was followed by flooding of the lungs with fresh water or with sea water. In a control group, apnea was permitted to continue for a comparable period of time. Resuscitation was then attempted with intermittent positive pressure breathing utilizing room air (IPPB/air) for a period of 10 minutes.

This treatment resulted in survival of all dogs subjected to obstructive asphyxia without flooding of the lungs. Each of the dogs subjected to obstructive asphyxia followed by flooding of the lungs with fresh water died as the result of ventricular fibrillation within 3 minutes of the start of resuscitative efforts.

When the lungs were flooded with sea water following obstructive asphyxia, IPPB/air was effective in partially reoxygenating the arterial blood and in supporting circulation. Following the cessation of artificial ventilation there was an immediate resumption of spontaneous respiration, a transient rise in the aortic pressure and an increase in the pulse pressure. However, in each case 9–31 minutes after cessation of IPPB/air the dog died in asystole, with marked cyanosis and signs of pulmonary edema.

The present study was undertaken to evaluate additional measures which might be utilized in the treatment of dogs subjected to the same sequence of obstructive asphyxia followed by flooding of the lungs with sea water. Prolonged intermittent positive pressure breathing with 100% oxygen (IPPB/$O_2$) seemed likely to produce better reoxygenation, and plasma infusion seemed indicated to correct the hypovolemia and hemoconcentration (2) resulting from sea-water flooding.

## METHODS

Except for the resuscitative maneuvers, the experimental protocol was identical with that in the earlier study (1).

Ten healthy mongrel dogs weighing between 6.0 and 12.8 kg were anesthetized with intravenous pentobarbital sodium (20 mg/kg b. wt.). In each instance an endotracheal tube was inserted and the cuff inflated. The dog was supine and breathing air spontaneously. A polyethylene catheter (o.d., 0.067 in.) was passed through a femoral artery into the aorta and a similar catheter was passed through a femoral vein into the inferior vena cava, and both catheters were connected to strain-gauge pressure transducers. Needle electrodes for recording the electrocardiograph were inserted into all four extremities. A double pneumograph (3) was placed over the chest and abdomen and connected to a strain-gauge transducer. Thus, aortic and inferior vena caval pressures, EKG and breathing movements were continuously recorded through appropriate amplifiers on a direct-writing Sanborn 4-channel recorder. In each dog 45 minutes was allowed after the injection of pentobarbital for the blood pressures, breathing and EKG to reach equilibrium. Then the endotracheal tube was clamped, at the end of an expiration. Thirty seconds after the last spontaneous breathing movement the endotracheal tube was unclamped and flooded with

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[1] This research was supported by the Research and Development Division of the Surgeon General's Office under Contract No. DA-49-007-MD-858.

sea water[2] for 30 seconds. The water was poured through a funnel so that the water level was maintained at 30 cm above the dog's heart. The endotracheal tube was then held horizontally, with the dog in the supine position to allow passive drainage for 30 seconds.

After this total of 90 seconds of apnea, IPPB/$O_2$ was begun at a rate of 30 inflations/minute and with tidal volumes of 25 ml/kg body weight. Whenever fluid or foam became visible at the external end of the endotracheal tube, ventilation was briefly interrupted and aspiration performed through the endotracheal catheter. The volumes of fluid poured into and drained passively or by suction from the trachea were measured. Five of the ten dogs received an intravenous infusion of dog plasma, 50 ml/kg body weight. The infusion was started 10 minutes after the start of artificial ventilation and was completed within approximately 30 minutes.

After 3 hours of IPPB/$O_2$ the dogs were disconnected from the respirator and observed.

In all dogs, 5 ml of arterial blood was drawn anaerobically into a heparinized syringe *a*) immediately before clamping the tracheal tube, *b*) immediately before the start of IPPB, *c*) after 10 minutes of IPPB, *d*) after 3 hours of IPPB and *e*) after 2 hours of spontaneous breathing of room air at the end of resuscitation. The blood was analyzed immediately for $O_2$ saturation and $CO_2$ content by the method of Van Slyke and Neill (4). Arterial blood was drawn and determination of the hematocrit made under conditions *a*), *c*) and *d*).

## RESULTS

The last spontaneous breathing effort was noted in each of the 10 dogs in from 2 minutes and 10 seconds to 3 minutes and 20 seconds following obstruction of the airway (table 1). When resuscitation was started 90 seconds after the last spontaneous breathing movement the aortic mean pressure had been depressed as much as 75% below the control value and the heart rate had slowed as much as 92%. At this time the arterial oxygen saturation was between 3.6% and 21.1% and the arterial $CO_2$ content was increased.

After 10 minutes of IPPB with 100% oxygen the arterial oxygen saturation was between 88% and 100% and the $CO_2$ content had fallen below the control level. The heart rate had increased in all dogs, while the aortic mean pressure had increased in five dogs and fallen in five since the start of resuscitation. In all dogs, however, the aortic mean pressure was depressed between 7% and 100% below the control level. At this time the hematocrit was elevated in all dogs.

After about 1 hour the airway was noted to be dry and no further fluid could be removed by tracheal suction in any of the 10 dogs. From 40 to 91 ml/kg of sea water had been poured into the endotracheal tube and from 14 to 33 ml/kg of fluid in excess of this volume had been recovered by passive drainage at the end of flooding and by tracheal aspiration during resuscitation.

[2] Atlantic Ocean water, collected near Ocean City, Md.

TABLE 1. *Treatment of Sea-Water Aspiration*

| | Time, min.: sec. | Aortic Press., (mm Hg) | Vena Caval Mean Press., mm Hg | Heart Rate, Beats/min. | Art. $O_2$ Sat. % | Art. $CO_2$, mEq/l. | Hct., % | Water, ml: Aspirated | Water, ml: Drained |
|---|---|---|---|---|---|---|---|---|---|
| *A. IPPB/$O_2$ Only** | | | | | | | | | |
| *Dog 1; wt., 11 kg* | | | | | | | | | |
| Obstruction | 0 | 220/130 | 0 | 90 | 100.0 | 22.6 | 45 | 740 | 780 |
| Start resusc. | 4:35 | 110/50 | 0 | 102 | 21.1 | 34.1 | ns | | |
| 10-Min. resusc. | 14:35 | 80/50 | 0 | 120 | 94.8 | 11.2 | 58 | | |
| End resusc. | 194:35 | 170/130 | 0 | 150 | 93.1 | 16.6 | 54 | | |
| *Dog 2; wt., 8.7 kg* | | | | | | | | | |
| Obstruction | 0 | 160/110 | 0 | 150 | 100.0 | 17.2 | 42 | 550 | 800 |
| Start resusc. | 4:30 | 90/20 | 6 | 18 | 15.9 | 25.3 | ns | | |
| 10-Min. resusc. | 14:30 | 140/110 | 0 | 144 | 100.0 | 15.2 | 67 | | |
| End resusc. | 194:30 | 160/110 | 6 | 150 | 93.7 | 12.6 | 56 | | |
| *Dog 3; wt., 12.8 kg* | | | | | | | | | |
| Obstruction | 0 | 160/100 | 5 | 192 | 100.0 | 21.3 | 48 | 550 | 750 |
| Start resusc. | 4:00 | 130/70 | 4 | 60 | 14.8 | 30.1 | ns | | |
| 10-Min. resusc. | 14:00 | 120/100 | 3 | 144 | 98.0 | 10.7 | 68 | | |
| End resusc. | 194:00 | 130/100 | 2 | 150 | 81.8 | 14.1 | 59 | | |
| *Dog 4; wt., 11 kg* | | | | | | | | | |
| Obstruction | 0 | 140/100 | 0 | 192 | 96.4 | 18.1 | 46 | 430 | 585 |
| Start resusc. | 4:20 | 150/90 | 2 | 42 | 20.9 | 27.0 | ns | | |
| 10-Min. resusc. | 14:20 | 70/50 | 2 | 120 | 88.0 | 10.7 | 59 | | |
| End resusc. | 194:20 | 80/50 | 0 | 130 | 81.2 | 13.0 | 54 | | |
| *Dog 5; wt., 10.9 kg* | | | | | | | | | |
| Obstruction | 0 | 160/110 | 2 | 186 | 89.4 | 19.0 | 45 | 480 | 700 |
| Start resusc. | 3:40 | 100/40 | 5 | 30 | 11.3 | 27.4 | ns | | |
| 10-Min. resusc. | 13:40 | 80/55 | 2 | 156 | 90.6 | 11.8 | 56 | | |
| End resusc. | 193:40 | 135/100 | 2 | 150 | 94.6 | 14.3 | 57 | | |
| *B. IPPB/$O_2$ and Plasma Infusion†* | | | | | | | | | |
| *Dog 1; wt., 7 kg* | | | | | | | | | |
| Obstruction | 0 | 175/105 | 2 | 180 | ns | ns | 42 | 600 | 760 |
| Start resusc. | 4:50 | 80/25 | 8 | 15 | ns | ns | ns | | |
| 10-Min. resusc. | 14:50 | 65/30 | 0 | 84 | ns | ns | 55 | | |
| End resusc. | 194:50 | 145/95 | 6 | 120 | ns | ns | 44 | | |
| *Dog 2; wt., 8 kg* | | | | | | | | | |
| Obstruction | 0 | 180/110 | 2 | 132 | ns | ns | 44 | 600 | 860 |
| Start resusc. | 3:42 | 44/10 | 2 | 30 | ns | ns | ns | | |
| 10-Min. resusc. | 13:42 | 60/40 | 0 | 96 | ns | ns | 57 | | |
| End resusc. | 193:42 | 150/110 | 3 | 120 | ns | ns | 38 | | |
| *Dog 3; wt., 12 kg* | | | | | | | | | |
| Obstruction | 0 | 175/120 | 2 | 170 | 100.0 | 20.1 | 45 | 580 | 840 |
| Start resusc. | 4:07 | 80/20 | 6 | 18 | 3.6 | 26.0 | ns | | |
| 10-Min. resusc. | 14:07 | 65/50 | 4 | 150 | 100.0 | 12.1 | 57 | | |
| End resusc. | 194:07 | 175/110 | 0 | 150 | 100.0 | 16.5 | 43 | | |
| *Dog 4; wt., 7 kg* | | | | | | | | | |
| Obstruction | 0 | 130/90 | 4 | 108 | 92.0 | 20.0 | 50 | 537 | 700 |
| Start resusc | 3:50 | 70/40 | 2 | 60 | 10.6 | 24.9 | ns | | |
| 10-Min. resusc. | 13:50 | 0/0 | 0 | 84 | 100.0 | 10.9 | 60 | | |
| End resusc. | 193:50 | 90/50 | 0 | 120 | 100.0 | 13.7 | 47 | | |
| *Dog 5; wt., 6 kg* | | | | | | | | | |
| Obstruction | 0 | 160/130 | 0 | 132 | 91.2 | 19.0 | 48 | 550 | 730 |
| Start resusc. | 4:45 | 70/40 | 0 | 15 | 18.0 | 23.7 | ns | | |
| 10-Min. resusc. | 14:45 | 65/50 | 0 | 78 | 94.7 | 10.6 | 60 | | |
| End resusc. | 194:45 | 90/60 | 0 | 108 | 94.4 | 9.8 | 40 | | |

ns = Not studied. * Result; pulmonary edema and death. † Result; survival in *dogs 1–4*, pulmonary edema and death in *dog 5*.

In each of the five dogs given plasma infusion (table 1*B*), beginning 10 minutes after the start of resuscitation, there was an immediate increase in pulse pressure and aortic mean pressure (fig. 1), with an accompanying

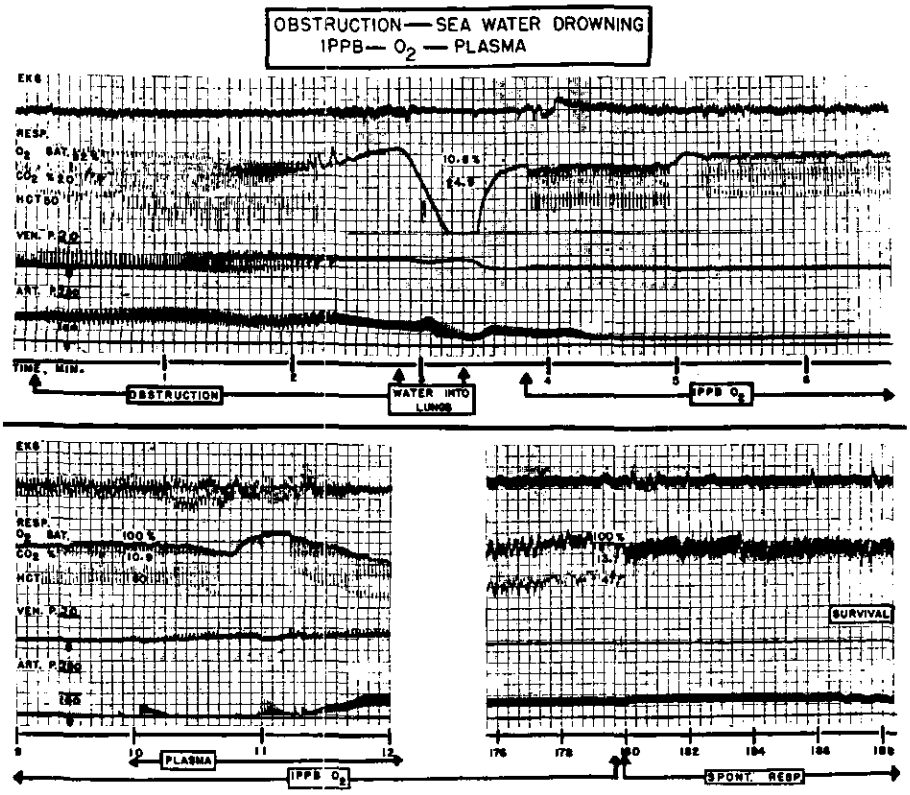


FIG. 1. Resuscitation of a dog subjected to sea-water drowning.

increase in vena caval pressure during the period of infusion. These changes were not observed in the five dogs not receiving plasma.

In the plasma-treated dogs at the end of 3 hours of IPPB/$O_2$ the arterial oxygen saturation was above 94.4%. The aortic mean pressure was between 4% and 48% below the control level and the hematocrit had returned to approximately control levels.

In those dogs not receiving plasma (table 1*A*), at the end of 3 hours of IPPB/$O_2$ the arterial oxygen saturation was between 81.2% and 94.6% and the aortic mean pressure was between 0% and 46% below the control level. *The hematocrit was still above the control value.*

All 10 dogs were then disconnected from the respirator and immediately began to breathe spontaneously on room air. Within a few minutes each of the plasma-treated dogs began to move and recover consciousness while those which had not received plasma remained comatose. After 2 hours of spontaneously breathing room air the plasma-treated dogs had arterial oxygen saturations of 90.6% or higher, while in the remaining dogs the arterial oxygen saturations were from 55.5% to 85.5%.

All of the dogs not treated with plasma died within 48 hours, with signs of pulmonary edema. One of the plasma-treated animals expired in a similar fashion within 12 hours, while the remaining four plasma-treated dogs survived, without evidence of permanent damage.

Macroscopic post-mortem examination of the dogs that succumbed after sea-water flooding revealed edematous, congested, heavy lungs with scattered areas of hemorrhagic consolidation.

Microscopic examination of the lungs of the dog which died after treatment with IPPB/$O_2$ and plasma infusion revealed homogeneous material filling many alveoli and bronchioles and some of the bronchi. The capillaries were engorged with erythrocytes. There were numerous areas of confluent air spaces with clubbing and rupture of the alveolar septa.

## DISCUSSION

This study was designed to evaluate certain resuscitative measures in the treatment of dogs prepared to simulate sea-water near-drowning in human beings.

It was demonstrated in an earlier experiment (1) that

dogs subjected to obstructive asphyxia without flooding (simulating laryngospasm) to the point of respiratory arrest could be resuscitated by IPPB/air for 10 minutes. However, when obstructive asphyxia was followed by flooding of the lungs with sea water, cessation of IPPB/air at the end of 10 minutes was followed by pulmonary edema and death within 30 minutes.

This experiment indicates that prolonged IPPB utilizing 100% oxygen provides better reoxygenation than does a shorter period of IPPB/air when the lungs have been flooded with sea water. Even with complete reoxygenation, the hemoconcentration and hypovolemia attendant upon loss of fluid and plasma protein in sea-water near-drowning lead to death.

When the intravenous infusion of plasma was utilized to correct this hypovolemia and hemoconcentration, combined with prolonged IPPB/$O_2$, four of five dogs survived.

Swann and Spafford (2) demonstrated loss of fluid from the circulation into the lungs and a rise in hematocrit in sea-water drowning in dogs. This fluid contained 2–4 gm % of serum proteins. Although we recovered from 14 to 33 ml/kg of fluid from the lungs in excess of the volume of sea water poured into the lungs, we feel that this represents only a portion of the loss of fluid from the circulation.

Estimation of the plasma volume based on elevation of the hematocrit at the end of 10 minutes of resuscitation reveals deficits of 172–301 ml in those dogs not treated with plasma. This does not necessarily represent the maximum plasma deficit which occurred during the period of resuscitation.

The volume of plasma infused in these experiments was selected empirically on the basis of these considerations. Plasma was selected for infusion on the basis of pilot experiments during which the use of dextrose solution or plasma-volume expanders failed to result in survival.

Moreover, the elevation of the hematocrit in those dogs not treated with plasma probably does not accurately reflect the degree of disturbance in circulation. The observations of Harding and Knisely (5) suggest that settling of blood cells and stasis of circulation may occur even with relatively unchanged arterial blood pressure. *In vivo* microscopy, as well as post-mortem morphological studies which may clarify the cause of death after near-drowning in sea water, should be carried out.

We are grateful to Mrs. Diane Keyes and to Dr. Sadao Morikawa for their assistance during these experiments.

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*Original Articles*

# Ultrastructural Alterations in Rat Lungs

*Changes After Intratracheal Perfusion With Freshwater and Seawater*

CAPT HOWARD E. REIDBORD, USAF (MC), WASHINGTON, DC,
AND WERNER U. SPITZ, MD, BALTIMORE

INVESTIGATIONS of the mechanisms of drowning have been concerned mainly with changes in blood volume,[1] electrolytes[2,3] and cardiopulmonary function.[4,5] Morphologic study of the lungs in human drowning and in analogous animal experiments has not been effective in elucidating the basic alterations that occur. Halmagyi[6] found no light microscopic change in the pulmonary architecture after introducing small quantities of fresh water into the lungs of rats and described focal intra-alveolar hemorrhage and edema after seawater was introduced. With massive pulmonary flooding, which occurs in most accidental drownings, the histologic changes may be severe. Distention of the alveoli, congestion of the capillaries, focal hemorrhages, and fluid within the alveolar spaces are found in most cases.[7] Such alterations are nonspecific, and a diagnosis of drowning made by these criteria alone is presumptuous. Neither a diagnosis of drowning nor differentiation of saltwater from freshwater drowning is possible solely on the basis of morphologic changes in the lungs.

Since significant movements of fluid occur in both directions across the air-blood barrier in experimental and human drowning,[1,2,5] exposure of the pulmonary tissue to solutions of varying tonicity, as encountered with freshwater and seawater, could be expected to result in structural changes. In addition, the direction of the major movement of fluid and the mechanism of death are known to be different in freshwater and saltwater drowning. Whereas water shifts from the alveoli into the circulation in freshwater drowning, resulting in hemodilution, water moves in the opposite direction in saltwater drowning, with consequent hemoconcentration.[1,2,5] Light microscopic studies have been inadequate in demonstrating morphologic alterations that might be correlated with these well-documented physiologic events.

This study was undertaken to examine the effects of fresh- and saltwater on the lung and, if possible, to differentiate saltwater from freshwater drowning. Simulation of drowning was accomplished by flooding the respiratory tract with fluid through the trachea, to avoid the variable effect of laryngospasm upon the introduction of the fluid. Ultramicroscopic examination of the pulmonary tissue was then performed. Review of the literature disclosed no report of the electron microscopic structure of the lungs under such conditions.

## Materials and Methods

Healthy adult Wistar rats,* weighing 300 to 400 gm and of both sexes, were used in the experiment. The animals were lightly anesthetized with intraperitoneal pentobarbital, and the anterior aspect of the neck was shaven. The single limb of a Y-shaped glass cannula was inserted into the trachea and was made airtight. One branch of the cannula was connected by polyethylene tubing to a buret filled with the perfusion fluid. The other limb of the cannula was open to room air. All perfusions were performed at the same pressure by adjusting the buret to a constant height (10 cm) above the animal's head. Two fluids were used: (1) tap water at 37 C and (2) seawater (salinity 2.9%) at 37 C.

Perfusion was begun by opening the buret and allowing the perfusion fluid to flow into the trachea while the air contained in the respiratory tract es-

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From the Aerospace Pathology Branch, Armed Forces Institute of Pathology, Washington, DC and the Office of the Chief Medical Examiner of Maryland, Baltimore.

Reprint requests to Armed Forces Institute of Pathology, Washington, DC 20305 (Capt Reidbord).

* The "Principles of Laboratory Animal Care" as promulgated by the National Society for Medical Research were observed during this study.

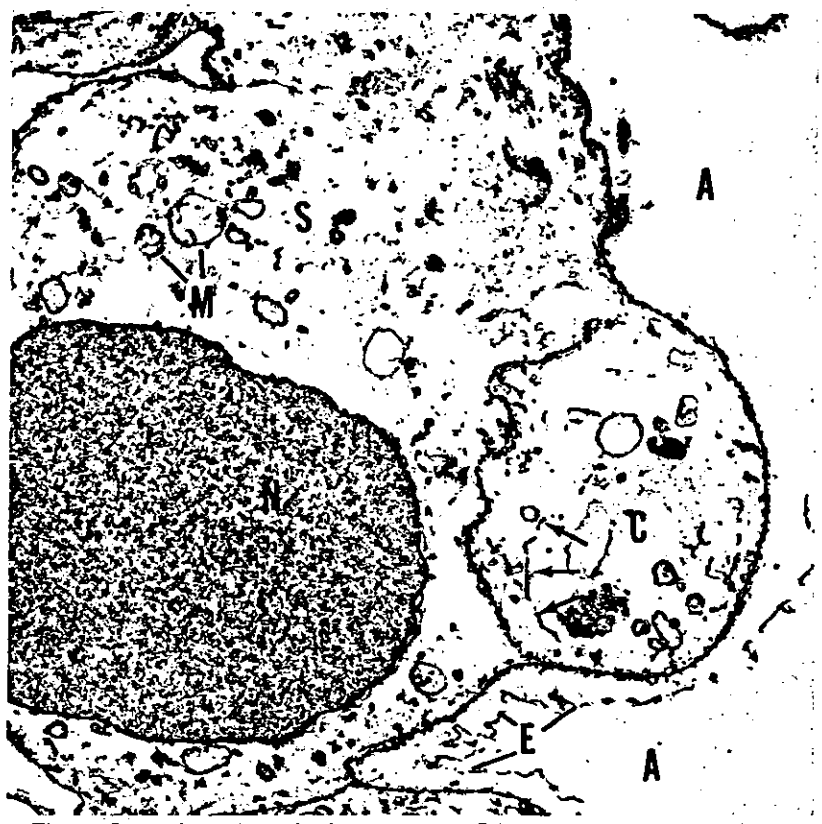



Fig 1.—Lung tissue from freshwater group. Cell margins are obliterated due to rupture of plasma membranes. Nuclei (*N*) are diffusely granular. Markedly altered mitochondria (*M*) can be discerned. Alveolar epithelium (*E*) is thickened and the cytoplasm clear. Complete absence of epithelium is noted in many areas. Capillary (*C*) endothelium (*arrows*) is extensively disrupted, and cellular debris is present in the lumen. Alveolar space (*A*). Septal area (*S*) (×12,000). (All illustrations are of tissue double stained with uranyl acetate and lead citrate.)

caped through the open limb of the cannula, which was then clamped shut. The animal was allowed to inspire the perfusion fluid until all respiratory motion ceased, at which time the thorax was immediately opened and a random cube of lung was removed. The tissue was fixed by mincing in 4 to 5 C phosphate-buffered 1% $OsO_4$.[9] Fixation was carried out for one hour at room temperature, and dehydration in ascending concentrations of ethanol was followed by embedding in Araldite or Epon.[10] Silver and silver-gold sections were obtained with glass knives; the sections were mounted unsupported on copper grids and double stained with uranyl acetate [11] and lead citrate.[12] An electron microscope (RCA EMU 3) was used. Thick sections 0.5$\mu$ to 1$\mu$ were stained with toluidine blue O. Six normal control animals were decapitated and the lung tissue handled in a manner identical to that in the experimental groups. Five animals were examined in the freshwater group, four in the seawater group.

## Results

*Control Group.*—The ultramicroscopic structure of the pulmonary tissue in the control animals was similar to that previously described in detail [13,14] and will not be repeated here.

*Freshwater Intratrachcal Perfusion.*—The gross appearance of the lungs of the rats in this group was similar. The lungs occupied the entire thorax, with some overlapping at the anterior margin. The cut surface was light pink to grayish white, and copious amounts of frothy fluid exuded from alveoli, which appeared moderately distended. The changes were uniform throughout both lungs.

Sections 0.5$\mu$ to 1.0$\mu$ thick showed widening of the alveolar septa. Capillaries appeared collapsed, and erythrocytes were reduced in number. The endothelial and septal cell nuclei appeared enlarged and more homogeneous than in the controls.

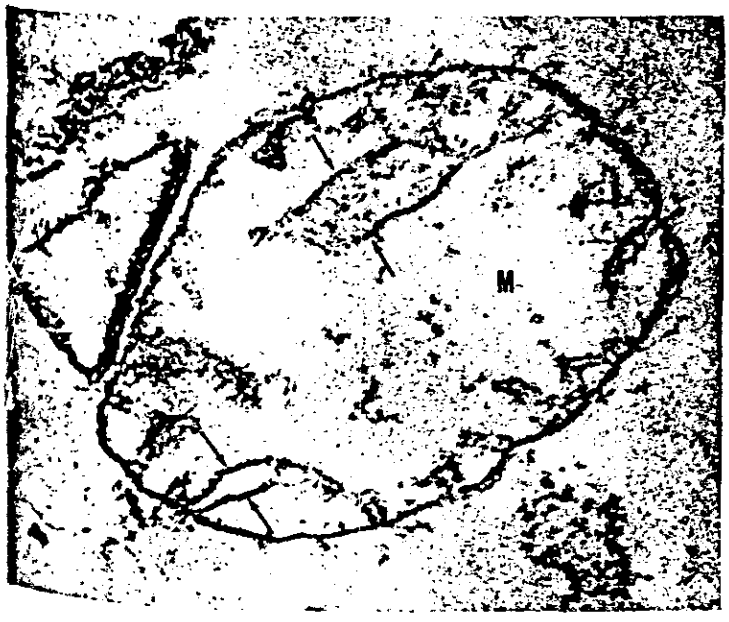
The extensive damage to the lungs observed in this group at first strongly suggested that the changes were artifacts of poor fixation or some other incorrect

Fig 2.—Lung tissue from freshwater group. Typical structure found in capillary lumina. Single- and double-membrane configuration is present (× 43,500).

preparative technique. Comparison with the control animals and with the saltwater group, however, established the severe damage to be the result of the fluid introduced into the lung. It should be noted that allowing tissue to remain in contact with fresh water would be expected to prpduce extensive damage, which might be interpreted as fixation artifact in the absence of adequate controls.

The ultrastructural findings in the lungs of all the animals in this group were similar and will be described together. The most striking feature was the obliteration of cell outlines, making recognition of normal relationship almost impossible (Fig 1). Extensive interruptions of the plasma membranes of endothelial, septal, and alveolar cells were evident, and fragments of cell membranes and cytoplasmic organelles were scattered about (Fig 1). Erythrocytes were only rarely seen, whereas normally the lumen of the vessel contains many red blood cells. Numerous cricular forms of various sizes were present in the lumina of the vessels. These structures were limited by single or double membranes of irregular contour, often forming a continuous outline (Fig 2). The origin of these structures was uncertain. Fragments of endoplasmic reticulum and mitochondria were present in vascular lumina and in the septal areas.

The mitochondria of the septal cells and endothelium in the most severely involved areas showed a uniform and distinctive swelling (Fig 3-5). There was loss of the normal double limiting membrane with rupture of the outer wall (Fig 4, *arrows*). Remnants of the outer layer could be seen as a blurred, discontinuous osmiophilic band. The normal density of the matrix was mark-




. Fig 3.—Lung tissue from freshwater group. Characteristic mitochondrial change seen in this group. Swollen mitochondrion (*M*) with decreased density of matrix, distortion of cristae and intracristal enlargement (*arrows*) (× 66,000).


Fig 4.—Lung tissue from freshwater group. Partial loss of outer membrane (*arrows*) is associated with early stage of mitochondrial (*M*) swelling. Endoplasmic reticulum (*ER*) (× 35,000).


Fig 5.—Lung tissue from freshwater group. Some of the dilated areas of the endoplasmic reticulum (*ER*) exceed mitochondria (*M*) in size. Circular contour of mitochondria is characteristic of more advanced swelling (× 21,600).

edly reduced, and the matrix granules were only rarely found. Some cristae appeared swollen, with focal blurring of the walls and fragmentation; others assumed elongated oval forms (Fig 3, *arrows*) and round configurations due to intracristal swelling. The changes were often so advanced that it was almost impossible to recognize the structure as a mitochondrion except for an occasional cristal remnant.

The rough-surfaced endoplasmic reticulum of the septal and alveolar cells was markedly dilated and in areas exceeded the enlarged mitochondria in size (Fig 4, 5). The characteristic electron-dense granules were often preserved, establishing identification. Faint strands of electron-dense material could be seen in the lumina of the endoplasmic tubules. The perinuclear continuation of the endoplasmic reticulum, the perinuclear cistern, was noticeably dilated, particularly at the point of junction with the cytoplasmic segment of the system.

Because of the severe disruption of the cells, recognition of the normal cytoplasmic structures was impossible in many areas. The Golgi apparatus could not be identified, although an occasional smooth-surfaced, flattened vacuole was noted. Dense bodies surrounded by single membranes were seen in the cytoplasm of septal cells and occasionally were found free in vessel lumina. Lipid droplets were present in the cytoplasm of septal cells. Septal bundles of collagen were separated by electron-lucent areas. The cytoplasmic ground substance tended to be clumped into varying-sized aggregates. The thin cytoplasmic extensions of the membranous pneumocytes (alveolar lining cells) showed clearing of the cytoplasm, dilatation of the endoplasmic reticulum and mitochondria, and disruption of the plasma membranes (Fig 1, *E*).

A distinctive loss of the normal distribution of nuclear chromatin was found in this group (Fig 1). The chromatin was finely granular and evenly distributed throughout the nucleus without the normal variations in density. The nuclear envelope was preserved as a double membrane with the inner layer accentuated by a uniform thin accumulation of chromatin. Small projections from the inner nuclear envelope into the perinuclear cistern were occasionally found.

*Seawater Intratracheal Perfusion.*—The gross appearance of the lungs of the rats in this group was similar to each other and did not differ significantly from that of the animals treated with freshwater. Occasional atelectatic areas were present in the posterior portions of the lower lobes.


Fig 6.—Lung tissue from seawater group. Capillary lumina (*C*) are enclosed by uninterrupted layers of endothelium. Alveoli (*A*) are lined by epithelium showing normal cytoplasmic density. Numerous vacuoles (*V*) are present in the capillary lumen and in the septal areas (*S*). Plasma membranes are preserved and cytoplasmic organelles are essentially normal as compared to those in the freshwater group (× 12,000).

Sections 0.5$\mu$ to 1$\mu$ thick revealed small, dark septal and endothelial nuclei, in contrast to the larger nuclei in the freshwater group. Red blood cells were frequently found in the capillary lumina. The thickness of the alveolar septa was less than in the freshwater group and similar to that of the controls.

The ultrastructural findings in the animals of this group were similar and will be described together. The architecture of the lung was preserved and the margins of the cells maintained (Fig 6), in contrast to the disruption evident in the first group. The mitochondria of the septal and alveolar cells appeared essentially normal. The double-layered external laminae of the mitochondria were well delineated, and the cristae appeared normal. The density of the matrix appeared unchanged, and matrix granules were present.

Most striking was the presence of many circular and irregularly rounded structures in vascular lumina, septal areas and alveolar spaces (Fig 6 and 7). These bodies varied from spherical to flattened cisternal structures and showed a clear central area. They varied from small vacuoles similar in size to endoplasmic reticulum to larger bodies approximately 1$\mu$ to 2$\mu$ in greatest dimension. The walls often appeared to be irregularly folded, with the configuration of a partially

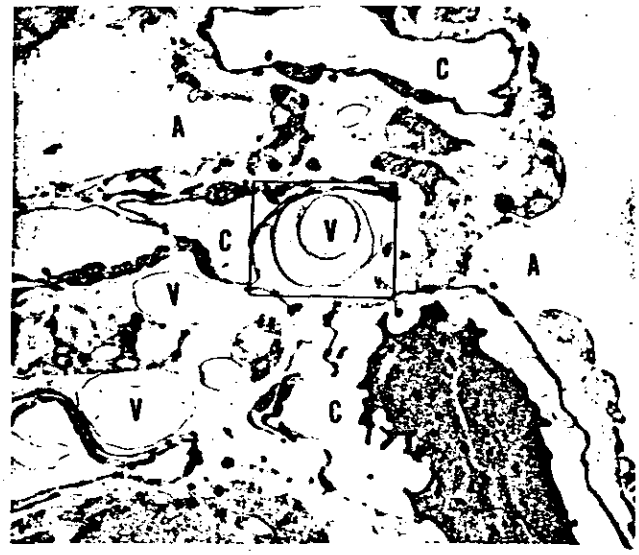



Fig 7.—Lung tissue from seawater group. Vacuoles (*V*) in septal area are most often bound by single membranes, but occasionally more complex structure is evident. Alveoli (*A*). Capillary (*C*) (× 10,800).

collapsed sphere (Fig 11). The limiting membranes were predominantly single layered, but many of the structures were surrounded by a double layer, and some were partially limited by both single and double layers (Fig 8). Because of the marked folding of the walls of these vesicular bodies, many limiting membranes had a blurred appearance in tangential sections. The bodies occasionally impinged upon surrounding structures, as indicated by indentation of adjacent nuclei. Structures similar to those just described have been infrequently observed in the lumina of vessels in the control animals but have not been seen in the septal areas of normal animals.

Indentations were seen projecting through either the alveolar cytoplasm (Fig 9), the endothelial lining, or both. These outpouchings were continuous with the basement membrane material and ranged from small elevations in the membrane to blebs that extended completely through the overlying epithelium or endothelium, maintaining continuity with the basement membrane by a narrow neck (Fig 9, *arrows*). This ap-

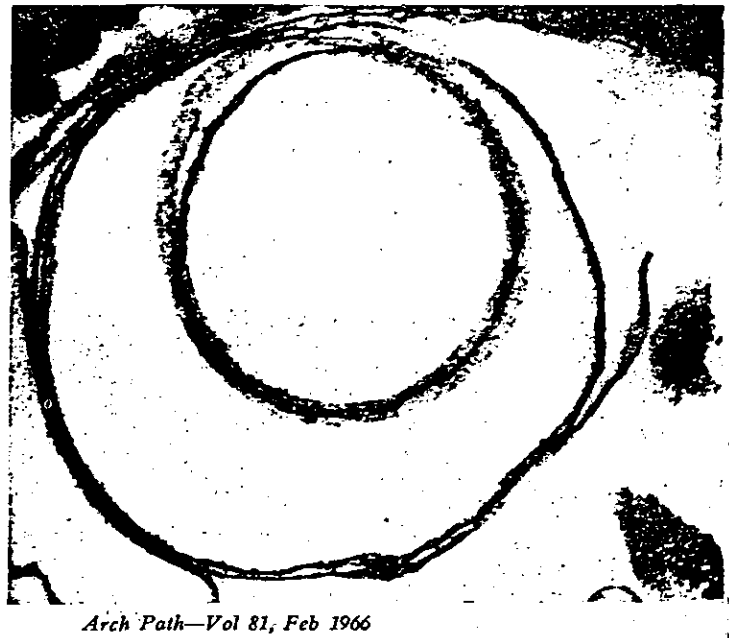


Fig 8.—Lung tissue from seawater group. Enlargement (area outlined in black in Fig 7) of vacuole reveals double-wall configuration similar to that in structures seen in the freshwater group (Fig 2) (× 56,300).

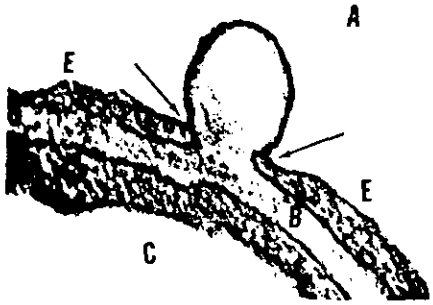



Fig 9.—Lung tissue from seawater group. Projection or bleb into alveolus (*A*) is continuous with basement membrane material (*B*). Alveolar epithelium (*E*) appears to be completely interrupted (*arrows*). Such a structure may represent passage of fluid-filled vacuole into alveolus (×51,300).

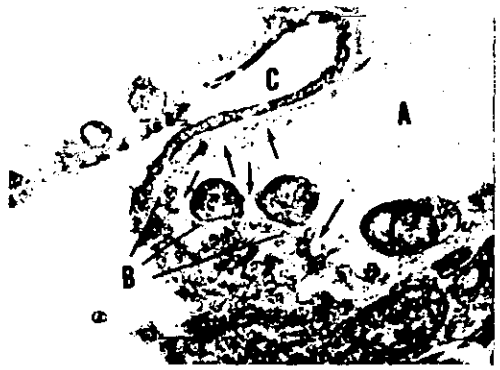



Fig 10.—Lung tissue from seawater group. Epithelium lining the alveoli (*A*) is discontinuous (*arrows*), and denuded basement membrane (*B*) is exposed. Such separations of the alveolar epithelium may result from the passage of vacuoles across the membrane, as in Fig 9 (×29,600).

pearance suggested that such structures accounted for some of the membrane-limited bodies in the vascular lumina and alveolar spaces.

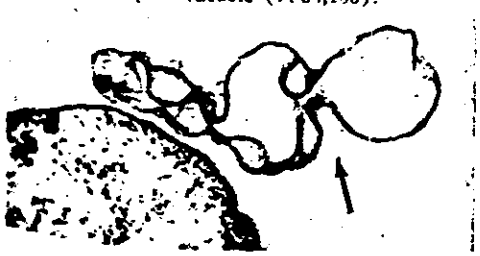
The cytoplasmic processes of the alveolar lining cells in this group were markedly changed from those in the normal animal. The basic alteration appeared to be a discontinuity of the alveolar cytoplasm, leaving denuded areas of basement membrane exposed to the alveolar space (Fig 10). The fragments of alveolar cell cytoplasm that remained were frequently increased in thickness. There was no indication of the swelling and cytoplasmic clearing found in the freshwater group.

## Comment

The introduction of fluid into the respiratory tract may produce damage to the architecture of the lung in two obvious ways. First, the cells of the lung are bathed in solutions that are significantly different in electrolytic and protein content from normal extracellular fluid. Second, the presence of the fluid in the alveoli interferes with or completely stops the interchange of gases across the alveolar wall, thereby rendering the whole animal hypoxic.

Hypoxia produced by reduced oxygen tension or total absence of oxygen results in only minor alterations in the structure of the air-blood interface.[15] The ultrastructural alterations found in other tissue following their removal from the body [16,17] do not to any large degree resemble the changes described in the freshwater flooding group. It is likely, then, that the severe structural alterations observed in the freshwater group were caused by the violent osmotic effect of the markedly hypotonic solution in contact with the cells and not by the hypoxia. On the other hand, the effects of the hypertonic seawater were considerably less damaging to the pulmonary tissue, and the more subtle changes of anoxia may be evidenced. This experiment did not attempt to distinguish between the effects of hypoxia and those resulting from the electrolytic and osmotic imbalances, but it would be pertinent to consider the morphologic change described in other tissues upon exposure to solutions of hypotonic or hypertonic composition.

Fig 11.—*Lung tissue from seawater group.* Irregularly folded structure (*arrow*) lying in alveolus resembles collapsed vacuole (×34,100).



Intact cells respond nonspecifically to irritating substances or alterations in the surrounding media. The general response involves changes in the mitochondria, swelling of the Golgi apparatus, and dilatation of the endoplasmic reticulum, with eventual rupture of the plasma membrane.[8] Swelling of cells in hypotonic solutions and shrinkage in hypertonic solutions was observed early in this century.[18] Cytoplasmic

vacuoles and foamy transformation of cytoplasm have been noted upon exposure of isolated cells and tissue slices to distilled water.[18,19] The precise structures that accounted for the foamy change were not clearly defined by the light microscope.[19] More recently, nuclear irregularity, clearing of the cytoplasm, and mitochondrial swelling were observed in leukocytes exposed to hypotonic solution, and considerably less change was noted upon exposure to hypertonic saline.[20]

Striking alterations were described in the mitochondria of the pulmonary cells in the freshwater group. Pathologic changes of mitochondria have been the subject of recent reviews.[18,21,22] Although much work has been done on the chemistry of mitochondrial swelling, electron microscopic observations under controlled conditions are few.[21,23,24] Of particular interest are the changes that occur upon exposure to hypotonic solutions. When exposed to water, mitochondria uniformly swell and the matrix becomes less dense. The outer limiting membrane forms blebs and is ruptured. Cristae are either unfolded or markedly distorted and are completely lost in some cases. The mitochondrion becomes spherical in contour and subsequently increases in volume; it may exceed five times the normal. These alterations are believed to be due to the osmotic effect of a markedly hypotonic medium, causing imbibition of water and an almost inverse linear relationship between mitochondrial volume and osmotic pressure of the medium.[22]

The mitochondrial alterations in the freshwater flooding group are similar to those described, as found upon exposure of mitochondria to hypotonic solutions in vitro. The ruptured outer membrane, spherical configuration, and decreased density of the matrix suggest severe osmotic swelling. The immediate and direct role of anoxia in producing these changes is felt to be minimal in light of recent work demonstrating minimal alterations of mitochondria in tissues anoxic for considerably longer periods than were in effect in this experiment.[16,17]

Vacuoles of various configuration were observed in the vessel lumina in both experimental groups and also in the interstitial area and alveoli of the seawater group. Their morphologic appearance and relation to surrounding structures suggested that they arose from the endothelium and, to a lesser extent, from the alveolar epithelium. Similar vacuoles may be found in the endothelium of pulmonary capillaries in normal lungs.[15,25,26] Such structures have also been described in pathologic states affecting the lung.[15,27-29] Schulz[15] concluded that the double-walled structures seen in the capillary lumen arise from endothelial vacuoles. Such a conclusion was also suggested by the material studied in the present experiment. The physiologic significance of these vacuoles is an unsettled matter, but their formation probably indicates that large shifts of fluid are occurring.[26] The presence of these double-walled structures in both experimental groups is felt to represent the morphologic expression of movement of fluid across the alveolar wall. This would be in accord with the experimental data that have established the existence of large shifts of fluid in both directions across the alveolar wall in freshwater and saltwater drowning.[2,30]

Distinctive invaginations of cell membranes were found in the seawater group and these projections extended into either the alveolar space (Fig 9) or the endothelial lumen. Such structures might be related to the movement of fluid across the alveolar wall. Vacuoles have been observed in the basement membrane substance, and during the process of transport across the alveolar septa they might assume some of the configurations noted. With the passage of the vacuoles into the alveolar space, a gap in the alveolar epithelium would occur. Such gaps were found with great regularity in the seawater group. These gross defects in the usually completely covered basement membrane might be expected to alter further the interchange of fluid across the alveolar wall. Similar but not identical changes in the alveolar epithelium with experimental pulmonary edema have been described.[29]

The severe disruption of the alveolar lining cells in the freshwater group was caused by the osmotic effect of the perfused fluid, while in the seawater group the irritative action of the hypertonic saline and the passage of vacuoles into the alveolar space resulted in the alveolar cell changes described.

## Summary

Seawater and freshwater were perfused into the respiratory tract of rats, and the ultrastructural architecture of the lung was

examined. A clear difference was found between the freshwater, saltwater, and control groups. The changes in freshwater pulmonary flooding appeared to be predominantly osmotic in nature, as indicated by severe cellular disruption, mitochondrial swelling, and endothelial destruction. In seawater perfusion, the lung structure was well preserved, although formation of vacuoles, discontinuity of alveolar lining cells, and swelling of cells were noted.

These findings were felt to represent the morphologic alterations resulting from the movements of large quantities of fluid across the alveolar-capillary region in addition to osmotic and hypoxic effects. The clinical, chemical, and physiologic differences between freshwater and saltwater drowning appear to be reflected in the ultrastructural morphology.

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# SURVIVAL AFTER 40 MINUTES' SUBMERSION WITHOUT CEREBRAL SEQUELÆ

HARALD SIEBKE HARALD BREIVIK
TORE RØD BJØRN LIND

*Departments of Anæsthesiology and Pædiatrics, Akershus Central Hospital, Nordbyhagen, Norway*

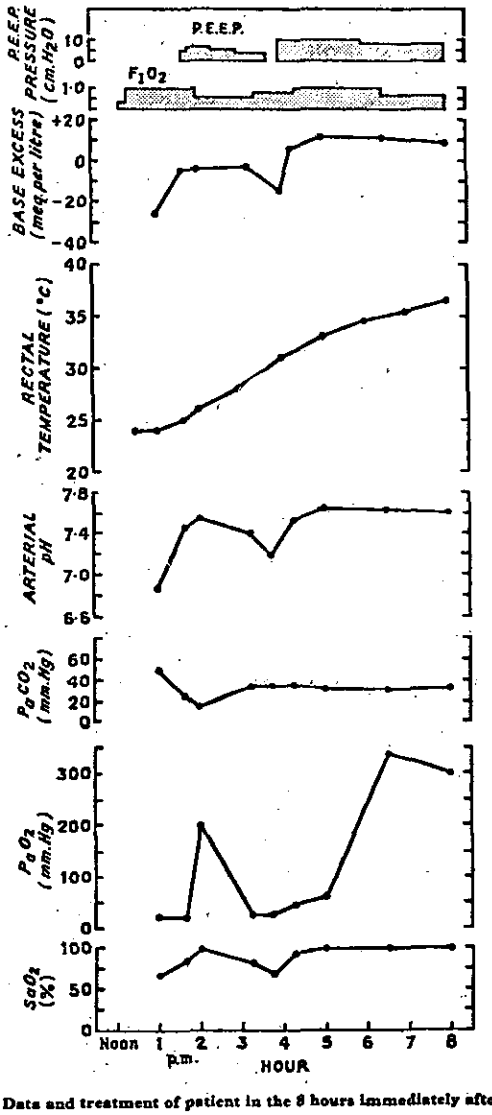
***Summary*** Cardiopulmonary resuscitation and rewarming were successful in a 5-year-old boy who had been submerged for 40 minutes in ice-cold fresh water. Severe metabolic acidosis was corrected by intravenous infusion of sodium bicarbonate solution before spontaneous circulation could be re-established. Fulminant pulmonary œdema developed after re-establishment of spontaneous circulation. This was efficiently reversed by positive-end-expiratory-pressure ventilation. During 2 days of treatment on a respirator the patient gradually regained consciousness; the endotracheal tube was then removed and the patient immediately started talking intelligently. The patient went through a period of slow cerebration and motor dysfunction but recovered rapidly, and on examination 13 months after the accident all findings were normal.

## Introduction

IT is often difficult to establish the exact duration of submersion in a case of drowning. Our patient was submerged for 40 minutes. This unusually long period was accurately recorded by the police and the fire brigade.

## Case-report

On Feb. 6, 1974, just before 11.30 A.M., a 5-year-old boy walked out on a partially frozen river and plunged into the water. Three people saw the accident from the opposite river bank, and, as the boy disappeared under the surface, one of them ran to a nearby house and called the police at exactly 11.30 A.M. From this moment the boy was completely and continuously submerged. The police requested frogmen from the fire brigade. The frogmen were stationed 25 kilometres from the site of the accident. Attempts by the policemen to locate the boy, while waiting for the frogmen, were unsuccessful. The frogmen arrived at the police station at exactly 12 noon, as shown by the records kept by the officer on duty. The accident happened about a kilometre from the police station, and the estimated time at which the frogmen dived for the boy was 12.05 P.M. The boy was found at the bottom of the river, 2·5–3 metres below the surface of the water. The ice was very thin at the site of the accident, and seemed to have broken under the boy. The attendant policemen saw no sign of air pockets between the water and the ice. The boy was carried ashore at 12.10 P.M. after being submerged for 40 minutes. Mouth-to-mouth ventilation was immediately started, and external cardiac compression was given in the ambulance. He arrived at the hospital at exactly 12.17 P.M. On arrival there was no sign of spontaneous respiration or circulation, his pupils were maximally dilated, and his skin was grey and cyanotic. His rectal temperature was 24°C. Cardiopulmonary resuscitation was continued with external cardiac compression and ventilation with 100% oxygen through an endotracheal tube. An intravenous infusion of sodium bicarbonate 4·2 g. per 100 ml. was started, and rewarming was attempted with warm-water bags. Ventricular fibrillation followed asystole after adrenaline (0·5 mg.) had been given twice intravenously. D.C. shock was given five times before ventricular fibrillation was converted to a stable but very slow sinus rhythm. However, there was no palpable pulse, and an infusion




**Data and treatment of patient in the 8 hours immediately after rescue.**

Measurements were made at 37°C with an Instrumentation Laboratories (model 313) blood-gas analyser and corrected to body-temperature using the Severinghaus blood-gas calculator.[1] $Sa_{O_2}$ (oxygen saturation of hæmoglobin) was calculated from $Pa_{O_2}$, arterial pH, base excess, and body-temperature using the nomograms of Kelman and Nunn.[2] 250 meq. (10 meq. per kg.) of sodium bicarbonate was given between the first and second measurements and 75 meq. between the fifth and sixth measurements. Note the pronounced improvement in calculated $Sa_{O_2}$ despite the slight changes in $Pa_{O_2}$, as pH was returned to normal by infusion of sodium bicarbonate. This is due to the increase in the affinity for oxygen of hæmoglobin as the pH rose.

of isoprenaline was started. This had no effect on the heart-rate, and since there still was no sign of spontaneous circulation, external cardiac compression was continued. At 1 P.M. arterial pH and blood-gas analysis showed very pronounced metabolic acidosis and hypoxæmia (see accompanying figure). The sodium bicarbonate infusion-rate was increased, and, after the pH had been returned to normal by the administration of about 10 meq. per kg. body-weight, a strong and regular pulse could be felt for the first time. This was about an hour after arrival at the hospital and 1 hour and 45 minutes after submersion. 75 ml. of mannitol (15%), frusemide (30 mg.), and hydrocortisone (100 mg.) was given intravenously. A Foley catheter was inserted, revealing a large diuresis. In spite of this, severe pulmonary œdema rapidly developed, resulting in very stiff lungs, a worsening of the hypoxæmia, and copious frothy œdema fluid pouring out of the endotracheal tube. The pulmonary œdema was completely reversed within 30 minutes by ventilation with a volume-controlled respirator with a positive end-expiratory pressure (P.E.E.P.) of 10 cm. water. The pronounced improvement in the pulmonary compliance and arterial oxygenation allowed the proportion of oxygen in the inspired gases ($F_{IO_2}$) to be reduced from 1 to 0·6 (see figure).

Steroid treatment was continued (dexamethasone 12 mg. four times a day), mannitol infusions were repeated twice during the first 18 hours, and prophylactic antibiotic treatment was started.

At about 3 P.M. hypoxæmia and acidæmia again developed and worsened, despite increasing the $F_{IO_2}$ to 0·8. A leaking cuff was discovered and it was difficult to maintain P.E.E.P. Arterial oxygenation did not improve until the defective endotracheal tube was replaced, the P.E.E.P. was restored to 10 cm. water, and the acidosis was corrected with sodium bicarbonate (see figure). During the next few hours the $F_{IO_2}$ could gradually be reduced to 0·5. However, a chest X-ray still showed pronounced congestion and infiltration of both lungs. Though his pulmonary function improved, respirator treatment was continued until 8 A.M. on Feb. 8. A chest X-ray taken 5 days after the accident showed a normal appearance.

The urine and plasma appeared pink 2 hours after admission, indicating hæmolysis. Unfortunately, free hæmoglobin was not estimated. Urinary output was high (1600 ml. during the first 18 hours), and the colour of the urine gradually returned to normal.

At 2.40 P.M. the patient had extremely pronounced hypokalæmia (1·6 meq. per litre), which was confirmed in a sample taken at 3 P.M. Urinary potassium was 3·8 meq. per litre, and serum sodium, chloride, glucose, and osmolality were normal. Potassium was added to the intravenous infusion, and 5 hours later serum-potassium was 2·9 meq. per litre.

The rectal temperature remained unchanged until the circulation was re-established and the patient was placed on a warm-water mattress. Active warming of the patient was discontinued when the rectal temperature had reached 30°C. Thereafter the temperature increased spontaneously, reaching 37°C 8 hours after arrival. Afterwards it remained normal.

His pupils were widely dilated for about 30 minutes after spontaneous circulation had been re-established. They then contracted and reacted normally to light. Shortly afterwards the patient had gasping respiratory movements. These increased in force and frequency, so that partial curarisation was needed to control ventilation. In the evening of Feb. 6 the patient began to move his eyes and extremities. The next morning an electroencephalogram (E.E.G.) showed generalised but slight dysrhythmia. The following evening the patient reacted to verbal commands. On the morning of Feb. 8 he seemed to be completely conscious and the endotracheal tube was removed. He immediately talked intelligently, asking for his glasses and telling us that he had been in a hospital once before. An E.E.G. showed some regression of the generalised dysrhythmia.

On Feb. 9 the boy was transferred from the intensive-care unit to the pædiatric department, where he remained in bed for the next 2 days. Steroid therapy was gradually withdrawn during the next 6 days. On Feb. 11 he was able to take a few steps, and 2 days later he managed the stairs, but his gait was unsteady. Coordination of his hand and finger movements was poor and he needed help with eating and drinking during the first week. A neurological examination on Feb. 12 revealed cerebellar dysfunction (positive Romberg test, poor coordination, and slight dysdiadochokinesis). During the first days in the pædiatric department, the patient had slightly slowed cerebration. His memory was poor; he repeated the same questions several times a day, and 3 months later he could recall only a few details of his stay in hospital.

The patient was discharged on Feb. 14 to celebrate his fifth birthday at home. According to his parents, he became mentally and physically normal within a few days of arriving home. During the spring he learnt to ride a bicycle.

On June 24 neurological examination showed further improvement, with only slight incoordination persisting. At the last neurological examination on March 20, 1975, he was completely normal.

The patient was tested by a clinical psychologist on five occasions from March 12 to April 18. This psychologist has considerable experience in evaluating patients with traumatic brain injuries. She found the patient to be intellectually and emotionally normal for his age.

## Discussion

This patient survived submersion lasting 40 minutes and had no apparent neurological sequelæ 13 months after the accident. We have no reason to doubt the reported duration of submersion, or that he was completely submerged all that time. His rectal temperature of 24°C on admission also indicates a lengthy submersion.[3]

Our patient was treated according to accepted principles.[4] The importance of adequate correction of acidosis, as indicated by arterial pH and blood-gas analysis during primary resuscitation, is well illustrated. Mechanical ventilation with P.E.E.P. had a beneficial effect on the severe pulmonary œdema in our patient. Secondary pulmonary œdema ("secondary drowning"), which occurs hours after the resuscitation, is caused by destruction and washout of surfactant by aspirated water,[5] resulting in alveolar collapse and leakage of plasma into the alveoli. Modell et al.[6] have demonstrated that mechanical ventilation with P.E.E.P. significantly increases the oxygen tension of arterial blood in dogs after drowning in sea water. They successfully applied this principle to two cases of near drowning in sea water.[6] Without P.E.E.P., secondary pulmonary œdema or alveolar collapse often caused hypoxæmia, necessitating high inspired oxygen concentrations and subsequent oxygen damage to the lungs with a fatal outcome even in cases where the patient had regained consciousness.[7,8]

The value of steroids in the treatment of aspiration pneumonitis is still debatable.[9–11] However, large doses of steroids may have a beneficial effect on the

post-ischæmic encephalopathy. Mannitol was given to counteract brain swelling.

The successful outcome in this case was probably due to the rapid cooling of the body in cold water. At a temperature of 24°C the oxygen requirement of the brain is considerably reduced [12,13] and adenosine triphosphate is preserved, thus protecting membrane stability.[14] The diving reflex, which has been demonstrated in human volunteers [15] and is potentiated in cold water,[16] may have further delayed brain deterioration.

Hypokalæmia has been reported in other cases of near drowning.[17] In our patient it was severe despite the obvious hæmolysis. We assume this to be the result of rapid correction of the acidosis with sodium bicarbonate, which causes an exchange of hydrogen and potassium ions across the cell membranes.[18] Rapid metabolism of the infused glucose as the body-temperature increased may also have contributed to the intracellular movement of potassium.

This case emphasises the importance of attempting resuscitation even in cases of lengthy submersion.

Requests for reprints should be addressed to H. S., Department of Anæsthesiology, Akershus Central Hospital, N1474 Nordbyhagen, Norway.

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TEXAS REP. BIOL. MED. 5:423-437. 1947.

# FRESH WATER AND SEA WATER DROWNING: A STUDY OF THE TERMINAL CARDIAC AND BIOCHEMICAL EVENTS*

H. G. SWANN, MARSHALL BRUCER, CORNELIA MOORE AND BETTY LEE VEZIEN

Of the many European studies of drowning (reviewed by Cot, 1931), the French investigators in general agree that when submersion has not been so long as to vitiate observation, the victims are either white ("pale") or cyanosed ("bleu") (Martin, 1932). In the "white" victims death is ascribed to "syncope," with little or no water aspirated and little or no froth in the respiratory passages. In the cyanosed victims death is ascribed to obstructive asphyxia, much water being aspirated and much froth being found in the respiratory passages. Cot (1931) writes that 10–15 per cent of all victims of drowning are of the "white" type.

The mechanism of death in drowning with cyanosis is still controversial. Although it has long been disputed (Moritz, 1944), water has been clearly shown in the lungs of animals drowned in solutions containing such chemical tracers as dyes, bismuth salts or ferricyanide. These solutions are found to penetrate deep into the lungs during drowning, even to "complete inundation of all the alveoli" (Martin, 1932). Much water passes into the blood stream and dilutes the red cells, chlorides, etc. (Moritz, 1944). In sea water drowning, on the other hand, there is an increase in chlorides in the left heart which is ascribed to the diffusion of the concentrated sea water (3.6% salts) into the blood from the lungs. Martin (1932) feels that the aspirated water mechanically blocks the pulmonary circuit, making even more difficult the task of an already anoxic myocardium. But Cot (1931), calling attention

*From the Department of Physiology, The University of Texas Medical Branch, Galveston. This paper reports, in a preliminary manner, a portion of the results obtained in a program of research into the efficacy of resuscitating procedures. The program is sponsored by the Air Materiel Command, Wright Field, Ohio, under Contract No. W 33-038 ac-14379. The coöperation of the Aero Medical Laboratory, Wright Field, is gratefully acknowledged. Received for publication August 11, 1947.

to the high protein content of the fluid found in the lungs of the drowned victims, suggests that the aspirated water causes a fulminating pulmonary edema and that it is the edematous fluid which "drowns" the victim.

Moritz (1944) has recently summarized the blood chemical changes that occur during drowning. In general terms, whatever blood constituent is measured, after fresh water drowning left heart blood is found to be more dilute than right heart blood. Conversely, after sea water drowning, right heart blood is found to be more dilute than left heart blood.

Banting and his associates (Banting, Hall, Janes, Leibel and Lougheed, 1938; Lougheed, Janes and Hall, 1939) studied some aspects of fresh water drowning comprehensively, employing dogs in their experiments. They reported a rapid fall in arterial oxygen content, a rise followed by a fall, in arterial carbon dioxide, and the occurrence "sometimes" of ventricular fibrillation. They also reported that some animals "drowned" with little or no water in the lungs, a reflex closure of the glottis and complete apnea effectively preventing the aspiration of water while the animals were submerged.

In this study we have reinvestigated the problem, attempting in especial to obtain a detailed analysis of the cardiac and biochemical events during the actual process of drowning.

## Methods

Healthy dogs of about 8 Kg. were employed in our experiments. Under local procain anesthesia both femoral arteries were exposed; one was cannulated for blood pressure measurement and the second cannulated with a Lindeman transfusion needle to obtain arterial blood samples. To measure venous pressure, a catheter (Balfour tubing, O.D. 7/64") was inserted into a femoral vein; the tube was then pushed toward the heart until its tip lay in the inferior vena cava about 2 cm. above the diaphragm. At autopsy, the position of the tip was determined with precision.

The arterial blood pressure was recorded optically with a water-filled glass Bourdon tube as the pressure-sensitive element, of the kind described by Kubicek, Sedgwick and Visscher (1941). The Bourdon tube was connected to the cannula with

41 cm. of Tygon tubing. This system had a natural frequency of 64 vibrations per second; it recorded diastolic pressures equal to, but systolic pressures about 10 mm. Hg lower than, the pressures recorded while using connections of lead tubing rather than Tygon tubing. With large pulse pressures, the systolic error approached 20 mm. Hg. Systolic pressures reported in this paper, then, are low by 10–20 mm. Hg.

Intrathoracic pressure, taken from a cannula which was inserted under local procain anesthesia, and venous pressure were also recorded optically with more sensitive glass Bourdon tubes. In this paper, the "effective venous pressure" is defined as follows: the pressure in the inferior vena cava minus (or plus, according to sign) the intrathoracic pressure. Both were measured at the end of diastole and during an expiratory movement when the intrathoracic pressure curve was relatively flat.

Electrocardiograms and heart sounds were recorded intermittently throughout the experiments, using a Sanborn "Stethocardiette."

An 8-ml. arterial blood sample was drawn under oil every minute during the experiment. Potassium fluoride was then added as an anticoagulant. These whole blood samples were analyzed thus:

*Oxygen* and *carbon dioxide* content of whole arterial blood, in duplicate, by the manometric method of Van Slyke and Neill (1924).

*pH* with a glass electrode ("Electron-Ray pH Meter" of Cambridge Instrument Co.).

*Lactic acid* of whole blood, by the method of Mendel and Goldscheider (1925). In our hands, this analysis was not satisfactory; the values reported here are correct only to the nearest 60 mgm. per cent.

*Chloride* of whole blood by the method of Whitehorn (1921).

The *densities of whole blood and of plasma* by the falling-drop method of Hamilton and Barbour (1926). From these were deduced, by employing the nomogram of Phillips et als. (1943), the *plasma proteins* and *hemoglobin*. Some hemoglobin estimations were checked photocolorimetrically and

showed little variation from densiometric measures, even under extreme conditions of hemolysis, hemoconcentration and hemodilution.

To accomplish the experimental drownings, a cone-shaped metal mask (described by Jackson, 1939, except that two rubber gaskets were used), was slipped over the dog's muzzle and bandaged with rubber sheeting at the junction of head and mask. The water to be used in the drowning was contained in a reservoir at a height quickly adjustable so that the level of reservoir water was the same as that of the dog's mouth. In this way, no water pressure was exerted upon the animal's respiratory passages. At zero time, the mask was flooded with fresh or sea water from the reservoir.

## Results

### A. *Fresh Water Drowning.*

Complete data were obtained on five dogs during experimental drowning with fresh water. A few incomplete observations were made on one more animal. Since, in general,

Table I

*Fresh Water Drowning—Dog No. 76*

| | Minutes | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
| Arterial oxygen volumes % | 21.0 | 8.5 | 3.8 | 2.8 | 2.5 | .... | 4.1 |
| Arterial carbon dioxide, volumes % | 43.6 | 51.3 | 47.3 | 37.9 | 31.7 | .... | 33.2 |
| Lactic acid, whole blood, mgm. % | 80 | 70 | 65 | 89 | 89 | .... | 82 |
| pH | 7.45 | 7.37 | 7.37 | 7.27 | 7.16 | .... | 7.18 |
| Plasma proteins, gm. % | 6.5 | 6.8 | 6.7 | 4.7 | 4.6 | .... | 6.2 |
| Hemoglobin, gm. % | 22.5 | 18.8 | 18.2 | 9.7 | 7.1 | .... | 3.8 |
| Density of whole blood, gm./ml | 1.0734 | 1.0658 | 1.0626 | 1.0427 | 1.0362 | .... | 1.0335 |
| Chlorides, whole blood, mE/L | 91 | 80 | 62 | 59 | 53 | .... | 44 |
| Pulse rate | 105 | 34 | 34 | 56 | Fibrillation at 3.42 | .... | — |
| Arterial blood pressure mm. Hg | 262/117 | 362/128 | 350/120 | 367/118 | 35 | 23 | 12 |
| Effective venous blood pressure, cm. $H_2O$ | 5 | 64 | 5 | 15 | 24 | 23 | 22 |

the data follow a consistent course in this preliminary report, the observations on only one dog (No. 76) will be described in detail. These are shown in Table I, with a graph of the changes in figure 1A.

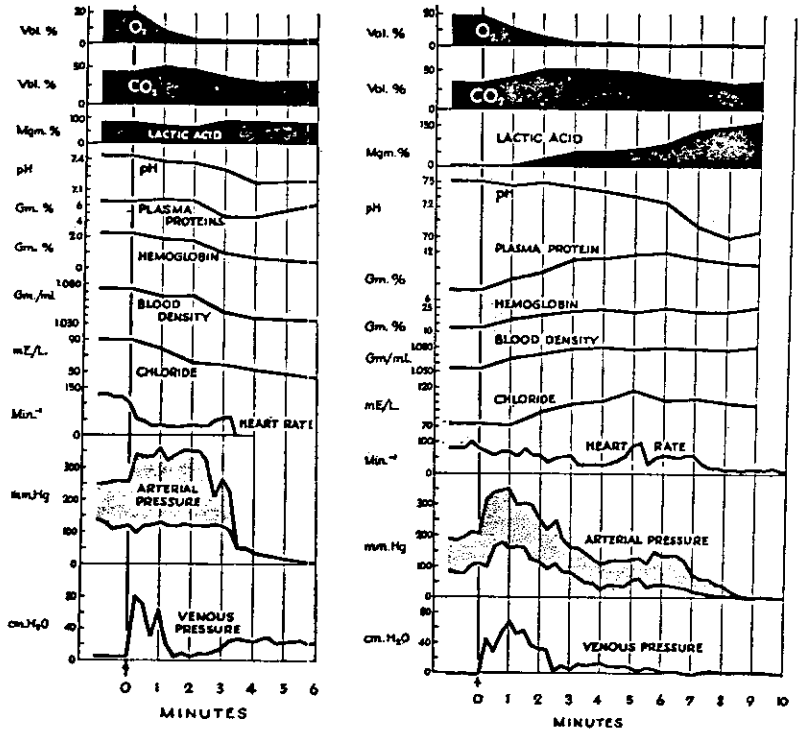


FIGURE 1

A. Fresh water drowning—Dog No. 76.

B. Sea water drowning—Dog No. 82.

1. *Blood gases.* During fresh water drowning, the arterial oxygen content dropped rapidly from 21.0 to 3.8 volumes per cent at two minutes after the start. The whole blood carbon dioxide content rose rapidly from its pre-drowning control value of 43.6 volumes per cent to 51.3 at one minute, and then slowly fell to 31.7 volumes per cent.

2. *pH.* The pH fell rapidly to the terminal value, at cardiac arrest, of about 7.1. This increased acidity occurred although there was a concurrent fall in carbon dioxide content. No consistent increase in whole blood lactic acid was observed.

3. *Hemodilution.* The blood density, hemoglobin, plasma proteins and whole blood chlorides all decreased rapidly. In dog No. 76, hemodilution commenced at one minute after the start and continued for the next five minutes. Its magnitude can be appreciated from the change in whole blood density, which dropped from 1.0734 at zero minutes to 1.0335 at six minutes. A considerable hemolysis occurred terminally, the *plasma* at the sixth minute containing 2.8 gm. per cent hemoglobin. It is this hemolysis which was probably responsible for the terminal rise in plasma proteins.

Hemodilution occurred in all five dogs; its course in each dog is shown in figure 2, employing whole blood density as the criterion of hemodilution. In dog No. 72, it was relatively

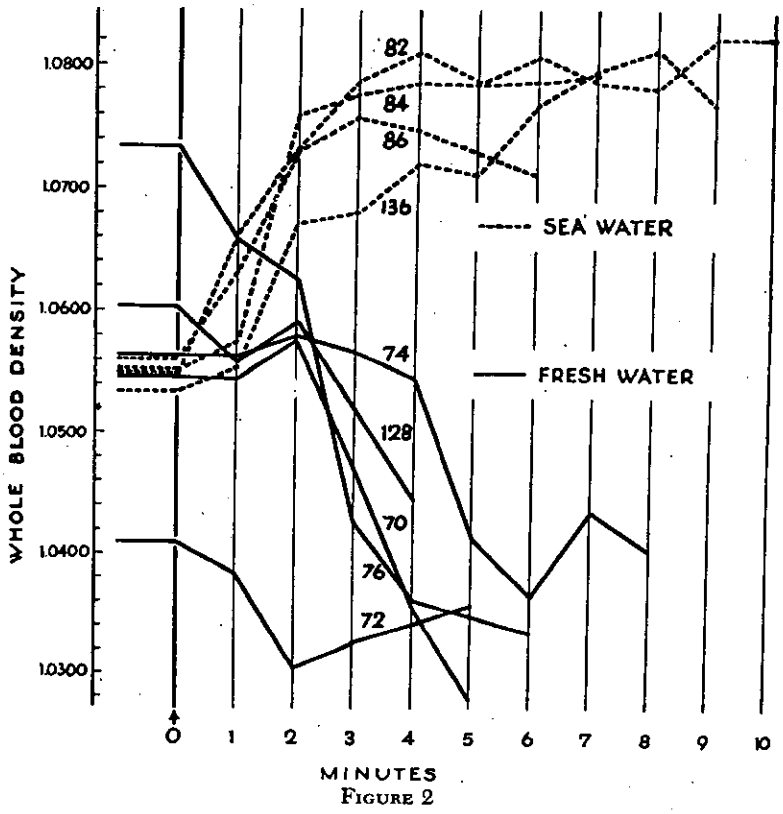


FIGURE 2

Changes in blood density during drowning.

mild, but in the other four it was violent. In four of the dogs, it was delayed until the second to fifth minute, but in the other dog it appeared at the first minute.

4. *Heart.* The systolic arterial blood pressure, but not the diastolic, rose rapidly and then levelled off. At this time the pulse rate was very slow. The ventricles fibrillated abruptly 3.4 minutes after drowning started, at a time when the blood pressure was still well sustained. Electrocardiograms, blood pressure records and heart sounds all confirmed this abrupt event. Ventricular fibrillation took place in four of the six dogs which were drowned in fresh water; the time of its occurrence is shown for these four dogs in Table II. (In two dogs, including one not shown in the table, it did not occur.)

TABLE II

*Data on Five Dogs Drowned in Fresh Water and Four Dogs Drowned in Sea Water*

| No. | Type of Drowning | Time of Ventricular Fibrillation, min. | Weight of Lungs of Drowned Dogs, gms. | Normal Weight of Dogs' Lungs, gms.* | Excess Weight of Drowned Dogs' Lungs, gms. | Volume of Water Diluting (+) or Removed from (—) Blood |
|---|---|---|---|---|---|---|
| 70 | FRESH WATER | 3.5 | 378 | 52 | 326 | +0.66 |
| 72 | | .... | 147 | 76 | 71 | +0.12 |
| 74 | | 5.6 | 238 | 77 | 161 | +0.39 |
| 76 | | 3.4 | 303 | 76 | 227 | +1.2 |
| 128 | | 3.2 | 411 | 100 | 311 | +0.37 |
| 82 | SEA WATER | .... | 360 | 100 | 260 | —0.34 |
| 84 | | .... | 343 | 77 | 266 | —0.31 |
| 86 | | .... | 159 | 80 | 79 | —0.25 |
| 136 | | .... | 280 | 96 | 184 | —0.34 |

*These figures were obtained from dogs killed by obstructive asphyxia. In each case, the lungs from a dog of the same body weight serve as controls.

5. Throughout the period of drowning, the effective venous pressure was high. At cardiac arrest it remained high (22 cm. $H_2O$), due probably to an increased blood volume (see below).

6. At autopsy, just after death, the right heart was found to be grossly relaxed, but the left—both chambers—hard and empty. Large quantities of froth and fluid flowed spontaneously from the nostrils. The lungs, particularly in their dependent parts, were hemorrhagic; they were soggy and tremendously enlarged, virtually filling the opened thoracic cage; they did not collapse spontaneously. A hemostat was clamped on the trachea and the lungs were then dissected free. They floated in water, as did the lungs of all the dogs in this series. The weight of the lungs was compared with that of similar dogs killed by obstructive asphyxia (Table II). The drowned dogs' lungs were heavier by a considerable amount; indeed, the excess fluid they contained was equal to roughly one-half of the vital capacity of dogs of this weight (500–700 ml.).

B. *Sea Water Drowning.*

Complete data were obtained on four dogs during experimental drowning in sea water. A few incomplete observations were also made on a fifth animal. Again, in this preliminary report, the data from only one dog, typical of the group, will be presented (Table III and figure 1B, dog No. 82).

The changes in blood gases and pH were like those observed in fresh water drowning, but blood lactic acid rose considerably.

The most conspicuous difference in behavior between the two types of experimental drowning lay in the changes in the blood concentration; all indices indicated a strong hemoconcentration, the converse of the hemodilution observed in fresh water drowning. It occurred in all dogs tested, as shown in the measurements of whole blood density, and was rapid and violent (figure 2).

In sea water drowning, none of the five animals tested had ventricular fibrillation. The blood pressure was lower and the pulse pressure, instead of being about 200 mm. Hg as in fresh water drowning, was about 100 mm. Hg at about the

TABLE III

*Sea Water Drowning—Dog No. 82*

| | Minutes | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Arterial oxygen, volumes % | 18.4 | 11.2 | 6.2 | 3.2 | 2.9 | 1.3 | 1.1 | 1.6 | 1.7 | 1.1 | .... |
| Arterial carbon dioxide, volumes % | 34.8 | 42.0 | 52.6 | 52.7 | 51.5 | 49.1 | 41.2 | 39.0 | 34.7 | 36.8 | .... |
| Lactic acid, whole blood mgm. % | 0 | 0 | .... | 53 | 55 | 65 | 86 | 133 | .... | 163 | .... |
| pH | 7.53 | 7.46 | 7.51 | 7.44 | 7.39 | 7.32 | 7.25 | 7.07 | 7.00 | 7.04 | .... |
| Plasma proteins, gm. % | 7.3 | 8.7 | 9.6 | 11.1 | 11.3 | 11.8 | 12.0 | 11.3 | 10.8 | 10.6 | .... |
| Hemoglobin, gm. % | 13.0 | 17.8 | 20.8 | 23.2 | 24.4 | 22.8 | 25.5 | 23.1 | 23.0 | 25.4 | .... |
| Density of whole blood, gm./ml. | 1.0547 | 1.0662 | 1.0733 | 1.0787 | 1.0810 | 1.0787 | 1.0807 | 1.0787 | 1.0782 | 1.0822 | .... |
| Chlorides, whole blood, mE/L | 74 | 73 | 89 | 99 | 103 | 117 | 104 | 106 | 101 | 97 | .... |
| Pulse rate | 81 | 68 | 58 | 57 | 30 | 88 | 58 | 59 | 17 | 15 | 10 |
| Arterial blood pressure, mm. Hg. | 213/107 | 352/160 | 250/116 | 164/76 | 110/30 | 125/56 | 139/44 | 79/23 | 41/7 | 15/0 | 5/0 |
| Effective venous blood pressure, cm, $H_2O$ | —1 | 68 | 32 | 5 | 13 | 8 | 2 | 1 | 2 | 2 | 0 |

second minute. The blood pressure fell to zero at about the ninth minute. The effective venous pressure was well sustained throughout, but at cardiac failure, it was close to zero, in contrast with the high post mortem venous pressure observed in fresh water drowning. These several differences in the arterial and venous pressures between the two types of drowning may be ascribed to the postulated differences in blood volume (see below).

At autopsy, the appearance of the lungs was similar to that observed in fresh water drowning. In these dogs' lungs, as in the lungs from dogs drowned in fresh water, large amounts of fluid were present. The actual weights and computed excess weights are shown in Table II.

## Discussion

The movement of water into the blood stream in fresh water drowning has been studied by Brouardel and Vibert (1880) and by Karpovitch (1933). They showed that it occurred even though the esophagus had been previously tied off to prevent entrance of water into the blood by way of the gastrointestinal tract. Furthermore, it has long been known that the pulmonary epithelium has an enormous capacity for absorption (Colin, 1873). Winternitz (1920) showed that dogs can absorb as much as 3000 ml. of saline from the lungs in 30 minutes. As Moritz points out (1944), the nature of the water movement will depend, among other things, upon the differences in osmotic pressure between intrapulmonic fluid and capillary blood. It seems clear that the flow of water into the blood in fresh water drowning is a matter of movement of aspirated hypotonic water into the isotonic blood, and that the flow of water from the blood into the lungs in sea water drowning is a matter of movement of isotonic blood water into the aspirated hypertonic intrapulmonic sea water.

The rapidity of the flow of water into, or out of, the blood is shown by the rapidity of the changes in blood density. It is possible to deduce from these changes the quantity of water involved in the movement, thus: the amount of water necessary

to dilute the blood to the low densities observed in fresh water drowning may be estimated by formula (1):

$$V = \frac{C_s - C_m}{C_m - 1} \qquad (1)$$

V equals the volume of water added to one volume of blood;
$C_s$ equals the density of blood at zero time; and
$C_m$ equals blood density at maximal dilution.

By this formula, the diluting volumes of the five dogs' bloods were found to range from 0.12 to 1.2, as shown in Table II. In other words, each milliliter of the blood of dog No. 76 was diluted with 1.2 milliliters of water. The blood volume was presumably enormously increased. This phenomenon is due to the aspirated water and not to the accompanying obstructive asphyxia, since in obstructive asphyxia, the maximal change in whole blood density observed in a series of five asphyxiated animals was from 1.0585 to 1.0540 (Swann, 1947).

A similar computation was made for sea water drowning, employing formula (2):

$$V = \frac{C_m - C_s}{C_m - 1} \qquad (2)$$

$C_m$ equals blood density at maximal concentration.

The volumes of water removed from the blood of the four dogs are shown in Table II. In these dogs, therefore, from a quarter to a third of the fluid originally in the blood was lost over a period of four minutes; their blood volumes were probably markedly decreased.

Besides these movements of water, other movements of molecules across the pulmonary epithelium have been suggested: Cot (1931) feels that drowning may be a matter of fulminating pulmonary edema, citing in evidence the reports that the drowned victim's lung fluid is rich in protein. Furthermore, still another movement is that of the salts in sea water; these evidently pass into the blood stream, for Jetter and Moritz (1943) found large quantities (15.3 mgm. %) of magnesium in the plasma of a dog drowned in sea water.

In sea water drowning, in summary, there have been postulated three rapid movements of molecules across the pulmonary

epithelium: one, water from the blood stream into the intrapulmonic spaces; two, protein from the blood stream into the intrapulmonic spaces; and three, salts from the intrapulmonic spaces into the blood stream. Two of these movements are in one direction, but the third is in the reverse direction. In fresh water drowning, two such movements are thought to take place, the two being in opposite directions: one, water into the blood from the lungs, and two, protein into the lungs from the blood. It is apparent that further analyses of these complex changes, especially with chemical tracers, is necessary before they can be fully understood. From our study it is apparent that the hemodilution or hemoconcentration is very rapid and of great magnitude in most dogs.[1] In our series, all animals presumably aspirated fluid, whereas in the dogs investigated by Banting and associates (Banting et als., 1932; Lougheed et als., 1933), some animals (figures not given) died without water in the lungs. This recalls Cot's statement (1931) that some human victims of "drowning"—10%–15%—aspirate no water but die of "syncope."

Ventricular fibrillation occurred in four of six dogs drowned experimentally in fresh water, but in none of five dogs drowned in sea water. Ventricular fibrillation is to all practical purposes an irreversibly fatal accident in and of itself (Wégria, 1944). Because of this, the hearts of the dogs which were drowned in fresh water failed, on the average, much sooner than those drowned in sea water. This suggests that the chances of successful resuscitation of dogs drowned in fresh water will, in future studies, be found to be far less than the chances of those drowned in sea water.

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[1]Thanks to the coöperation of Dr. N. D. Schofield, Department of Pathology, we have analyzed the blood of one man who was drowned. The victim fell into the sea at 7:08 A.M., his body was recovered at 8:50 A.M., and blood samples from the right and left ventricles were obtained at 11:00 A.M. The density of the whole blood from the right ventricle was 1.0811. Using formula (2) (see above), and assuming that his blood density before drowning was 1.060, this indicates that about 0.26 volume of water was removed from this victim's blood, a change of the same order of magnitude as was found in our four dogs. The lungs of the victim were also full of fluid; they weighed 1,720 gms., or about 1,120 gms. more than the wet weight of the lungs of a man of like size dying from causes other than drowning.

Banting and associates (Banting et als., 1932; Lougheed et al., 1933) reported fibrillation occurring in (fresh water?) drowning, but present no figures. In our data there is a hint that fibrillation does not happen when the dog does not aspirate much water, since dog No. 72, with small hemodilution and a small amount of water in the lungs, did not have a ventricular fibrillation. This hypothesis awaits confirmatory data. Because, however, of the frequency of fibrillation in our series, it seems probable that such an accident is not uncommon in fresh water drowning of humans. The cause of fibrillation in the dogs is being sought, with the hypothesis in mind that some ionic unbalance, a known cause for fibrillation (Garrey, 1924), is at its basis.

Finally, these findings in experimental drowning in dogs must be applied with caution to drowning in men. Our data were obtained on animals which were not under general, but under local, anesthesia, so from this viewpoint our data are not artificial. However, the animals could not swim, they were under restraint, they were not exhausted by swimming efforts, etc., and so should be considered to have been under artificial conditions in some respects. Since, however, the data dealing with the blood changes in human drownings (Moritz, 1944) are matched so very closely by our findings on dogs, we feel confident that the data herein reported can be carried over to drowning in humans with considerable confidence.

## Summary

Measurements of the terminal cardiac and biochemical events in dogs during experimental drowning have been made, including blood oxygen, carbon dioxide, lactic acid, pH, chloride, hemoglobin, plasma protein, systolic and diastolic arterial pressure, venous pressure, heart rate, and electrocardiograms.

The blood oxygen declines toward zero within three minutes after the start of drowning, but the carbon dioxide, after a transitory rise, falls to the normal range. The pH declines to about 7.1. In fresh water drowning, there is an abrupt and marked hemodilution, as indicated by rapid declines in the plasma protein, hemoglobin, chloride, etc. From 0.1 to 1.2 ml.

of water are estimated to dilute each ml. of blood. In sea water drowning, the converse—a strong hemoconcentration—occurs, with 0.3 ml. of water estimated to have been rapidly removed from each ml. of blood.

In fresh water drowning ventricular fibrillation commonly occurs (four out of six dogs) after three to five minutes of submersion. Fibrillation was not observed in any of the five dogs drowned in sea water. During sea water drowning, the heart fails about nine minutes after submersion.

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# DYSBARIC OSTEONECROSIS

Articles selected by Professor D. N. Walder
University of Newcastle Upon Tyne
ENGLAND

# 8

# DYSBARIC OSTEONECROSIS

D. N. WALDER

Over the years most writers have attributed the first description of dysbaric osteonecrosis to Twynam (1888). In fact, as the bone in his patient (a caisson worker) was obviously infected, the condition described was probably osteomyelitis. This leaves the paper by Bassoe, and Bornstein and Plate, both published in 1911, tied for the honour of the first description of dysbaric osteonecrosis.

A good early description of clinical findings, radiologic appearances, and histology of dysbaric osteonecrosis occurring in compressed air workers was reported in a paper by Kahlstrom, Burton, and Phemister in 1939.

Although many reports of bone lesions attributed to working in hyperbaric conditions continued to appear over the years, these were nearly all in men who attended hospital because they had symptoms, and it was not until 1960 that Golding et al. were able to report the first radiological survey of men working on a compressed air contract still in progress. Both men who had suffered from decompression sickness and men who had not were considered; thus some indication of the prevalence of the condition was obtained.

Similarly, although bone necrosis in a diver was first reported by Grutzmacher in 1941 there had been no attempt to assess the prevalence of the condition until the 1960s. Reports appeared concerning Royal Navy divers (Harrison, 1971), U.S. Navy divers (Harvey and Sphar, 1976), and North Sea commercial divers for whom the British had set up a comprehensive monitoring scheme (Thickett and Evans, 1976). The prevalence of bone necrosis in all these groups is remarkably similar and contrasts favourably with the prevalence found in Japanese shellfish divers by Ohta and Matsunaga (1974). Since the latter carry out their diving without taking advantage of recognized decompression procedure, the figures serve to emphasize the importance of controlled decompression as a factor in prevention of this condition.

However, because the association between suffering from decompression sickness and acquiring bone necrosis does not appear to be absolute, other factors connected with a hyperbaric work environment have been considered as possibly providing a link between cause and effect. For example, Hills (1977) has given a good review of possible aetiologic factors which may be the cause of bone necrosis. These include the suggestion that too rapid compression could be the initiating cause. An important piece of clinical evidence in the argument of compression versus decompression as the precipitating event is found in a paper by James (1945), in which he considers men who were very slowly, that is, in 2½ to 3 h, compressed to the equivalent depth of 120 ft of seawater, but rapidly decompressed during a submarine escape episode. Three out of five of these men traced in later years had bone necrosis.

A point of fundamental importance in the study of bone necrosis has been establishment of a classification of radiologic appearances. This first appeared in 1966 in the *Journal of Bone and Joint Surgery* (Decompression Sickness Panel Report, 1966). A more profusely illustrated version of the same classification is found in the book by Davidson (1976).

Current research into bone necrosis is progressing simultaneously along several lines. First, there are studies of the epidemiology of the condition as exemplified by publication of the 1977 EUBS Symposium on Bone Necrosis from the MRC Decompression Sickness Central Registry in Newcastle (Evans and Walder, 1976). Second, there are studies of human bone lesion material collected at operations or post mortem examinations. Specimens from the latter source have enabled relatively early bone lesions to be studied in toto. Much of this work has been reported by Mary Catto (1976). Third, there is experimental work designed to reveal the cause of the condition. This requires use of animal models, such as described by Smith et al. (1974), Cox (1973), and Chryssanthou (1976). In this context it might be significant that aseptic bone necrosis is not often found in aviators. They certainly experience decompression sickness but hardly ever develop bone necrosis. The position is well summarized by Allen et al. (1974). What to make of this piece of evidence is at present not yet clear.

Much effort has been expended in testing more sensitive and quicker methods of diagnosis than radiology. For instance, the place of radioisotope bone-scanning in diagnosis of bone necrosis has been examined, together with the possibility of using a non-localizing test in the form of a biochemical marker of bone damage (Gregg and Walder, 1977) to pinpoint men who should be scanned.

# DYSBARIC OSTEONECROSIS

D. N. WALDER

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# DYSBARISM-RELATED OSTEONECROSIS

## Proceedings of a Symposium on Dysbaric Osteonecrosis

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# U.S. AIR FORCE EXPERIENCE IN HYPOBARIC OSTEONECROSIS

THOMAS H. ALLEN
JEFFERSON C. DAVIS
CORRIN J. HODGSON

Hypobaric osteonecrosis has indeed occurred following military flight. Hodgson *et al.* (1968) presented this history from the files of Wilford Hall USAF Hospital:

> A 45-year-old B-29 crew member in combat was subjected to two episodes of rapid decompression to 35,000 and 45,000 foot altitudes within one week in 1953. On both occasions the aircraft was required to remain at altitude for an hour or more. He experienced pain . . . in several joints . . . and his symptoms required several days to resolve each time. After the second episode, he never was fully free of discomfort in the left hip joint. . . . In 1962, he was medically retired with a diagnosis of "aseptic necrosis of the left hip due to caisson [*sic*] disease. . . ."

By 1965, this man's hip required surgical repair, and the femoral head was replaced with a prosthesis. See Hodgson *et al.* (1968), Fig. 4.

From RAF experience the following case history was recorded by D. I. Fryer (1969): In about 1955, after 20 years of unpressurized aircraft flying, a 43-year-old photo-survey pilot suddenly suffered joint pains at 27,000 feet for a period of 6 hours. After he landed, he was confined to bed for 4 days suffering from severe pain in all his extremities. Between 1963 and 1967 he experienced 2 similar episodes, and on 6 other flights he had moderately severe shoulder and elbow bends. In May 1967 he experienced a sharp pain in his left shoulder associated with a "thunk" sound. Radiographs showed an impending "separation of a fragment from the head of the humerus." Six weeks later a jarring within this joint was distinctly heard and felt. The fragment had indeed separated.

Aside from J. H. Allan's (1945) claim of "calcific deposits and aseptic necrosis as predisposing factors in bends pain," these two cases apparently are the only specific accounts of disabling hypobaric osteonecrosis in the literature. They can be compared with 18 subatmospheric decompression sickness (DCS) fatalities (Fryer, 1969) in the USAF, RAF, RCAF, and USN from 1943 to 1958 (none since) and with 46 severe DCS cases successfully treated by compression, chiefly to 2.8 atm, between 1941 and the present time (as compiled by author J.C.D.). In both above-referenced cases, note that joint pain had persisted after landing, that there had been several such episodes, and that bone damage was found several years later.

Three reports (Ratnoff, 1943; Berry and Hekhuis, 1960; Hodgson *et al.*, 1968) exist dealing with roentgenography of bones and joints in men who in their regular duties were often exposed to simulated altitudes. The earliest (Ratnoff, 1943) concerned 21 military men who had undergone repeated exposures of 4 to 2 hours, or less, to altitudes of 35,000 and 40,000 feet. X-ray films of both hip joints were examined. "In none of the subjects were the roentgenographic changes described in caisson workers noted. Lesions of doubtful significance were present in two subjects, neither of whom had a history of bends."

In 1958, 623 USAF altitude-chamber men were X-rayed; the results on 579 of them were described by Berry and Hekhuis in 1960. Of this number, anterior-posterior views of the humeri, radii, ulnae, femorae, tibiae, and fibulae revealed not a single lesion that might be attributable to pressure changes. In the interim between 1958 and a follow-up study conducted in 1966 (Hodgson *et al.*, 1968), the X-rays of the additional 44 men were examined. An immature lesion was found in the midshaft of one right femur (see Fig. 2 of that study).

In their 1966 follow-up study, Hodgson *et al.* (1968) were unable to obtain X-rays on 459 of the entire sample. Although 291 of the original 623 men were still enlisted in the Air Force in December 1965 and 279 were in locations at which they could be reached, only 164 responded to the request for X-rays. In this second survey, it was found that the immature lesion mentioned

above had become "a mature intramedullary infarct" (see Fig. 1 of that study). It was 4 cm long and filled the entire thickness of the medulla. This man had a history of 6 attacks of bends.

In the 1966 study, as well, an additional case of aseptic bone necrosis was found in a man who had a history of 5 episodes of bends (see Hodgson *et al.*, Fig. 3). The lesion, 1 cm in diameter, was a round radiolucent area in the neck of the left humerus, just distal to the epiphysis. The lesion was "surrounded by a rim of increased bone density, and contained a few flecks of calcification. The 1958 X-rays are cut off just below the area of this lesion, so its onset cannot be documented."

Only 44 of the 164 respondents in the 1966 study had no history of DCS. Hence the *apparent* incidence of bony lesions may have been 2/120 among the altitude-chamber men who had suffered various mild forms of DCS, chiefly bends. To recapitulate, from 1958 to 1966 a lesion in one man had progressed to a mature medullary infarct of the femur. A lesion in a second man may or may not have been present earlier, but it was distinctly affecting the neck of the left humerus in 1966.

Even given the obvious deficiencies of the cited studies, it is possible to guess at the overall incidence of hypobaric osteonecrosis among men abruptly exposed to simulated high altitudes. From 1943 to 1966 the number was perhaps $(2+2)/(21+164)$, or 2.2% at the most. More likely the number could be as low as $(0+2)/(21+623)$, or 0.31%. Only the 2 fliers whose histories were given above have been disabled by hypobaric osteonecrosis; both of them had often suffered persistent postflight pain. They were fortunately not among the 18 known fatalities of subatmospheric DCS. On the other hand, they were unfortunately not among the 46 who were successfully treated from 1941 to date for severe reaction to hypobaric exposure.

In sum, disabling hypobaric osteonecrosis had indeed occurred — twice, surely. Initial X-ray films of 623 altitude-chamber men showed low incidences of bony lesions; it is difficult for obvious reasons to check an entire sample of that size 8 years later. Beginning in 1966 many USAF altitude-chamber operators have also been exposed regularly to 3 and 6 atm and are decompressed in exact accordance with U.S. Navy tables used in treatment of DCS. The 1966 USAF study was therefore biased toward a "last chance" attempt to find osteonecrosis in these operators before they began working in diving chambers as well. Because of this bias, only 2 cases of comparatively evident lesions were uncovered. Three cases of bone islands were excluded, plus one of endosteal scalloping, which could have yielded 6 cases, all told, out of 164 respondents in the 1966 study, had we chosen to use more liberal interpretative criteria at the time.

Of more importance, none of the original 623 men apparently suffered from or reported "postflight" symptoms of severe DCS. It is therefore felt that only those who have been afflicted with severe postflight reactions should be studied now and in the future. In other words, after treatment of such reactions by means of oxygen breathing at 2.8 atm, those individuals should be clinically observed in subsequent years.

The sequelae of severe DCS affecting the bones could thus be contrasted to the total of 46 incidences following subatmospheric exposure, recorded between 1941 and January 1972, that were successfully treated. Finally, it should be clear that the currently accepted treatment of altitude DCS persisting at ground level may prevent development of hypobaric osteonecrosis.

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## DISCUSSION 2

**Dr. ELLIOTT:** Osteonecrosis is not just a question of X-ray changes. Some real problems are generated for the afflicted individual. I should like to cite a quotation from Alnor (1963), which may be of interest to Dr. Fairchild and his associates: "Of the 65 men kept under observation for more than 10 years in the German study, only 22 of them remained free of radiological evidence of lesions. Of the 43 with lesions, 17 had symptoms, and 7 were totally unable to work." So, for the men concerned, it is indeed a very real problem.

**Dr. KINDWALL:** I should like to ask Dr. Beckman what method of selection was used in picking the 27 divers of the Gulf of Mexico survey. Was it slanted toward men who indeed had symptoms? Was there anything other than pure random choice involved?

**Dr. BECKMAN:** There was no selection whatsoever.

**Dr. HARRISON:** I should like to congratulate Dr. Fagan on his survey and to reinforce one or two points that he made. He commented on how very subtle some of these early lesions are, and how very difficult it is to recognize them. He also stressed that the lesions are frequently multiple. His point is well taken, I think, that the frogleg position is rather an improvement over the British straight A-P X-ray of the hips.

Dr. Fagan also demonstrated something that has concerned many of us — *i.e.*, the association of these vague densities with what we now recognize as lesions. By "vague densities" I mean an area that one cannot with certainty identify as a bone island or accept as evidence of aseptic bone necrosis. Experience seems to indicate that these densities are certainly much more common in divers than in a comparable nondiving population.

Dr. Fagan also made the very relevant point that when one begins a roentgenographic survey and makes the initial readings, one does not want to know anything at all about the divers. The survey must begin as a blind reading. In later evaluations of the lesions, of course, some knowledge is helpful.

**Dr. JONES:** In our opinion there is a very definite association between metaphyseal lesions and irregular osteosclerotic lesions in epiphyseal regions. I think serial evaluation of the multiple features previously conceived of as "bone islands" may actually show that they are focal areas of necrosis.

**Dr. WORKMAN:** We have done 152 bone surveys on our own divers and on applicants seeking employment as divers; we have also done 10 planograms (tomograms) of these men. We made the routine films suggested by England's Medical Research Council.

Ten planograms were done of suspicious areas that we could not otherwise define. Ten of the 152 men studied had lesions of the head of the humerus. One was bilateral, with compaction of subchondral bone and disruption of cartilage. Three of these happened to be company divers and seven were diver applicants. Planograms were repeated on two subjects one year later; there was no perceptible change in the lesions in the mid-head of the humerus. As Dr. Fagan has shown, the lesions were radiolucent, sclerotic areas, with disruption or irregularity of the trabeculae. We found that planograms are extremely helpful in defining these things — much more so, I think, than the best cone spots we could get.

We refused 35 applicants for employment because of multiple bone lesions in which early stages of aseptic necrosis could not be excluded, or because of other hypertrophic joint changes that we felt were risky in active divers. Several of our older divers have been active for 10, 15, or perhaps 25 years; I am impressed that most have no lesions that we considered positive for osteonecrosis.

**Dr. WALDER:** We have done a survey of 230 professional civilian divers, men sent to us by an organization called the Construction Industry Research and Information Association. They were thus unselected by us. To date we have found 3 definite and 12 suspect positive lesions in the group.

**Dr. ELLIOTT:** That low incidence is very encouraging. I think we should remember that similar results have been reported in other surveys. One I would like to mention was reported by Graczyk (1970), who examined 67 Polish divers, all of whom had 10 or more years' diving experience. He found lesions in only 5 men, a 7% incidence. So there appear to be groups of divers in whom the incidence is less than that found in the majority of surveys. But the criteria of diagnosis in the Polish survey may not have been the same as those used by the Medical Research Council or the same as those used by the German authors.

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# COMPRESSED AIR DISEASE

By: Bassoe, P.

J. Nerv. & Mental Dis., 38: 368-369; 1911.

Dr. Bassoe has tabulated the main points in the history and examination of 161 affected caisson workers, studied in connection with an investigation carried out under the auspices of the Illinois State Commission on Occupational Diseases. Some of the men examined had their acute attacks many years ago; others during the present year. Of the 161 men 89 had various affections of the ears causing permanent impairment of hearing in 85 cases; 141 gave a history of "bends:" that is, severe muscular and articular pains; 34 had paralysis, most generally transient and affecting the legs-although three men have permanent partial paralysis of one arm and two of both legs; 11 present more or less chronic joint pain and stiffness. One of these men who developed an affection of the hip immediatly after working his second shift in compressed air twelve years ago has been an invalid ever since and presents the typical X-ray picture of arthritis deformans. He had been in perfect health before these two exposures to compressed air. One man with signs of caisson myelitis had a spontaneous fracture of the patella eleven years after the acute attack, which had consisted of numbness in both lower extremities followed by pain; 12 men now present signs of some degree of permanent cord disease; 13 were delirious or unconscious during the acute attack; 33 complained of vertigo as a prominent symptom; 6 of vomiting during the acute stage and 11 of incontinence or retention of urine; 5 had numbness without paralysis; 6 had blind staggers; that is labyrithine vertigo with nystagmus, and two "chokes". Several men gave a history of large swellings of the soft parts of the chest wall or in the vicinity of joints. Dr. Bassoe had not seen them at this stage but agrees with Heller, Mager and Schrotter, that the swellings are due to vaso-motor disturbance of central origin, not of local liberation of gas ("tumeurs gazeuses") as has been claimed by French writers. He considers the nitrogen bubble theory of Paul Bert fully proven both by the observations on human beings and the abundant experimental work recorded in the literature. The cases treated by immediate "recompression" had fared much better than those not so treated.

Dr. E.L. Cornell had seen about 75 cases of caisson disease among 110 men employed last summer near Helena, Mont. He examined all of the applicants for work and rejected all who showed signs of arterio-sclerosis, heart disease, nephritis, chronic diseases such as tuberculosis and syphilis or any defects of the ears. He found the men to be of a rough type, addicted to drink and overeating. He cited several cases, most of which were instances of pains. One patient had a large swelling in the left side of the chest. The swelling was very hard, the overlying skin was not reddened, and no crepitus could be elicited. It lasted about three days. In one case there was a very severe supraorbital pain lasting several hours.

Professor Carlson inquired if gas bubbles were frequently observed in the aqueous humor or other portions of the eye.

Dr. Bassoe replied that in the Philosophical Transactions of the Royal Society for 1670 are recorded experiments by Robert Boyle, who placed many kinds of animals in bell jars from which the air was exhausted and observed bubbles in the aqueous humor of a snake. Aside from the nystagmus connected with "blind Staggers" no eye symptoms had occurred in his own cases. In the discussion of a paper on caisson disease read by Dr. John E. Owens in 1908, Dr. Frank Allport had related a case of total blindness from hemorrhagic effusions in the choroid, retina and vitreous. The swelling in the chest wall mentioned by Dr. Cornell is of interest as well as the supraorbital pains which also had been present after rapid exit in many of Dr. Bassoe's cases, and which he ascribed to retention of compressed air in the frontal sinuses.

ABSTRACT

Catto, M.

Pathology of aseptic bone necrosis.

In: Davidson, J.K., et al. Aseptic necrosis of bone, p. 3-100. New York, American Elsevier Publishing Co., 1976.

Careful examination of bones of patients at risk should be carried out at necropsy even if clinical radiographs are negative. It is from the examination of early lesions rather than of the late stages when secondary changes complicate the picture that some hint of the pathogenesis may be obtained and the natural history of these conditions further elucidated. Equally, it is important to examine bones with radiological changes for, especially in less common conditions, the basic information on the nature of the underlying tissue alterations is still not known and remains a source of speculation and controversy. The slab radiograph, that is a low-voltage radiograph on fine-grain film of a slice of bone about 3 or 4 mm thick, is a helpful intermediate step in the translation of the pathology to the clinical radiograph. The same radiological picture is sometimes produced by different pathological changes and it may be unwise to transfer interpretations from one condition to another just as it is in transferring uncritically deductions on aseptic necrosis produced in animals to the human situation... Ancillary techniques such as arteriography, tetracycline labelling, histochemistry, microradiography and densitometry are being increasingly used and may do much to make up for the limitations of conventional histology. If the most is to be gained from any investigation, it must be through the cooperation of the pathologist with clinicians and radiologists. (From author's conclusions)

# UNDERSEA BIOMEDICAL RESEARCH

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# Dysbaric osteonecrosis in mice

C. P. CHRYSSANTHOU

*Department of Pathology, Beth Israel Medical Center, New York, N.Y. 10003, Department of Pathology, Mount Sinai School of Medicine of the City University of New York, New York, N.Y. 10029*

Chryssanthou, C. P. 1976. Dysbaric osteonecrosis in mice. Undersea Biomed. Res. 3(2): 67-83.–The histopathology of dysbaric osteonecrosis and the influence of the number of exposures, compression rate, and obesity on the incidence and latency of the lesion were studied in 438 mice (2505 bones were examined). The animals were subjected to 75 psig air pressure for 2-6 hours (single or multiple exposures). Compression was rapid or stage. Decompression was *safe*. Osteonecrosis developed in the epiphysis of the tibia and/or femur in 34.1% of obese and in 5.8% of thin animals after a latent period of 2 to at least 12 months. It was concluded that: 1. dysbaric osteonecrosis appears to be independent of decompression sickness; 2. in obese mice the incidence is higher and the latent period shorter; 3. multiple exposures result in higher incidence and earlier lesions than single exposure; 4. the incidence is lower with stage than with rapid compression; 5. the pathogenesis of osteonecrosis may involve several factors (circulatory impairment by extravascular or intravascular bubbles, emboli, thrombi, vasoactive substances, gas-induced osmosis, autoimmunity) acting in concert or in sequence.

dysbarism
bone
bubbles
histopathology
ischemia
osmosis
fat embolism
susceptibility
aseptic bone necrosis
obesity
compression rate
repetitive diving
pathogenesis

Dysbaric osteonecrosis has recently been recognized as a major hazard in individuals subjected to large changes in ambient pressure. The latest statistics leave little doubt that this potentially disabling disorder is alarmingly widespread in divers and compressed-air workers. The incidence of the disease determined in relatively extensive surveys ranges from 4% in Royal Navy divers (Elliott and Harrison 1970) to 50-60% in Japanese diving fishermen (Kawashima, Torisu, Hayashi, and Kamo 1973; Ohta and Matsunaga 1974). This wide variation in the incidence can be attributed to the difference in the conditions of dysbaric exposure. Certain factors such as degree of pressure, duration of exposure, rate of decompression, and frequency of exposure are known to influence the incidence of the lesion. The effect of other factors, including rate of compression and obesity, remains to be assessed. In addition it remains to be determined whether the latent bone lesions are associated with acute manifestations of decompression sickness. Such uncertainties in our understanding of dysbaric osteonecrosis reflect our ignorance of the etiology and pathogenesis of the disorder.

An animal model for dysbaric osteonecrosis could provide some answers to these important questions. It would enable one to evaluate the influence of various factors on the incidence, severity, and latency of the lesion under controlled experimental conditions. Furthermore, an animal model could be used for studies on the etiology and pathogenesis as well as on the prevention and treatment of the disease.

Dysbaric osteonecrosis has been experimentally produced in several animal species including mice (Antopol, Kalberer, Kooperstein, and Chryssanthou 1964), rabbits (Horvath and Vizkelety 1973), and miniature swine (Smith and Stegall 1974). The mouse as a model for such studies permits large scale experiments to be conducted to provide statistical validation. In addition, large numbers of animals may be subjected simultaneously to compression/decompression in the same chamber, thus ensuring exposure to identical environmental conditions.

This report deals with studies on the histopathology of dysbaric osteonecrosis in mice and on the influence of obesity, number of exposures, and rate of compression on the incidence and latency of the lesion.

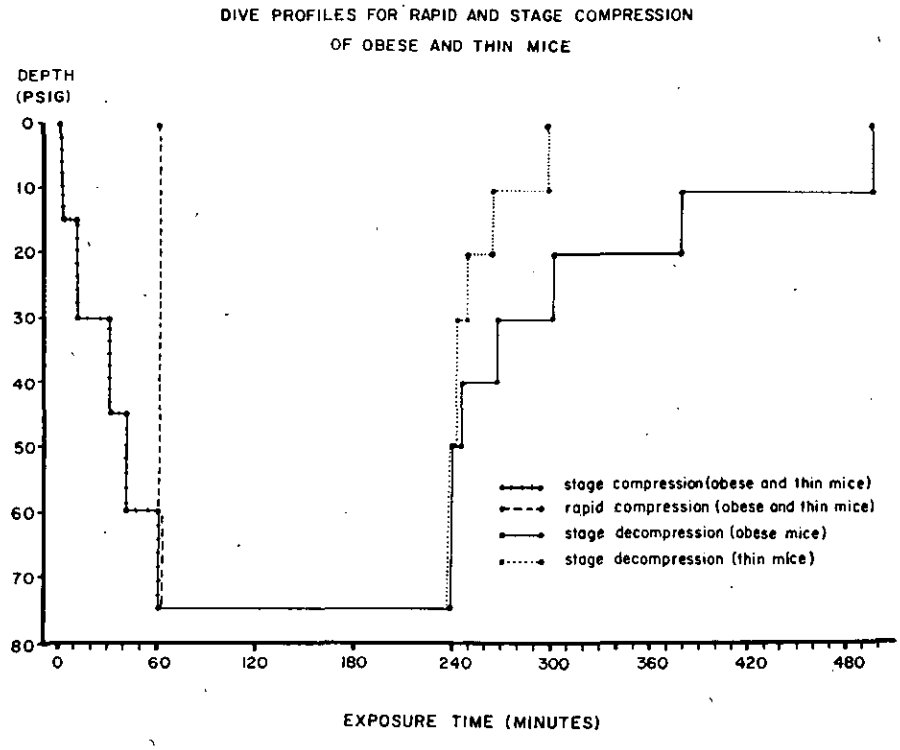


Fig. 1. Compression/decompression schedules for thin and obese mice.

## MATERIAL AND METHODS

A total of 580 male hereditarily obese hyperglycemic mice and their thin siblings were used. They were obtained from Jackson Memorial Laboratories, Bar Harbor, Maine. There were two weight ranges of obese animals: 38-60 gm (average 54 gm) and 61-90 gm (average 78 gm). Thin mice weighed 18-35 gm (average 24 gm). All animals were housed in metal cages in animal rooms with controlled temperature (72 ± 2° F) and relative humidity (50%) and were fed Wayne Lab-Blox and water ad libitum. They were kept under these conditions for a stabilization period of at least 3 weeks before they were used.

The animals in each weight range were randomly divided into an experimental group (subjected to dysbaric conditions) and a control group (kept at ambient pressure). Prior to the initiation of the experiments both control and experimental animals were numbered and their corresponding weights recorded. The experimental animals were subjected to 75 psig (6.12 ATA) air pressure for 2-6 hours in a hyperbaric chamber (Bethlehem Corporation Model 1836 HP) with controlled temperature (72 ± 2° F) and relative humidity (50%). Bottom time for thin mice was longer (4-6 hours) than for obese mice (2-3 hours). Figure 1 shows the dive profiles employed. Compression for both obese and thin mice was either rapid (to 40 psig in 30 s, to 75 psig in 60 s) or stage. Stage compression involved stops at 15, 30, 45, and 60 psig for 10, 20, 10, and 20 min respectively. Decompression was always stage with stops at 50, 30, 20, and 10 psig for 2, 5, 15, and 30 min respectively for thin mice and at 50, 40, 30, 20, and 10 psig for 5, 25, 35, 75, and 120 min respectively for obese mice. The animals were subjected to these conditions once (single exposure) or 3-8 times (multiple exposures) at weekly intervals. Upon reaching surface the animals were immediately removed from the chamber and observed for signs of decompression sickness (e.g. chokes, scratching, twitch) for at least 1 hour.

The animals died or were sacrificed at intervals up to 17 mo after initiation of dysbaric exposure. The bones of the extremities and, in some animals, the sternum were removed and fixed in 10% neutral buffered formalin for at least 3 days. Prior to fixation the soft tissue surrounding the bone was carefully trimmed off. Following fixation the bones were decalcified (Omega Decal solution) for a minimum of 24 hours and stored in 80% alcohol until processing by autotechnicon. The latter process consisted of sequentially treating the specimen for 1 hour with each 10%, 95%, 95%, 95%, 95%, and 100% alcohol, chloroform, paraffin (paraplast), and paraffin. The specimens were then embedded, cut (5-6 micron section), and stained with hematoxylin-eosin.

Bones of animals that died within 24 hours were examined to observe acute histologic changes but were not included in the statistics of dysbaric osteonecrosis. Also excluded from the studies were animals that were autolyzed or cannibalized after death as well as those in which processing of tissue was unsatisfactory. Because of these eliminations the statistical data of this report are based on 438 animals and a total of 2505 examined bones (Table 1).

In the statistical analysis of the results, the chi square test with Yates correction was used for comparison of distribution frequencies and the Pearson's correlation coefficient for testing dependence of two variables.

## RESULTS

With the dive profiles used in these studies, thin mice did not exhibit apparent clinical manifestations of decompression sickness except for an occasional animal. In obese mice signs of decompression sickness were observed in about 7% of the animals. Mice which developed decompression sickness usually died within 24 hours after decompression.

TABLE 1

Number of bones histological examined

| | Compressed/ Decompressed | | Controls | | |
|---|---|---|---|---|---|
| | Obese | Thin | Obese | Thin | Total |
| Femur | 316 | 378 | 72 | 110 | 876 |
| Tibia | 316 | 378 | 72 | 110 | 876 |
| Humerus | 191 | 237 | 4 | 34 | 466 |
| Sternum | 51 | 156 | 36 | 44 | 287 |
| TOTAL | 874 | 1149 | 184 | 298 | 2505 |

## HISTOLOGIC FINDINGS

Histologic examination of the bones of animals that died within 48 hours after decompression revealed pronounced hyperemia of the bone marrow with occasional hemorrhagic foci (Fig. 2). In addition, gas bubbles were present in the diaphysis and epiphysis of the bones, particularly in obese mice. The bubbles appeared as round or oval clear spaces of varying size, equaling in a few instances the diameter of the medullary canal. Often they were irregularly shaped, their smooth outline distorted by bony trabeculae protruding into the bubble (Fig. 3).

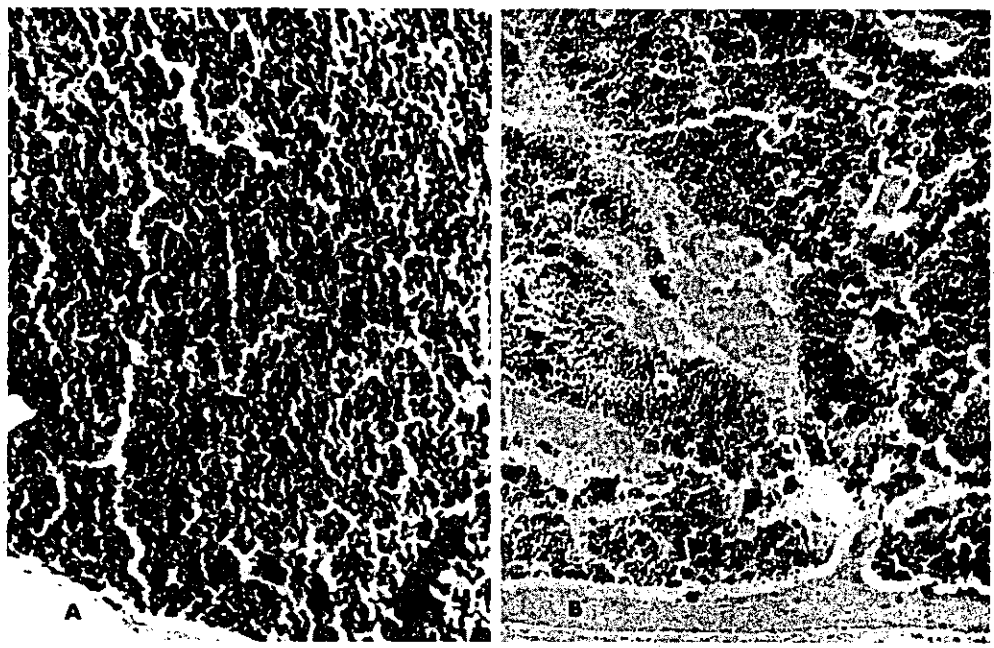


Fig. 2. Tibial bone marrow of a thin mouse. A. Control (not compressed/decompressed). B. 48 hours after exposure to compression/decompression. Note the marked congestion and hemorrhagic foci. (Hematoxylin-eosin, original magnification 25.2×.)

Fig. 3. Femoral diaphysis of an obese mouse 40 min after the last of six exposures to compression/decompression. The large empty spaces are gas bubbles, their spherical or oval shape being distorted by bony trabeculae. (Hematoxylin-eosin, original magnification 25.2×.)

Histologic evidence of osteonecrosis appeared after a period of at least 2 mo following the initial dysbaric exposure. The necrotic lesion always involved the spongy tissue of a part or of the entire epiphysis. In early stages of the lesion, the osteocytes in epiphyseal trabeculae exhibited pyknosis and karyorrhexis and the marrow cells showed indistinct cellular boundaries and loss of nuclear staining.

In more advanced lesions the lacunae in the necrotic trabeculae were devoid of osteocytes and the intertrabecular marrow spaces contained amorphous masses of granular debris (Fig. 4) and sometimes fragments of necrotic bone. Haversian canals, when [illegible] they could be observed in necrotic areas, appeared empty or contained debris from disintegrated tissue. Several microcracks (fissures) were seen between lamellae, usually extending to the surface of the trabeculae (Fig. 5) and, in some cases, resulting in tissue fragmentation. A few microscopic fissures were also seen in control animals with no evidence of osteonecrotic lesion, thus raising the possibility of artifacts or of alterations unrelated to dysbaric exposure and making the significance of this finding questionable.

In some cases necrotic epiphyseal trabeculae appeared fractured and occasionally collapse of the articular surface was observed. In other cases there was erosion of the articular cartilage and of the subjacent bone of the epiphysis with formation of concave defects, sometimes associated with epiphyseal collapse (Fig. 6). These alterations of the articular surface resembled osteoarthritic changes as reported by Sokoloff (1956).

At later stages fibrovascular tissue invaded intertrabecular spaces and replaced necrotic marrow (Figs. 7 and 8). Sometimes vascular connective tissue showing evidence of osteoclastic activity could be seen surrounding partially resorbed bone fragments (Fig. 7). Appositional new bone formation was observed in only few cases. Deposition of new bone on preexisting necrotic trabeculae resulted in thickening of these structures. Figure 8 shows new bone formation in apposition to necrotic bone tissue from which it is sharply demarcated. Figure 8 also shows areas of hematopoietic and adipose tissue elements within the vascular connective tissue, suggesting reconstitution of the necrotic marrow.

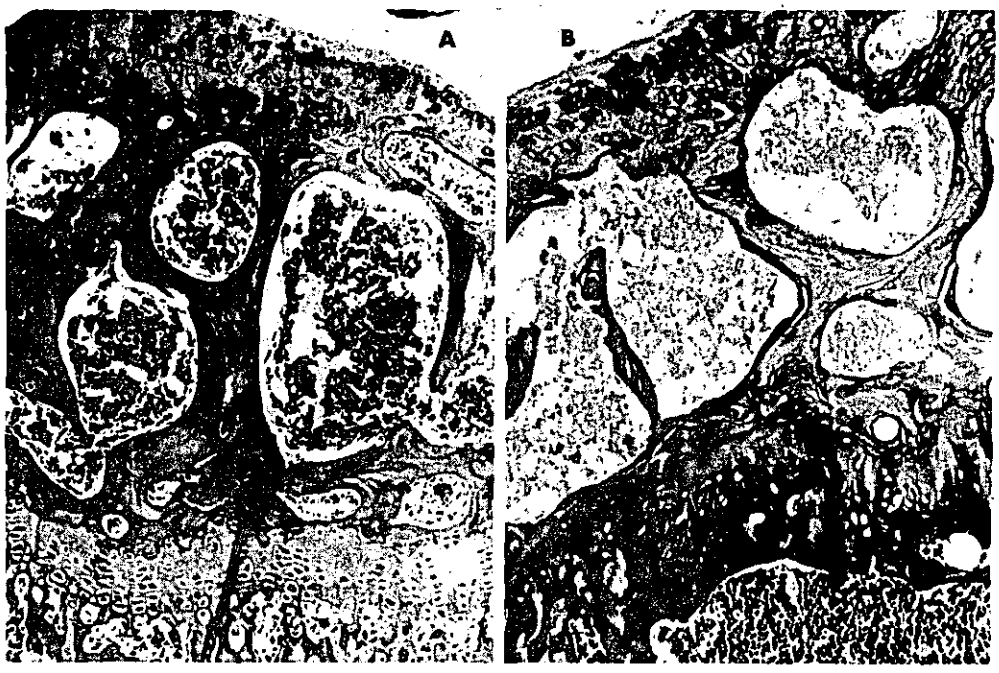


Fig. 4. Epiphysis of the proximal end of the tibia of a thin mouse. A. Control (not compressed/decompressed). B. 5 mo after multiple exposures to compression (rapid)/decompression. Note the necrotic trabeculae with empty lacunae and microcracks and the intervening marrow spaces containing granular debris. Normal bone marrow can be seen in the lower portion of the microphotograph. (Hematoxylin-eosin, original magnification 25.2×.)

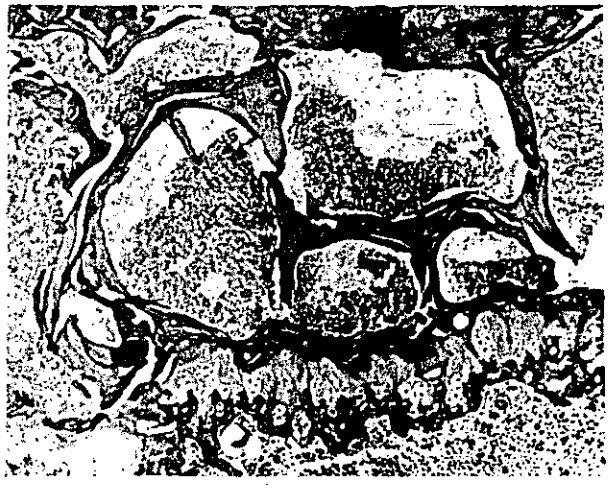

Fig. 5. Epiphysis of the proximal end of the tibia of an obese mouse 4 mo after multiple exposures to rapid compression/decompression. Necrotic trabeculae exhibit lacunae devoid of osteocytes and multiple microcracks some of which extend to the trabecular surface. The intertrabecular spaces in the necrotic area contain amorphous masses of granular debris. (Hematoxylin-eosin, original magnification 25.2×.)

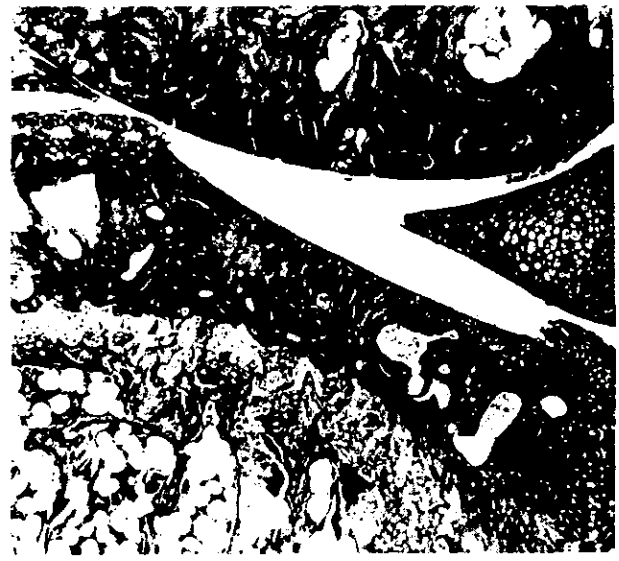

Fig. 6. Knee joint of an obese mouse 4 mo after repeated exposures to compression (rapid)/decompression. The epiphysis is collapsed. The articular cartilage and the subjacent epiphyseal bone are eroded with formation of a concave defect. (Hematoxylin-eosin, original magnification 25.2x.)

Fig. 7. Area in the epiphysis of the proximal end of the tibia of an obese mouse 11 mo after hyperbaric exposure. Note fibrous connective tissue surrounding fragments of partially resorbed bone. A few multinucleated osteoclasts can be seen around the necrotic bone. (Hematoxylin-eosin, original magnification 64x.)

## INCIDENCE AND LATENT PERIOD

The incidence of dysbaric osteonecrosis was 34.1% in obese and 5.8% in thin animals (Table 2). The lesion was also seen in 4 of 46 control obese mice but in none of 45 control thin animals. Definite osteonecrotic changes became histologically evident after a period of at least 2 mo following the initial exposure to compression/decompression. Table 3 shows that, in a period up to 4 mo after exposure, the incidence was 12.9% in obese and 0% in thin

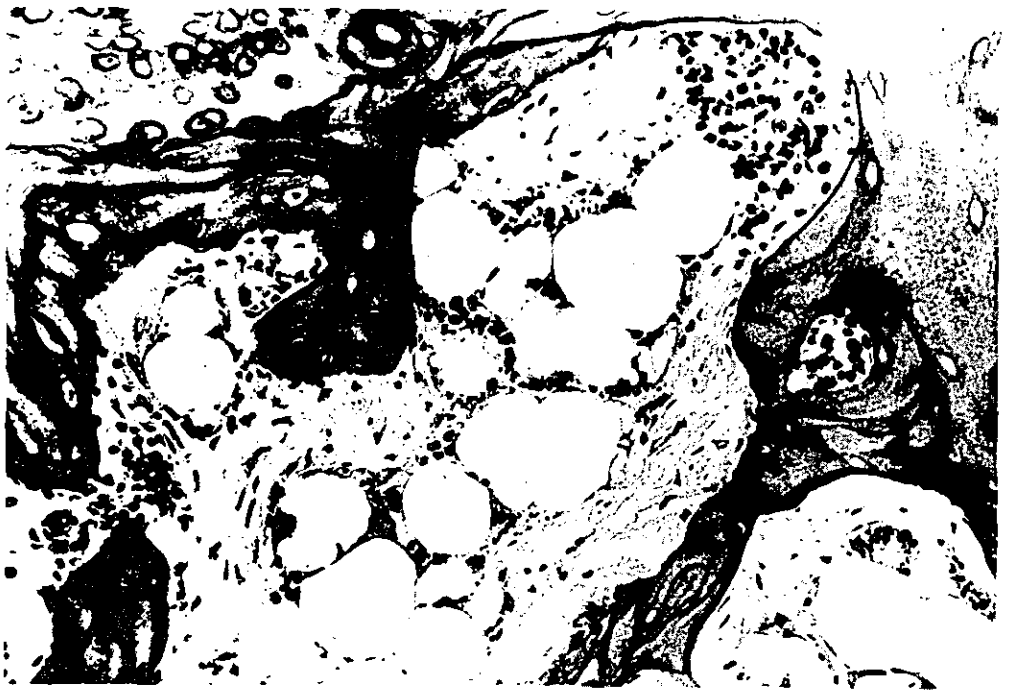

Fig. 8. Area in the epiphysis of the proximal end of the tibia of an obese mouse 10 mo after hyperbaric exposure. Necrotic trabeculae and subchondral bone with empty lacunae are evident. New appositional bone with lacunae containing viable osteocytes is sharply demarcated from the adjacent necrotic tissue (left). The vascular connective tissue which has replaced the necrotic marrow contains areas with hemotopoietic and adipose tissue elements. (Hematoxylin-eosin, original magnification 64X.)

mice. In animals that died or were sacrificed 4 mo after exposure or later, however, the incidence increased to 47.4% in obese and to 7.4% in thin mice. In fact there was a significant correlation between incidence and time period following exposure. Figure 9 shows this correlation in obese mice subjected to a single dysbaric exposure. These results indicate that the post exposure latent period varies—ranging from 2-3 mo to at least 9 mo inasmuch as the incidence of dysbaric osteonecrosis was higher in the 9-12 mo than in the 6-9 mo period.

## DISTRIBUTION

In most cases dysbaric osteonecrosis in mice was observed in the epiphysis of the proximal end of the tibia bilaterally (38%) or unilaterally (62%). The femur was involved in some cases, with the lesion usually localized in the distal end. Osteonecrotic changes in the head of the femur were seen only occasionally. Table 4 shows the distribution of the lesion in the various bones.

## INFLUENCE OF OBESITY

There was a striking difference in the incidence of osteonecrosis between obese mice and their thin littermates (Table 5). Obesity also influenced the latent period; osteonecrotic changes appeared earlier in the heavier mice. In animals with an average weight of 78 gm,

TABLE 2

Incidence of dysbaric osteonecrosis in mice

| | Compressed/ Decompressed | Controls | Probability |
|---|---|---|---|
| Obese | 34.1%(54/158)* | 8.7%(4/46) | $.001<P<.01$ |
| Thin | 5.8%(11/189) | 0% (0/45) | N.S.† |

*(Number of animals with lesions/total number of animals)

† Not significant

TABLE 3

Incidence of dysbaric osteonecrosis in mice in the early and late periods following hyperbaric exposure

| Type | 0 - 4 Mo | 4 Mo or more | Probability |
|---|---|---|---|
| Obese | 12.9%(8/62)* | 47.9%(46/96) | $P<.001$ |
| Thin | 0%(0/40) | 7.4%(11/149) | $.1<P<.2$ |

*(Number of animals with lesions/total number of animals)

TABLE 4

Distribution of osteonecrotic lesions

| | | |
|---|---|---|
| Tibia (*Prox. end*) | 80.8% | (80/99)* |
| Femur (*Total*) | 15.1% | (15/99) |
| Femur (*Head*) | 3.0% | (3/99) |
| Femur (*Dist. end*) | 12.1% | (12/99) |
| Sternum | 2.0% | (2/99) |
| Humerus (*Dist. end*) | 1.0% | (1/99) |
| Ilium | 1.0% | (1/99) |

*(Number of specified bones with lesions/total number of bones with lesions)

20.5% of the lesions appeared within the first 3 mo after exposure (Table 6). None of the mice weighing 54 gm or less developed osteonecrosis during this period.

## INFLUENCE OF THE NUMBER OF EXPOSURES

Obese animals subjected to multiple dysbaric exposures had a significantly higher incidence of dysbaric osteonecrosis than animals exposed only one time. In thin mice the number of lesions was too small to reflect the possible effect of the number of exposures on the incidence of osteonecrosis. The number of exposures also influenced the latent period. In mice subjected to multiple exposures (rapid compression), lesion incidence within 3 mo following initial exposure was 25%. In contrast, none of the animals with a single exposure (rapid compression) developed osteonecrosis within the same period.

## INFLUENCE OF THE RATE OF COMPRESSION

The incidence of dysbaric osteonecrosis in mice subjected to stage compression, was significantly lower than in animals exposed to rapid compression. Table 8 shows the respective frequencies of lesions in obese and thin mice subjected to multiple exposures with rapid or stage compression.

## INFLUENCE OF VARIOUS FACTORS IN COMBINATION

In this investigation obesity, rapid compression, and multiple exposures produced a statistically significant increase in the incidence of dysbaric osteonecrosis. The combined effect of two of these factors was greater than that produced by each of them individually and a combination of three factors influenced the incidence of the lesion to a greater degree than any combination of two factors. The effect of various combinations is compared in Fig. 10. Incidence of osteonecrosis was lowest (0%) in thin mice subjected to stage compression and highest in obese mice subjected to rapid compression and multiple exposures.

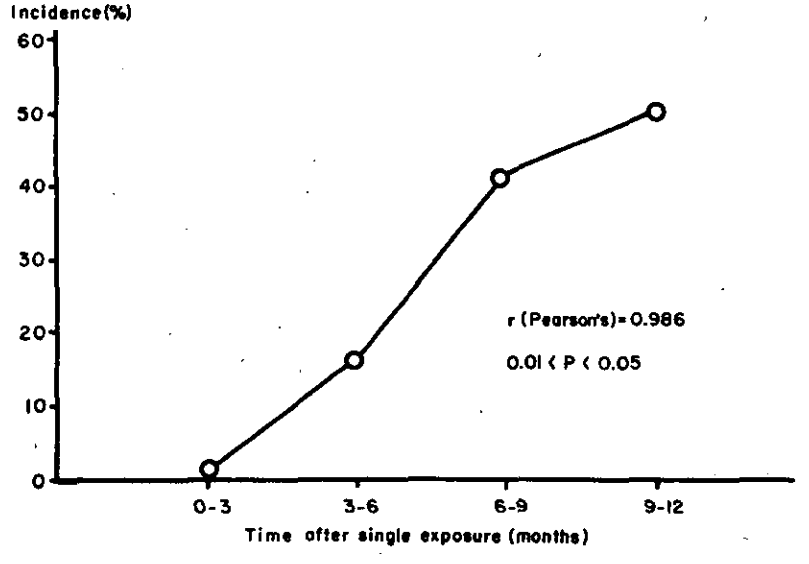


Fig. 9. Correlation of the incidence of dysbaric osteonecrosis with post-exposure interval in obese mice ubjected to a single compression (rapid)/decompression.

TABLE 5
Influence of obesity on the incidence of dysbaric osteonecrosis in mice

| Type | Average weight (g) | Incidence | Probability |
|---|---|---|---|
| Thin | 24 | 5.8%(11/189)* | $P<.001$ |
| Obese | 54 | 26.3%(15/57) | |
| Obese | 78 | 38.6%(39/101) | |

*(Number of animals with lesions/total number of animals)

TABLE 6
Influence of obesity on the latency of dysbaric osteonecrosis

| Type | Average weight (g) | Percent of animals with lesions | | Probability |
|---|---|---|---|---|
| | | 0 - 3 mo | > 3 mo | |
| Thin | 24 | 0(0/11)* | 100(11/11) | |
| Obese | 54 | 0(0/15) | 100(15/15) | $.02<P<.05$† |
| Obese | 78 | 20.5(8/39) | 79.5(31/39) | |

* (Number of animals with lesions in period/total number of animals with lesions)
† Statistical probability of difference in the latency between the 78- g group and the 24- and 54- g groups combined.

TABLE 7
Influence of the number of hyperbaric exposures on the incidence of dysbaric osteonecrosis in mice subjected to rapid compression

| Type | Single exposure | Multiple exposures | Probability |
|---|---|---|---|
| Obese | 28.3%(19/67)* | 47.3%(27/57) | $.02<P<.05$ |
| Thin | 6.7%(6/89) | 5%(5/100) | N.S.† |

*(Number of animals with lesions/total number of animals)
† Not significant

TABLE 8

Influence of the rate of compression on the incidence of dysbaric osteonecrosis in mice with multiple exposures

| Type | Rapid compression | Stage compression | Probability |
|---|---|---|---|
| Obese | 47.3%(27/57)* | 23.5%(8/34) | $.02<P<.05$ |
| Thin | 7.1%(5/70) | 0% (0/30) | N.S.† |

*(Number of animals with lesions/total number of animals)
† Not significant

The effect of obesity can be seen by comparing columns 1, 2, and 3 with 4, 5, and 6 respectively. Comparison of columns 4 and 6 demonstrates the effect of compression rate; of columns 5 and 6, the effect of the number of exposures.

## DISCUSSION

The results presented indicate that dysbaric osteonecrosis can be experimentally produced in mice. Diagnosis was made conservatively. Morphologic changes in osteocytes or bone marrow cells, although they may represent early manifestations of a lesion, did not suffice by themselves to make a diagnosis of osteonecrosis. Nor did the absence of osteocytes in lacunae in focal areas constitute adequate evidence of bone necrosis unless it was associated with other alterations (e.g. necrosis of bone marrow, invasion by fibrovascular tissue, appositional new bone formation, etc.). It is therefore possible that the incidence of dysbaric osteonecrosis has been underestimated because some lesions may have been missed either in their early phases before they were fully manifested or at late stages because of almost perfect restitution of necrotic tissues; the latter, however, is not very likely since *creeping substitution* was seen only rarely. The fact that reparatory changes were infrequent is an indication that in most cases there was a severe defect in blood supply. The high incidence of lesions in the proximal end of the tibia and the distal end of the femur may be related to circulatory peculiarities and postural characteristics of the mouse.

None of the control thin mice developed bone necrosis. The occurrence of lesions in four of the control obese mice could be associated with the obesity. Obesity and hyperlipidemia have been considered predisposing factors in nondysbaric aseptic bone necrosis (Conti and Sciarli 1973; Welfling 1973). Obese mice have a fatty liver and it has been suggested that the fatty liver is capable of spontaneously releasing embolic fat globules into the circulation (Owens and Worthington 1962).

In animals subjected to compression/decompression, obesity influenced the incidence of osteonecrosis more than any other factor studied in these experiments. It was previously reported that the degree of obesity in mice correlates with their susceptibility to

decompression sickness (Antopol et al. 1964). These correlations, however, do not imply that the delayed dysbaric osteonecrosis is associated with the acute manifestations of decompression sickness. On the contrary, the animals which developed dysbaric osteonecrosis did not exhibit signs of decompression sickness. Dysbaric osteonecrosis, therefore, appears to be independent of decompression sickness, at least in mice. This observation is consistent with the well-known fact that delayed bone lesions have been detected in divers and compressed-air workers who did not manifest acute symptoms and signs of decompression sickness.

The increased susceptibility of obese mice to dysbaric bone necrosis may be related to the high solubility of nitrogen in fat and the higher content of fat in the bone marrow of obese animals. Fatty bone marrow exchanges nitrogen slowly and decompression could cause great supersaturation of dissolved gas in this tissue with the potential of generating gas bubbles over relatively long periods of time. Gas bubbles were seen in the diaphyseal and epiphyseal marrow of obese mice, even after a period of several days following decompression.

It is tempting to apply the above considerations to a possible explanation of the fact that dysbaric osteonecrosis can be produced without preceding manifestations of decompression sickness. *Safe* decompression tables are considered adequate as long as they prevent development of decompression sickness. It is conceivable, however, that safe decompression, while keeping gas-tension levels below those required to produce acute manifestations of decompression sickness, may permit supersaturation of the long half-time fatty bone marrow with subsequent bubble formation. In addition, it is known that gas bubbles may be present

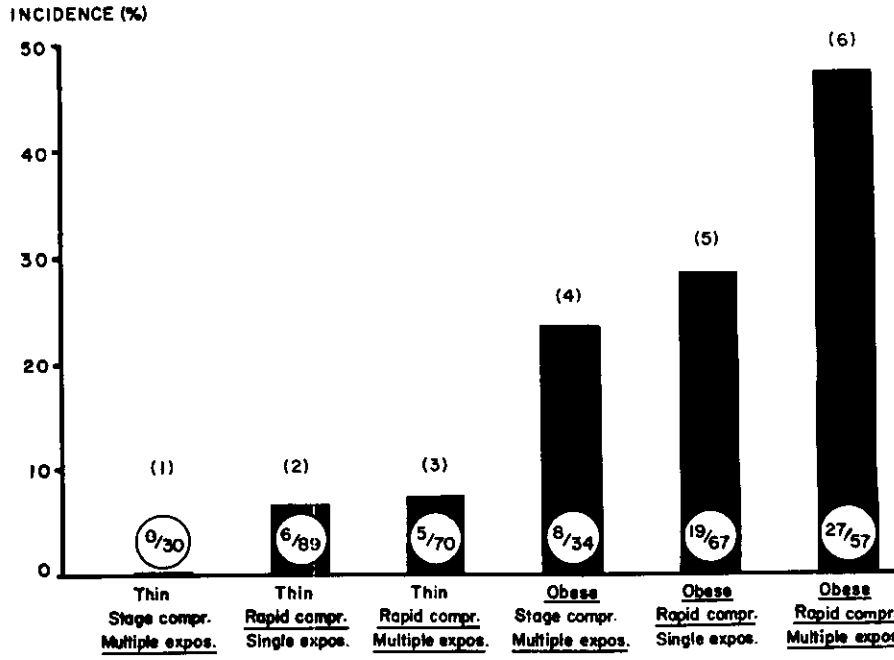


Fig. 10. Influence of obesity, rate of compression, and number of exposures in various combinations on the incidence of dysbaric osteonecrosis. Factors which were shown to increase the incidence are underlined. Comparison of the incidences in columns 1,2, and 3 with those in columns 4,5, and 6 shows the influence of obesity. The effect of the rate of compression is shown when columns 4 and 6 are compared and the effect of the number of exposures when columns 5 and 6 are compared.

even after routine asymptomatic decompression (Behnke 1967). These asymptomatic gas bubbles were referred to as "silent." They may be "silent" in terms of decompression sickness but not in terms of dysbaric osteonecrosis. Harvey (1974) has stated that ". . .the low tolerance of bone for inert gas supersaturation, may precipitate development of lesions (osteonecrotic) when present day decompression tables are followed." If this is so, decompression tables may require recalculation in consideration of the longer half-time tissues and the occurrence of silent bubbles.

Extravascular gas bubbles released from fatty elements of the bones could, within the rigid confines of the osseous tissue, exert sufficient pressure to compress blood vessels. Initially this would affect the veins, which are more susceptible to pressure, thus resulting in stasis. This is consistent with the hyperemia and hemorrhagic foci observed in the bone marrow of animals that died within 48 hours after decompression. These circulatory alterations could produce anoxia which in turn could precipitate necrotic bone changes. Circulatory impairment and ischemia could also be caused by arterial obstruction produced by intravascular bubbles. It has been reported, however, that only a small percentage of vessels remains blocked after gas embolization (Duff 1954) and arterial air embolism failed to produce bone infarction (Kahlstrom 1939).

These speculations should not limit pathogenetic considerations to the direct effects of gas bubbles. Circulating nitrogen bubbles could trigger a chain of secondary events including aggregation of platelets and erythrocytes, coalescence of unstable lipids and changes in the coagulation mechanism. Anyone of these alterations might result in vascular obstruction and anoxia in the bones. Fat embolization could also result from disruption of fatty tissue by expanding gas bubbles. Experimental production of aseptic bone necrosis by fat embolization following intraaortic oil infusion was recently reported by Jones, Sakovich, and Anderson (1974). The possible implication of fat embolization in the pathogenesis of dysbaric osteonecrosis merits further exploration. The hypothesis that embolization may be involved in the mechanism of dysbaric osteonecrosis is further supported by the observation that introduction of artificial emboli (glass beads) into the common iliac artery of rabbits produced femoral osteonecrotic lesions (Walder 1974). Regarding the possible role of thrombotic material, it should be mentioned that administration of anticoagulants and platelet inhibitors in animals did not prevent development of dysbaric osteonecrosis (Smith and Stegall 1974).

Blood-gas interface phenomena can result not only in platelet and lipid changes but also in the release or activation of vasoactive substances (Chryssanthou 1973; Chryssanthou, Waskman, and Koutsoyiannis 1974). It is of interest in this respect that intrarterial administration of vasodilator substances causes a redistribution of blood flow in the limb by increasing the flow through the muscles at the expense of that through the bone marrow (Semb 1971). This decrease of blood flow could render the bone more vulnerable to extravascular or intravascular factors that cause ischemia.

In all of the above postulated mechanisms, the protagonist is the gas bubble, which directly or indirectly causes circulatory impairment. Alternatively there is the possibility that factors other than, or in addition to gas bubble-related events may play a role in the pathogenesis of dysbaric osteonecrosis. It has been suggested that gas-concentration gradients resulting from rapid pressure changes can produce osmotic changes and fluid shifts that could contribute to the production of bone lesions (Hills 1970). Consequently the rate of compression becomes a factor that may influence the development of bone changes. Supporting this hypothesis is our finding that, with rapid compression, the incidence of dysbaric osteonecrosis is higher than with stage compression. It has also been reported that

the severity and frequency of hyperbaric arthralgia are reduced in divers subjected to slow compression rates and that gas-induced osmosis is implicated in this phenomenon (Bradley and Vorosmarti 1974). Another speculation on the pathogenesis of dysbaric osteonecrosis implicates altered immunity and dysproteinemia. This hypothesis of an autoimmune process is based on the latency of bone lesions and on the observation of rouleaux formation, amyloidosis, and long delayed membranous glomerulitis in some animals with dysbaric osteonecrosis (Antopol et al. 1964). Changes induced by high $P_{O_2}$, which in turn may influence development of osteonecrosis is still another factor that merits consideration.

It is evident from the foregoing discussion that the mechanism of dysbaric osteonecrosis is still unclear. The various concepts that have been presented involve several diverse pathogenetic factors which can be summarized as follows:

1. Factors causing circulatory impairment: *a*. extravascular pressure (e.g. by growing gas bubbles); *b*. vascular obstruction by emboli (e.g. fat, gas bubbles); *c*. vascular obstruction by thrombotic material (e.g. fibrin, platelets); *d*. vasodilator substances causing decreased blood flow in bones.
2. Factors not associated with blockade of blood supply: *a*. gas-induced osmotic shift of fluids; *b*. autoimmunity and dysproteinemia.

Further experimentation and additional clinical and epidemiological studies are needed before the relative importance of the postulated pathogenetic factors can be assessed. It is reasonable at this juncture, however, to propose that the pathogenesis of dysbaric osteonecrosis involves several of the above mentioned factors acting in concert or in sequence.

The findings of the present study regarding the latency in the development of bone necrosis and the influence of multiple dysbaric exposures are consistent with well-known observations on human subjects. The influence of obesity and of the rate of compression on the incidence of the disease in man has not yet been established. Although the results of the present investigation indicating an increased incidence of dysbaric osteonecrosis in obese and in rapidly compressed animals must be extrapolated with caution, they should draw attention to the possible role of these factors in the development of the lesion in humans.

## CONCLUSIONS

1. Dysbaric osteonecrosis can be experimentally produced in mice, particularly, in obese strains.
2. There is a latent period ranging from 2 to 9 mo or possibly more.
3. In obese mice the incidence is greater and the latent period shorter than in thin siblings.
4. With multiple exposures, the incidence is higher and the latent period shorter than with single exposure.
5. With stage compression, the incidence is lower than with rapid compression.
6. Dysbaric osteonecrosis in mice appears to be independent of decompression sickness.
7. The pathogenesis of dysbaric osteonecrosis may involve several initiating and contributing factors that act in concert or in sequence.

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Chryssanthou, C. P. 1976. Ostéonécrose dysbarique chez la souris. Undersea Biomed. Res. 3(2): 67-83.–L'histopathologie de l'ostéonécrose dysbarique et l'influence du nombre d'expositions, de la vitesse de compression et de l'obésité sur la fréquence et la latence des lésions ont été étudiées chez 438 souris (2,205 os examinés). Les animaux ont subi des pressions de 75 psig pendant 2-6 heures (expositions uniques ou multiples). La compression a été soit rapide, soit par paliers; la décompression a été *sans danger*. Après une période de latence de 2-12 mois, 34,1% des souris obèses et 5,8% des souris maigres avaient developpé une ostéonécrose épiphysaire tibiale ou fémorale. Les conclusions suivantes s'imposent: 1. l'ostéonécrose apparaît indépendente de la maladie de la décompression; 2. la fréquence de l'ostéonécrose augmente, et la période de latence se raccourcit chez les souris obèses; 3. la fréquence de l'ostéonécrose augmente et la période de latence se raccourcit après des expositions multiples; 4. la fréquence reste plus restreinte avec une compression par paliers; 5. la pathogénèse de l'ostéonécrose peut impliquer plusieurs facteurs (gêne circulatoire due aux bulles intra- ou extravasculaires, embolies, thromboses, substances vasoactives, osmose gazeuse, autoimmunité) qui agissent ensemble ou en séquence.

| | | |
|---|---|---|
| dysbarie | ischémie | obésité |
| os | osmose | vitesse de compression |
| bulles | embolie graisseuse | plongées répétées |
| histopathologie | susceptibilité | pathogénèse |
| | ostéonécrose aseptique | |

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# Simulated Caisson Disease of Bone

P. T. COX

## Introduction

In spite of progressive improvements in decompression techniques which have resulted from recent advances in knowledge of the physiological changes that occur during hyperbaric exposure and decompression, there is still a risk of developing potentially disabling bone lesions for men who dive to depths of 180 feet or deeper for short periods or who are exposed to lesser pressures for longer times. The inability to eliminate the risk totally is in some part due to the fact that the aetiology of Caisson disease of bone is not fully understood, though several plausible explanations have been suggested.

The basic pathological change in the bones is the appearance of areas of aseptic necrosis. These characteristically occur in the upper end or shaft of the femur or humerus, or the shaft of the tibia. Because of the similarity of the pathological appearance of these lesions to those developing after an incident known to result in obstruction to the osseus blood supply (e.g. fracture of the surgical neck of the femur, or dislocation of the hip), it is assumed that the cause of this is the obstruction to the blood supply of the relevant areas of bone.

It has been demonstrated that a period of something like 6 to 12 hours ischaemia (11, 14) is necessary to induce bone death. It is most unlikely that the vascular obstruction is situated in the venous system as the venous drainage of bone is generally considered to be profuse, with many collateral connections (8). The venous drainage could only be obstructed by a very widespread process. Also, venous obstruction would be expected to cause an increase in the intraosseus pressure, and this has not been observed to occur at least for any prolonged period at decompression (9, 7).

Arterial obstruction could occur as a result of the impaction of embolic particles, vascular thrombosis, or external pressure on the vessel walls. Gas bubbles, which have been detected in the arterial system at severe (13) and even so-called safe decompression (4) are usually assumed to be the cause of the vascular obstruction. Other embolic particles, e.g. aggregates of platelets or red blood cells or fat emboli which develop at decompression, possibly secondarily to the presence of intravascular gas bubbles, might also cause the required degree of vascular obstruction.

If Caisson disease of bone is due to circulating arterial embolic particles it is difficult to understand why nectrotic areas only develop in certain locations in a relatively small number of bones and are not generally distributed.

Intraosseus vascular obstruction due to the local development of extravascular gas bubbles causing a local increase in pressure has also been postulated as a cause of Caisson disease of bone, but the experiments carried out by Kasler *et al.* and Harrelson and Hills would indicate that this is unlikely.

Lack of knowledge about the exact nature of the vascular obstruction is due to three factors. First, the absence of pathological material showing the early stages of the condition; second, the paucity of knowledge of all the complex changes that occur in the constituents and circulatory behaviour of the blood in large and small vessels at hyperbaric exposure and decompression; and third, the great difficulty which has been found in simulating the lesions of Caisson disease of bone in man in experimental animals exposed to hyperbaric conditions. Most of the experiments have been carried out on small animals, in which bubbles developing at decompression probably only last for a short time compared to their duration in man (10). So it would appear that small animals such as rats and mice are unsuitable as models for this purpose. Recent reports (12) suggest that the repeated exposure of miniature swine to hyperbaric conditions results in the development of bone lesions having some similarity with those that develop in humans.

In an attempt to determine whether bone changes would develop in the limb of an animal to which arterial emboli had been introduced and to investigate the location and nature of any such changes, an animal model has been

developed in which artificial embolic particles are used to mimic gas emboli.

## Materials and Methods

Glass microspheres were used as the embolic particles. They are made in various sizes, and are opaque to X-rays. One potential disadvantage is their relatively high specific gravity, which should theoretically cause their preferential streaming in the circulation. However, our results, and the reported results of others (2, 6) indicate that when used in the smaller sizes, this effect is negligible.

Very small quantities of spheres (total volume including air space never more than 0.1 ml) with diameters in the range from 2 $\mu$ to 65 $\mu$ were injected in saline suspension directly into the unobstructed left external iliac artery of anaesthetised adult New Zealand white rabbits. The femur was studied because Caisson disease in man causes more disability when it involves the hip joint than when it involves the shoulder joint.

The arrangement of the blood supply to the rabbit's femur is similar to that in man, except for the fact that in the rabbit the vessels in the ligamentum teres are branches of the femoral artery, and do not arise from the internal iliac system. The microspheres could therefore be expected to be distributed to all the hard tissues and the majority of the soft tissues of the left leg.

In all, 40 rabbits were used. Standard radiographic examination of the whole of the left leg was carried out where appropriate at 14 day intervals. Each animal was killed at some time between 2 days and four months after the injection. After death the vessels of both legs of 15 animals were perfused with a 20 % suspension of Micropaque, a radio-opaque contrast medium, through the aorta.

Standard radiographic examination of the excised left femur was carried out in all cases. In addition some bones were examined by *microfocal radiography*. This has a much greater power of resolution than standard radiography. *Routine histological* sections were prepared from the head, neck and upper shaft and the midshaft regions of the excised left femora. The results of these examinations were compared with the results of similar examination on 4 normal control animals and on the right femur of 15 animals injected with microspheres.

## Results

Serial radiological examination of the live animals showed the development of thickening of the cortex, and occasionally subperiosteal new bone formation affecting the femoral shaft, normally at the posterior aspect of the midshaft, in a number of animals on the injected side. No changes were ever noted at the lower end of the femur, or in the tibia. Radiological examination of the excised bones showed an increase in the density of some of the femoral heads (Fig. 1).

In those specimens injected with Micropaque it could be seen that in the main nutrient artery to the shaft of the bone its principal ascending and descending trunks were normal but many of the smaller branches running towards the ends of the bones were blocked. The main trunk of the artery supplying the femoral head, which is a branch of the medial circumflex femoral artery, appeared normal, but again many of the smaller branches to the femoral head did not fill with Micropaque.

*Histological examination* of the femoral head revealed necrotic changes in 11 cases out of the total of 40 rabbits (Fig. 2). The changes were detectable from four days after the injection of the spheres. Dead bone trabeculae and necrosis of the marrow were seen. The necrotic area subsequently revascularized with replacement of the marrow and the laying down of appositional new bone on the surface of the necrotic trabeculae.

Bobechko and Harris demonstrated in 1960 that this appositional new bone is responsible for the radiographic increase in density mentioned above.

Histological examination of the femoral shafts showed changes in 15 cases. Cortical changes which developed in 14 animals, frequently accompanied patchy necrosis of the marrow, which developed in 4 cases. In the majority of cases, there was some osteocyte loss in the central and inner cortical lamellae, with cortical thickening due to subperiosteal and

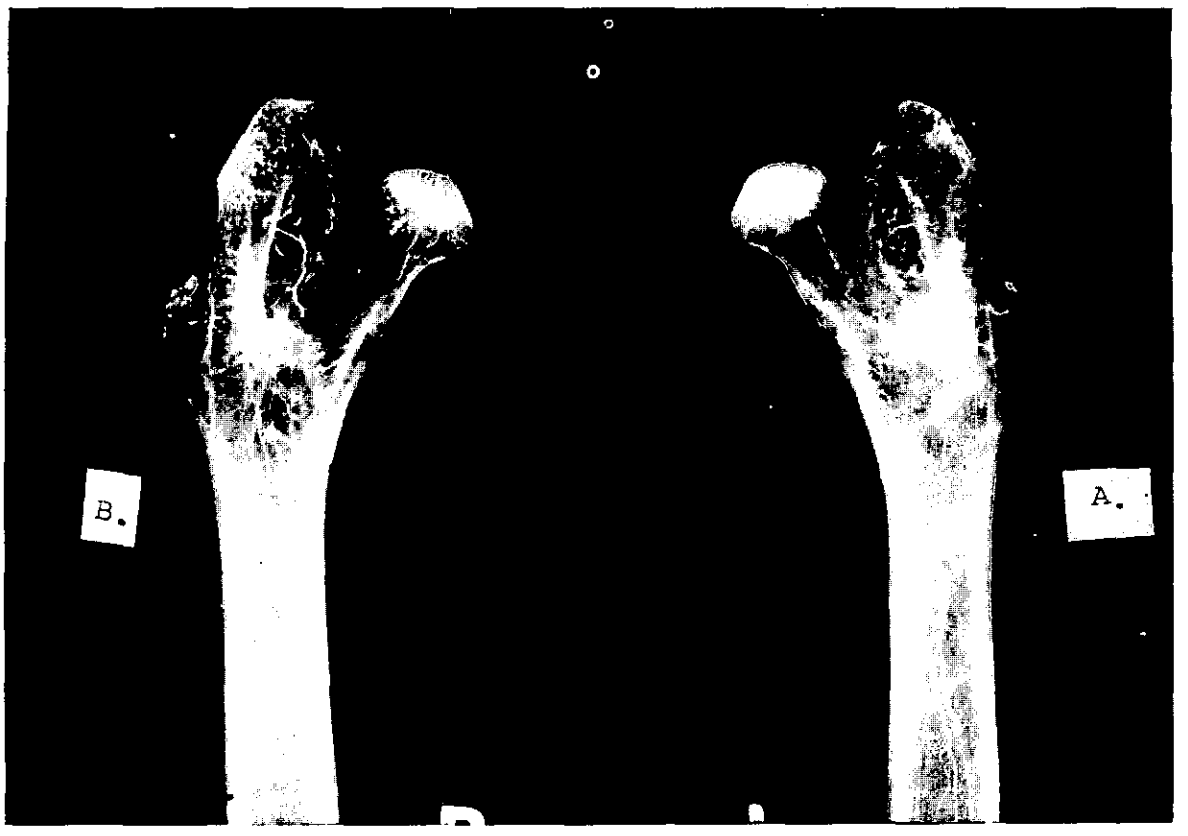


*Fig. 1. Radiographs of excised rabbit femora. (a) After injection of microspheres showing an increase in the density of the femoral head. (b) Normal control.*

occasionally endosteal new bone formation. In 3 cases the changes were more severe with complete necrosis of all layers of the cortex, which was gradually removed by osteoclastic activity, and the formation of some endosteal new bone and a thick layer of subperiosteal new bone (Fig. 3).

## Discussion

In all cases angiography revealed normal nutrient and epiphyso-metaphyseal vessels running into the femur. Many medium sized intraosseus branches of these vessels did not fill with radio-opaque material. The resolution of the radiological examination would definitely demonstrate spheres obstructing vessels of this size, and as this type of obstruction was not demonstrated in any case, it must be assumed that the spheres lodge in arterioles and cause a slowing of the flow and possibly thrombosis in more proximal vessels.

The lesions produced in the rabbit femora had many features of Caisson disease of bone and we feel fairly confident in attributing them to the vascular obstruction produced by the impaction of the microspheres. The main dissimilarity between the lesions in the femoral heads of the rabbits and those occurring in humans was that complete revascularization occurred in the rabbit, compared with the partial revascularization that is seen to occur in juxta-articular lesions in man. This is probably due to the great difference in size between the rabbit and human femoral head. In the rabbit only a short distance has to be travelled by the granulation tissue. The fact that collapse of the necrotic bone did not take place in the rabbit is

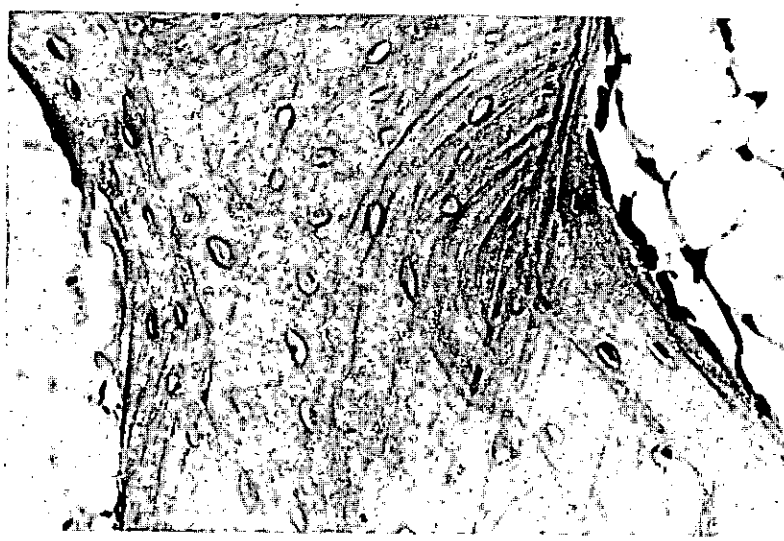

*Fig. 2. Necrotic rabbit femoral head after injection of microspheres. Empty osteocyte lacunae in the centre of a trabeculum, with appositional new bone laid down at the surface.*

*Fig. 3. Transverse section of completely necrotic femoral shaft from rabbit after injection of microspheres. Necrotic cortex is seen at the upper part of the picture. A revascularised marrow infarct is separated from the cortex by an area of endosteal new bone.*

not surprising, in view of the low load bearing requirement of the hip joint in the caged animal.

Lesions developing in the femoral shafts differed in a number of aspects from those observed in humans. Cortical thickening, which is occasionally present in humans (3) and subperiosteal new bone formation which is only very rarely present in humans (5) developed frequently in the rabbit, while the typical necrotic medullary lesion with a calcified wall, that frequently develops in the human, was not seen in the rabbit. The reason for this latter feature is again probably due to the small size of the rabbit bone, allowing relatively rapid and complete revascularization of the necrotic area.

## Conclusion

It would appear that the injection of embolic particles into the artery supplying the lower limb of the rabbit indicates that the arterial supply of the femoral head and to a lesser degree the shaft is poor in that it may be relatively easily obstructed. It also produces avascular necrotic bone lesions of the femur in sites that correspond to those that occur in Caisson disease of bone and implies that the aetiological agent in Caisson disease of bone may be the embolic occlusion of osseous vessels.

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Dr. P.T. Cox
Medical Research Council
Decompression Sickness Team
Department of Surgery
Royal Victoria Infirmary
Newcastle-Upon-Tyne NE1 4LP
England

# *Aseptic necrosis of bone*

*Edited by*

J. K. Davidson

*Consultant Radiologist in Administrative Charge, Western Infirmary, Glasgow, and Honorary Clinical Lecturer, University of Glasgow*

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CHAPTER 4

# Dysbaric osteonecrosis

John K. DAVIDSON

Aseptic necrosis of bone is a late complication of exposure to high-pressure environments. It is a major hazard to those involved in tunnel construction or caisson work when the pressure of air is greater than 2 atmospheres absolute (ATA). It occurs less frequently in divers. Very rarely the condition develops in those exposed to low-pressure environments such as flying at altitudes exceeding 18,000 feet in non-pressurised aircraft.

The condition has been variously called – caisson disease of bone, caisson arthrosis, pressure-induced osteoarthropathy, barotraumatic osteoarthropathy, aseptic necrosis of bone of caisson workers, barotraumatic arthropathy, aseptic barotraumatic osteonecrosis, arthopathia etc. In fact, 49 different names have been used and this is understandable when the aetiology and pathological development have not been clearly understood. Credit for the term dysbaric osteonecrosis is given to the Symposium sponsored by the National Institute for Occupational Safety and Health presented by the Marine Biochemical Institute and the Undersea Medical Society at Galveston in 1972. The term applies to compressed air, tunnel and caisson workers, divers and those aviators who are exposed to low-pressure environments.

For a better understanding of the condition it is clearly important to have some knowledge of the working environment of this group of men and of decompression sickness which they are liable to develop.

## *4.1 Working environment*

Men working in caisson, or in tunnels being built through water-bearing ground are rarely exposed to pressures exceeding four atmospheres absolute (ATA) or 44 lbs per square inch gauge (p.s.i.g.) and in this country the standard shift is of 8 hours duration. Compressed air is required in tunnel construction to prevent water seeping through the bed of the river and so flooding the workings. The pressure of air varies with the height of the water immediately above and also the porosity of the ground. When men are

* Many of the data in this chapter are derived from the records of the M.R.C. Decompression Sickness Registry.

about to work in compressed air, either in a tunnel or caisson, they enter a manlock, where, within a few minutes, the pressure is raised to that of the working chamber (Fig. 4.1.). The men then enter the working chamber where they remain for periods of time varying according to the particular job which they have to do, the majority remaining for an eight-hour shift. On completion of their work the men re-enter the manlock and are decompressed to atmospheric pressure. The decompression procedure, which is specified by legislation with subsequent modifications (Work in Compressed

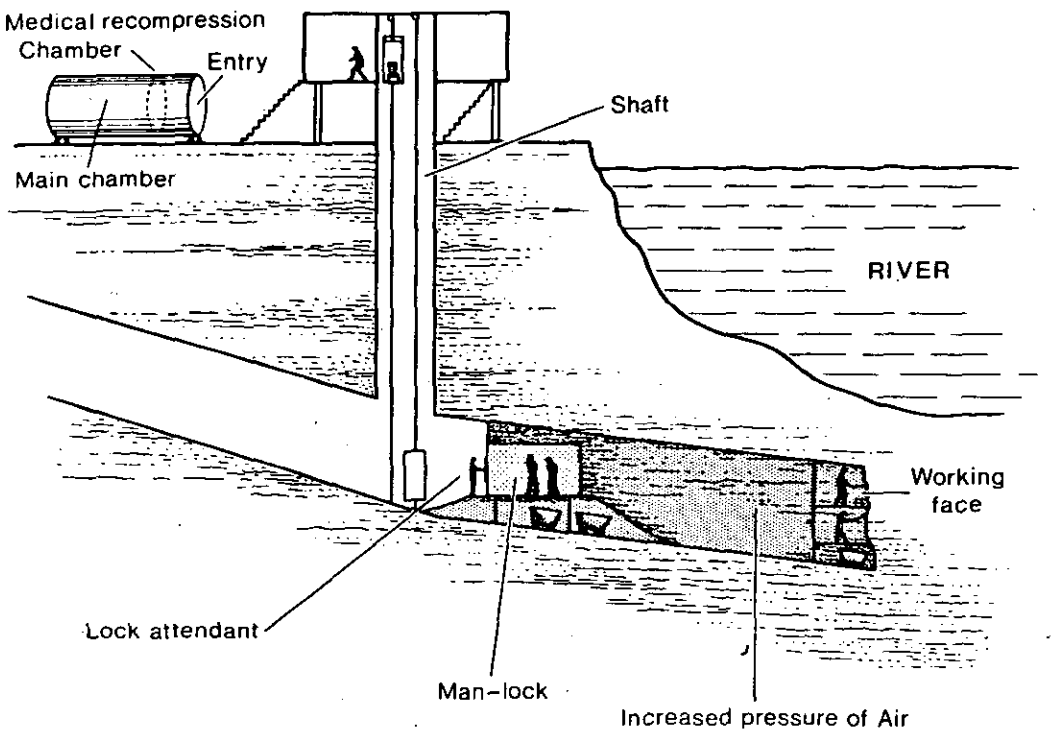


Fig. 4.1. Diagram showing tunnel construction using compressed air.

Air Special Regulations, 1958; Blackpool Trial Decompression Table, 1966) depends upon the pressures to which they have been exposed and the length of the exposure. For an exposure of six hours to 3 ATA (29 p.s.i.g.) the decompression time would be approximately 67 min (1958 Tables) and 115 min on the modified Blackpool Tables. Following a shift the men remain on the surface at the working site for an hour because it is in the first hour that symptoms and signs of the more serious Type II decompression sickness are most likely to develop. Should these symptoms and signs occur, the men are immediately recompressed in a separate medical recompression chamber.

Compressed air was first used in tunnelling at the Hudson River in New York in 1879 and Boycott (1906) reported a 25 percent mortality which dropped to one percent

with the introduction of a medical recompression lock. Fatalities are now very rare and the incidence of decompression sickness is considerably reduced.

A Medical Code of Practice has been produced by the Construction Industry Research and Information Association (CIRIA 1973). It is intended that this should be applied for work in compressed air in tunnels, caissons or other pressure chambers. Other recommendations have been published for divers and these include 'The Principles of Safe Diving Practice 1972' by the CIRIA Underwater Engineering Research Group and 'The Report by Committee on Diver Training and Performance Standards 1972' by the Society for Underwater Technology. All three documents provide valuable and practical information.

Divers are also exposed to a hyperbaric environment. For approximately every 33 feet of descent into sea water the pressure increases by 1 ATA, the figures varying slightly between salt and fresh water (Fig. 4.2). Although divers may go to a depth of

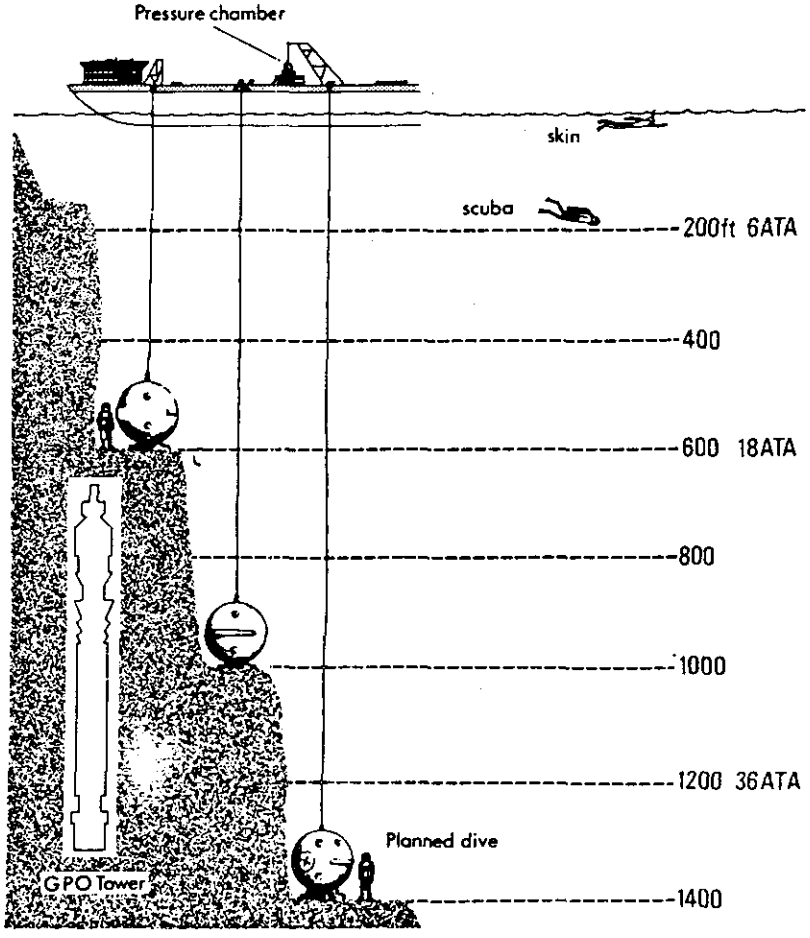


Fig. 4.2. Diagram showing diving depth in relation to pressure.

several hundred feet and are, therefore, exposed to higher pressures than tunnel workers, their period of exposure is usually considerably shorter. Diving is becoming increasingly common in the United Kingdom. Currently there are over six hundred commercial divers involved in oil exploration in the North Sea, over 350 Royal Navy divers and recreational divers can be counted in their thousands. The exact number and rate of increase is not known. Divers may work from a diving bell or be connected to the surface by continuous airlines. More commonly, especially for recreation, use is made of self-contained underwater breathing apparatus (Scuba) and those who use it are referred to as Scuba divers. As for tunnel workers, the decompression period depends on the depth and length of time to which men have been exposed. For example for a dive of 15 min at 120 feet the decompression time would be 12 min, for a dive of one hour at 180 feet the time would be about 4 h and for 30 min at 600 feet the decompression time would be approximately 36 h. Currently the change is made from air to oxyhelium mixtures at about 180 feet. Saturation dives are being carried out where the diver remains at pressure for periods of 4–10 days. Experimental simulated dives using gas mixtures have been made to 2000 feet.

Symptoms of decompression sickness may also develop when changing rapidly from normal atmospheric pressure to a lower pressure of air, as when flying at over 18,000 feet in non-pressurised aircraft. Similarly, astronauts would be liable to develop symptoms if they lost their cabin pressure or their space-suit became punctured during extravehicular activity (McIver, 1968). A further group liable to develop decompression sickness are those involved in hyperbaric medicine where pressures of air from 3 ATA to 6 ATA have to be used (Ledingham and Davidson, 1969). Staff members must be decompressed in the same way as tunnel workers or divers. This form of therapy has an established place in the treatment of carbon monoxide poisoning, gas gangrene and other conditions.

### *4.2 Decompression sickness*

The symptoms and signs which may develop in people who return to normal atmospheric pressure after working at high pressure, or who are exposed to low pressure after having been in normal atmospheric pressures, are collectively referred to as decompression sicknesses.

At present there is no known decompression procedure which will prevent all men at all times from developing decompression sickness. This may commence during decompression or within a few hours of its completion. There are two types of decompression sickness; Type I is less serious and there is no constitutional upset. It consists of pain in one or more of the limbs and the joint is characteristically held in a semi-flexed position – often referred to as the 'bends'. The pain will persist for some considerable time unless the patient is recompressed when symptoms are relieved, presumably because the causative bubble goes back into solution. Similar less-severe pain, is referred to as the 'niggles'.

Type II decompression is potentially more serious and always accompanied by a constitutional upset. The symptoms and signs may include any of the following ± nausea or vomiting with or without epigastric pain, hypotension, pallor or sweating

and there will be additional features depending whether the respiratory, cardiovascular or neurological system is involved. It may end in permanent paralysis or even death. Cardiovascular symptoms are thought to result from a bubble entering the coronary circulation causing anginal pain and arrythmia. Similarly neurological symptoms may result from bubbles entering the cerebral circulation causing limb weakness or even paralysis. Severe headaches may occur with visual defects, flashing of light or scotomata. Should a bubble enter an anterior spinal artery then a severe quadriplegia may result. Respiratory symptoms of dyspnoea or coughing ('the chokes') may occur.

All cases should be treated by immediate recompression in a separate recompression chamber. The pressure is increased until all symptoms and signs are relieved when the pressure is reduced to that of the normal atmosphere. Empirical procedures of Griffiths (1960, 1967), have generally been the basis of treatment. Griffiths points out that, by using the lowest pressure to relieve symptoms, further absorption of gas is avoided.

The incidence of Type I and Type II decompression sickness is expressed as the 'bends rate'. This is the number of cases treated by recompression expressed as a percentage of the number of decompressions. Comparison of decompression sickness rates from different contracts can be misleading because of the numerous variables which have to be considered (Walder, 1967). For example, if the pressures have been relatively low with a low turnover of the labour force, then the 'bends rate' will be less than on a contract where the pressure is high and the turnover of labour is high. The basic information is liable to be unsound because some men do not consider the less severe Type I pain ('the niggles') to be of importance and consequently this may not be recorded. Other variable factors include the length of shift, differences in temperature and humidity and disciplinary problems (McCallum, 1968). The incidence of Type I varies from 0.29–2.6% and is usually around 1.05–1.5% of all compressions over 18 p.s.i.g. The potentially more serious Type II is less frequent with an overall rate of approximately 0.02%.

Sinus pain, odontolgia and earache may result from variation of pressure in air-containing cavities occurring during compression or decompression.

Apart from dysbaric osteonecrosis, other long term chronic effects of decompression include paralysis and psychiatric illness (Rozsahegyi, 1967) but these aspects have tended to be neglected.

### *4.3 Aetiology of decompression sickness*

It is commonly believed that the condition results from nitrogen gas bubbles forming during decompression. During a prolonged exposure to a hyperbaric environment the body tissues become saturated with the gases found in air and they become equilibrated with the surrounding atmosphere. The partial pressure values of nitrogen in the alveoli, venous and arterial blood and in the tissues are identical. Oxygen and carbon dioxide on the other hand become physiologically active and are of little consequence in bubble formation but not in growth. During decompression the pressure within a lung alveolus is reduced while the partial pressure of gas in the bloodstream remains temporarily unaltered. Therefore, a pressure gradient is formed across the alveolar membrane

driving nitrogen from the blood to the air. Provided the decompression is well controlled, that is, sufficiently slow, then the nitrogen will be removed from the tissues. However, if the decompression is too rapid there will be insufficient time for nitrogen to be cleared from the tissues which become supersaturated and bubbles form.

The aetiology is not clearly understood and the literature is voluminous. Evidence that bubbles are the cause of decompression sickness is circumstantial but there is no other reasonable explanation and this theory accounts for the effectiveness of recompression when bubbles go back into solution.

Bubbles may result from pulmonary damage. Should an individual hold his breath while ascending rapidly to the surface in a submarine escape training tank then the intrapulmonary pressure becomes higher than the surrounding hydrostatic pressure. Rapid ascent with a closed glottis will result in overdistension of the lungs with interstitial emphysema and possibly massive air embolism. Similarly, pulmonary air trapping from occlusion of a bronchiole could result in the rapid formation of a cyst which might rupture and discharge gas into the interstitial tissue and pulmonary circulation so causing decompression sickness. Walder (1963, 1966) demonstrated that cyst formation and air embolism are possible in pig lungs, which have a similar structure to the human lung. If saturation with gas is already present then air embolism could initiate further bubble formation. Of interest to radiologists is the paper by Collins (1962) who reported lung cysts associated with Type II decompression sickness in a 20-year-old diver whose earlier chest radiograph was normal. Davidson (1964a and c) also reported a large subpleural bulla in an autopsy chest radiograph on a tunnel worker who died immediately following decompression. The same paper reported the results of routine chest radiography in compressed-air workers which had little effect on the incidence of Type I or Type II decompression sickness. Moreover no pulmonary cyst or bulla developed in 293 men who worked in compressed air for six to twelve months and were known to have a normal chest radiograph initially. However, chest radiography is recommended in divers and the presence of a cyst or bulla would be an absolute bar to diving.

Decompression sickness may result either from gas coming out of solution to form bubbles or pulmonary 'air trapping' causing the injection of air into the circulation. The actual distinction is difficult or even impossible in life, the essential feature being that the treatment for both conditions is virtually the same.

Recently there has been some interesting work on micro-embolism formation. Platelet aggregation is believed to take place during decompression at the liquid/gas interface and increased platelet adhesiveness has been demonstrated. If this is a cause of decompression sickness then management should include the use of anticoagulants (Philp et al., 1972).

### *4.4 Dysbaric osteonecrosis*

The first paper on osteonecrosis in a compressed-air worker came from Twynham in Australia in 1888. While osteomyelitis was clearly present in this patient and dysbaric osteonecrosis was probably not the diagnosis, exposure to a high-pressure environment was at least considered a possible cause. The radiographic appearances were first

described by Bornstein and Plate (1911/12) and independently by Bassoe (1913) the former reporting bone necrosis affecting the shoulder or hip joints in three tunnel workers. Since then there have been many reports (Davidson, 1964b and c, 1965; Davidson and Golding, 1970) and in fact there are over 130 publications from many countries throughout the world including France, U.S.A., Britain and Germany in that order of frequency. The publication by Roszahégyi (1956) gives a thorough and complete review of the subject including a superb summary of published cases up to 1955.

Prior to 1947 publications on dysbaric osteonecrosis were confined to compressed-air workers and until then it was felt that the diagnosis could not be made unless the man had experienced decompression sickness. Subsequently, large radiographic surveys showed that dysbaric osteonecrosis could occur in a significant percentage of those men who had not previously been treated for decompression sickness. For this reason the Reports by the M.R.C. Decompression Sickness Panel (1960, 1966 and 1971) are of particular interest. In fact the Report in 1966 of 241 men working at the Clyde Tunnel in Glasgow (1955–1963) was the first radiographic skeletal survey carried out in a large group of symptom-free men. Bone lesions were found in 19.0% of the men and 10.0% of the lesions were juxta-articular and potentially disabling. The findings were related both to the occupational history and the incidence of decompression sickness.

Of particular value is the annotated bibliography on dysbaric osteonecrosis prepared by Werts and Shilling (1972). This provides short abstracts and analysis of the literature including compressed-air workers, divers and aviators. The project was supported by the Office of Naval Research of the U.S. Navy so that the latest information in underwater activity would be available.

Because of the shorter exposure time to pressure compared with compressed-air workers, it was thought that divers did not develop osteonecrosis. Lesions were first reported by Seifert (1936) and there have been over thirty reports since then. The lesions are identical with those found in compressed-air workers but the incidence is less. One of the most interesting reports is that by James (1945) who found osteonecrosis in three of the five survivors who escaped from a submarine (H.M.S. Poseidon) which sank twelve years previously in 120 feet of water (4.75 ATA). These lesions apparently followed a single exposure to a hyperbaric environment for approximately three hours. There are several Japanese reports and of particular interest is that by Ohta and Matsunaga (1974) who found a 50.5% incidence of osteonecrosis in 301 divers who collected shellfish. Osteonecrosis was found in 4% of 350 Royal Navy Divers examined by Elliot and Harrison (1970).

Dysbaric osteonecrosis is rarely recorded in aviators. Classical changes have been reported in the head of the left humerus of a 43-year-old pilot who, during a period of 20 years had flown regularly in unpressurised aircraft at altitudes of up to 25,000 feet. He had three severe episodes of Type I 'bends' at widely spaced intervals (Fryer, 1969). Similar cases are reported by Markham (1967) and Hodgson et al. (1968). Other cases of osteonecrosis in aviators have been recorded but the case reports indicate that steriod therapy has been given at some time or another; consequently it is not possible to be certain that exposure to a low-pressure environment has been the cause

of the bone lesion. Radiographic surveys of those exposed to low pressures have been made and the most interesting is that by Hodgson et al. (1968).

### *4.5 Pathological and radiological correlation*

Compared with the extensive literature on the radiology, very little has been written about the pathological changes. An accurate interpretation of the density changes seen radiologically can only be made if the concurrent pathological changes are understood. The first report was by Kahlstrom et al. (1939a) who reviewed earlier cases and added four of their own. Necrotic areas were present in the head of the femur, head of the humerus, and in the shaft of the femur, tibia and fibula. A few months later (1939b) they reported three similar cases of osteonecrosis in men who had never been in a hyperbaric environment. The radiological and histological features are identical in all cases and both reports were of a high standard. Other publications of interest include those by Swain (1942), Kahlstrom and Phemister (1946), De Sèze et al. (1963) and the report by the M.R.C. Decompression Sickness Panel (1966).

As with osteonecrosis from other causes, when an area of bone is deprived of blood supply it dies and this can be recognised histologically within a few days by acellularity of the bone marrow and later by the absence of osteocytes in the bone lacunae. Initially necrotic bone is radiographically indistinguishable from living bone. It is only after a period of several months when the repair processes have been started that radiological changes become evident. During the process of revascularisation, granulation tissue grows from the narrow spaces of the living bone into the necrotic marrow, often accompanied by the laying down of new bone on the surface of dead trabeculae. Histologically this can be recognised and the dead trabeculae with osteocytes absent from the lacunae are covered with a new layer of bone. For some reason, which is not clearly understood, the process of repair sometimes becomes arrested. New bone continues to become heaped up forming a zone of thickened trabeculae. This causes an overall increase in bone bulk with an absolute increase in radiographic density. It is at this stage, at least six months after the ischaemic episode, that positive radiological changes of increased density become apparent. In dysbaric osteonecrosis the ischaemic episode is painless and the precise moment of occurrence cannot be identified. Consequently positive radiological changes are calculated from the first exposure to a hyperbaric environment known to produce such changes. If serial radiographs are taken at intervals of approximately six months then positive changes are likely to become evident at six months to a year after the first exposure. On the other hand, without serial radiographs, symptomless bone lesions may not be identified until many years after exposure to a hyperbaric environment.

Weight bearing or excessive physical activity may cause a structural failure in damaged bone with collapse of the articular surface into the underlying necrotic bone. The articular cartilage with a shallow layer of underlying bone may sequestrate. Following collapse, osteophytes will form at the margins of the joint surface. The report by Swain (1942) and the M.R.C. Panel Report (1966) are of particular value. Both report compressed-air workers who died after having considerable experience of this type of work. In the M.R.C. Panel Report (1966) sections of the head of the humerus and the

head of the femur showed that a large proportion had been necrotic but had been revascularised. Subarticular necrotic bone was separated from the living bone by a layer of thickened trabeculae which appeared radiologically as a serpiginous dense layer. Between this layer and the remaining necrotic bone was a layer of fibrous tissue which was thought to indicate that further revascularisation was unlikely. Swain records a structural failure of the head of the right humerus with sequestration and a similar dense curvilinear layer. The articular cartilage of two-thirds of the head was found to be devitalised with a mosaic appearance due to irregular fissures. A similar appearance was present in the head of the left humerus where about one-third of the articular surface was involved. The zone of thickened trabeculae separated necrotic from living bone and this corresponded to the dense curvilinear opacity seen on the radiographs.

The radiological changes within the shaft of the bone consist of areas of increased density which progress to calcification. The reports by Kahlstrom et al. (1939a and b) relate the radiological and pathological changes. The areas of increased density seen radiologically in the medulla may also be due to new bone layed on dead trabeculae. The very dense areas are probably due to calcification of the fibrous capsule which surrounds the necrotic area, and even to calcification of the dead marrow itself. Considerable cortical thickening is sometimes seen adjacent to a medullary lesion but the explanation of this is not clear. (See Section 2.8.)

### *4.6 Radiological investigation*

The basic skeletal survey, recommended by the MRC Decompression Sickness Registry, should include views of the head and proximal parts of the shafts of the humerus and femur on each side and projections of each knee including the distal two-thirds of the shaft of the femur and the proximal third of the shaft of the tibia.

The early demonstration of dysbaric osteonecrosis demands high quality radiographs which clearly demonstrate the bone trabeculae. This will require the optimum screen/film combination, an adequate ratio grid and a focal spot size of 1 or 1.2 mm. A smaller size with a high-speed rotating tube should be used if this is available. Gonad protection should always be used. A list of recommended projections and specimen radiographs illustrating these views should be available for the radiographer. Where possible the radiographs should be checked before the patient leaves the X-ray room or Department and preferably this should be done by the radiologist responsible for the interpretation. It is of considerable advantage to have the surveys done in as few centres as possible so that the radiography technicians become closely involved in the work and are fully aware of the problems in interpretation and the need for high quality radiographs.

#### *4.6.1 Shoulder joint*

The object is to obtain a radiograph of the entire articular cortex of the humeral head in unobscured profile. An 18 × 24 cm (10/8) film is recommended. An antero-posterior projection of each shoulder is taken with the patient lying supine and the trunk rotated to bring the scapula on the side to be radiographed flat against the table top. With the arm in the supine position (palm up), pulled down and abducted 10° the beam is

centred one inch (24.5 mm) below the tip of the coracoid process of the scapula. The beam should be collimated by bringing in the diaphragms to show only the head and the proximal third of the shaft of the humerus. This view should show a clear joint space. The patient should hold his breath while the film is exposed (Fig. 4.3.).

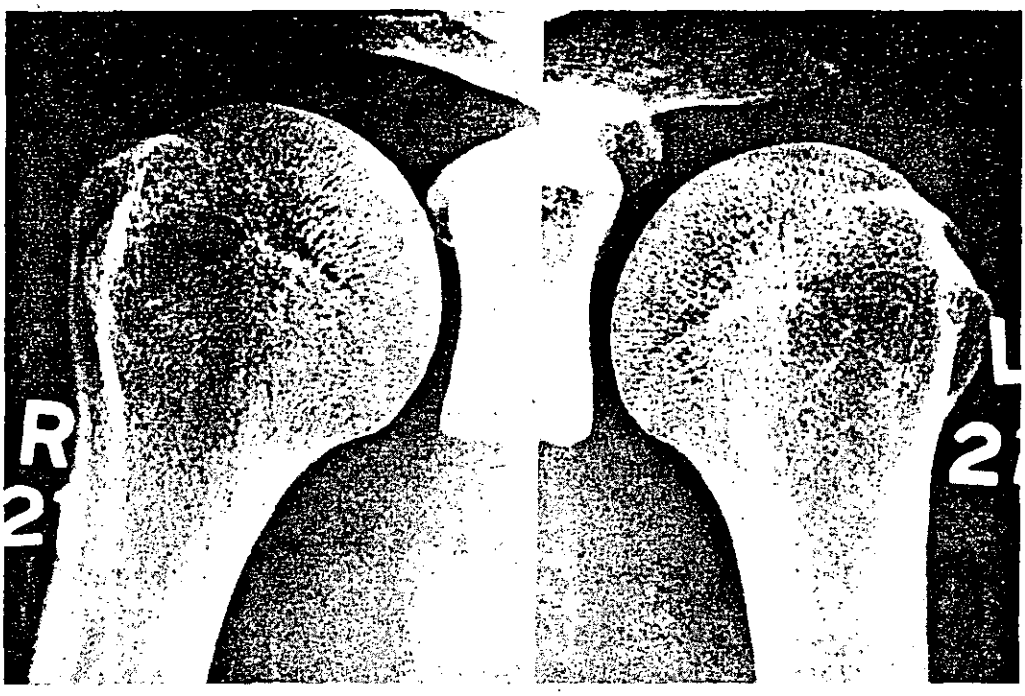


Fig. 4.3. Sample projection of both humeral heads showing good trabecular detail. No overlying bone. The joint space is clearly defined.

*4.6.2 Shoulder joint with arm in internal rotation*

An 18 × 24 cm (19/18) film is recommended. An antero-posterior projection of each shoulder joint is taken with the patient placed in a supine position and the trunk rotated to bring the scapula on the side to be radiographed flat against the table top. The humeral head is then internally rotated by turning the forearm to the prone position (palm down), with the elbow slightly flexed and the humerus abducted approximately 10°. The beam is centred 1 inch (24.5 mm) below the tip of the coracoid process of the scapula. The beam should be collimated by bringing in the diaphragms to show only the head and the proximal third of the shaft of the humerus. The patient should hold his breath during the exposure.

*4.6.3 Hip joint*

The object is to obtain a radiograph demonstrating the head of the femur. To obtain comparable radiographs at serial follow-up, the femoral neck should be in a standard position. A 24 × 30 cm film (10/12) is recommended. A separate antero-posterior projection of each hip joint is taken with the patient placed in a supine position and the foot on the side under investigation kept at 90° to the table top. The beam should be centred over the head of the femur, that is, 1 inch (24.5 mm) below the mid point of the line joining the anterior-superior iliac spine and the mid point of the upper border of the pubic symphysis. The beam should be collimated by bringing in the diaphragms to show only the head, neck and immediate subtrochanteric area of the femoral shaft. The edge of the gonad protector should be as near to the femoral head as possible but not obscuring it (Fig. 4.4.).

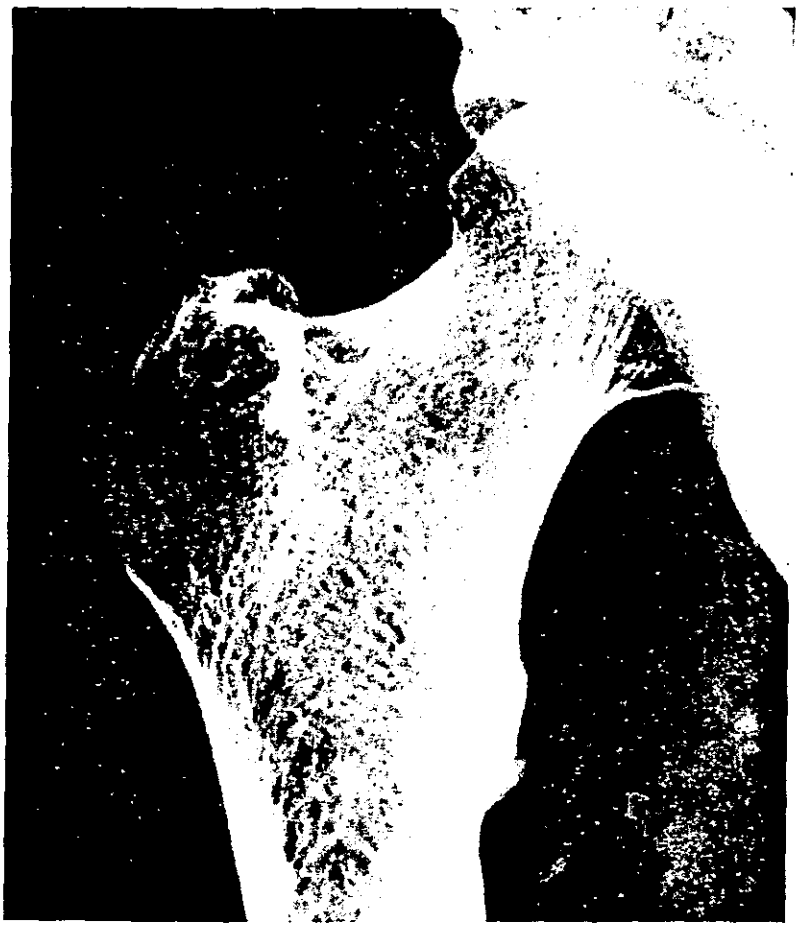

Fig. 4.4. Sample radiograph of the femoral head.

*4.6.4 Knee joint*

The object is to ensure a comparable density between the lower two-thirds of the femur and the upper third of the tibia. It is recommended that the kV is lowered, the mA raised and use made of a grid. Two projections are used. A 30 × 40 cm film (15/12) is recommended for both. An antero-posterior projection of each knee is made with the knee extended to include the lower two-thirds of the femur and the upper third of the tibia and fibula. The beam should be centred at the level of the upper border of the patella.

A lateral projection of each knee joint is made with the patient rotated so that the lateral border of the knee to be examined is against the table. The opposite leg should be positioned so that a line through both anterior-superior iliac spines is at right angles to the table top. In this way the projection of the knee joint is more likely to be a true lateral. The field should include the lower two-thirds of the femur and the upper third of the tibia and fibula. The beam should be centred at the level of the upper border of the patella (Fig. 4.5.).

Should there be doubt in the diagnosis then the following additional views may be of value.

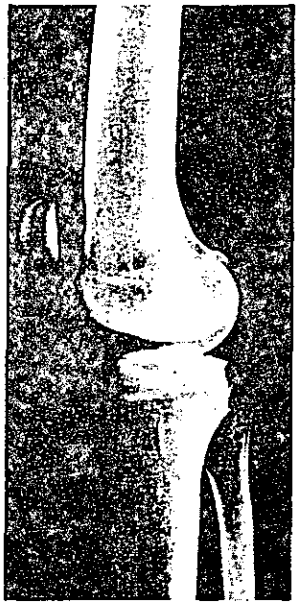

Fig. 4.5. Sample lateral projection including the distal two-thirds of the femoral and the proximla third of the tibial shaft.

*4.6.5 Hip joint with leg in lateral position*

A 24 × 30 cm (10/12) film is recommended. A lateral projection of the hip joint

increases the potential radiation dose to the gonads. However, it may be of value in identifying an early lesion particularly when there is a structural failure with a translucent subcortical band. A separate lateral projection of each hip joint is taken with the patient supine. The knee and hip on the side to be examined are flexed so that the foot is flat on the table top directly opposite the other knee. The thigh is then abducted maximally and the knee supported by a sandbag. The beam is centred over the head of the femur, that is, 1 inch (24.5 mm) below the mid point of the line joining the anterior-superior iliac spine and the upper border of the pubic symphysis. The projection should include the head, neck and immediate subtrochanteric region of the femur.

*4.6.6 Further comments*

The gonads must always be protected from ionizing radiation by a lead shield. If this is done, estimation of the radiation dose received by the patient indicates that the basic skeletal survey can be safely repeated at intervals of six months.

It is debatable whether the routine surveys should include the additional projections. However, when doing this type of work, it is not always practical or easy to recall a man for a repeat or extended radiographic examination. In this situation it is worthwhile to include the additional projections as they may help to indicate more clearly whether or not an abnormality is present. When the recall is easy then the survey should be confined to the basic views.

Probably the greatest fault lies in underpenetration of the radiographs. Because of this trabecular detail is not clearly seen and consequently small dense areas close to the joint surface will not be identified. During the process of repair, granulation tissue

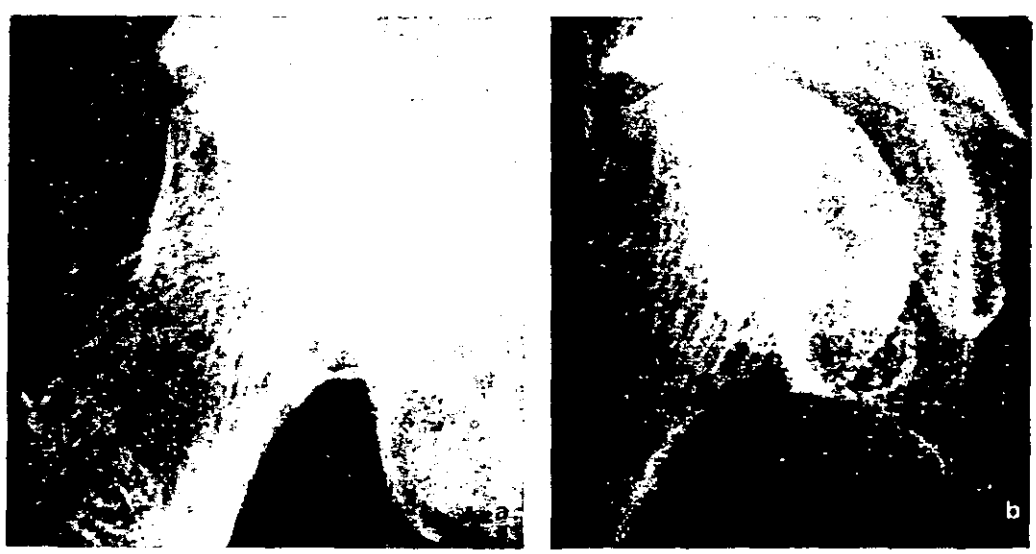


Fig. 4.6. (a) Underpenetration of the left femoral head and the trabecular structure is not clearly defined. (b) Repeat radiograph with increased kilovoltage clearly defining osteonecrosis with a dense layer in the right femoral head and an intact articular cortex.


Fig. 4.7. Serial radiographs. On the left the humeral head is underpenetrated, trabecular detail is not seen and it is impossible to identify possible osteonecrosis; in the centre a better quality radiograph has defined positive osteonecrosis with spherical segmental opacities adjacent to an intact articular cortex – positioning is unsatisfactory with overlying glenoid; on the right positioning is better but the radiograph is grossly overpenetrated and the lesion is not well defined.

Fig. 4.8. Malrotation of the shoulder joint resulting in the superior border of the greater tuberosity appearing as a dense layer which could be misinterpreted as osteonecrosis.

Fig. 4.9. (Left) Inadequate exposure of the distal femoral shaft with trabecular detail not defined and an early lesion could be missed.

Fig. 4.10. (Right) Inadequate projection in that the radiograph does not include the distal two-thirds of the femoral shaft or the proximal third of the tibial shaft.

Fig. 4.11. Radiograph of the left shoulder including most of the left upper zone of the lung. The X-ray projection is too large with consequent loss of detail of the left humeral head. The examination should be repeated with adequate coning and improved positioning.

Fig. 4.12. Faulty screen contact with loss of trabecular detail and a blurring effect.

grows from the living bone into the necrotic bone and new bone is laid on the trabeculae causing an overall increase in bone bulk. Therefore, there is more tissue for the X-rays to penetrate and, unless the kilo voltage is increased possibly as much as 10 kV, a pale, under-penetrated radiograph will result. When this happens small dense areas will not be identified and this is one of the commonest causes of misinterpretation and failure to identify osteonecrosis (Figs 4.6 and 4.7). Other difficulties in interpretation arise from malrotation of the shoulder joint resulting in the superior border of the greater tuberosity appearing as a dense layer which could be misinterpreted as osteonecrosis (Fig. 4.8). Further faults will arise from inadequate projection, exposure etc. (Figs 4.9–4.12).

Tomography may be required to improve definition particularly in the femoral head and sometimes in the humeral head where detail is obscured by overlying bone. In general, however, good quality radiographs preclude the need for frequent use of tomography.

Xero radiography provides good detail and is of value in delineating the edge of a lesion more clearly. As yet the technique is not widely used but the radiation dose is high. Further investigation such as special projections or tomography may be indicated by the clinical situation. Cox (1972) reported the results of isotope organ scanning

using $^{87}Sr$ in compressed-air workers with radiological evidence of osteonecrosis. There was good correlation in the head of the humerus and femur in both positive and negative cases indicating that osteonecrosis can be detected by isotope scans using strontium.

### *4.7 Classification of bone lesions*

The following classification was prepared by the M.R.C. Decompression Sickness Panel following the first radiographic skeletal survey at the Clyde Tunnel in Glasgow (Panel Report 1966) and subsequently reported by Davidson and Griffith (1970). This classification is now generally accepted.

Lesions are primarily classified into two broad groups:

*(a) Juxta-articular lesions* These involve or are adjacent to an articular cortex occurring in the head of the humerus or femur. The lesions may either give rise to disabling symptoms when first seen or may do so in the future and are therefore considered to be potentially disabling.

*(b) Head, neck and shaft lesions* These lesions are situated at some distance from the joint surface and rarely, if ever, give rise to symptoms.

#### *4.7.1 Juxta-articular lesions*

##### *4.7.1.1 Dense areas with an intact articular cortex (Figs 4.13, 4.14 and 4.36)*

The dense areas lie adjacent to an intact articular cortex and are found more commonly in the head of the humerus than in the head of the femur; the diameter of the areas of density varies between 3 and 20 mm. Trabeculae passing through the dense area appear

Fig. 4.13. (Left) Very small dense areas with intact articular cortex at the head of the humerus. Early changes of osteonecrosis.

Fig. 4.14. (Right) Tomograph of the left shoulder defining more clearly the extent of the dense area. The articular cortex is intact.

to be thickened and fused. The margins are indistinct compared with those of a bone island (see Section 4.15) and the adjacent bone is of normal density. In the femoral head, detail is obscured by the overlying acetabulum and consequently lesions at this site are identified much less rapidly. Tomography or a 'frog lateral' projection help with further definition.

*4.7.1.2 Spherical segmental opacities (Figs 4.15 and 4.16)*
Areas of density (4.7.1.1) may be spherical in shape and, when confluent, the appearance is that of a 'snowcap' as described by Poppel and Robinson in 1956. Occasionally a 'pseudo-snowcap' may be seen. This results from a minor variation in the radiographic projection and can be distinguished from a definite abnormality by the presence of trabeculae running through the area of apparent increased density.

Fig. 4.15. (Left) Spherical segmental opacities in the head of the left humerus adjacent to an intact articular cortex. Typical 'snowcap' lesions.

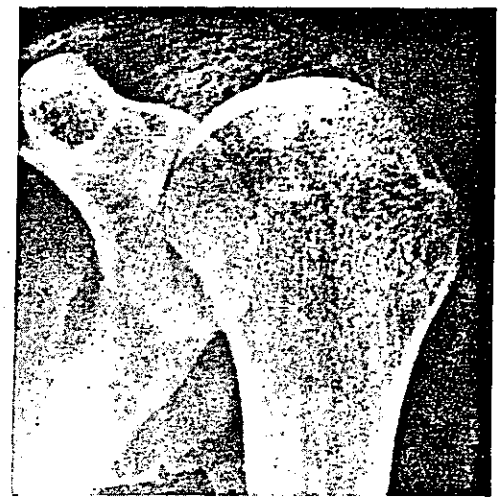

Fig. 4.16. (Right) Further example of spherical segmental opacities adjacent to an intact articular cortex with the patient remaining symptom free.

*4.7.1.3 Dense layer (Figs 4.17–4.19)*
The dense layer may be curved or serpiginous. It may extend to the intact articular surface on each side enclosing as much as two-thirds of the joint surface. Usually there is a mild concavity towards the articular surface. The width of the layer varies between 2 and 5 mm and the margins vary from being well-defined to indistinct. The necrotic bone between the dense layer and the articular cortex is usually radiographically indistinguishable from the living bone on the opposite side, but there may be additional areas of increased density on the shaft side of the dense layer. The lesion is seen more commonly in the humerus. In the femoral head the dense layer tends to follow a large S-shaped course, but, as in the case of localised areas of density, the appearance is

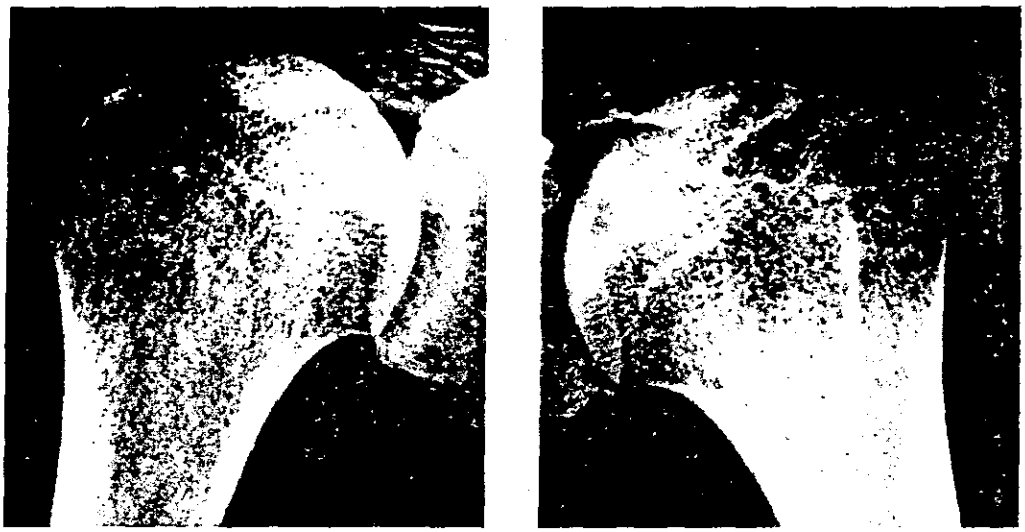

Fig. 4.17. Bilateral serpiginous dense layers involving both humeral heads. Articular cortex is intact on both sides and no symptoms were present.

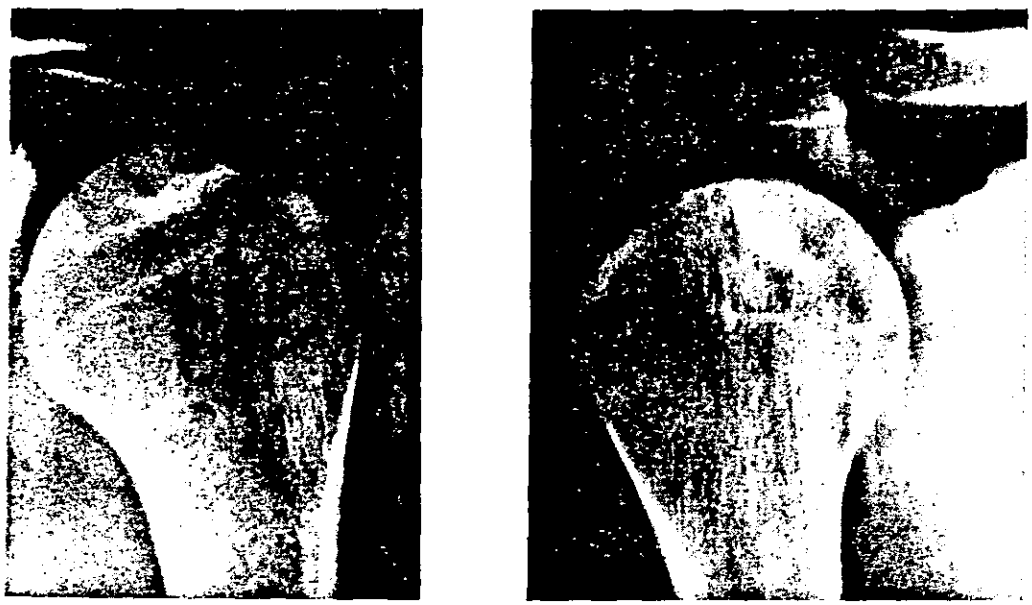

Fig. 4.18. (Left) Dense curvi-linear layer (5 mm in width) enclosing about two-thirds of the articular cortex. Typical juxta-articular dense layer in a man of 28 years who has worked for four months in compressed air at pressures up to 3ATA. Patient never had Type I or type II bends and had no shoulder joint symptoms.

Fig. 4.19. (Right) Tomograph of the right shoulder showing a dense layer with an intact articular cortex. No symptoms were present. The dense layer represented new bone laid on the trabeculae of dead bone, causing an absolute increase in radiographic density.

frequently obscured by the overlying acetabulum. Tomography is again required to define lesions more clearly. This layer type of lesion presents a typical appearance, and could be described as a hallmark of dysbaric osteonecrosis.

*4.7.1.4 Structural failure*

The articular cortex collapses into the underlying necrotic bone at the point of the greatest stress and the radiological appearances depend upon the degree of structural failure. In addition to the above changes there is sometimes a triangular area of increased bone density with its apex extending towards the shaft.

*(a) Translucent subcortical band (Figs 4.20 and 4.21)* This is found in the head of either the humerus or the femur. The translucency appears as a fine line immediately under the articular cortex and parallel to it, extending for as much as two-thirds or more of the joint surface. This appearance has been described as the 'radiolucent crescent sign' (Norman and Bullough, 1963). The translucency represents a fracture through the necrotic bone but at this stage the articular surface has not yet collapsed and is intact.

Fig. 4.20. (Left) Fine translucent subcortical band in a juxta-articular lesion involving the left femoral head – a good example of the 'radiolucent crescent sign'. The translucent band, is, in fact, a fracture through necrotic subcortical bone.

Fig. 4.21. (Right) Fine translucent subcortical band involving the head of the right humerus. Several dense areas involve a large segment of the bone under the joint surface. The dense areas result from revascularisation and represent new bone laid on the trabeculae of dead bone. The translucency is a fracture through necrotic bone. Limitation of movement was noted with a painful arc on abduction.

*(b) Collapse of the articular surface (Fig. 4.22)* In the femoral head as much as half the posterior weight-bearing area of the articular cortex may collapse and in the humeral head up to one-third or more may be involved. The middle third of the humeral articular surface (also probably the point of greatest stress) is affected. At the margins of the collapsed segment there is clearly defined 'step' formation, but in the initial stage the articular cortex may still be intact.

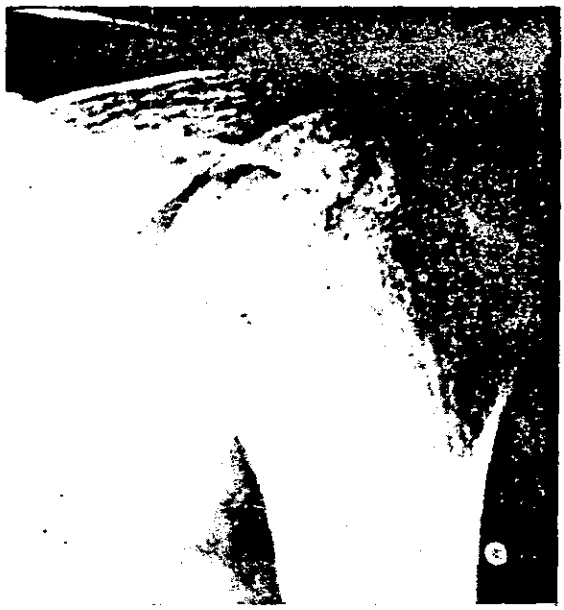

*Fig.* 4.22. Structural failure with early collapse of the articular surface inferiorly and a translucent subcortical band involving the middle third of the head of the humerus. Extensive areas of increased density form a triangle with the apex extending towards the proximal shaft of the humerus.

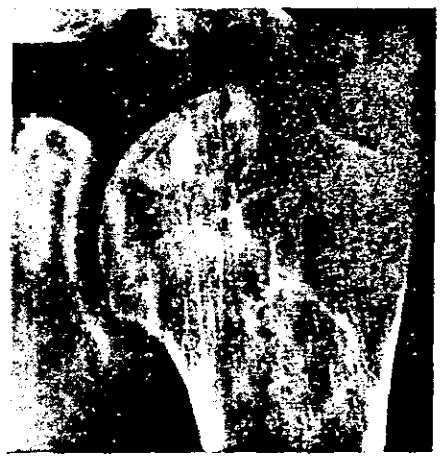

Fig. 4.23. (Left) A large part of the articular cortex has sequestrated. Dense areas are present in the adjacent bone. Patient was an experienced compressed-air worker for many years and had experienced Type I and II bends on several occasions.

Fig. 4.24. (Right) Tomography of the left shoulder joint demonstrating extensive dense areas involving the head of the humerus and extending to the shaft. A sequestrum has been demonstrated involving the upper part of the articular surface and bounded by a fine translucent band. As yet the sequestrum has not collapsed into the subarticular bone.

*(c) Sequestration (Figs 4.23–4.27)* The articular cortex may break up into several necrotic segments which become depressed into underlying bone so that the joint surface appears to be totally disorganised. If the area of sequestration is single and large and not yet depressed, it appears to be separated from the head by a translucent band which represents a fracture through the necrotic area. In the femur, sequestra may lie below the level of the articular surface.

*4.7.1.5 Osteoarthritis (Figs 4.28 and 4.29)*

Osteoarthritis with osteophyte formation usually follows structural failure. In the humeral head the osteophyte characteristically develops at the inferior margin of the articular cortex, and may increase in size rapidly. In the femoral head, osteophytes may develop at either the superior or inferior margin and be of considerable size.

The glenoid fossa and the acetabulum are not severely affected by osteoarthritis and the joint space is usually still visible in the earlier stages.

*4.7.2 Head, neck and shaft lesions*

*4.7.2.1 Dense areas (Fig. 4.30)*

These lesions are similar to the dense areas already described in the juxta-articular group. The margins are indistinct and ill defined. The lesions lie at a considerable distance from the joint surface and are most often seen in the distal shaft of the femur or the proximal shaft of the tibia. Less commonly they may be found in the proximal shaft of the humerus.

*4.7.2.2 Irregular calcified areas (Figs 4.31–4.34)*

This is the most frequent abnormality, is often bilateral and forms 39% of all patients. It is commonly situated in the distal shaft of the femur, the proximal shaft of the tibia and the proximal shaft of the humerus. These areas of calcification are found only in the medulla. In the early stages the calcification tends to form faint short linear strands, only identified on good quality radiographs. Later it is more dense, sometimes oblong or rectangular in shape, extending over several centimetres and occupies the full width of the medulla. Lesions in the femoral and tibial shaft are seen more clearly in the lateral radiographs.

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Fig. 4.25. (Upper) Multiple areas of sequestration involving the head of the right humerus in an experienced compressed-air worker.

Fig. 4.26. (Lower left) Complete disorganisation of the articular surface of the head of the left humerus, with collapse and sequestration of the cortex. One of the most severe cases as similar changes were present in the opposite humerus and in both femoral heads. This patient worked for 11 months in compressed air at pressures up to 28 p.s.i.g. and never experienced Type I or II bends. Probably had no previous compressed-air experience.

Fig. 4.27. (Lower right) Axillary projection demonstrating sequestration of the articular surface of the head of the humerus with partial collapse.

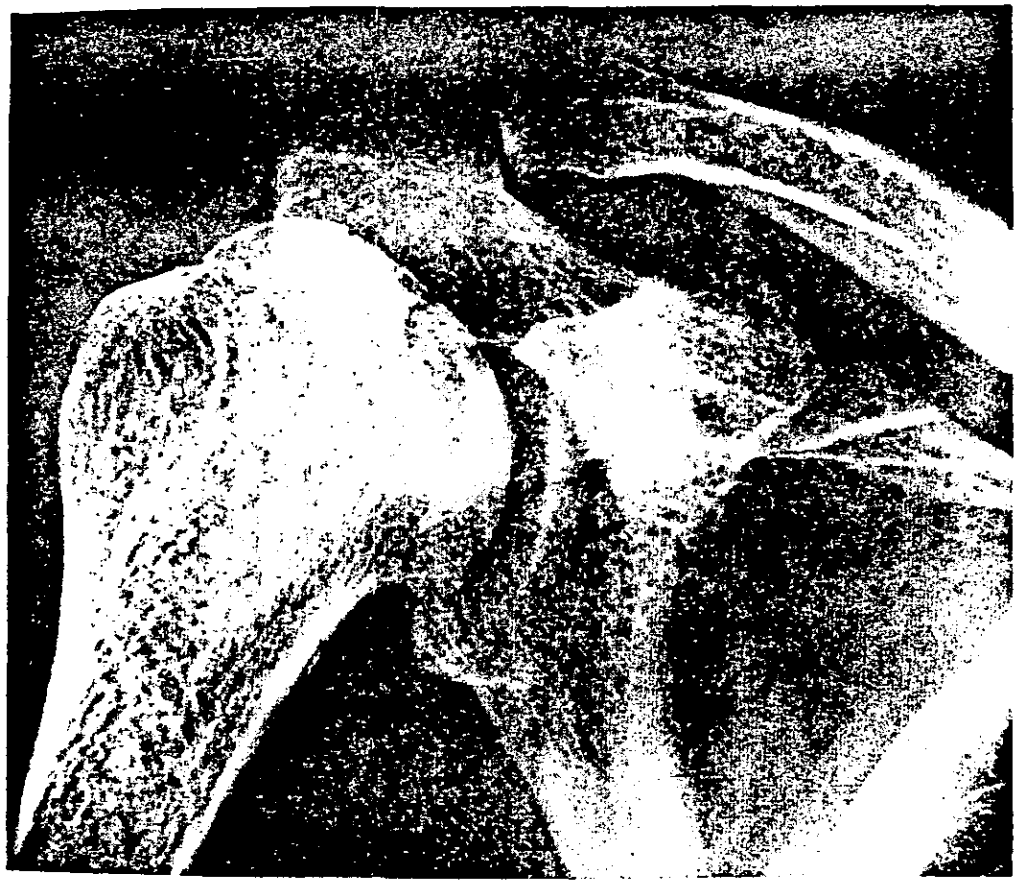
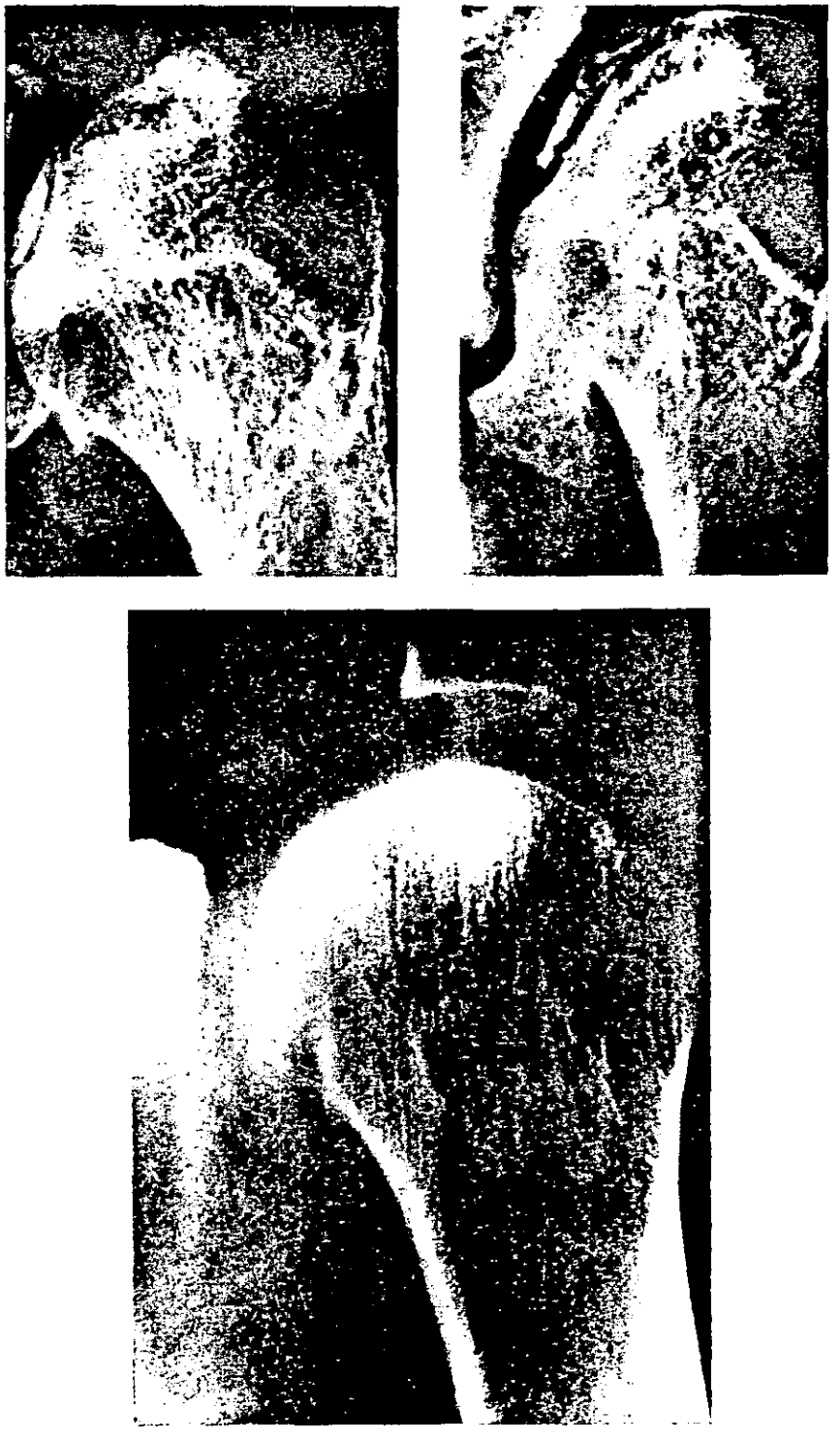


Fig. 4.28. Tomograph of the left femoral head demonstrating severe secondary osteoarthritis in a very experienced compressed-air worker. Well-developed marginal osteophytes are present and there is increased density of the femoral head. A defect is present in the articular surface and the appearances suggest that a sequestrum has become attached to the acetabulum.

Fig. 4.29. (Upper) Marginal osteophytes developing in the head of the left humerus during a period of 3½ years. In the later radiographs the inferior marginal osteophyte is much larger. The sequestra and dense areas are more defined.

Fig. 4.30. (Lower) Tomography of the head and neck of the left humerus, demonstrating a large dense area in the proximal shaft of the left humerus. This is an example of a head, neck and shaft lesion and is very unlikely ever to cause symptoms.



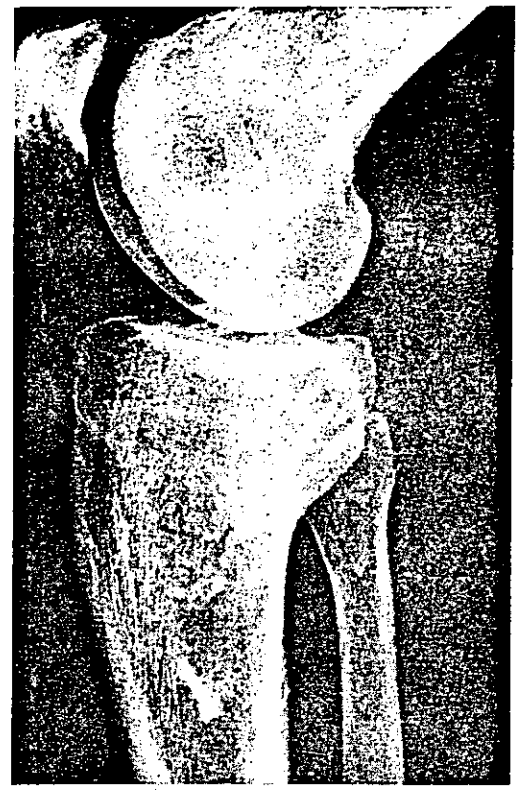


Fig. 4.31. (Left) Extensive calcification involving the proximal shaft of the tibia.

Fig. 4.32. (Right) Irregular calcified areas of proximal shaft of the tibia. Typical example of a head, neck and shaft lesion.

*4.7.2.3 Translucent areas (Fig. 4.35)*

These are uncommon and their true nature is difficult to explain; they are found in the distal shaft of the femur and proximal shaft of the humerus occupying the whole width of the medulla and are several centimetres in length with scalloping of the endosteum. It is thought that the translucency represents a necrotic area, the margins of which will subsequently calcify. These are not to be confused with cystic areas in the femoral neck (Fig. 4.75) which are not considered to be osteonecrosis.

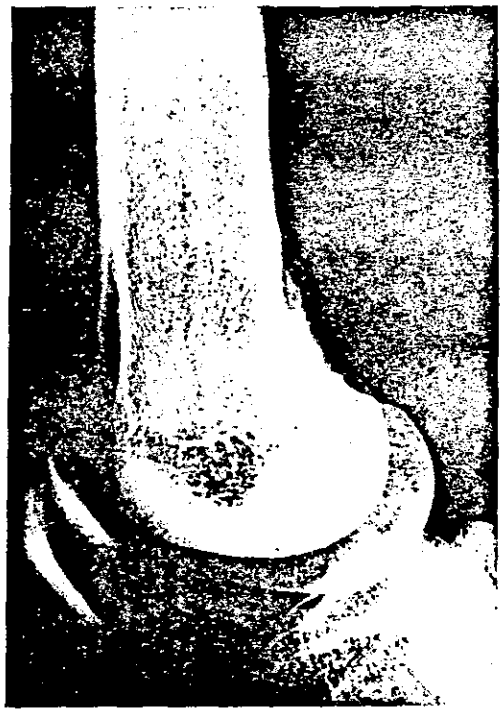


Fig. 4.33. (Left) Extensive calcification involving a large part of the distal shaft of the femur and occupying the full width of the medulla.

Fig. 4.34. (Right) Irregular calcified areas in the distal shaft of the femur.

### *4.8 Progress of bone lesions*

The M.R.C. Decompression Sickness Registry has skeletal radiographs of 1694 compressed-air workers. Of these about 600 have been examined radiographically more than once, about 150 on three occasions and over 20 on five occasions. Consequently it has been possible to follow a number of cases radiologically over the years. Dense areas or a dense layer adjacent to an intact articular cortex may remain static for several years and, as long as the articular cortex is intact, the patient remains symptom free (Figs 4.36–4.40). Others may progress from dense areas adjacent to the articular cortex, through the dense layer to structural failure of the joint surface and secondary osteoarthritis, symptoms beginning when structural failure occurs (Figs 4.41–4.51). It is not uncommon for a lesion to develop so rapidly that involvement of the joint surface with

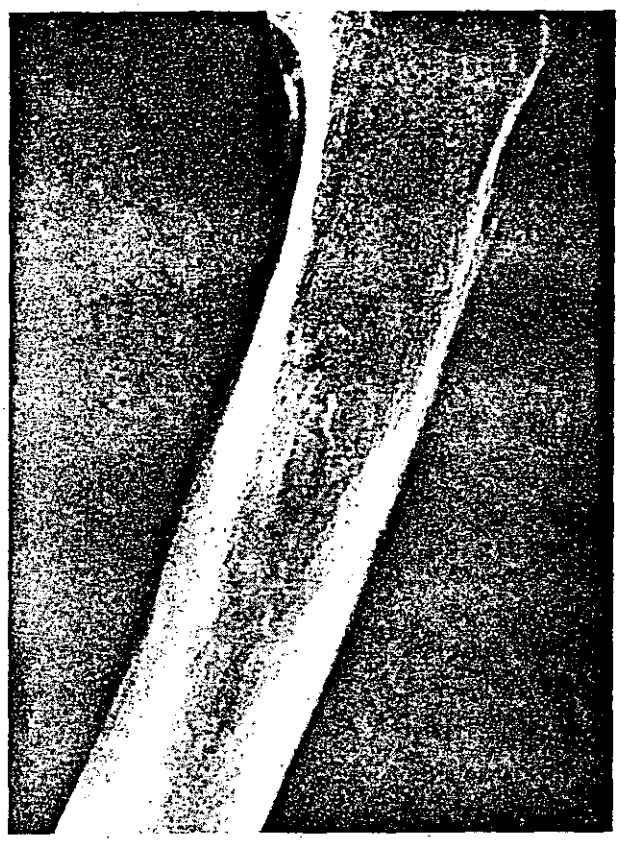


Fig. 4.35. Cortical thickening demonstrated in the distal shaft of the femur affecting both the anterior and posterior surfaces. Endosteal erosions are present. Faint calcified areas are present within the medulla. The appearances suggest increased translucency in the medulla in the area bordered by the cortical thickening.

associated symptoms occurs within eighteen months of the first exposure to a hyperbaric environment (Figs 4.52–4.54). There is no way of identifying those men who may develop a bone lesion and, furthermore, there is no way of predicting if a lesion will remain static or go on to structural failure and secondary osteoarthritis.

Similarly it has been possible to follow a number of shaft lesions developing radiologically. These appear first as faint areas of increased density and progress to irregular calcification in the shaft of the femur or tibia (Figs 4.55–4.57).

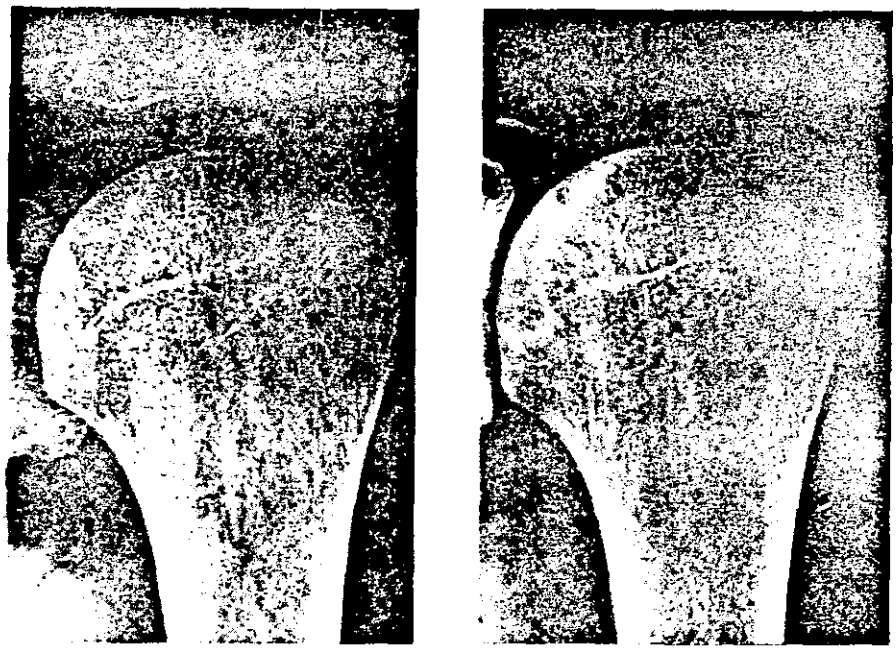


Fig. 4.36. On the left, January 1963, ill-defined dense areas with an intact cortex, the appearances being those of early osteonecrosis. On the right, February 1965, a serpiginous dense layer has developed enclosing approximately two-thirds of the articular surface which remains intact.

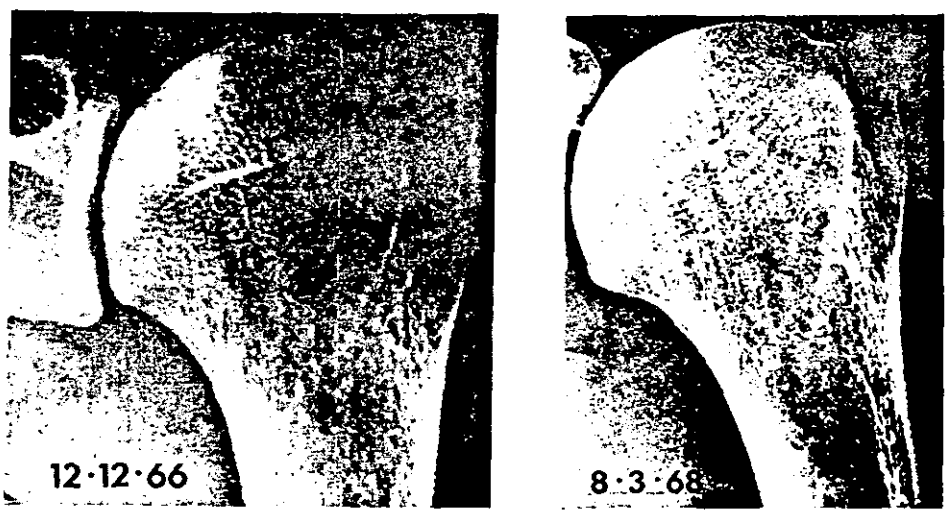



Fig. 4.37. (Left) Same case as Fig. 4.36 almost 4 years after the original radiograph. Well-defined dense areas in the head of the humerus.

Fig. 4.38. (Right) Same case five years after the original radiograph, dense areas remain unchanged and the articular surface is intact. The patient remaining symptom free.

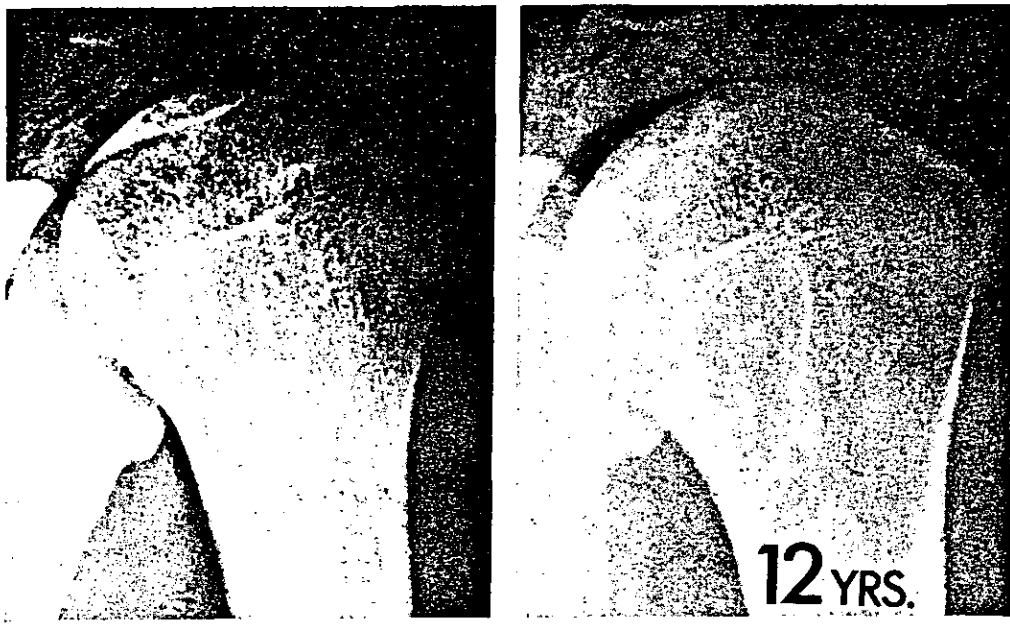



Fig. 4.39. Follow-up over 12 years. On the left ill-defined dense areas with an intact articular cortex. On the right, 12 years later, areas of increased density and the cortex has remained intact. Structural failure has not taken place and symptoms have not developed.

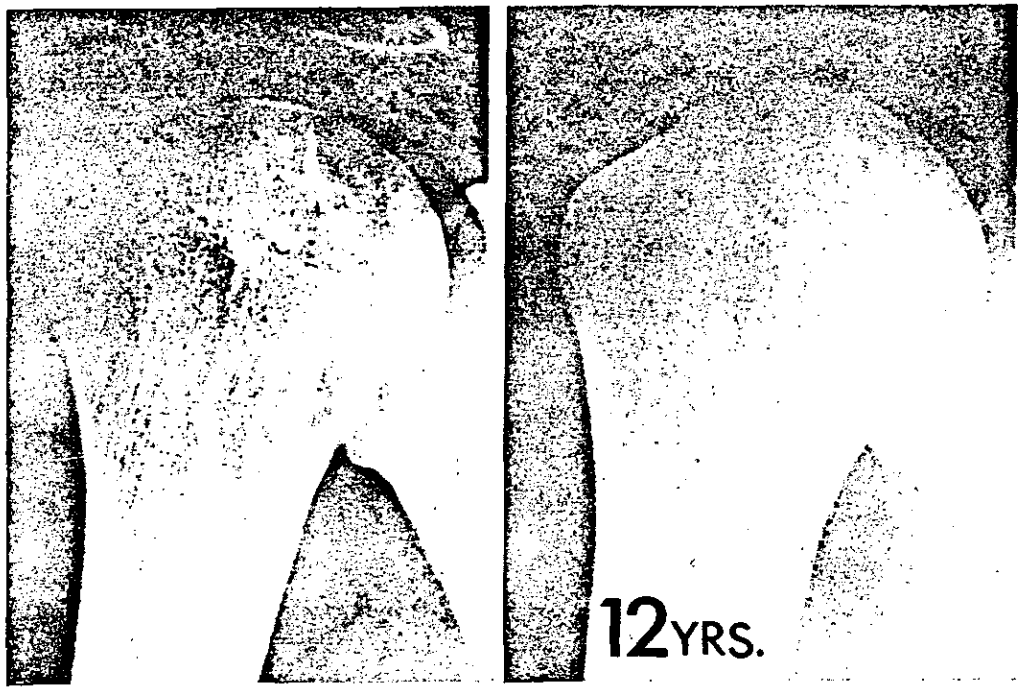



Fig. 4.40. On the left dense curvi-linear layer with an intact cortex. On the right, 12 years later the area of increased density has become slightly larger, extending towards the articular cortex which remains intact.

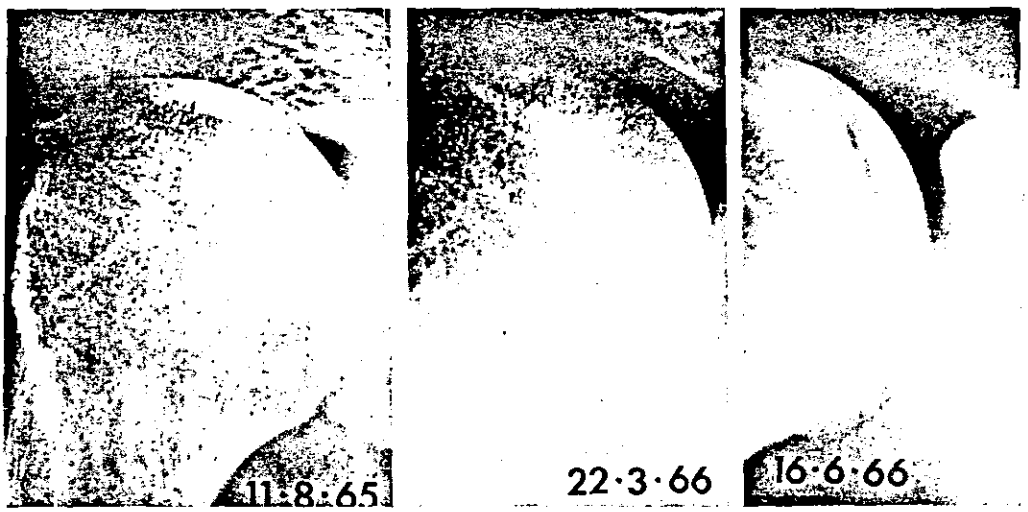



Fig. 4.41. On the left note bone island in the head of the left humerus with possible increase in density just inferior. In the centre dense layer is now becoming apparent just distal to the bone island. On the right, *10 months after the original radiograph*, a large part of the articular surface has sequestrated and deep to this a dense curvi-linear layer is more clearly defined on the tomograph.

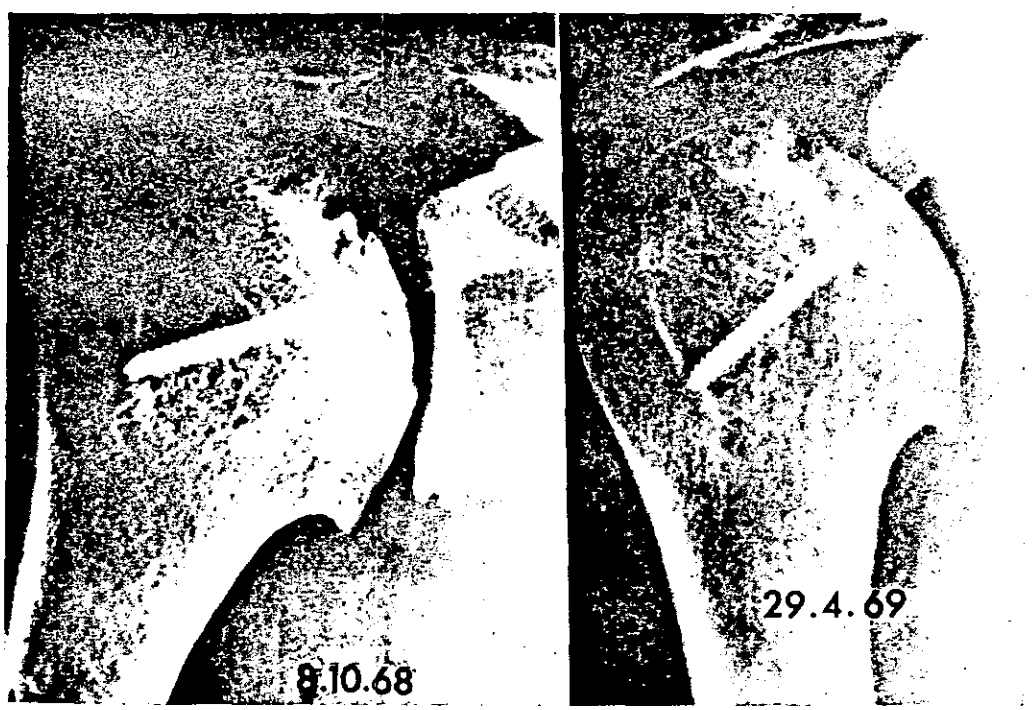



Fig. 4.42. Same case following fixation of the sequestrated area with a screw, secondary osteoarthritis is becoming apparent with marginal osteophytes developing inferiorly.


Fig. 4.43. Same case four years later.

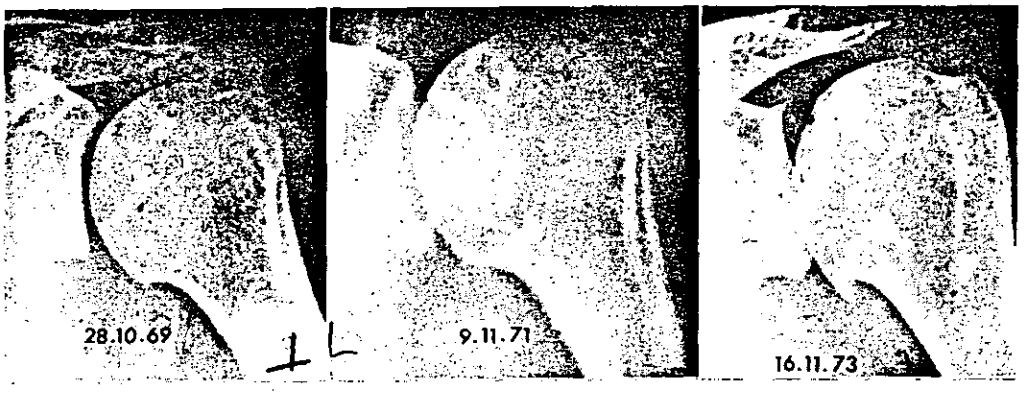



Fig. 4.44. Serial radiographs showing a dense layer with an intact cortex progressing to structural failure with sequestration and evidence of secondary osteoarthritis over four years.

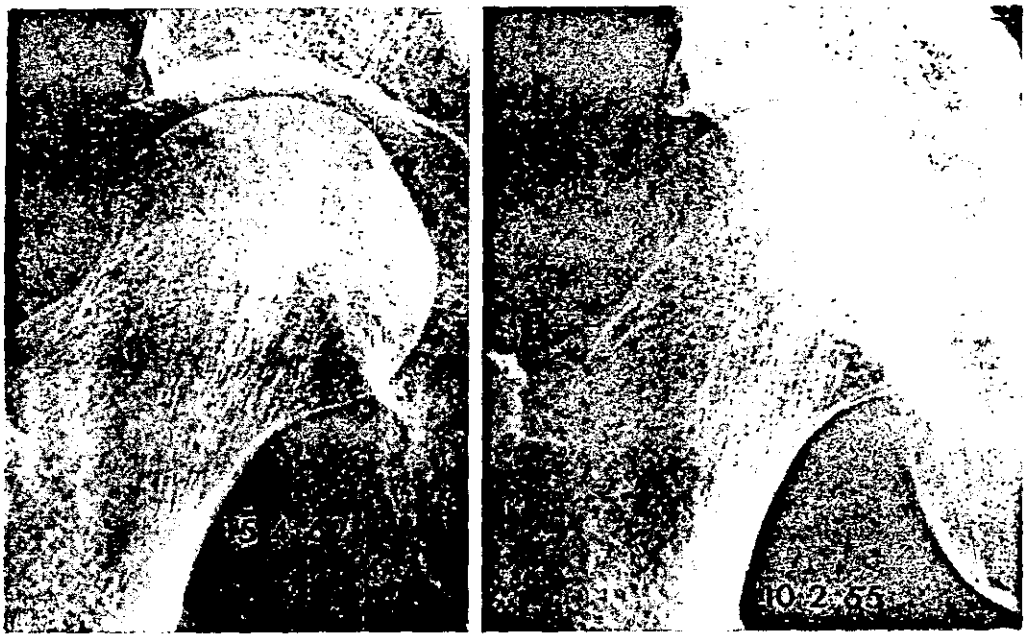



Fig. 4.45. On the left a normal radiograph of the left femoral head. On the right, almost three years later, dense layer becoming apparent enclosing the inferior part of the articular surface which remains intact.

Fig. 4.46. Same case two years later where tomography shows a serpiginous dense layer (arrow) with sequestration of part of the articular surface inferiorly (arrow).

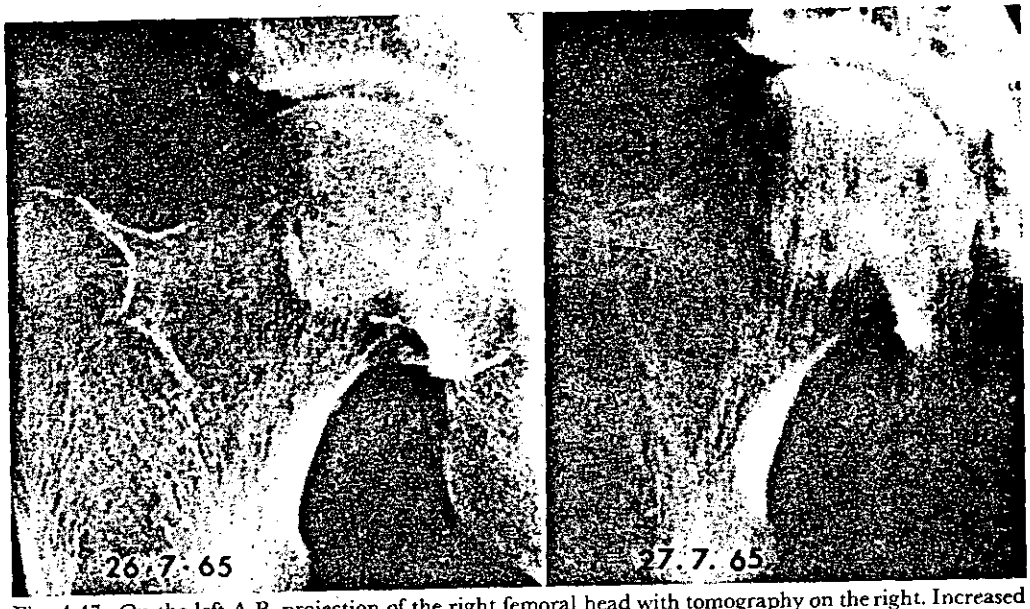



Fig. 4.47. On the left A.P. projection of the right femoral head with tomography on the right. Increased density involving a large part of the femoral head with an intact cortex.

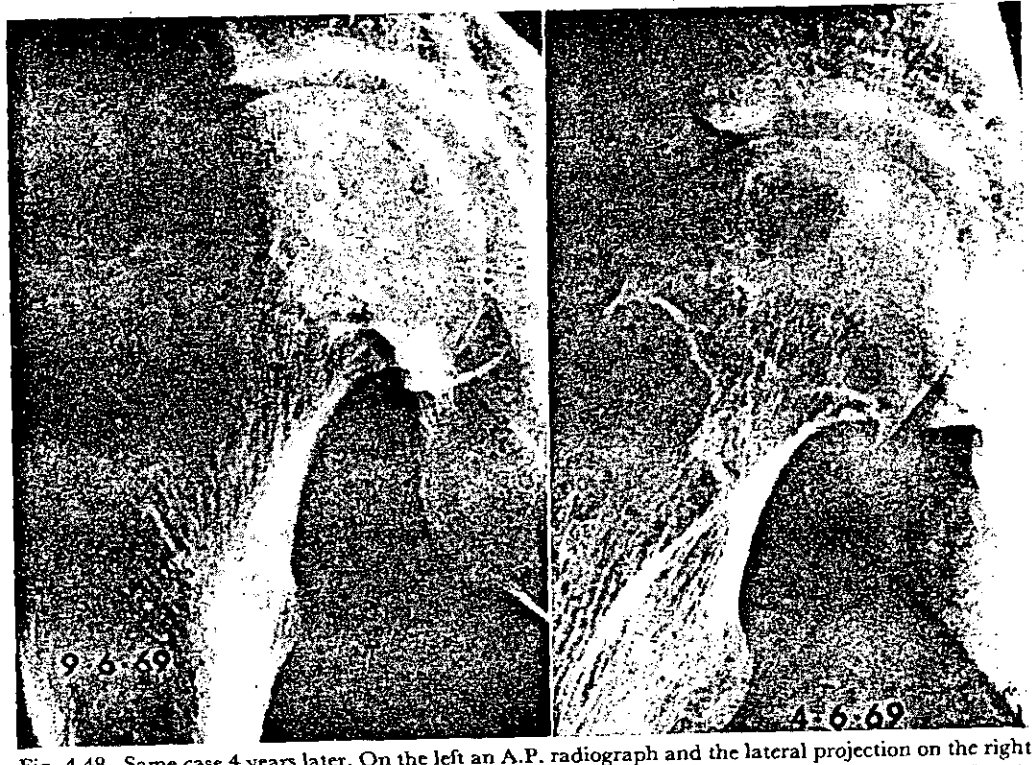



Fig. 4.48. Same case 4 years later. On the left an A.P. radiograph and the lateral projection on the right shows sequestration of a large portion of the postero-superior aspect of the articular surface. This is bounded by a dense serpiginous layer inferiorly.

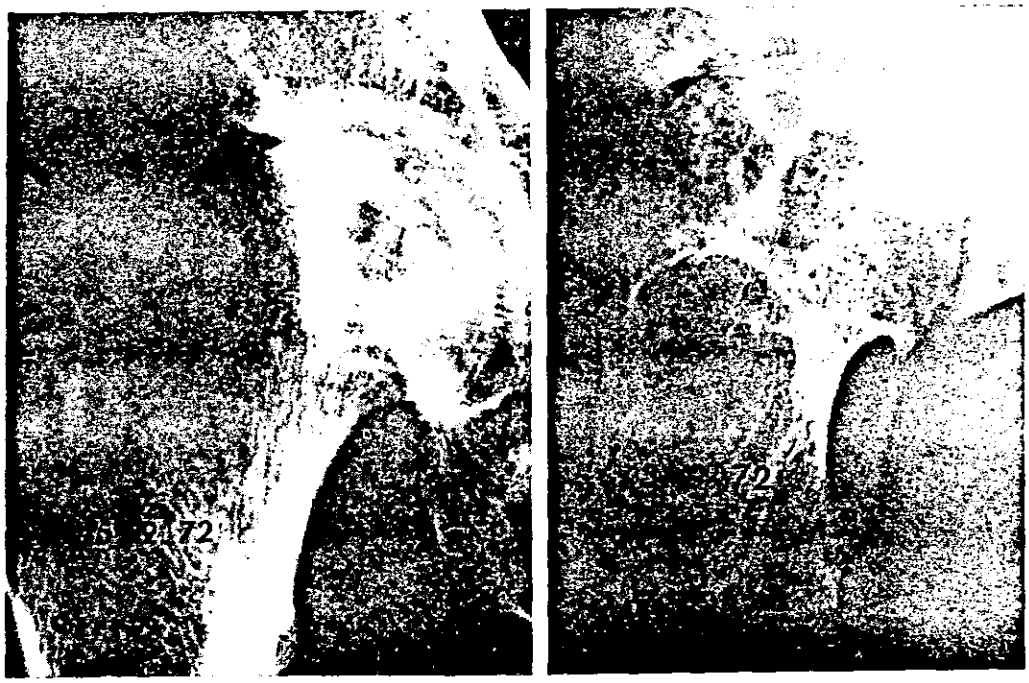


Fig. 4.49. Same case 7 years after the original radiograph with the sequestration, and increased density more prominent.

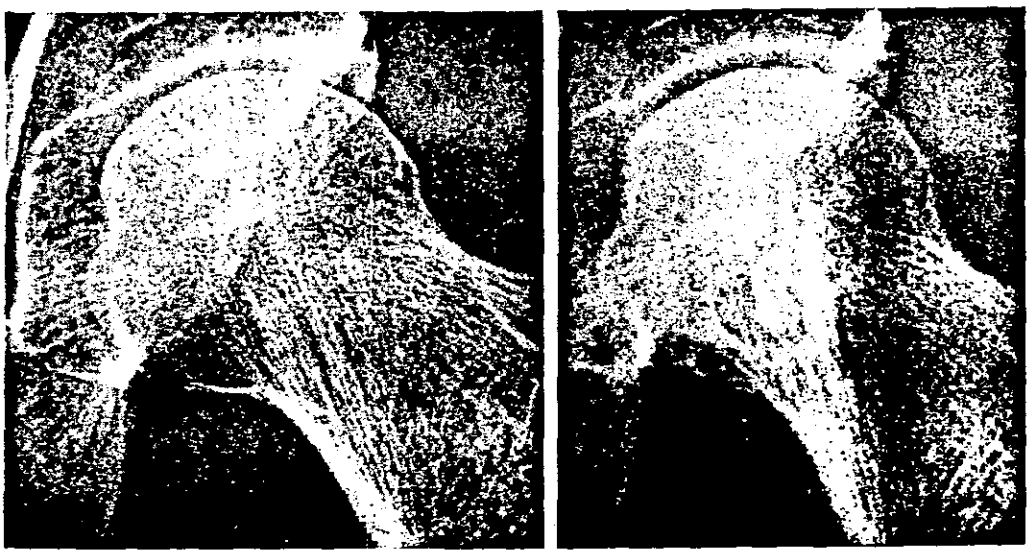


Fig. 4.50. On the left the femoral head shows no abnormality. On the right 2 years later a dense serpiginous layer involves the femoral head and extends into the inferior aspect of the neck.

Fig. 4.51. Same case as Fig. 4.50. On the left four years after the original radiograph, increased density of the femoral head is more marked. On the right, 8 years after the original radiograph, because of persistent pain and disability, an arthroplasty has been carried out with excision of the left femoral head.

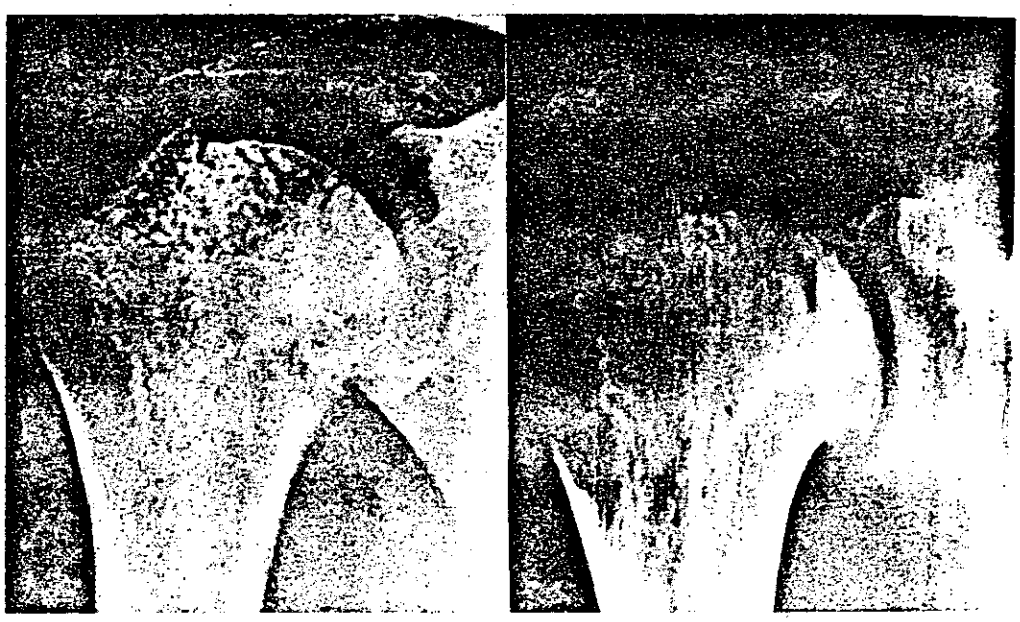


Fig. 4.52. Collapse of the articular surface of the right humeral head, more clearly defined on the tomograph (right). Several fragments have sunk into the underlying necrotic bone with 'step' formation of the margin and dense areas involve the head of the humerus and extend to the shaft. This 32-year-old man with no previous compressed-air experience was exposed for two consecutive days at the Clyde to pressures to 24½ p.s.i.g. On each occasion he had severe type I bends treated by recompression. Two years later he presented with pain in both shoulders and radiological examination demonstrated collapse of the articular cortex on the right and sequestration in the head of the left humerus.


Fig. 4.53. Same case as Fig. 4.52. On the left, two years after the original radiograph, insertion of bone chips and excision of the greater tuberosity. On the right, same case after the original radiographs


Fig. 4.54. Same case as 4.52 and 4.53. Originally there was sequestration of the head of the left humerus and eventually this arthroplasty was carried out.

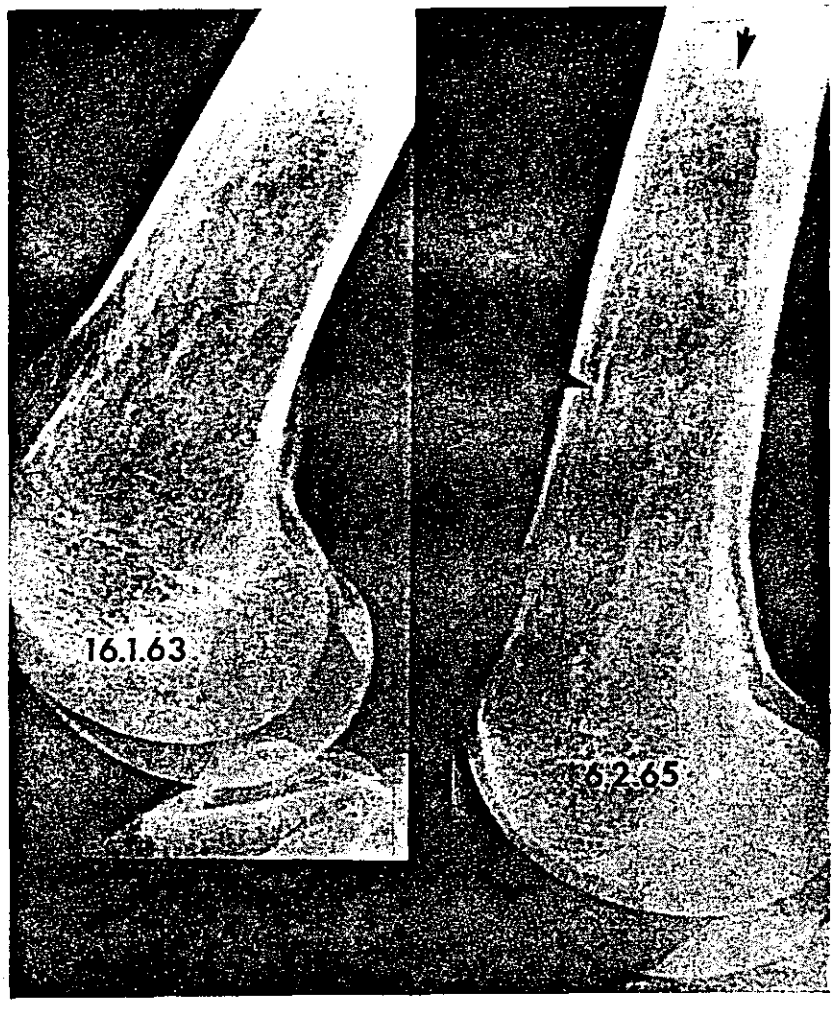



Fig. 4.55. Calcification developing in the distal shaft of the femur. On the left (16.1.63) no abnormality. On the right, (6.2.65) early calcification is present (arrows). Note the importance of good quality radiographs showing trabecular detail. If this is not present then early calcification will not be defined.

It has been possible to study the radiographs of two compressed-air workers of over 30 years experience. One showed extensive osteonecrosis of both humeral heads, both femoral heads and the distal shafts of both femora (Figs 4.58–4.62). The other had lesions in both humeral heads (Figs 4.63 and 4.64). Both are interesting in that the joint surfaces have remained intact and the patients are still symptom free. Radiologically, the lesions have developed as circumscribed patterns apparently enclosing a necrotic area.

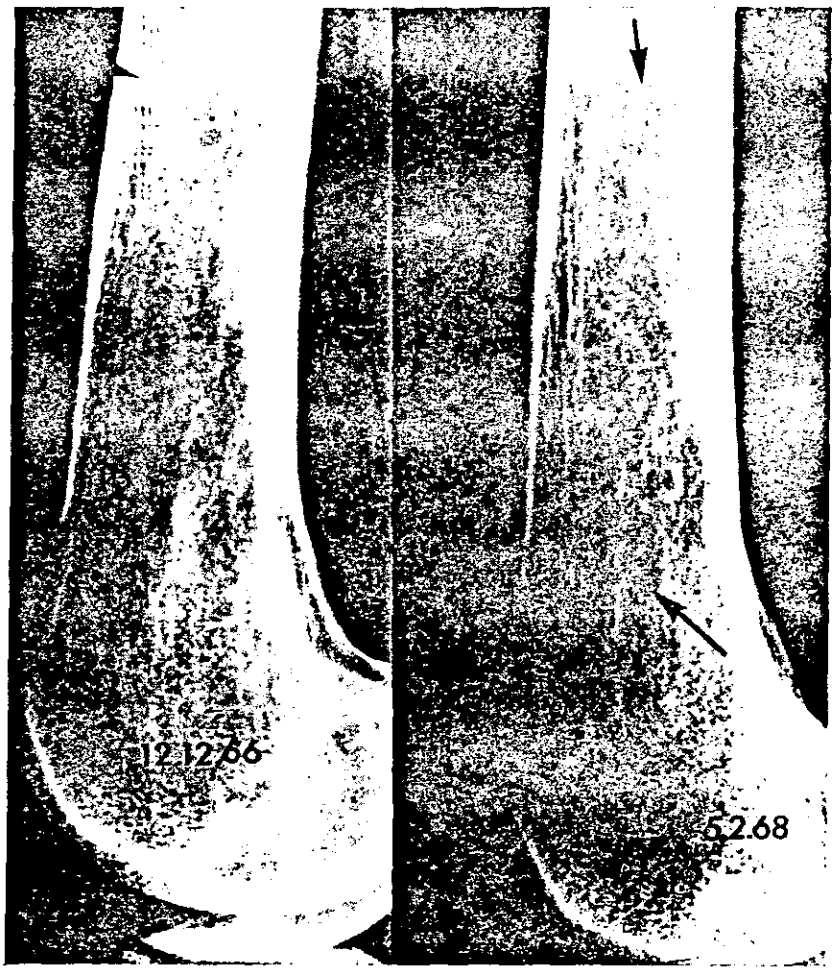



Fig. 4.56. Same case as Fig. 4.55. On the left, 12.12.66 calcification is more clearly defined. On the right 5.2.68 calcification now more marked occupying the full width of the medulla.

In the survey of 301 Japanese divers (Ohta and Matsunaga, 1974) changes in bone structure could be followed in 144 men who were examined at least twice during the three years survey. Sixteen lesions were classified as 'segmental opacities' and none advanced to a structural failure. However, of the six lesions classified as 'linear opacities', structural failure developed in five. Three further lesions, first classified as 'head, neck and shaft' lesions at the proximal end of the femur, were later classified as juxta-articular. The authors comment that these may have been originally juxta-articular because the lesion was not clearly defined at the early examinations. Ohta and Matsunaga modified the M.R.C. classification slightly.

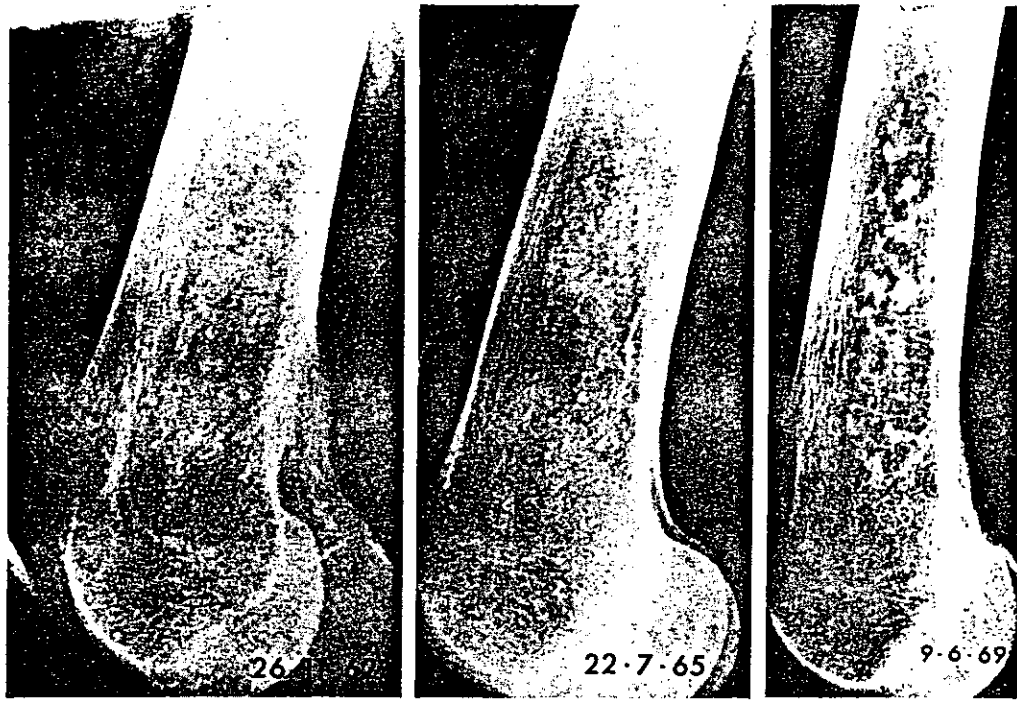
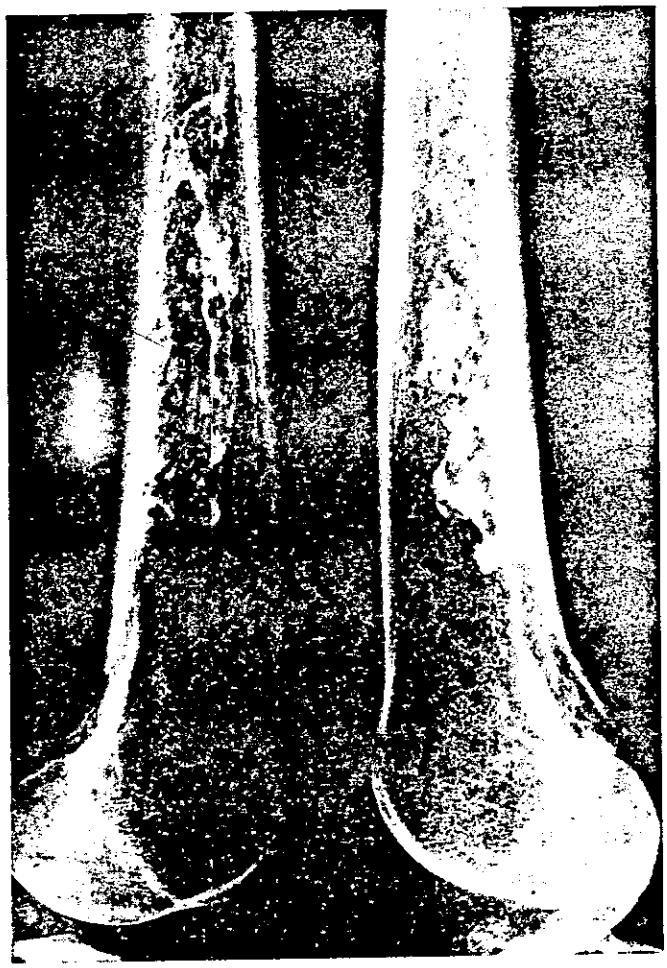



Fig. 4.57. Showing calcification developing in the distal shaft of the left femur over a 7 year period. On the left early calcification is, in fact, present. Again this would be missed on a poor quality radiograph.

Fig. 4.58. On the left A.P. projection of the left humeral head. On the right tomography giving better definition. Note serpiginous dense layer enclosing a large part of the head of the humerus adjacent to an intact articular cortex. Note also Figs. 4.59–4.62.



Figs 4.58–4.62. This man worked for approximately two years in compressed air about thirty years previously and had not been exposed to a hyperbaric environment since. Bone necrosis involves both femoral heads, both humeral heads and the distal shafts of both femora. The articular surface has remained intact and there are no joint symptoms. Attending hospital with chronic bronchitis and emphysema. Skeletal radiographs taken because of previous occupational history.

Fig. 4.59. Extensive bilateral calcification occupying the full width of the medulla and the distal shaft of the femur.

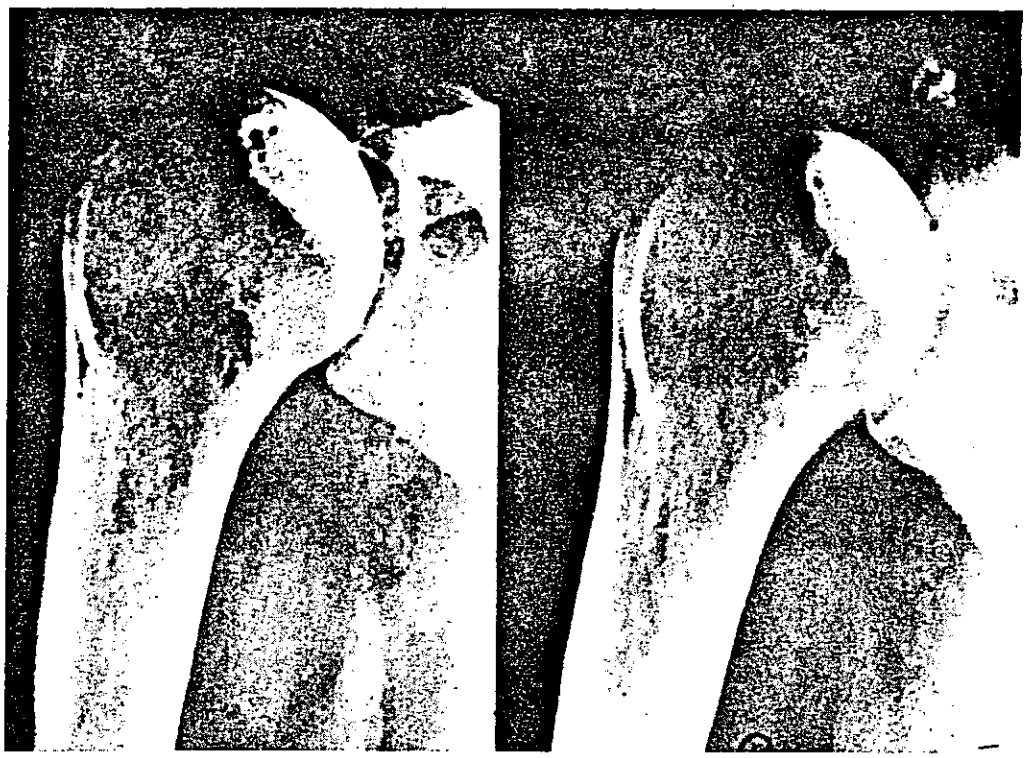


Fig. 4.60. A.P. radiograph and tomograph of the right humeral head showing serpiginous dense layer enclosing a large part of the head with an intact cortex.

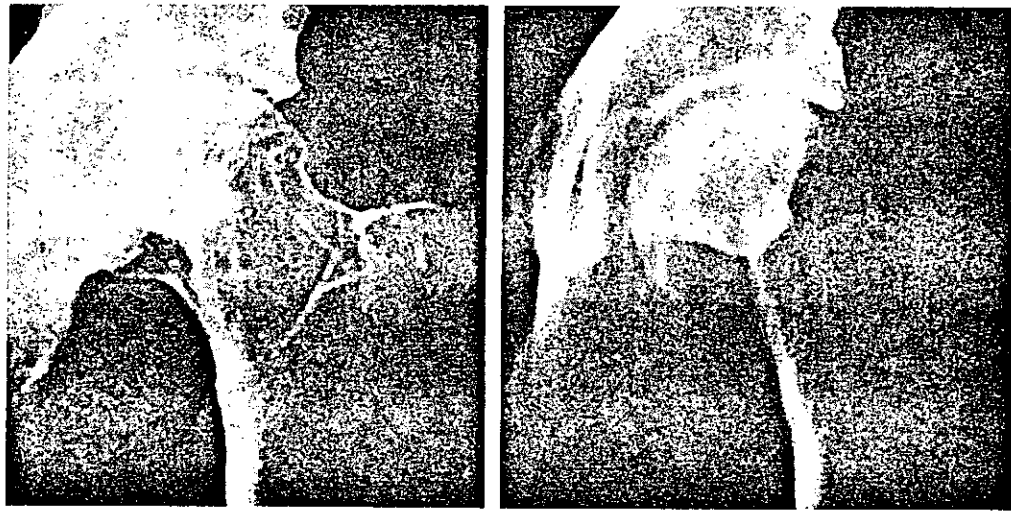


Fig. 4.61. A.P. radiograph and tomograph of the left femoral head showing serpiginous dense layer enclosing a large part of the head of the femur and intact cortex.

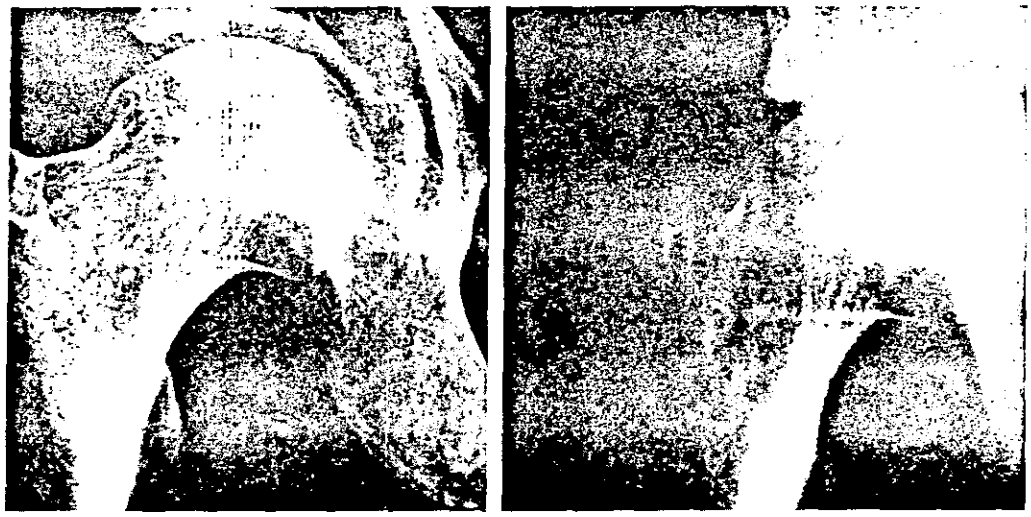


Fig. 4.62. A.P. radiograph and tomograph of the right femoral head showing serpiginous dense layer enclosing a large part of the head of the femur and intact cortex.


Fig. 4.63. (Left) Tomograph defining a dense layer enclosing an oblong area in the head of the right humerus with an intact cortex. Note also increased density in the proximal shaft of the right humerus.

Fig. 4.64. (Right) Same case as Fig. 4.63. Radiograph 6 years later showing increased density virtually unchanged. This man has more or less continuous experience in compressed air over almost 30 years.

### 4.9 Frequency of lesions

Regarding frequency, while it is known that lesions will progress through their natural history and that radiology only records that particular episode, it is of value to know how often one might except to find various types of radiographic abnormality when carrying out survey work.

In July 1972 the Registry had skeletal survey radiographs of 1694 compressed-air workers, 334 of whom showed 820 positive lesions. The frequency of these lesions is as follows:

| Lesion | Frequency (%) | Symptoms |
|---|---|---|
| Juxta-articular (4.7.1) | | |
| Dense area with an intact articular cortex (4.7.1.1) | 15½ | absent |
| Spherical segmental opacities (4.7.1.2) | 5 | absent |
| Linear opacity (dense layer) (4.7.1.3) | 6½ | absent |
| Structural failure (4.7.1.4) | | |
| (a) translucent subcortical band | ½ | present |
| (b) collapse of the articular cortex | 2 | present |
| (c) sequestration | 3 | present |
| Osteoarthritis (4.7.1.5) | 5 | present |
| Head, neck and shaft (4.7.2) | | |
| Dense area (4.7.2.1) | 20 | absent |
| Irregular calcified area (4.7.2.2) | 40 | absent |
| Translucencies and cysts (4.7.2.3) | 2 | absent |
| Cortical thickening | – | – |

#### 4.9.1 Prevalence in compressed-air workers

Estimates of the prevalence of bone lesions in compressed-air workers vary from zero (Lewis and Paton, 1957) to 75% (Bell et al., 1942). Many publications report the results of radiographic examinations on selected groups and consequently the incidence of bone lesions will be high. For this reason the radiographic surveys carried out by the M.R.C. Decompression Sickness Panel at the Dartford Tunnel (Panel Report 1960); at the Clyde Tunnel (Panel Report 1966) and the Tyne Road Tunnel (Panel Report 1971) are of particular interest, the object being to radiograph as many men as possible including those with previous experience in compressed air and those who have had none. The main problems in determining the number of men affected by bone lesions, apart from the fact that it is a voluntary procedure, are that it is difficult to carry out radiographic examination of all men at risk, and that follow-up radiographs are required for several years after ceasing work in compressed air. It is known that in this type of civil engineering work there is an exceptionally high turnover of the labour force, due partly to the arduous nature of the work and also to the fact that a large number are itinerant labourers. For example, at the Dartford Tunnel altogether 1200 compressed-air workers were employed, while the total labour force was never more

than 320 men at any one time. A total of 1362 men were employed at the Clyde Tunnel and 55% left after less than four months.

Hospital X-ray departments are often at some distance from a tunnel site and only a few men can be persuaded to attend usually because this has to be done in their spare unpaid time. This difficulty was overcome at the Tyne Road Tunnel where X-ray apparatus was installed in the medical centre. However, it is not always possible to staff these units on a full-time basis. Surveys have been more successful at other civil engineering contracts where a commercial portable X-ray unit visits the site for a continuous period of one or two weeks. Men can then have their radiographic examination before or at the end of a shift which may be at any time of the day or night.

At the Clyde Tunnel the 241 men included in the survey were those remaining towards the end of the contract in which a total of 1362 workers had been employed. Forty-seven men (19%) of the 241 examined had a bone lesion and the lesion was next to the joint surface in 25 of these men (10%) and so liable to cause symptoms. Of the 241 men, 18 had previous experience of compressed air and of these nine (50%) had a bone lesions. Of the remaining 223 with no previous experience in compressed air, 38 (17%) had a bone lesion.

At the Tyne Road Tunnel 171 of the 641 men employed in the contract were studied. Seventy-nine men (17%) had a definite bone lesion and in 20 of these (12%) the lesions were next to a joint surface. Of the 171 men, 47 were known to have worked in compressed air before and of these, 14 (29.8%) had a definite bone lesion; in the remaining 124 men without previous exposure to compressed air, 14 (12.1%) had a definite lesion.

One of the major difficulties is that it is impossible to identify the causative exposure. It is clear that the pathological process results from an ischaemic episode which appears to be painless. It is estimated that about 4 to 12 months should elapse between the causative episode and the time when bone changes are radiologically evident. The interval depends on the extent of the necrotic area, the amount of revascularisation with laying down of new bone, the thickness of the overlying tissues and, not least, the quality of the radiograph.

When comparing the prevalence of bone necrosis in various contracts it is necessary to consider the interval between the man's first exposure to compressed air at a critical pressure and the radiographic examination, to be certain that sufficient time has elapsed for a bone lesion to become apparent radiologically. For example, when comparing groups of men without previous experience in compressed air, if the average interval between the first exposure and the radiographic examination was 1½ years at one centre, and only nine months at another, then the figures would not be strictly comparable. From the studies at the Clyde and the Tyne Tunnels the proportion of men with bone lesions is higher in men with previous experience than in those without experience. This could mean that the lesions have had time to become apparent or that the previous experience was either more extensive or at higher pressures.

An interesting study at the Tyne Road Tunnel related the time of detection of bone lesions to the first exposure to compressed air. No bone lesions were demonstrated in men who were examined within the first three months after exposure. One had a suspected lesion six months after starting work and the first definite lesion was evident nine months after the first exposure. In those with twelve months experience, two had

definite osteonecrosis and two were thought to have suspected lesions. At 15 months yet two more men had definite lesions. Further cases of definite osteonecrosis were found in those with eighteen months experience (one case): twenty-four months experience (three cases) and twenty-seven to thirty-nine months experience (six cases).

In 1972 the M.R.C. Decompression Sickness Registry had radiographs of the shoulders, hip and knee joints of 1694 compressed-air workers. Three hundred and thirty-four men (19.7%) had positive lesions. In many other cases it was not possible to be certain whether or not definite osteonecrosis was present and in 229 men (13.5%) a diagnosis of suspected osteonecrosis was made. Seventy-five of these men were subsequently re-classified as positive on follow-up over five to six years. In the U.S.A., Nellen and Kindwall (1972) reported a 35% incidence of osteonecrosis in 169 compressed-air workers employed in Milwaukee, many of whom had been treated for decompression sickness. The overall incidence of juxta-articular lesions was 25%.

Dysbaric osteonecrosis is undoubtedly a major health hazard to compressed-air workers. Young men, often in their twenties, may be severely and permanently disabled. The success of the decompression procedure should no longer be judged by the incidence of Type I decompression sickness (the bends rate) but by the incidence of potentially serious Type II and of bone lesions.

*4.9.2 Prevalence in divers*

Numerous publications report osteonecrosis in divers. Of the ninety German divers reported by Herget (1948a, b, 1952), twenty-nine had dysbaric osteonecrosis. In 1953 Slordhal examined thirteen civilian divers in Norway and found that three had osteonecrosis. In Germany, Alnor (1953) found 72 cases of osteonecrosis among 131 divers, the interesting point being that of 65 men followed for more than 10 years, only 22 managed to remain clear of bone necrosis. Of the 43 with lesions, 17 had symptoms and 7, in fact, were no longer able to work. In 29 Bulgarian divers reported by Kiryakov (1964), bone lesions were demonstrated radiographically in 19. Fournier and Jullien (1965) considered the incidence of bone lesions in French divers to be more than 17% having found lesions in 22 divers in a series of 132 men.

From Japan, Asahi (1968) examined a group of 79 men who had been diving for sea food since the ages of 15–16 years. The radiographic examination included views of both femoral heads, both humeral heads and both knees and, when interpreting the radiological appearances, the classification adopted by the M.R.C. Decompression Sickness Panel was used. Osteonecrosis was found in 15 (19%). The incidence was 28.6% in those with a longer diving experience of over three years. A similar report by Ohta and Matsunaga (1974) described the results of a radiographic survey of 301 fishermen also diving for sea food in another part of Japan. Positive osteonecrosis was found in 15% of divers aged 16–19 years and in 76% of those over 40 years of age. The overall incidence of osteonecrosis was 50.5%. These men dive many times a day and know little of the physiological problems involved or the correct methods of decompression. Each year three to five men died from accidents or from decompression sickness.

Probably the most interesting report was that by Elliot and Harrison (1970) who

carried out radiographic skeletal surveys on as many divers in the Royal Navy as possible. Of the 350 symptomless men examined, 14 were found to have definite evidence of osteonecrosis, an incidence of 4%. This incidence is much less than in the commercial divers in Japan, the reason being that surveillance and regulations are strict, whereas there were no regulations for shell divers in Japan. The M.R.C. Decompression Sickness Registry in 1974 had skeletal radiographs of 604 commercial divers and definite evidence of osteonecrosis was present in eighteen (3%). Of 420 men who had dived to depths below 180 feet, 17 were found to have osteonecrosis, an incidence of just over 4%.

Dysbaric osteonecrosis is undoubtedly a hazard in diving. In a well supervised environment the incidence appears to be much less than in compressed-air workers.

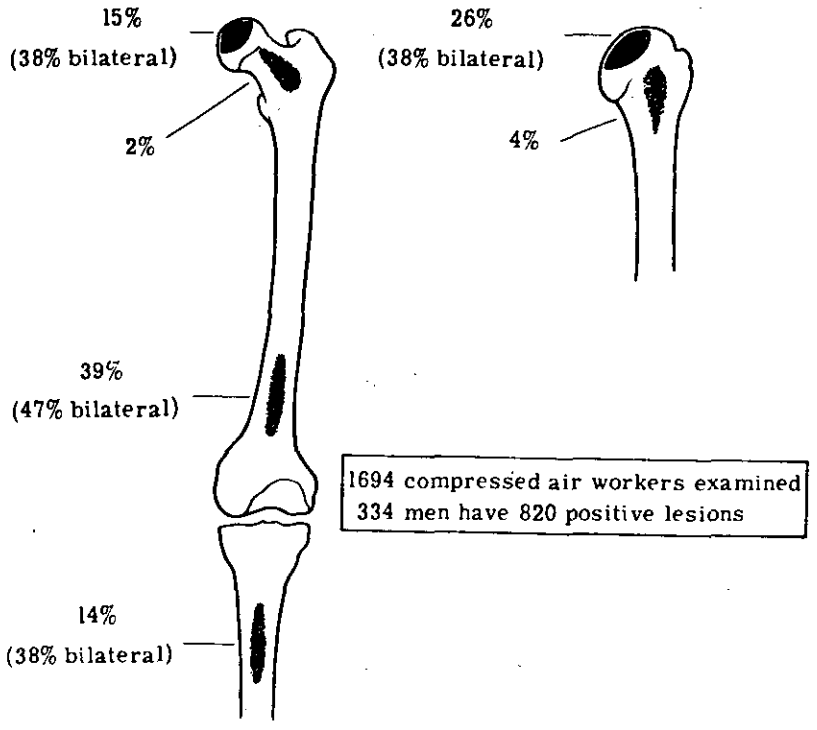
*4.9.3 Prevalence in low-pressure environment*

Amongst those exposed to pressures below atmospheric, Coburn (1956) found a 15.5% incidence of osteonecrosis in 40 low-pressure chamber operators in the U.S. Navy and the changes are reported to be similar to those following exposure to compressed air. Berry and Hekhuis (1960) could find no evidence of osteonecrosis in a radiographic survey of 579 low-pressure chamber operators in the U.S. Air Force. Radiographic examination included the shoulder, hip and knee joints and approximately half of the men had experienced decompression sickness. As a follow-up, Hodgson et al. (1968) contacted 164 of the 579 men originally examined and a bone lesion was demonstrated in the distal shaft of the femur in one man and the proximal shaft of the humerus in another. The lesion in the femoral shaft was present at the earlier survey but apparently less well defined. In the other case the shaft of the proximal humerus had not been fully included at the original examination. In a subsequent paper, Coburn (1970) commented on the possibility of having included 'normal' bone islands as positive evidence of osteonecrosis in his report in 1956. He indicated that U.S. Navy Personnel were having more frequent decompressions and that while osteonecrosis occurs in those exposed to pressures below atmospheric it is extremely rare.

*4.10 Distribution of lesions in compressed-air workers*

The Decompression Sickness Registry in 1972 had skeletal radiographs of 1964 compressed-air workers. Of these, 334 men had 820 positive lesions. The distal shaft of the femur was the most common sites with 39.0% of all lesions and 47% were bilateral (Fig. 4.65). The next most frequent site was juxta-articular lesions in the humeral head with an incidence of 26% and of these 38% were bilateral. Juxta-articular lesions in the femoral head formed 15% and 14% of lesions were in the shaft of the tibia. Over a third of all lesions were bilateral. Lesions were not significantly more numerous on one side than on the other. Symptoms and disability arise from those juxta-articular lesions which develop structural failure at a joint surface. Fortunately, these lesions situated in the distal femoral shaft remain symptomless. More than half of the affected compressed-air workers have more than one bone lesion. The prevalence of multiple bone lesions was studied in 281 compressed-air workers with 629 lesions.

DYSBARIC OSTEONECROSIS




M.R.C. Decompression Sickness Registry — July 1972

Fig. 4.65. Showing distribution of bone lesions in 1694 compressed-air workers.

Very few of the earlier reports on compressed-air workers included radiographic surveys and consequently it is not possible to get any idea of the distribution of lesions.

| Number of lesions/man | Number of men | % Total men affected |
|---|---|---|
| 1 | 114 | 40 |
| 2 | 75 | 27 |
| 3 | 34 | 12 |
| 4 | 38 | 13 |
| 5 | 13 | 5 |
| 6 | 4 | 3 |
| 7 | 2 | |
| 8 | 1 | |
| TOTAL | 281 | 100 |

Often the radiographic examination only included the affected joint. For this reason the attempted survey work of the M.R.C. Decompression Sickness Panel is of particular value in assessing the frequency and site of lesions.

### *4.11 Distribution of lesions in divers*

In the survey of 301 Japanese divers (Ohta and Matsunaga, 1974), 152 men had 231 lesions. Again the commonest site was the distal shaft of the femur followed by the head of the humerus and then the head of the femur (Fig. 4.66). The authors report a greater number of head, neck and shaft lesions in the head of the humerus and the head of the femur than in other series. Lesions of the upper humerus and femur were more frequently unilateral than bilateral but not significantly more numerous on the right than on the left. As in compressed-air workers approximately one-third of all lesions were bilateral. Sixty of the divers (39.5%) had a solitary lesion and 92 (60.5%) had multiple lesions.

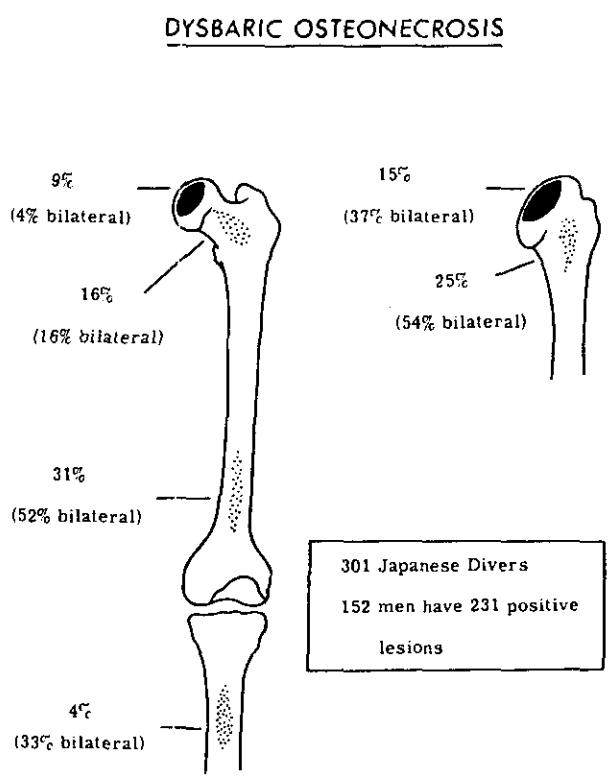



Fig. 4.66. Showing distribution of bone lesions in 301 Japanese divers.

Elliot and Harrison (1970) in their review of 350 Royal Navy divers found 37 lesions in 14 divers and the head of the humerus was the most common site. The Decompression Sickness Registry has radiographs of 604 commercial divers and 18 men were found to have 19 lesions between them. Eight lesions were juxta-articular in the head of the humerus and 10 were in the distal shaft of the femur. The lesions were bilateral in one case.

### *4.12 Relation of bone lesions to occupational history*

#### *4.12.1 Working pressure and number of decompressions in compressed-air workers*

When the incidence of bone lesions is related to the pressure of air it is quite clear that lesions are more common in those who have worked at a higher pressure and also in men who have experienced a greater number of exposures. From the data available both these factors are compounded because contracts with a high pressure of air normally continue for a longer period and consequently the number of exposures is greater.

The following data from the Clyde Tunnel relates the maximum pressure and number of decompressions.

Bone lesions and maximum pressure experienced

| Maximum gauge pressure (p.s.i.g.) | Men with bone lesions | Men without bone lesions | Total |
|---|---|---|---|
| 18 | 1 (6%) | 17 | 18 |
| 25 | 3 (10%) | 27 | 30 |
| 30 | 10 (11%) | 83 | 93 |
| 34 | 24 (29%) | 58 | 82 |
| Total | 38 (17%) | 185 | 233 |

There is a significant association between lesions and pressure. ($\chi^2 = 14.0$, d.f. $= 3$, $P = 0.01$)

Bone lesions and decompressions

| Number of decompressions | Men with bone lesions | Men without bone lesions | Total |
|---|---|---|---|
| 300 | 5 ( 8.6%) | 53 | 58 |
| 300–599 | 4 ( 7.4%) | 50 | 54 |
| 600–899 | 8 (19.0%) | 34 | 42 |
| 900 and over | 21 (30.4%) | 48 | 69 |
| Total | 38 (17.0%) | 185 | 223 |

There is a significant association between lesions and number of decompressions. ($\chi^2 = 15.3$, d.f. $= 3$, $P = 0.01$).

So far no bone lesions have been detected in men who have only been exposed to pressures of less than 2.16 ATA (17 p.s.i.g.)

*4.12.2 Relation of bone lesions to diving depth*

Of the 604 commercial divers whose records are held by the Decompression Sickness Registry, only one man was found to have a bone lesion of the 184 who have dived to only 180 feet or less. Osteonecrosis was found in 17 of the 420 men who had dived to depths deeper than 180 feet. All the 420 men diving to a depth greater than 180 feet have five years or more experience – the average being twelve years. At a level of about 180 feet a change is usually made from air to an oxyhelium mixture.

Ohta and Matsunaga (1974) in their survey of 301 divers found it difficult to obtain precise information about diving experience. However, statements regarding maximum working depths were accepted. In general lesions increased in proportion to the depth of diving with a significantly higher incidence in those who dived over 100 feet. The incidence also increased in proportion to the length of diving experience, being highest in men with over ten years experience. Moreover, the incidence of lesions was higher in those who had a history of decompression sickness but no significant statistical relationship could be established.

*4.12.3 Relation of bone lesions to duration of exposure in compressed-air workers*

In the United Kingdom the standard shift length is of eight hours duration. While the majority of men work a full shift of six to eight hours there is a group of non-shift workers – electricians, carpenters and engineers etc. who usually spend shorter periods in compressed air. There are no reliable data of the incidence of bone lesions in these men who have worked as non-shift workers because on occasions they do work full shift. The length of working shift is important when comparing the effectiveness of procedures in this country with those in the U.S.A. where decompression times are longer and the shift length is reduced as the pressure increases. Moreover a split shift system is used in certain States (Nellen and Kindwall, 1972).

*4.12.4 Relation of decompression sickness to bone lesions*

Roszahégyi and Fried (1963) showed a relation between decompression sickness and bone necrosis. While there appears to be some relationship between the history of Type I bends and the bone lesions it is not absolute. Several factors must be taken into consideration. The diagnosis and treatment of Type I or Type II bends depends on the man reporting his symptoms and then being treated. In most contracts only those cases treated by recompression are recorded. Many may experience mild symptoms, 'the niggles', and prefer to manage these with analgesics or alcohol rather than be recompressed. Moreover, men are not paid for time spent under treatment.

While there is no precise relationship between the incidence of Type I decompression sickness and bone lesions, significantly more of the men with bone lesions have been treated for Type I decompression sickness.

Bone lesions and bends

| | Bends | No bends | Total |
|---|---|---|---|
| Men with bone lesions | 17 | 21 | 38 |
| Men without bone lesions | 25 | 160 | 185 |
| Total | 42 | 181 | 223 |

($\chi^2 = 18.1$, d.f. = 0.001)

A man who has never been recompressed for decompression sickness may develop a bone lesion and one with frequent treatment for 'bends' may never develop a bone lesion. An interesting point is that bone lesions are more liable to occur when the attack of 'bends' has required several recompressions to cure rather than after the attacks which only require one recompression.

The incidence of bone lesions in compressed-air workers following a single attack of bends

| | Single recompression required | Multiple recompressions required | Total |
|---|---|---|---|
| Men with lesions | 11 | 14 | 25 |
| Men without lesions | 32 | 10 | 42 |
| Total | 43 | 24 | 67 |

($\chi^2 = 7.06$, d.f. = 1, $P = 0.01$

The number of bone lesions included is small but the criteria for selection were so rigorous – only men known to have been recompressed after one attack of decompression sickness and who have subsequently developed a bone lesion could be included.

### *4.13 Relation of bone lesions to age*

Many of the men who developed bone lesions are under thirty years of age. At the Clyde Tunnel the distribution amongst those with no previous experience in compressed air is as follows: 20–24 years, 3; 20–29 years, 11; 30–34 years, 8; 40–44 years, 4; 45–49 years, 2.

At the Tyne Road Tunnel three men – all between the ages of 22 and 34 years – were known to have severe bone necrosis of the femoral heads and still had marked disability after surgical treatment.

### *4.14 Relation of bone lesions to fatness*

It has been held for long that fat men are liable to decompression sickness. Boycott et al. (1908) drew attention to this and quoted Vernon (1907) who pointed out that nitrogen dissolves five times more easily in fatty tissues.

Measurements of skin-fold thickness were made and related to bone lesions at the

Tyne Road Tunnel and no relationship was found between bone lesions and either fat score or the lean score.

## *4.15 Differential diagnosis of bone lesions*

The radiographic changes of dysbaric osteonecrosis must be differentiated from other causes of aseptic necrosis of bone, possibly the most common being necrosis developing in the femoral head following either dislocation of the hip or from fracture of the femoral neck. Other conditions associated with bone necrosis must be borne in mind – steroid therapy; sickle cell anaemia; osteochondritis dissecans and Gaucher's disease. Idiopathic necrosis of the femoral head is considered to be a rare condition in Britain.

Osteoarthritis of the shoulder joint may give rise to difficulties in differential diagnosis. While this is an uncommon site for osteoarthritis, typical changes include narrowing of the joint space, marginal osteophyte formation and subarticular sclerosis. It is the subarticular sclerosis which can be confused with the increased density in osteonecrosis (Fig. 4.67). In dysbaric osteonecrosis the joint space is not likely to be diminished at least in the earlier stages (Fig. 4.68).

Fig. 4.67. Osteoarthritis of the left shoulder joint. Note narrowing of the joint space, osteophyte formation inferiorly, both on the articular surface of the humerus and on the glenoid. Note also subarticular increased density.

Calcification in the shaft of the bone must be differentiated from an enchondroma (Fig. 4.69) and in the early stages this can be extremely difficult, particularly with a poorly calcified enchondroma. Faint, fine short linear strands over an area 2–3 cm in diameter favour osteonecrosis, while foci of calcification in the medullary enchondroma tend to be more circular, whorled and are in close apposition, covering a smaller area. In the later stages differentiation is much more easy as the calcification in osteonecrosis occupies an area up to 4–5 cm in length and often the whole width of the medulla.

Where there is definite evidence of osteonecrosis in a man who has been exposed to a hyperbaric environment and particularly when the lesions are multiple and bilateral, then dysbaric osteonecrosis is a likely diagnosis. It is important to exclude other causes and enquiries should be made concerning any earlier fracture of the femoral neck or dislocation of the hip, previous cortisone therapy and any history of heavy drinking. The possibility of hepatic cirrhosis, pancreatic disease, and rheumatoid arthritis or gout should also be borne in mind. Laboratory investigations should include

Fig. 4.68. Severe osteoarthritis of the right hip joint with partial subluxation. Note the marked narrowing of the joint space, subarticular sclerosis, both sides of the joint space involving the femoral head and the acetabulum and note also the marginal osteophytes superiorly.

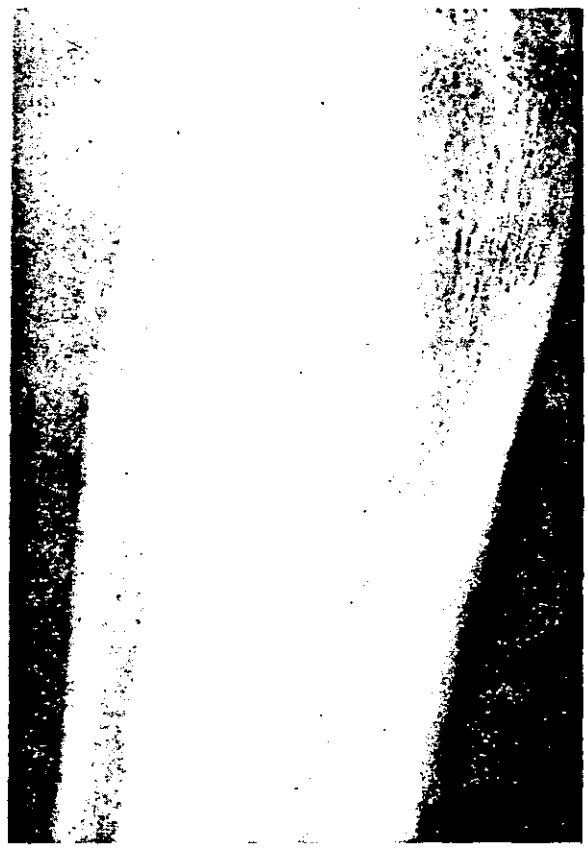


Fig. 4.69. Circular and whorled areas of calcification lying in close apposition covering the small area in the shaft of the tibia. This is likely to be an enchondroma.

liver function tests, blood sugar estimations, haemoglobin studies to exclude haemoglobinopathy, and serology to exclude rheumatoid arthritis or syphilis. If other causes have been excluded then the diagnosis of dysbaric osteonecrosis can be made with confidence.

Differentiation from a bone island may be difficult. They are usually compact, ovoid or oblong in shape with well-defined margins and usually remain unchanged in appearance (Figs 4.70 and 4.71) Occasionally they may enlarge (Fig. 4.72; Kim and Barry, 1964). The difficulties arise when trying to identify the earliest changes of osteonecrosis which appear as small areas of increased density which tend to be irregular in shape with an ill-defined margin and may have thickened trabeculae running through them (Fournier and Jullien, 1959; Mosinger and Jullien, 1961). Good quality radiographs demonstrating trabecular detail are essential in identifying the earliest changes of osteonecrosis. Tomography can be of help in defining these lesions more clearly.

To assess whether bone islands were more common in commercial divers, the Decom-

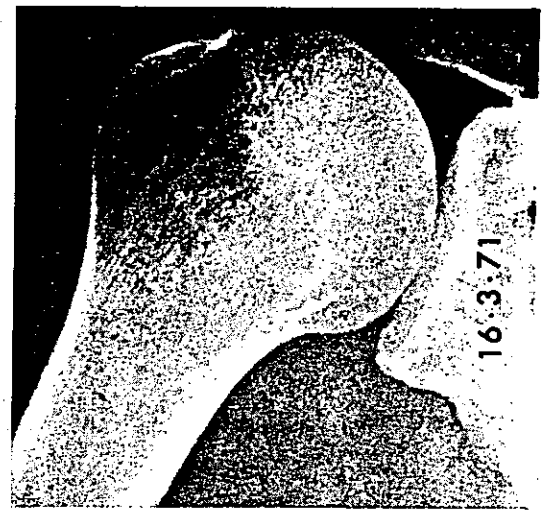



Fig. 4.70. (Left) Well-defined bone island in the intertrochanteric area of the right femur. Note also sclerosis of the superior aspect of the femoral neck with a small cyst surrounded by a sclerotic margin.

Fig. 4.71. (Right) Small bone island in the head of the right humerus overlying the anatomical neck.

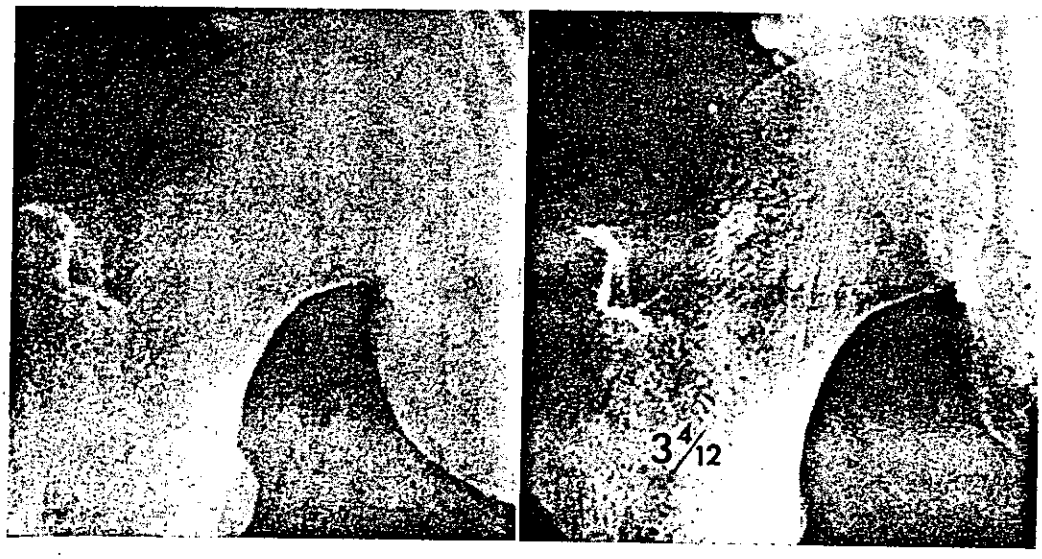



Fig. 4.72. Bone island superiorly in the left femoral neck, probably increasing in size over three years and four months.

pression Sickness Registry reviewed 100 commercial divers within the age group 23–40 years, all having had at least four years experience and having dived to 100 feet or more. These were compared with 100 controls of the same age group who had been declared medically fit to dive or to work in compressed air and were examined radiologically before being exposed to pressure. Bone islands were found in 40 divers and 36 controls. In addition, multiple bone islands were present in 19 divers and 12 controls. The available evidence does not confirm the theory that bone islands are more common in divers than in non-divers.

Small cysts with fine sclerotic margins are sometimes seen near the greater tuberosity of the humerus (Figs 4.73 and 4.74) and may be associated with tears of the rotator cuff (Campbell Golding, 1962). Similar lesions are seen in the neck of the femur at the insertion of the joint capsule and have been observed on serial radiographs (Fig. 4.75). Like the shoulder joint it may be that these cystic areas result from tears of the capsule, with synovium and fluid entering the subcortical bone. Fournier and Jullien (1965) in a good review of dysbaric osteonecrosis described these small cysts as microgéodes and interpreted them as positive evidence of bone necrosis. However, these changes are found in people not exposed to a hyperbaric environment and moreover there is no pathological report confirming that these radiological appearances are osteonecrosis.

Similarly, cortical thickening and sclerosis of the superior aspect of the femoral neck may cause difficulty in interpretation (Fig. 4.76). This finding is present in those who have never been exposed to a hyperbaric environment and there is no pathological evidence to support that this is osteonecrosis. Neither small cysts with fine sclerotic margins either in the humerus or femoral neck nor cortical thickening in the femoral neck are generally accepted as definite evidence of osteonecrosis.

Increased translucency of the inferior aspect of the femoral head may cause some difficulty in diagnosis (Fig. 4.77) but this is not of significance and results from variation in normal trabecular structure.

## *4.16 Medico-legal problems*

The compensation laws in most nations are inadequate. The problem is highlighted in many French reports (Tara, 1956; Tara and Françon, 1959; Tolot, 1966) where there is frequent reference to the ten-year statute of limitation and the need to extend this time for those involved in this type of work. Dysbaric osteonecrosis is a late complication of exposure to hyperbaric environment and a man may not develop symptoms until years after leaving work in compressed air. For this reason litigation may not commence until several years after exposure. Moreover, as there is no way of identifying the precise time of an ischaemic episode the affected man may not know at which particular contract he developed a lesion. Both Jullien et al. (1954) and the Panel Report (1961) underline the need to reduce the incidence of osteonecrosis and recommend compulsory radiography of the joints of all compressed-air workers.

Compensation and insurance claims are a major factor in civil engineering work involving the use of compressed air. In 1972, in the U.S.A., it was estimated that 2½ million dollars would probably be paid out in claims to men with dysbaric osteonecrosis.

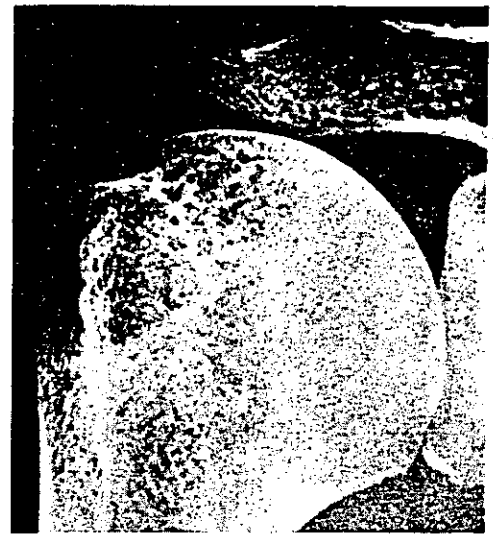


Fig. 4.73. (Left) Small cysts with fine sclerotic margins in the region of the greater tuberosity and anatomical neck of the right humerus. These are believed to be associated with tears of the rotator cuff.

Fig. 4.74. (Right) Larger cystic areas with fine sclerotic margins overlying the anatomical neck of the right humerus. This is not considered to be osteonecrosis.


Fig. 4.75. On the left, no significant bone abnormality in the left femoral head or neck. In the centre, 33 months later, cystic area in the femoral neck with well-defined thin sclerotic margins. On the right, 22 months later, sclerosis is occurring in the cystic area which is gradually disappearing. This is not considered to be osteonecrosis.

Fig. 4.76. Sclerosis superiorly in the right femoral neck, again not considered to be osteonecrosis.

## *4.17 Aetiology of dysbaric osteonecrosis*

The pathological and radiological features of dysbaric osteonecrosis in the femoral head are similar to traumatic osteonecrosis developing after a femoral neck fracture or dislocation of the hip when there is obstruction to the blood supply. Because of this it is assumed that there is a vascular obstruction to the affected bone in dysbaric osteonecrosis. It is known that bone death will result after 6–12 hours of ischaemia (Rösingh and James, 1969; Woodhouse, 1964). Venous drainage is profuse with extensive collateral circulation (Harrison and Gossman, 1955) and, while impaired venous drainage has been demonstrated at venography in osteonecrosis, a widespread process would be necessary if this were the primary cause in dysbaric osteonecrosis. Arterial obstruction could result from the impaction of embolic particles, vascular thrombosis or extravascular obstruction. Bubbles are known to be present in the arterial system both at 'severe' (Walder et al., 1968) and at 'safe' decompressions (Evans et al., 1972). Moreover it is known that platelet aggregation may occur at the

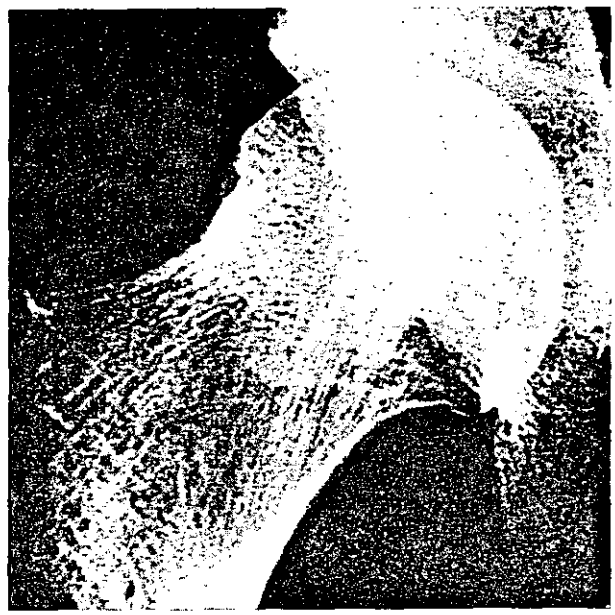


Fig. 4.77. Increased translucency of the inferior aspect of the femoral head which is believed to result from variation in the normal trabecular structure and is not of significance.

liquid/gas interface and result in microemboli (Philp et al., 1972) and this could be a cause of vascular obstruction.

If arterial obstruction is the cause of dysbaric osteonecrosis it is difficult to understand why only certain areas of bone become necrotic. It has been suggested that extravascular bubbles may develop within bone and, because of the rigid trabeculae, an expanding bubble may occlude the vessel.

The aetiology is not clearly understood. There is little information on the pathological change in the early stages and, until recently, dysbaric osteonecrosis had not been reproduced experimentally (Pirastu and Perra, 1960; Averyanov and Mikhailov, 1962; Antopol et al., 1964). Most experiments had been carried out using small animals in which bubbles would only last for a short time compared with man.

Recently Cox (1973) used glass microspheres as embolic particles which were injected into the unobstructed external iliac artery of rabbits. Serial radiography carried out at intervals of 14 days shows cortical thickening of the shaft on the affected side. Radiographic examination of the excised bone showed increased density of some of the femoral heads. Histological evidence of osteonecrosis was present in 11 out of the 40 rabbits and was detectable from four days after the injection. Later changes, up to four months, included the laying down of new bone on dead trabeculae. Bobechko and Harris (1960) related the radiological and histological changes and found that the increased radiological density in the necrotic femoral head resulted from new bone

laid down on the dead trabeculae and causing an overall increase in bone mass. The lesions produced by Cox were similar to those of dysbaric osteonecrosis, one difference being that complete revascularisation occurred in the relatively small femoral head of the rabbit. Another very interesting report is that by Stegall and Smith (1972) who produced radiological evidence of calcification and sclerosis in the femoral shaft of miniature pigs who were exposed to a hyperbaric environment for several hours daily over several months. Possibly because of the variation in blood supply, none showed radiological evidence of osteonecrosis in the femoral head. The same authors reported increased platelet adhesiveness and suggested that microembolism may result in osteonecrosis.

As the head of the humerus in man is so frequently affected in osteonecrosis it is tempting to suggest that bubbles would rise to the highest point and so cause ischaemia. Moreover lesions are more frequent in the distal shaft than in the head and neck of the femur. This hypothesis was investigated (Panel Report 1970) and bone lesions in the distal femoral shaft were related to leg length. While sitting during decompression the knees, in those with long legs, would be above the level of the hip and below in those with short legs. If bubbles rose to the higher point in the femur, lesions would be more common in the distal shaft than in those with long legs. However, there was no statistical evidence to support this. In fact, there were many flaws in the arguement not least being that men may well lie down during a lengthy decompression.

Variation of pressure within the bone medulla has been studied and Shaw (1963) reported that the blood flow in bone was found to relate directly to the marrow pressure. Harrelson and Hills (1970) in a series of hyperbaric experiments in dogs demonstrated a significant fall in marrow pressure during compression. This observation might be of significance as tunnel workers and divers are compressed rapidly.

### *4.18 Mangement and treatment*

Various operations have been carried out for a collapsed humeral and femoral head. Bone grafting and drilling appear to be unsuccessful (Figs 4.42, 4.51, 4.53 and 4.78), and arthroplasty gives better results (Fig. 4.54). If the pain and disability in the shoulder joint is sufficiently severe then an arthrodesis may be required (Fig. 4.79). In general, however, orthopaedic treatment is unsatisfactory, particularly in an active young adult and early diagnosis offers the best prognosis.

The management of a symptom-free diver with positive radiological evidence of osteonecrosis depends on the site of the lesion. The diver with a juxta-articular lesion should be advised to give up diving and even then further deterioration in the progress of the lesion may not be arrested. The lesion may well go on to a structural failure and arthritis. A shaft lesion will almost certainly remain symptomless. The diver should be told of its presence and, because it may indicate some form of susceptibility he should be advised to avoid very deep diving. The policy of diving companies seems to vary and some will only employ divers where there is no evidence of osteonecrosis.

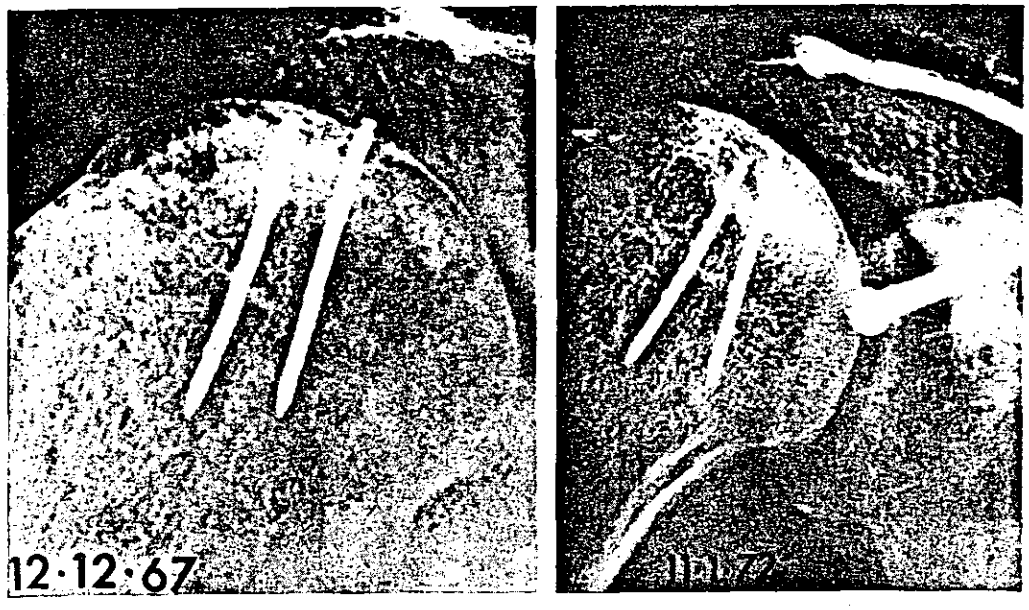



Fig. 4.78. Osteonecrosis of the right humeral head with a structural failure and fine translucent subcortical band managed by internal fixation of the necrotic segment. On the right, 4 years later showing further increased density.

### *4.19 Prevention*

Dysbaric osteonecrosis is a major hazard to compressed-air workers and may be an increasing hazard to divers, particularly now that dives are being made to greater depths and for longer periods.

As radiology provides the only method whereby osteonecrosis can first be recognised, it is clearly important that those at risk have regular surveillance. Any attempts to reduce the incidence by varying decompression times and the length of exposure etc. should be monitored by a radiological survey. The radiology must be of a high standard showing good trabecular detail and those involved in interpretation must be experienced in this condition and have a high index of suspicion. Care must be taken to avoid either over-interpretation causing a sense of alarm, or under-interpretation, resulting in a false sense of security.

Regular surveillance is important and the findings must be related to the occupational history. Only in this way would it be possible to assess the effectiveness of varying decompression schedules and exposure times in reducing the incidence of this disabling condition.

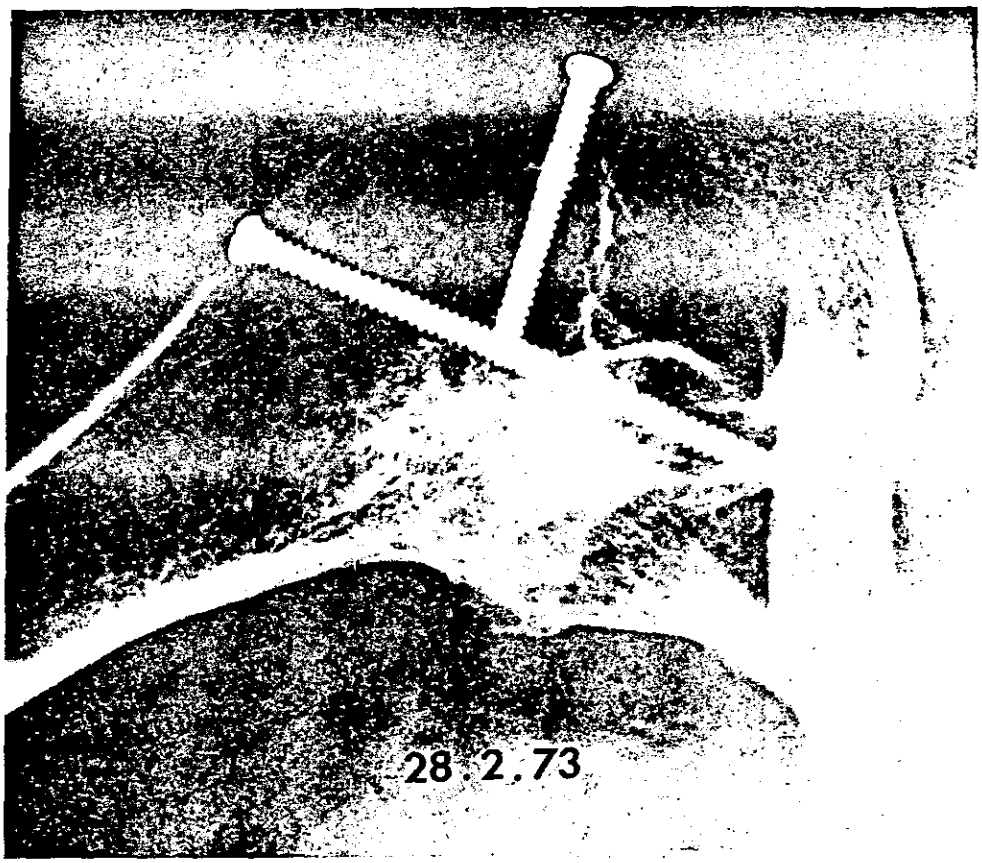



Fig. 4.79. Arthrodesis of the right shoulder joint in a diver who previously had sequestration of a large part of the articular cortex of the humerus.

*Acknowledgements*

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# BONE LESIONS IN COMPRESSED AIR WORKERS

## With Special Reference to Men who Worked on the Clyde Tunnels 1958 to 1963

REPORT OF DECOMPRESSION SICKNESS PANEL, MEDICAL RESEARCH COUNCIL*

Prepared by

R. I. McCallum and D. N. Walder

with the assistance of

R. Barnes, M. E. Catto, J. K. Davidson, D. I. Fryer, F. C. Golding and W. D. M. Paton

*From the Medical Research Council Decompression Sickness Registry, University of Newcastle upon Tyne, England*

Chronic disease of bone is one of the hazards of working in compressed air. The lesion is variously described as caisson disease, avascular necrosis or aseptic necrosis of bone. In this paper we use the term " aseptic necrosis of bone." Although the first report of bone necrosis in a compressed air worker has been attributed to Twynam (1888), his description was rather that of osteomyelitis; the infection which was clearly present in his patient is, by definition, absent in aseptic necrosis.

The radiographic appearances of aseptic necrosis of bone caused by decompression were first described by Bornstein and Plate (1911) and independently by Bassoe (1913).

Bone necrosis in compressed air workers has often been reported in single cases or in small series of cases but, in general, these reports lack sufficient detail from which to identify the causative factors. In British literature there are reports by Walker (1940), Swain (1942), McCallum, Stanger, Walder and Paton (1954), Thomson and Young (1958), and Bucky (1959). In American literature there are reports by Coley and Moore (1940), Rendich and Harrington (1940), and Poppel and Robinson (1956). In European literature there are reports 1) from France by Charles, Cavigneaux, Fuchs and Tara (1948), Bourret, Fraisse and Fraisse (1948), Fischgold, Coville and Doassans (1948), Raymond (1948), Bétoulières and Boulouys (1952), Guitard (1953), Ravault, Merer, Roche and Rayneau (1953), Roche and Rayneau (1953), Bureau, Horeau and Lemeillet (1955), Tarn (1956), Fournier and Jullien (1959), Raymond (1960), and Nicolet, Merer and Jaffres (1961); 2) from Italy by Balestra and Molfino (1949), Angei and Cossu (1954), Mauro (1959), Mauro and Saggese (1959), Francia and Quaglia (1959), and Molfino (1961); 3) from Germany by Rettig (1951), Schröder (1956), Liess (1956), and Fründ (1956); and 4) from Hungary by Déak and Rózsahegyi (1956). Other reports include those by Horvath (1958), Meesters (1958) and Kaczurba (1962) from Europe; and by Rose (1962) from New Zealand. Reference should be made to Rózsahegyi (1956) for a summary of cases of aseptic necrosis of bone in compressed air workers published in the literature before 1955.

The typical bone lesions described in these papers were often bilateral and were situated in the proximal end of the humerus and in the proximal or distal ends of the femur. Symptoms were present only when an articular surface had become involved, and sometimes this did not occur until a considerable time after the last exposure to compressed air. The articular surface of the humeral head was affected more often than the articular surface of the femoral head,

* Medical Research Council Decompression Sickness Panel 1965

Mr D. N. Walder (*Chairman*)
Mr H. V. Hempleman (*Secretary*)
Professor Roland Barnes
Dr A. H. Baynes
Dr M. J. Catton
Dr P. J. Chapman
Dr J. K. Davidson
Wing Commander D. I. Fryer
Dr F. Campbell Golding
Dr P. D. Griffiths
Dr R. I. McCallum
Dr B. McStay
Professor W. D. M. Paton
Dr E. C. Poulton
Dr W. R. Tidy
Dr R. F. Tuckett

and the articular surfaces of the knee joints were never involved. Not all the men with radiographic evidence of bone necrosis were said to have experienced symptoms of acute decompression sickness.

**Diagnosis**—Several papers demonstrate the similarity of the radiographic changes of bone necrosis after work in compressed air to those from other causes. Taylor (1943) reported aseptic necrosis of bone in a series of fifty patients. Twelve had been exposed at some time to high atmospheric pressure, but thirty-eight had never been in compressed air although they were said to have the "same characteristic lesions" as the others. Kahlstrom, Burton and Phemister (1939) and Bucky (1959) also described bone necrosis in patients who had never been in compressed air.

The difficulty of differentiating between secondary osteoarthritis following aseptic necrosis of the head of the femur and osteoarthritis from other causes is discussed by Jullien, Leandri and Desanti (1954), Mosinger and Jullien (1961) and Gaultier, Fournier, Gervais and Ract (1962).

The value of macroradiography (Reboul, Delos, Delorme, Groc, Bordron and Carraze 1955) and tomography (Roche, Devic, Genevois and Marin 1956; Suntych and Suntychova 1961) in the detection of early lesions of bone necrosis has been clearly shown.

**Pathology**—Compared with the extensive literature on the radiographic appearances of the bones of compressed air workers, little has been written about the pathological changes of the affected areas. The pathology of this condition was first described by Kahlstrom, Burton and Phemister (1939). They observed areas of bone necrosis in which the lacunae of the trabeculae were devoid of cells and were surrounded by walls of patchily calcified and partly ossified dense connective tissue. The cases studied were all of long standing and had marked secondary changes of osteoarthritis. Similar descriptions of pathological findings have also been given by Swain (1942) and de Sèze, Durieu, Brux, Guéguen and Welfing (1951).

**Single exposures**—The possibility that a single exposure to compressed air may produce bone necrosis has been raised from time to time. Barbara and Isola (1939) described the development of bone necrosis in the head of the femur, and in the heads of both humeri, in a man aged thirty-two after one exposure to four atmospheres absolute pressure for four hours. Guillain and Grossiord (1943) recorded a case of bone necrosis after a single exposure of four hours. Taylor (1944) mentioned that in one of his cases there had been only one exposure to compressed air. Perhaps most convincing is the experience of James (1945), who, twelve years after the incident, found aseptic necrosis of bone in three of the five survivors from the submarine H.M.S. *Poseidon*, which sank in 1931 in 120 feet of water (4·75 atmospheres absolute). Lesions were present in the neck of the left humerus of one man, and in both femoral and humeral heads of a second man; there were lesions in the shaft of the left femur and head of the left humerus in a third man. The changes apparently followed a single exposure to compressed air of approximately three hours.

**Prevalence of bone lesions in compressed air workers**—From the evidence published so far it is not possible to assess accurately the prevalence of aseptic necrosis of bone in compressed air workers. One of the earliest reports of radiographic findings in a group of compressed air workers appears to be that of Bell, Edson and Hornick (1942). These authors examined thirty-eight men and found aseptic necrosis of bone in 75 per cent. As these men were a selected group of workers who were claiming compensation, it is difficult to assess the significance of the findings.

Nicolas (1949) stated that one in twenty (5 per cent) of compressed air workers showed radiographic evidence of bone necrosis. Cavigneaux, Charles, Fuchs and Tara (1949) found that the bone radiographs of forty-eight out of 125 caisson workers (38 per cent) were abnormal. Lewis and Paton (1957) failed to find any bone lesions in twenty caisson workers. Mungo and Sessa (1958) examined the radiographs of the hips, shoulders and knee joints of forty-seven compressed air workers and reported abnormalities in fourteen (34 per cent). From the very

well reproduced radiographs in this paper it can be seen that many of the abnormal findings resembled bone islands and some of the changes appeared to be indefinite.

In an investigation by the Medical Research Council's Decompression Sickness Panel (Golding, Griffiths, Hempleman, Paton and Walder 1960) during the construction of the Dartford tunnel, when radiographs were taken of shoulders, hips and knee joints, ten of eighty-three (12 per cent) experienced compressed air workers with a history of one or more attacks of bends had demonstrable bone changes, as did three of twenty without a history of treatment for bends. It was pointed out that the extent to which bone changes occur in men without symptoms has scarcely been explored.

Rózsahegyi and Fried (1963) found aseptic necrosis of bone in 22 per cent of sixty-six compressed air workers employed on the construction of the Budapest underground. Many of these men were symptom-free and no close relationship was found between decompression sickness and bone changes, but the authors stated that the more attacks of bends a man suffered, the more likely he was to develop bone necrosis.

**Aseptic necrosis of bone in divers**—Aseptic necrosis of bone appears to be much less frequent in divers than in compressed air workers. Ronald (1953) described one case in Britain, and Herget (1948) in Germany found aseptic necrosis in thirteen of forty-seven divers (28 per cent). The lesions were said to have the same features as those found in compressed air workers and to occur more frequently in the head of the humerus than in other bones. Other cases of bone necrosis in divers were reported, one by Sartor (1947), two by Dale (1952), three by Slørdahl (1953) and three by Pirastu and Perra (1960). More recently Kirjakov (1964) has also reported bone changes in divers.

**Aseptic necrosis of bone in aviators**—Aseptic necrosis of bone in those exposed to sub-atmospheric decompression is the subject of conflicting reports. Ratnoff (1943) found no radiographic evidence of bone necrosis in the hip joints of twenty-one men up to two and a half years after they had been exposed intermittently to simulated altitudes of about 35,000 feet in low pressure chambers, and Allan (1943) found no changes in three other men exposed to low pressures. Coburn (1956) claimed to have found evidence of bone necrosis in 17 per cent of forty low pressure chamber operators in the United States Navy. Berry and Hekhuis (1960), in a radiographic survey of 579 low pressure chamber workers in the United States Air Force, were unable to find evidence of bone necrosis in the shoulders, hips or knee joints, although approximately half these men had experienced acute decompression sickness. The length of exposure and the time interval between the first exposure and radiographic examination were not stated.

## THE CLYDE TUNNELS

Two parallel tunnels have been constructed under the Clyde between Linthouse and Whiteinch where the river is 400 feet wide; they lie about twenty-one feet below the river bed in sandstone and shale overlaid by glacial and alluvial deposits. Work in compressed air began in February 1958 and continued with breaks of a few weeks in free air until January 1963 (Fig. 1). Early in the contract, when the air pressure was being increased from 10 pounds per square inch gauge to 32·5 pounds per square inch gauge over a period of three months, the incidence of decompression sickness rose appreciably, so that it was decided to lengthen by an average of seven minutes the statutory decompression times for exposures of four hours or more for the remainder of the contract (Haxton and Whyte 1965).

**Radiographic investigation**—This paper reports an investigation of 241 men who had worked at pressures up to 35 pounds per square inch gauge on the construction of two tunnels under the River Clyde at Glasgow. A further six men also employed at that time refused examination. Radiographs were taken of major joints and the adjacent bone shafts: 1) to determine the prevalence of bone lesions; 2) to provide information about the time of onset of radiological changes; and 3) to attempt to relate these changes to working pressure and length of exposure.

The investigation was carried out in November 1962 when, with the help of the contractors, arrangements were made for the men to attend a nearby hospital.

Antero-posterior radiographs of the hips and shoulders and antero-posterior and lateral views of the knee joints were taken. As much as possible of the femur and tibia was included to detect shaft lesions. It had been found during the Dartford tunnel investigation (Golding and colleagues 1960) that lateral views of the lower end of the femur were essential to detect early lesions in this region because the antero-posterior film did not always show them clearly.

The contractors' agent and a member of the Medical Research Council Decompression Sickness Panel explained to the men the purpose of the investigation. The men were also given a leaflet pointing out that the survey was part of medical research into the diseases of tunnel workers. If a significant radiological abnormality was found the patient was informed at interview and arrangements made for him to obtain further medical advice if he so wished. If no significant lesion was found the man was informed by letter.

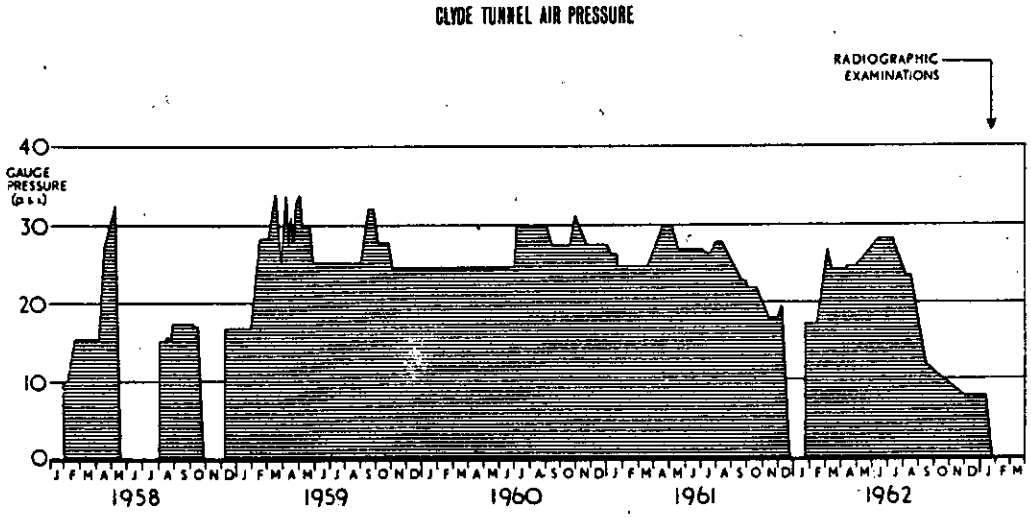


FIG. 1

Simplified diagram of the air pressures used during construction of the Clyde tunnels. Because work was proceeding simultaneously on more than one tunnel face, all the men were not necessarily working at the same pressure. Only the highest pressure in use at any one time is shown.

All the radiographs were examined twice by each of two radiologists (F. C. G. and J. K. D.) working separately, and once by both radiologists working together. Although the radiologists knew that all the radiographs were of men who had worked in compressed air, they did not know which of the men had been treated for decompression sickness. The radiographs were classified as showing definite, doubtful, or no evidence of aseptic necrosis. Lesions were described according to site as " juxta-articular " when close to an articular surface, or " head, neck or shaft " (Table I).

**Results**—Evidence of bone necrosis was found in forty-seven men (19 per cent) and doubtful evidence in a further nineteen. This latter group has been excluded from the following analysis. Some men with lesions also had doubtful lesions (Table I).

There were altogether thirty-three juxta-articular lesions, of which twelve involved femora and twenty-one involved humeri. Both femora were affected in three men, and one femur was affected in six men. Both humeri were affected in six men, and one humerus was affected in nine men. Head, neck or shaft lesions were found in thirty-four men and were seen more frequently in lower limbs (thirty-five lesions) than in upper limbs (twenty-three lesions). It is remarkable how infrequently the tibia was involved (seven lesions), but only part of the upper

## TABLE I

MEN WITH AT LEAST ONE RADIOGRAPHIC BONE LESION

J = Juxta-articular lesions. S = Head, neck or shaft lesions. Doubtful lesions are preceded by a question mark

| Case number | Humerus | | Femur (upper) | | Femur (lower) | | Tibia (upper) | | History of work in compressed air before Clyde contract |
|---|---|---|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left | Right | Left | |
| 1 | J | J | — | — | — | — | — | — | Yes |
| 2 | J | J | S | — | — | — | — | — | Yes |
| 3 | J | J | — | — | — | — | — | — | *No* |
| 4 | ?S | — | J | J | S | — | — | — | Yes |
| 5 | S | S | — | S | — | — | — | — | No |
| 6 | S | — | — | — | — | — | — | — | No |
| 7 | — | — | S | — | — | — | — | — | No |
| 8 | — | J | — | ?S | — | — | — | — | No |
| 9 | — | — | S | — | — | — | — | — | No |
| 10 | — | ?J | — | ?J | S | S | S | — | No |
| 11 | — | — | — | — | S | ?S | — | — | Yes |
| 12 | J | — | — | ?J | — | — | — | — | No |
| 13 | — | ?S | — | — | — | — | S | — | Yes |
| 14 | — | S | — | — | — | S | — | — | No |
| 15 | — | J | — | — | — | — | — | — | No |
| 16 | S | S | J | J | — | S | — | — | No |
| 17 | S | S | — | — | — | — | — | — | No |
| 18 | — | — | — | — | S | — | — | — | No |
| 19 | J | J | — | — | — | — | — | — | No |
| 20 | S | S | SJ | J | — | — | — | — | Yes |
| 21 | — | — | — | — | — | S | — | — | No |
| 22 | J | — | — | — | — | — | — | — | No |
| 23 | — | SJ | — | — | — | — | — | — | No |
| 24 | — | — | — | — | S | S | — | — | Yes |
| 25 | J | J | — | — | — | — | — | — | *No* |
| 26 | J | J | — | — | — | — | — | — | No |
| 27 | — | S | — | — | — | ?S | — | — | No |
| 28 | — | J | ?J | — | — | — | — | — | No |
| 29 | — | — | J | — | S | S | S | S | No |
| 30 | S | S | — | — | — | — | — | — | No |
| 31 | ?S | S | ?S | — | ?S | — | — | — | No |
| 32 | J | — | — | — | — | — | — | — | No |
| 33 | — | S | — | — | S | S | — | — | No |
| 34 | — | — | S | S | ?S | — | — | — | No |
| 35 | S | — | — | — | — | — | — | — | Yes |
| 36 | — | J | — | J | — | — | — | — | No |
| 37 | — | — | J | — | S | — | — | — | Yes |
| 38 | S | — | — | — | — | — | — | — | No |
| 39 | — | SJ | — | — | — | — | — | — | No |
| 40 | ?S | S | — | J | — | — | — | — | No |
| 41 | — | ?S | — | ?S | S | S | — | — | No |
| 42 | — | — | — | J | ?S | — | — | — | *No* |
| 43 | S | — | — | — | — | S | — | — | No |
| 44 | S | S | — | — | — | — | — | — | No |
| 45 | — | — | — | — | S | S | S | S | No |
| 46 | — | — | — | — | — | — | S | — | No |
| 47 | — | — | — | SJ | — | — | — | — | No |

end of the bone was visible in the radiographs. No lesion was seen in those parts of the pelvis, scapula, clavicle and ribs included on the radiographs.

Of the forty-seven men with one or more bone lesions, thirty-eight claimed that the Clyde contract was their first experience of work in compressed air; so in these men any bone changes characteristic of aseptic necrosis may reasonably be ascribed to working on this particular contract.

**Computer analysis**—One of the most important problems requiring a solution is the precise nature of the relationship between the occurrence of a bone lesion and exposure to compressed air. For each man information was available about the number of decompressions to which he had been exposed during the Clyde contract, the air pressures at which he had worked and his history of treatment for simple bends (Type I decompression sickness) and the more serious manifestations (Type II decompression sickness—Golding and colleagues 1960), and whether or not he had ever worked in compressed air before this contract.

All the above information, together with the results of the radiological examination of the bones, was abstracted on to record sheets from which it was transferred to punched tape for analysis by a Pegasus computer in the University of Newcastle upon Tyne.

### MEN WHO HAD NEVER BEEN EXPOSED TO COMPRESSED AIR BEFORE THE CLYDE CONTRACT

**Bone lesions and decompressions**—The 223 men who first experienced work in compressed air in this contract were divided into those with and those without a bone lesion and classified according to the number of decompressions experienced (Table IIA). It can be seen that as a group the men with bone lesions had experienced significantly more decompressions than those without a bone lesion ($p<0.01$). Further analysis of these figures shows that as the number of decompressions increases there is a corresponding rise in the proportion of men with bone lesions. This increases from 8·6 per cent in men who experienced fewer than 300 decompressions to 30·4 per cent in men who experienced more than 900 decompressions (Table IIB).

**Bone lesions and maximum pressure experienced**—If the men are grouped according to the maximum pressure at which they worked in this contract it can be seen that the proportion of men with bone lesions increases significantly among those who were exposed at some time to pressures over 30 pounds per square inch gauge (Table III).

**Bone lesions and decompression sickness.** *Type I decompression sickness (bends)*—In the group of men with one or more bone lesions 45 per cent were known to have been treated for bends, whereas in the group without bone lesions only 14 per cent were known to have been so treated, a difference which is statistically significant (Table IV). We found no statistically significant relationship between the sites of the bone lesions and the sites of bends.

*Type II decompression sickness*—Only nine cases of Type II decompression sickness occurred in those without previous compressed air experience and there was no tendency for this type of decompression sickness to be associated with the development of bone lesions (Table V).

### MEN WHO HAD BEEN EXPOSED TO COMPRESSED AIR BEFORE THE CLYDE CONTRACT

**Bone lesions and decompressions**—In the eighteen men with a history of exposure to compressed air in other contracts no association between bone lesions and the number of decompressions during the Clyde contract was evident (Table VI).

**Bone lesions and maximum pressure experienced**—The presence or absence of a bone lesion was not related statistically to the maximum pressure at which a man had worked during this contract (Table VII).

**Bone lesions and decompression sickness**—It was not possible to show any statistically significant association between the number of men with bone lesions and the number with a previous history of decompression sickness of either Type I (bends) or Type II. However, no information

TABLE II

BONE LESIONS AND DECOMPRESSIONS IN THOSE WITHOUT PREVIOUS COMPRESSED AIR EXPERIENCE

A. Men with and without bone lesions (total 223)

| Number of decompressions | Number of men without bone lesions | Number of men with bone lesions |
|---|---|---|
| 1–74 | 10 | 1 |
| 75–149 | 12 | 1 |
| 150–224 | 15 | 2 |
| 225–299 | 16 | 1 |
| 300–374 | 10 | 0 |
| 375–449 | 13 | 3 |
| 450–524 | 12 | 0 |
| 525–599 | 15 | 1 |
| 600–674 | 8 | 2 |
| 675–749 | 9 | 2 |
| 750–824 | 7 | 1 |
| 825–899 | 10 | 3 |
| 900–974 | 3 | 5 |
| 975–1,049 | 7 | 2 |
| 1,050–1,124 | 5 | 2 |
| 1,125–1,199 | 5 | 1 |
| 1,200–1,274 | 2 | 1 |
| 1,275–1,349 | 9 | 3 |
| 1,350–1,424 | 3 | 2 |
| 1,425–1,499 | 3 | 1 |
| 1,500–1,574 | 1 | 2 |
| 1,575–1,649 | 3 | 1 |
| 1,650–1,724 | 7 | 1 |
| Total number of men | 185 | 38 |
| Average number of decompressions | 646 (S.E.±34) | 908 (S.E.±72) |
| Difference | 262 (S.E.±81) ($p<0.01$) | |

B. Men with bone lesions

| Number of decompressions | Total men | Men with bone lesions | Percentage with bone lesions |
|---|---|---|---|
| <300 | 58 | 5 | 8·6 |
| 300–599 | 54 | 4 | 7·4 |
| 600–899 | 42 | 8 | 19 |
| 900 and over | 69 | 21 | 30·4 |
| Total | 223 | 38 | 17 |

TABLE III

*BONE LESIONS AND MAXIMUM PRESSURE EXPERIENCED IN THOSE WITHOUT PREVIOUS EXPOSURE TO COMPRESSED AIR*

| | Maximum gauge pressure (*pounds per square inch*) | | | | Total |
|---|---|---|---|---|---|
| | 18 | 25 | 30 | 34 | |
| Men with bone lesion | 1 (6 per cent) | 3 (10 per cent) | 10 (11 per cent) | 24 (29 per cent) | 38 (17 per cent) |
| *Men without bone lesion* | 17 | 27 | 83 | 58 | 185 |
| Total | 18 | 30 | 93 | 82 | 223 |

There is a significant association between lesion and pressure ($x^2 = 14$, d.f. $= 3$, $p<0.01$)

TABLE IV

BONE LESIONS AND TYPE I DECOMPRESSION SICKNESS (BENDS) IN THOSE WITHOUT PREVIOUS COMPRESSED AIR EXPERIENCE

| Number of recompressions for Type I decompression sickness (bends) | Men with bone lesions | | Men without bone lesions | |
|---|---|---|---|---|
| 1 | 8 | | 11 | |
| 2 | 7 | | 7 | |
| 3 | 1 | 45 per cent | 2 | 14 per cent |
| 4 | 1 | | 2 | |
| 5 | 0 | | 1 | |
| 8 | 0 | | 2 | |
| 0 | 21 | (55 per cent) | 160 | (86 per cent) |
| Total | 38 | | 185 | |

Significantly more of the men with lesions have at least one bend
$x^2 = 18{\cdot}1$, d.f. $= 1$, $p < 0{\cdot}001$

TABLE V

BONE LESIONS AND TYPE II DECOMPRESSION SICKNESS IN THOSE WITHOUT PREVIOUS COMPRESSED AIR EXPERIENCE

| Number of recompressions for Type II decompression sickness | Men with bone lesions | Men without bone lesions |
|---|---|---|
| 1 | 2 | 5 |
| 2 | 0 | 2 |
| 0 | 36 | 178 |
| Total | 38 | 185 |

TABLE VI

BONE LESIONS AND DECOMPRESSIONS IN THOSE WITH PREVIOUS COMPRESSED AIR EXPERIENCE

| | Without bone lesions | With bone lesions |
|---|---|---|
| Number of men | 9 | 9 |
| Average number of decompressions | 1,090 | 1,156 |
| Range of number of decompressions | 498–1,652 | 662–1,536 |
| Difference between average number of decompressions | 66 (S.E. 173) (not significant) | |

TABLE VII

BONE LESIONS AND MAXIMUM PRESSURE EXPERIENCED IN THOSE WITH PREVIOUS EXPOSURE TO COMPRESSED AIR

| | Maximum gauge pressure (*pounds per square inch*) | | Total |
|---|---|---|---|
| | 30 | 34 | |
| Men with bone lesion . | 3 | 6 | 9 |
| Men without bone lesion | 3 | 6 | 9 |
| Total . . . | 6 | 12 | 18 |

TABLE VIII

BONE LESIONS AND TYPE I DECOMPRESSION SICKNESS (BENDS) IN THOSE WITH PREVIOUS COMPRESSED AIR EXPERIENCE

| Number of *recompressions for* Type I decompression sickness (bends) | *Men with* bone lesions | *Men without* bone lesions |
|---|---|---|
| 1 | 4 | 3 |
| 2 | 0 | 2 |
| 7 | 1 | 0 |
| 0 | 4 | 4 |
| Total . . | 9 | 9 |

TABLE IX

BONE LESIONS AND TYPE II DECOMPRESSION SICKNESS IN THOSE WITH PREVIOUS COMPRESSED AIR EXPERIENCE

| Number of recompressions for Type II decompression sickness | Men with bone lesions | Men without bone lesions |
|---|---|---|
| 1 | 4 | 2 |
| 2 | 2 | 1 |
| 0 | 3 | 6 |
| Total . . | 9 | 9 |

TABLE X

BONE LESIONS IN MEN WITH AND WITHOUT PREVIOUS COMPRESSED AIR EXPERIENCE

| | Men with previous compressed air experience | Men without previous compressed air experience |
|---|---|---|
| Total number of men | 18 | 223 |
| Number with bone lesions | 9 (50 per cent) | 38 (17 per cent) |
| There is a significant association $x^2=9{\cdot}5$, d.f. $=1$, $p<0{\cdot}01$ | | |

TABLE XI

RECOMPRESSIONS FOR TYPE I DECOMPRESSION SICKNESS IN MEN WITH AND WITHOUT PREVIOUS COMPRESSED AIR EXPERIENCE

| Number of recompressions for Type I decompression sickness (bends) | Men with previous compressed air experience | Men without previous compressed air experience |
|---|---|---|
| 1 | 7 | 19 |
| 2 | 2 | 14 |
| 3 | 0 | 3 |
| 4 | 0 | 3 |
| 5 | 0 | 1 |
| 6 | 0 | 0 |
| 7 | 1 | 0 |
| 8 | 0 | 2 |
| | 56 per cent | 19 per cent |
| 0 | 8 (44 per cent) | 181 (81 per cent) |
| Total . . | 18 | 223 |
| $x^2=11{\cdot}2$, d.f. $=1$, $p<0{\cdot}001$ | | |

TABLE XII

RECOMPRESSIONS FOR TYPE II DECOMPRESSION SICKNESS IN MEN WITH AND WITHOUT PREVIOUS COMPRESSED AIR EXPERIENCE

| Number of recompressions for Type II decompression sickness | Men with previous compressed air experience | Men without previous compressed air experience |
|---|---|---|
| 1 | 6 | 7 |
| 2 | 3 | 2 |
| | 50 per cent | 4 per cent |
| 0 | 9 (50 per cent) | 214 (96 per cent) |
| Total . . | 18 | 223 |
| $x^2=44{\cdot}5$, d.f. $=1$, $p<0{\cdot}001$ | | |

TABLE XIII

SHIFT AND NON-SHIFT WORKERS WITH BONE LESIONS

| | | |
|---|---|---|
| Without previous compressed air experience (223) . . . | Non-shift (28) 3 (11 per cent) | Shift (195) 35 (18 per cent) |
| | $x^2=0{\cdot}467$, $p>0{\cdot}3$. Not significant | |
| With previous compressed air experience (18) . . . | Non-shift (3) 3 (100 per cent) | Shift (15) 6 (40 per cent) |
| | $p=0{\cdot}103$. Not significant | |
| With and without previous compressed air experience (241) . | Non-shift (31) 6 (19·4 per cent) | Shift (210) 41 (19·5 per cent) |

was available about the number of decompressions, working pressures, or periods of work in previous contracts, details which might allow a full consideration of the risks to which these men had been exposed (Tables VIII and IX).

### COMPARISON BETWEEN MEN WITH AND WITHOUT PREVIOUS EXPOSURE TO COMPRESSED AIR

Fifty per cent of men with a history of exposure to compressed air before the Clyde contract had bone lesions compared with only 17 per cent of those men without a history of previous exposure to compressed air (Table X).

Men with previous experience of work in compressed air had a much higher prevalence of both Type I (bends) and Type II decompression sickness during the Clyde contract than had men without previous exposure (Tables XI and XII). There was no statistically significant difference between the proportion of men with bone lesions in shift workers, who usually spend periods of eight hours in compressed air, and non-shift workers, who usually spend periods of less than four hours in compressed air (Table XIII), whether they had had experience of compressed air work previous to this contract or not.

TABLE XIV

AGE COMPOSITION OF THE MEN IN THE SURVEY

| Age (*years*) | Without previous compressed air experience | | With previous compressed air experience | |
|---|---|---|---|---|
| | With bone lesion | Without bone lesion | With bone lesion | Without bone lesion |
| 15–19 | 0 | 6 | 0 | 0 |
| 20–24 | 3 | 34 | 0 | 0 |
| 25–29 | 11 | 44 | 0 | 0 |
| 30–34 | 8 | 41 | 2 | 3 |
| 35–39 | 8 | 31 | 2 | 3 |
| 40–44 | 4 | 22 | 1 | 0 |
| 45–49 | 2 | 4 | 0 | 2 |
| 50–54 | 0 | 1 | 2 | 1 |
| 55 and over | 2 | 2 | 2 | 0 |
| Total . | 38 | 185 | 9 | 9 |

The age composition of the men in the survey is shown in Table XIV. In men without previous compressed air experience there is no significant difference in the proportion with bone lesions above the age of forty years compared with those below the age of forty years ($\chi^2=0{\cdot}327$).

### SUMMARY

Evidence from the Clyde contract suggests that: 1) the greater the number of decompressions that a man experiences the higher the risk of acquiring a bone lesion, but no evidence was obtained that the risk of acquiring a bone lesion differed between shift and non-shift workers (Table XIII); 2) lesions were more likely to occur after exposures to pressures above 30 pounds per square inch gauge; 3) among men without previous exposure to compressed

air those who had suffered at least one attack of bends were more likely to have a bone lesion than those men who had never suffered from bends. In spite of this general relationship, the probability of having a bone lesion did not increase with the number of attacks of Type I decompression sickness suffered. For example, two men in the survey with no previous experience of compressed air work, each of whom had suffered from eight attacks of bends in the course of 1,622 and 1,654 exposures to compressed air, had no bone lesions.

### CONTROLS

Fifty unselected men taken on at the Tyne tunnel, who, as far as could be ascertained, had had no previous experience of compressed air work, were examined radiographically as they presented themselves for shift work to determine the presence or absence of bone lesions. The radiographs were presented independently to two radiologists (F. C. G. and J. K. D.) among other radiographs of experienced compressed air workers. In none of the bones of the fifty men were any lesions of aseptic necrosis reported.

FIG. 2

FIG. 3

Figure 2—Juxta-articular lesion. Dense areas. Figure 3—Juxta-articular lesion. Spherical segmental opacity.

The age distribution of this control group was not identical with that of the group of Clyde workers without previous compressed air experience who developed bone lesions, but, as has been shown above (Table XIV), in the latter there was no statistically significant association between age and the presence of a bone lesion.

## RADIOGRAPHIC FINDINGS IN THE CLYDE WORKERS

The bone lesions seen in compressed air workers are indistinguishable radiologically from aseptic necrosis from other causes. Diagnosis is based primarily on the presence of patches of increased density in the affected area, but areas of decreased density may also be seen.

The radiographic appearances of the bone lesions in the Clyde group of men resembled some of those described in the literature. We have classified the radiographic lesions found in compressed air workers as follows.

JUXTA-ARTICULAR LESIONS

These occur in the head of the humerus or femur, or both, and may be bilateral. They are in close proximity to the articular cortex of the bone, which may collapse with distortion or breakage of the unsupported articular cartilage. In this event symptoms may arise.

**Dense areas with an intact articular cortex** (Fig. 2)—These lesions are commonly found in the head of the humerus and, less frequently, in the femoral head. They are often bilateral and multiple and they appear as small dense areas close to, and often touching, the intact articular cortex. Their margins, unlike those of bone islands, are irregular and the trabeculae passing through them appear to be thickened or fused. The surrounding bone is normal.

**Spherical segmental opacities** (Fig. 3)—Opacities shaped like the segment of a sphere are found in the head of the humerus and less frequently in the head of the femur. This lesion appears to correspond to what Poppel and Robinson (1956) described as a "snow-cap," but their description is imprecise. At a later stage these lesions may collapse or become sequestrated (see below).

FIG. 4
Juxta-articular lesion. Rarefied area bounded by linear opacity.

**Linear opacity** (Fig. 4)—This lesion occurs commonly in the head of the humerus and rarely in the femoral head; it is sometimes bilateral. The linear opacity, which may be curved or serpiginous, varies in thickness and density. Its ends extend to the articular cortex on each

FIG. 5

FIG. 6

Figure 5—Juxta-articular lesion. Structural failure: transradiant subcortical band. Figure 6—Juxta-articular lesion. Structural failure: collapse of articular cortex.

side so that as much as two-thirds of the joint surface, as seen in the radiograph, is sometimes included by it. The bone between the dense layer and the articular cortex sometimes shows a decrease in density. The bone on the shaft side of the linear opacity sometimes contains small dense areas. In some cases the dense line appears to follow the old epiphysial line.

**Structural failure.** *Transradiant subcortical band* (Fig. 5)—This lesion is found in the heads of humeri and femora, and appears as a transradiant line below the articular cortex. In some instances the transradiancy underlies as much as two-thirds of the articular surface. This transradiancy probably represents a fracture line (Norman and Bullough 1963).

*Collapse of the articular cortex* (Fig. 6)—Occasionally the middle third or more of the articular cortex of the head of the humerus and up to half of the articular cortex in the "weight-bearing" area of the femoral head on one or both sides collapses.

Sometimes a large intact segment or several small fragments of the articular cortex sink into the subcortical bone. There is a clear "step formation" at the junction with the normal articular cortex. In the adjacent bone there is frequently a large triangular density with its apex extending towards the shaft of the bone.

FIG. 7

FIG. 8

Figure 7—Juxta-articular lesion (tomograph). Structural failure: sequestration of cortex. Figure 8—Juxta-articular lesion with osteoarthritis.

*Sequestration of part of the cortex* (Fig. 7)—A large segment of the articular cortex of the humerus or femur appears to have separated but it is not depressed below the level of the articular surface. Occasionally small fragments of articular cortex appear to be detached. The remainder of the bone head sometimes shows increased density.

**Osteoarthritis** (Fig. 8)—Osteoarthritis with osteophyte formation may follow aseptic necrosis involving the articular cortex of the humerus or femur when the lesion is long standing. Characteristically the glenoid and acetabulum are not affected until a very late stage and the joint space is usually of normal width.

### HEAD, NECK AND SHAFT LESIONS

These are situated at a distance from the articular cortex and are believed to remain symptomless.

**Dense areas** (Fig. 9)—These lesions are commonly found in the neck and proximal shaft of femur and humerus. Less commonly they are present in the distal shaft of the femur or proximal shaft of the tibia. The lesions are usually multiple and bilateral. Occasionally a large area of bone is involved, but the lesions are usually small and ill-defined, and it can be difficult to distinguish between them and bone islands. A typical site for this lesion is the upper margin of the femoral neck.

**Irregular calcified areas** (Fig. 10)—These lesions are commonly situated in the distal shaft of the femur, in the proximal shaft of the tibia, and in the proximal shaft of the humerus. They

are found only in the medulla. They are frequently bilateral and multiple and consist of irregularly calcified areas of varied size and distribution. In some cases they form a circular

FIG. 9

FIG. 10

Figure 9—Head, neck and shaft lesions. Dense areas. Figure 10—Shaft lesion. Irregular calcified area.

FIG. 11
Neck lesion. Cyst.

cluster and in other cases a continuous broad strip several centimetres in length with ill-defined margins. Lesions at the lower end of the femur are more clearly demonstrated in a lateral than in an antero-posterior radiograph.

**Transradiant areas and cysts** (Fig. 11)—Transradiant areas, sometimes surrounded by a sclerotic margin in which case we have called them cysts, are found in the head and neck of the humerus and in the neck of the femur. They may be as large as two centimetres in diameter and are occasionally seen close to the articular surface of the head of the humerus or femur. When a transradiant area is situated close to the humeral cortex its margin may follow the shape of the bone. These lesions were best seen in tomographs.

## PATHOLOGY

In order to interpret the radiological appearances correctly they must be correlated with the underlying histological changes.

The first histological confirmation that the radiological changes in the bones of compressed air workers were the results of aseptic necrosis was afforded by Kahlstrom, Burton and Phemister (1939). Since then further reports have been made by Phemister (1940), Walker (1940), Swain (1942), de Sèze and colleagues (1951), McCallum and colleagues (1954), and Laufer (1957). Many of these reports are brief and all of them concern patients with symptoms due to collapse of the joint surface.

In 1962 the Medical Research Council Decompression Sickness Panel obtained the left humerus and the right femur from a compressed air worker who died during treatment for decompression sickness during another contract. This case has been reported in detail elsewhere (Bennison, Catton and Fryer 1965). Although this man had been employed in compressed air work for fourteen years, he had never complained of symptoms suggesting that he had aseptic necrosis of bone. At necropsy both bones showed a normal contour and external appearances, but on section areas of necrosis were apparent in the humeral head and shaft and in the femoral head.

Death of an area of bone is recognised histologically by acellularity of the bone marrow and by absence of osteocytes in the bone lacunae. When revascularisation occurs the marrow may return virtually to normal, but recognisable unresorbed dead bone cores remain for a long time in the centre of the new bone trabeculae.

Histological examination of the humeral head showed, by the presence of unresorbed dead bone in the centre of many trabeculae, that all the head had at one time been dead (Figs. 12 to 14). Much had revascularised and only a fairly shallow subchondral saucer remained necrotic. The border between necrotic and revascularised zones was marked by a band of dense fibrous tissue. The trabeculae adjacent to the fibrous tissue on the revascularised side were very broad because of the deposition of a particularly thick layer of viable bone on the surface of unresorbed dead trabeculae, and this would account for the dense linear opacity seen in this region on radiographs.

It was evident then that the initial necrosis involved a larger area than the small lesion which was identifiable in a slab radiograph. The radiographically dense boundary of the lesion represented the most proximal point to which the revascularisation process had reached. It appeared unlikely that revascularisation would have progressed further in view of the avascular collagen in this zone. Even over the unrevascularised bone the articular cartilage was viable and of normal thickness.

The lesion in the shaft of the humerus was a few centimetres below the surgical neck. It had a pale necrotic centre with a dense fibrous boundary and occupied about half the width of the medullary canal. The presence of living bone on the surface of dead trabeculae showed that the necrosis had initially involved the whole width of the spongy bone and a small part of the endosteal surface of the cortex on both sides. The lesion was scarcely detectable in a radiograph of a thin transverse slice of bone at this point.

The histological changes seen in the femoral head were similar to those in the head of the humerus (Figs. 15 to 17). Necrosis had initially involved much of the head, crossing the

epiphysial scar, but extensive revascularisation and deposition of new bone had occurred and only a subchondral zone, chiefly in the lower part of the head, remained necrotic. Again, the revascularisation process appeared to have halted at a zone of dense fibrosis and the broad reossified trabeculae in the revascularised area resulted in an increase of radiological density. No evidence of thrombosis or recanalisation was seen in any blood vessel.

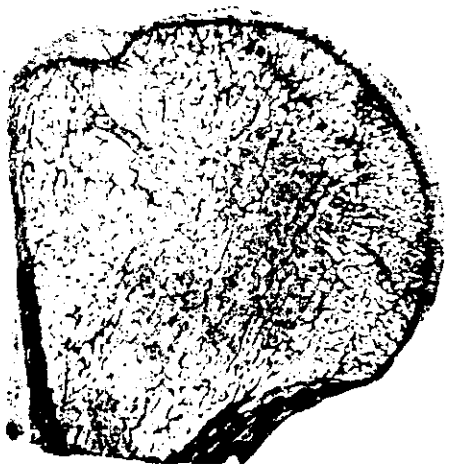

FIG. 12

FIG. 13

FIG. 14

Humeral head showing aseptic necrosis. Figure 12—Photomicrograph of whole humeral head. The contour of the humeral head is well preserved, the articular cartilage being of normal thickness and showing no degenerative changes. Beneath the articular cartilage there is a shallow saucer of dead bone bordered by a greyish line of fibrous tissue representing the farthest advance of the revascularisation process. Broad trabeculae are found immediately distal to this. They consist of living bone which has been laid down on unresorbed dead trabeculae. The dark material in the marrow spaces in the centre of the head consists of bone dust pushed into the marrow during sawing and is artefactual. Figure 13—The hatched area indicates the minimal extent of the original necrotic zone. Trabeculae within the revascularised area consist of dead bone covered by living bone. Figure 14—Slab radiograph. The irregular line near the joint surface represents the broad reossified trabeculae immediately behind the fibrotic revascularisation front.

In addition to the necropsy specimens described above, biopsy specimens obtained at operation were available from four Clyde tunnel workers, all of whom had severe joint symptoms with radiological evidence of collapse of a joint surface and of secondary degenerative changes. The histological appearances in these late cases in which collapse of an articular

surface had occurred bore a striking resemblance to " idiopathic " bone necrosis, of which an excellent description was given by Patterson, Bickel and Dahlin (1964).

In all four patients operated upon a major part of the joint surface consisting of viable articular cartilage with an underlying fringe of dead bone had partly separated. There was evidence of some revascularisation of the necrotic bone, and where this had occurred secondary osteoarthritic changes with remodelling of the articular surface had taken place with osteophyte and " cyst " formation.

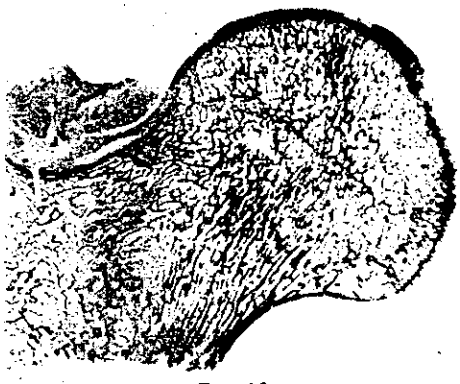

FIG. 15

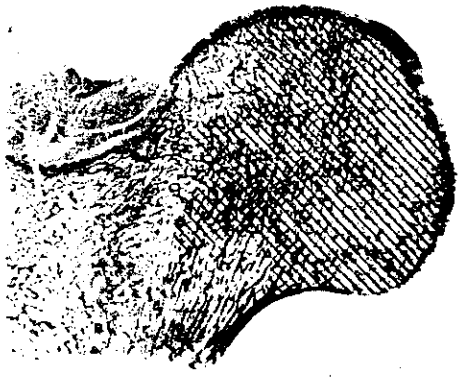

FIG. 16

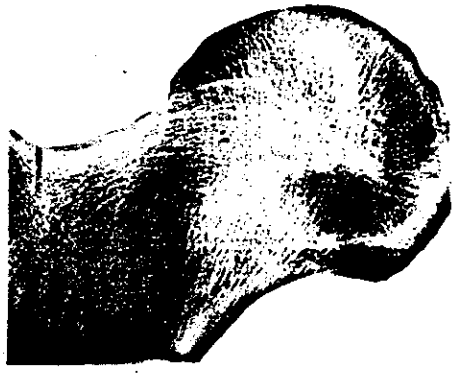

FIG. 17

Femoral head showing aseptic necrosis. Figure 15—Photomicrograph of femoral head and neck. The contour of the femoral head is unaltered and the articular cartilage of normal thickness. A zone of necrotic bone is outlined by a greyish line representing the fibrotic revascularisation front and behind this broad reossified trabeculae are seen. Figure 16—The hatched area indicates the minimal extent of the original necrotic zone. Trabeculae within the revascularised area are broader than normal due to living bone laid down on dead. Figure 17—Slab radiograph. The normal density of the necrotic bone is in marked contrast to the increased density in the revascularised zone which is especially marked at the necrotic margin.

A radiological " cyst " deep in the femoral head of one patient with a recently collapsed articular surface and no significant osteoarthritis was found to consist of a mass of granulation tissue, organising fibrin and fragments of dead bone.

There was evidence that more than one episode of ischaemia might have occurred in two patients, as shown by the presence of dead fibre bone on the surface of dead lamellar trabeculae. None of the biopsy material was heavily calcified.

In summary, then, it seems likely that not all the lesions of aseptic necrosis of bone are detectable by radiography, at least in the early stages, and that when radiographic changes are seen they may represent only a small part of the initial necrotic area. An increase of

radiological density may be the result of deposition of new bone on dead trabeculae or of marrow calcification, though the latter was minimal in these patients.

The articular cartilage may remain viable and of normal thickness even when the bone it covers is dead. Furthermore, sequestration of part of the joint surface leads to relatively little alteration in the cartilage. The notable changes seen at the joint surface following collapse are secondary degenerative ones and occur in the viable or revascularised part of the articular cortex. Cysts seen in radiographs may be associated with secondary osteoarthritis or may represent granulation tissue, organising fibrin and fragments of dead bone.

The cause of the failure of complete revascularisation is not clear but in our cases it seemed that it was not the result of the mechanical break in the cortex, nor of heavy calcification within the necrotic area.

## CLINICAL FEATURES

In our experience of the clinical features of aseptic necrosis of bone, based partly on the Clyde tunnel group of men, head, neck and shaft lesions do not cause symptoms, and the juxta-articular lesions are seldom painful before there is radiographic evidence of deformation of the articular cortex. In the shoulder, symptoms may commence suddenly when, for instance, a heavy bag of tools or a baulk of timber is picked up, presumably because of collapse of necrotic trabeculae supporting the articular cortex. In some men symptoms are insidious in onset, with pain in the shoulder radiating down the lateral aspect of the upper arm to about the level of the insertion of the deltoid muscle. Pain is commonly present in the shoulder when the patient lies in bed on the affected side.

When there is only slight deformation of the articular surface a full range of movement in the shoulder is usually retained, and the only abnormal physical signs are a painful arc of movement between 60 and 180 degrees of abduction, and difficulty in maintaining right-angled abduction of the upper arm against resistance. The clinical picture resembles that of a degenerative lesion of the shoulder cuff.

After collapse of the articular surface of the humeral head osteoarthritic changes develop and progressively restrict all movement of the shoulder joint.

Juxta-articular lesions in the hip rarely give rise to an acute onset of pain in the joint. The initial symptom is usually pain over the anterior aspect of the hip joint or trochanter radiating down the antero-lateral aspect of the thigh to the knee. The pain may at first be thought to be mild bends by the man if he is still engaged upon compressed air work, but it is not relieved by recompression. After a time the pain becomes more severe and may interfere with sleep. Later, movement at the hip is restricted, especially abduction and rotation. A useful range of flexion is usually retained, even when there are severe deformation of the articular cartilage of the head of the femur and associated arthritic changes in the joint.

## TREATMENT

Four of the men in this survey with juxta-articular lesions, one in the femur and three in the humerus, were treated surgically to alleviate pain because there appeared to be no reasonable prospect of restoring the joints to normality by prolonged rest and traction. In all of these the radiographs taken before operation showed considerable deformation and collapse of the articular cortex. In each case there was a narrow transradiant band running through the subcortical bone a few millimetres below the articular surface.

At operation on these patients the depressed area of articular cartilage was seen to have lost its sheen and to be pale yellow in colour. It could be detached, together with a narrow zone of necrotic bone, from the remainder of the head at the level of the transradiant band seen on the radiograph. Deep to the line of cleavage there was a zone of necrotic bone of varying depth overlying a layer of dense avascular fibrous tissue.

With the object of promoting revascularisation and healing of the overlying necrotic bone a number of holes were drilled through the avascular layer in each case. Although this manoeuvre has not resulted in any improvement in the range of movement of the affected joints it has reduced pain. For instance, one man who had a painful shoulder with limited movement now has less pain and is able to work as a builder's labourer. In the man with the juxta-articular lesion affecting the femoral head there was also a large cavity lined by granulation tissue. This was packed with cancellous bone autografts and, in addition, holes were drilled through the avascular layer. Although there has been no increase in the range of hip movement the joint is less painful and the patient is able to work as a baker.

## DISCUSSION

**Prevalence of aseptic necrosis in compressed air workers**—Estimates of the prevalence of aseptic necrosis in compressed air workers vary from zero (Lewis and Paton 1957) to 75 per cent (Bell, Edson and Hornick 1942). The main problems in determining the total number of men affected by aseptic necrosis of bone are 1) that in practice it is very difficult to radiograph all the men at risk; and 2) that repeated radiological examination for several years after work in compressed air ceases is necessary if all the affected men are to be detected.

The exact time at which the earliest radiographic evidence of aseptic necrosis appears after the causative exposure to compressed air is not known, but one man in this survey was found to have a bone lesion three months after starting work in compressed air. In most cases it is not possible to identify the particular exposure responsible for the lesion except when a lesion has followed a single exposure. Many lesions cause no symptoms for a long time and may never give rise to symptoms, so that such lesions will not be detected unless specifically looked for. In our experience the early radiographic changes of aseptic necrosis can easily be missed until attention is drawn to them by more marked changes in later radiographs.

Studies of groups of compressed air workers suffer from the fact that in this type of civil engineering work there is often an exceptionally high turnover of the labour force, due partly to the arduous nature of the work and the dangers of the environment, and partly to the fact that a high proportion are itinerant labourers who have no permanent home. For example, at the Dartford tunnel (Golding and colleagues 1960), although never more than 320 men were at work in compressed air at any one time, 1,200 compressed air workers were actually employed. At the Clyde tunnels 55 per cent of the men left after less than four months and 20 per cent after less than one month.

The 241 men included in the present survey were those remaining in employment towards the end of the contract in which a total of 1,362 compressed air workers had been employed. Forty-seven men (19 per cent) of the 241 showed radiographic evidence of aseptic necrosis of bone. Most of these lesions appear to have been acquired during this contract. Some men who only stayed for a few months and underwent relatively few decompressions nevertheless contracted aseptic necrosis of bone (Table II).

It can be expected that some of the 1,121 compressed air workers employed on the Clyde tunnels who were not included in this survey will also have acquired bone lesions, either during this contract or during previous work on a compressed air contract. In fact, it is known that up to May 1964 eleven of them have presented with disabling aseptic necrosis of bone at Glasgow hospitals.

If the men in our survey can be regarded as a representative sample then we could expect that about 19 per cent or approximately 250 of all the men who were at risk will have bone lesions. On the other hand, if there are no more men with bone lesions than those found to date (forty-seven in the survey and eleven since) the overall prevalence would be 4 per cent. Therefore, the prevalence of aseptic necrosis of bone in this contract up to the present date

is from 4 per cent to 19 per cent. As time elapses it can be expected that the number of bone lesions detectable radiologically in this group of men will increase.

These figures refer to all lesions, whether juxta-articular or in the head, neck and shaft of bone, but it is clear that the juxta-articular lesions are the more important clinically in that they may lead to disability. Of these, femoral juxta-articular lesions will probably lead to more severe disability than juxta-articular lesions in the humerus. In our survey 4 per cent of the 241 men had femoral juxta-articular lesions (three men having both sides affected) and 6 per cent had humeral juxta-articular lesions (six men having both sides affected).

**Diagnosis and differential diagnosis**—In this survey bone radiographs have been confined to the head and upper end of the humerus, head and upper end of the femur, lower end of the femur and upper end of the tibia for two reasons: 1) there was a limit to the time that could be spent on radiographing each individual, and 2) experience has shown that these are the common and most important sites for this type of lesion, although it is recognised that other sites, such as the shaft and lower end of the humerus, the tibia, the fibula, the ischio-pubic ramus, the acetabulum and the clavicle may also be affected (Bell, Edson and Hornick 1942).

The radiographic changes of aseptic necrosis of bone seen in compressed air workers must be differentiated from those of Gaucher's disease, sickle-cell anaemia, the arthropathy of steroid therapy, osteochondritis dissecans and the changes following dislocation or fracture. These conditions as well as calcified enchondromata and osteoblastic metastases, may have to be excluded by a careful study of the patient's history and by clinical tests. Idiopathic necrosis of the femoral head in adults (Merle d'Aubigné 1964) is considered to be a rare condition in Great Britain, and aseptic necrosis, when it occurs in a man with a history of exposure to compressed air, may, in our opinion, reasonably be attributed to his work if other causes can be excluded. The lesions of aseptic necrosis in compressed air workers are often multiple and bilateral. Analysis of the figures in Table I shows that using the $x^2$ test the likelihood of this symmetrical occurrence of lesions being due to chance is remote ($p<0{\cdot}001$).

It is usually still possible to detect the underlying characteristic changes of aseptic necrosis, even when they are complicated by secondary osteoarthritis. Under these circumstances the width of the joint space as seen in the radiograph is usually unaffected because the cartilage retains its normal thickness until late in the disease.

Some difficulty may be experienced in differentiating dense areas of aseptic necrosis of bone from the bone islands which are commonly found in the normal skeleton. Bone islands are usually composed of uniformly dense compact bone and are ovoid or oblong in shape (Kim and Barry 1964), whereas the lesions of aseptic necrosis tend to be irregular in shape and to have thickened trabeculae running through them (Reboul and colleagues 1955, Fournier and Jullien 1959, Mosinger and Jullien 1961). Tomography may help in differentiating between bone islands and aseptic necrosis by demonstrating the irregular outline of the latter.

In this survey radiographs showing areas of bone with only slight thickening of the trabeculae have been classified as normal but it is hoped to re-examine radiographically these areas later to see whether they develop into typical lesions of aseptic necrosis.

**Etiology**—It is obviously of paramount importance to know the factors which determine the risk that a man may acquire a bone lesion if this risk is eventually to be eliminated. A relationship has been shown between the number of decompressions and the prevalence of bone lesions (Table IIB), as well as between the maximum pressure experienced and the prevalence of bone lesions (Table III).

It is unfortunate that in the analysis of the data from the Clyde contract we have not found it possible to separate the effect of the number of decompressions to which a man has been subjected from those of the pressure at which he worked. In our sample the men who experienced pressures over 30 pounds per square inch gauge were also the men who had been employed the longest and therefore decompressed the most frequently (Fig. 1). It is hoped that separation of these two factors may be possible in the future using data from other contracts.

**Pathogenesis**—The usual explanation for the occurrence of aseptic necrosis of bone in compressed air workers is that during or after decompression bubbles of nitrogen arise in the blood and tissues, obstruct blood vessels and thus cause infarction. Campbell and Hill (1933) showed that in goats there was a slow rate of saturation of bone marrow with nitrogen. This, they claimed, was due to a " low circulation rate through marrow " and a " high fat content diminishing the rate of diffusion." Presumably in bone marrow there is also a slow rate of desaturation which would predispose towards the risk of both intravascular and extravascular nitrogen bubble formation during decompression after a prolonged exposure to compressed air. In man, areas of necrosis in the rigid tissue of bone might thus follow local interruption of its blood supply by bubbles within or without the vessels.

As the head of the humerus and the head of the femur are so frequently affected by aseptic necrosis in man it is tempting to suggest that posture is a factor. Thus, it could be argued 1) that because of gravity the upper end of a bone has a poorer blood supply than the lower end, and 2) that intravascular or extravascular bubbles within the cavity of bone might show a tendency to rise to the highest point before causing obstruction to the blood supply. On the other hand, lesions frequently occur in the lower end of the femur, and it would be difficult to explain these on this hypothesis unless it could be established that during decompression the affected men sat with their knees above the level of their hips.

However, direct evidence in support of the hypothesis that aseptic necrosis of bone in man is caused by infarction by gas emboli is lacking.

Experiments on animals in which air emboli were produced by injection (Kahlstrom, Burton and Phemister 1939), or gas bubbles induced by rapid decompression from very high pressures (Gersh 1945; Colonna and Jones 1948; Averyanov and Mikhailov 1962; Antopol, Kalberer, Kooperstein, Sugaar and Chryssanthou 1964), have not succeeded in producing lesions of aseptic necrosis of bone comparable to those found in man. In any case it is doubtful whether conclusions drawn from animals completely dissimilar to man in size and rate of metabolism, exposed to pressures well beyond the usual range normally employed in compressed air work and decompressed at very high rates, can be expected to throw light on the causation of aseptic necrosis in man.

Experimental evidence of the occurrence of bone infarction following embolism by agents other than gas bubbles is also difficult to find, but Kistler (1934) produced infarction in the femora of rabbits by embolism from the injection of gum acacia suspension of charcoal into the nutrient arteries.

Another possible approach to the problem of the pathogenesis of aseptic necrosis of bone in compressed air workers may be to look for factors common to it and to aseptic necrosis of bone associated with other conditions such as steroid therapy, sickle-cell anaemia, Gaucher's disease and aplastic anaemia.

**The relationship between bends and bone lesions**—By showing a statistical relationship between a bone lesion and attacks of bends we have confirmed the findings of Rózsahegyi and Fried (1963), but the following factors must be taken into consideration: 1) The diagnosis and treatment of the bends depends on the affected man reporting his symptoms and on their being judged to merit treatment. Men are not paid for the time spent under treatment in the medical recompression chamber and if they do not wish to report for treatment but prefer to put up with the pain or to relieve it by taking analgesics or alcohol, then there is no record of the attack. 2) Experience suggests that almost every shift worker exposed to pressures above 16 pounds per square inch gauge at some time or another suffers from a mild attack of bends which is not sufficiently severe to make him return for recompression and which he calls the " niggles." The differentiation between what is called the " niggles " and what is called the " bends " depends on a subjective judgement. For these reasons it must be assumed that every compressed air worker has probably suffered at some time or another from untreated mild bends. From the results of this survey we conclude that a bend severe enough to call for

treatment, even though it receives treatment, is a more likely precursor of bone necrosis than an untreated bend.

In the Clyde workers who had had no compressed air experience before this contract, 45 per cent of those with a bone lesion had been treated for the bends by the time the investigation was made. Thus the treatment of a bend does not necessarily prevent the onset of subsequent bone lesions. On the other hand, it is also possible that the bone lesions in these men arose from mild bends for which they did not receive recompression treatment.

Another factor which might reduce the closeness of the relationship between a bone lesion and the bends is the possibility that some bone lesions may result from interference with the bone circulation by symptomless bubbles, but at the moment we can neither confirm nor deny this suggestion.

**Bone lesions and shift lengths**—Aseptic necrosis of bone is rare in divers and this may be related to the fact that they spend much briefer periods under pressure than compressed air workers. It might be concluded from this that one way of avoiding bone lesions in tunnel or caisson workers would be greatly to shorten the shifts.

Tunnel workers who regularly spend six to eight hours in compressed air seem to be more prone to suffer from bends than men who are employed on a non-shift basis, such as electricians, carpenters and engineers, who usually spend periods of less than four hours in compressed air. For example, during the construction of the Dartford tunnel under the Thames (pressure range 18–28 pounds per square inch gauge) the bends rate on the Kent side was 1·03 per cent for men working for periods of over four hours daily and 0·05 per cent for men working for periods of under four hours daily (Golding and colleagues 1960) a difference of 0·98 per cent. It was found, however, that in the Clyde contract, in which the pressure varied from 18–32 pounds per square inch gauge, men with over four hours exposure to compressed air had a bends rate of 0·30 per cent whereas men with less than four hours in compressed air had a rate of 0·24 per cent, a difference of only 0·06 per cent. The proportion of men with bone lesions in shift and non-shift workers was the same (Table XIII), so that there is no confirmation from the Clyde investigation that limiting exposure to compressed air to four hours or less diminishes the risk of acquiring a bone lesion.

In 1936 the British Institution of Civil Engineers suggested a split shift system in which two spells of work in compressed air are separated by a period in free air. A system of split shifts was used by the Port of New York Authority in 1953 during the construction of the third tube of the Lincoln tunnel, but this did not prevent bone lesions. It is thought that the principle of the split shift system is unsound because it doubles the number of times each man is decompressed.

**Prevention of bone lesions**—It has recently become obvious that bone necrosis is a major hazard in compressed air work since it may lead to permanent disability if it affects the articular surface of the head of the femur or humerus. The prevalence of bone lesions is a much more realistic measure of the success of any particular decompression procedure than the bends rate.

Use of the present British Decompression Table (Ministry of Labour and National Service 1958) does not prevent bends, as rates of up to 4 per cent occur (Lewis and Paton 1957), but even if the decompression procedure was altered in such a way that bends were completely prevented there is no guarantee that bone lesions would be prevented.

There is no evidence that lengthening the decompression times given in the Decompression Table is harmful (Paton and Walder 1954), and on the Clyde, because it was noticed early in the contract that the bends rate was increasing when the pressure rose above 26 pounds per square inch gauge, the decompression times were increased by amounts varying from four to thirteen minutes, an average of seven minutes.

The overall bends rate on the Clyde was 0·29 per cent, which is better than, for example, that of the Dartford tunnel contract where it was 0·55 per cent and the Blackwall tunnel contract where it was 1·05 per cent. The proportion of attacks of severe decompression sickness

(Type II) in men working at 18 pounds per square inch and above on the Clyde was similar to that at Dartford and at Blackwall, being 0·0441, 0·0390 and 0·0421 per cent respectively. In spite of the apparent improvement in the bends rate in comparison with previous contracts, a large number of bone lesions were detected among men whose experience in compressed air was confined to this contract.

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.

**Management and treatment**—This radiographic survey of compressed air workers revealed many symptomless but potentially disabling bone lesions which might not otherwise have been detected for some considerable time. The advice which should be given to a compressed air worker with a view to preventing future disability from a symptomless lesion must be considered, as well as the question of the advisability of such a man continuing to work in compressed air once he has developed a bone lesion.

We have no evidence to enable us to assess the probability that a man with one or more bone lesions will suffer from additional bone damage in the form of fresh lesions or extension to existing lesions if he continues to work in compressed air, and this should be made clear to a man who already has one or more bone lesions.

If a man has symptomless juxta-articular aseptic necrosis in the head of one femur it seems reasonable to advise him to avoid any further exposure to compressed air on the grounds that although the risk of developing juxta-articular aseptic necrosis in his other femoral head may be small, the consequences of such an event could be grossly disabling.

If a juxta-articular bone lesion, particularly of the head of the femur, has progressed to give symptoms, it is likely that because of the pain the man will be unable to continue to work in compressed air and will seek treatment.

Our knowledge of the evolution of the bone changes of aseptic necrosis in compressed air workers is too meagre to enable us to define a programme of treatment for all cases. Head, neck and shaft lesions have not so far given rise to symptoms in this group of Clyde workers, so that the question of their treatment has not arisen.

Juxta-articular lesions, however, present a difficult therapeutic problem. These lesions are usually symptomless until deformation of the articular surface occurs from collapse of the underlying necrotic bone, probably as a result of the stress to which it is normally subjected. The changes are most severe in the weight-bearing area of the head of the femur, and in that part of the head of the humerus which is opposite the glenoid fossa when the arm is in a position of approximately right-angled abduction. Following deformation of the articular surface, pain on movement is a prominent symptom which becomes more severe if osteoarthritic changes supervene in the damaged joint. These observations suggest, firstly, that it is that part of the necrotic bone subjected to the greatest stress which collapses, and, secondly, that this might be avoided if the joint surfaces were protected from stress by traction and rest until repair of the necrotic bone had taken place. If the radiographic appearances are an accurate index of the process of repair, then the complete restoration to normal of necrotic bone may require many years of treatment, if indeed it can ever occur.

At present no surgical treatment has been shown to be entirely satisfactory: even though pain is relieved the results are either of a temporary nature or leave the man with some permanent disability.

The suitability of the following surgical procedures has to be considered.

*Stimulation of repair*—A technique which seems to offer the best prospect of success is that recommended by Phemister (1949) and by Bonfiglio and Bardenstein (1958) for the treatment of avascular necrosis of the femoral head complicating transcervical fractures of the femur. Bonfiglio and Bardenstein claimed satisfactory results in three-quarters of their patients. In this operation two holes, each one centimetre in diameter, are drilled under radiographic control from the subtrochanteric area of the femur into the necrotic part of the head. An

autogenous bone graft is driven into position along each hole so that one end of the graft lies immediately beneath the weight-bearing articular surface of the femoral head. These grafts, by breaking down the fibrous barrier between living and dead bone, may aid the advance of revascularisation into the necrotic zone. At the same time the grafts support the weakened part of the articular surface of the femoral head. Full weight bearing is not allowed until about twelve months after this operation but partial weight bearing may be allowed earlier.

If conservative surgery of this type were to have any prospect of success in compressed air workers with aseptic necrosis it would have to be undertaken well before the onset of symptoms. This would necessitate the regular radiographic examination of the femoral and humeral heads of men working in compressed air in order to detect early bone changes. Another difficulty would be that, as we have no evidence that all juxta-articular bone changes necessarily progress to give disability, it would be difficult to decide which patients required surgical treatment.

*Arthrodesis*—Arthrodesis is a suitable procedure for patients who have collapse of the articular cortex with secondary osteoarthritic changes affecting only one femoral head. It is probably the best operation for a fit and active man who wishes to return to moderately heavy work. If necrosis of the head of the femur is extensive, arthrodesis may be difficult to achieve and the insertion of a metallic prosthesis may be more satisfactory.

*Insertion of prosthesis*—When both femoral heads are involved the insertion of metallic prostheses is the best procedure if the patient is seriously disabled. In most patients the initial result is satisfactory, but it may not remain so. McCallum, Stanger, Walder and Paton (1954) reported the case of a compressed air worker with juxta-articular aseptic necrosis in both femoral heads, each of which was replaced by an acrylic prosthesis. The result was satisfactory for about three years, but further surgical treatment then became necessary. The modern metallic prosthesis is a better appliance than that used in 1952 but it may not be able to withstand indefinitely the stresses and strains of weight bearing in a heavy, active man.

*Osteotomy*—Osteotomy is not recommended for patients with juxta-articular aseptic necrosis of the head of the femur. It does not result in revascularisation of the necrotic area and further collapse and deformity of the weight-bearing surface of the head of the femur is inevitable.

**Recommendations for the future**—In order to obtain a clearer picture of the whole problem of decompression sickness and in particular of aseptic necrosis of bone in compressed air workers employed in civil engineering projects, some systematic means of acquiring data on the health of this unstable occupational group is required. In the past only limited information about specific contracts or individuals affected by bone necrosis has been obtained. What is now required is a continuous record of the medical history and compressed air experience of each worker over a period of years as he moves from job to job. For example, periodic radiographic examination of the bones of these men should be carried out. This is of increasing importance as it becomes evident that the success or otherwise of decompression procedures must be judged by the proportion of men subsequently found to have bone lesions.

Radiographic examinations of compressed air workers are already being carried out by the Medical Research Council Decompression Sickness Panel with the cooperation of civil engineering contractors.

The maintenance of adequate records of compressed air workers is extremely difficult because of the high turnover of labour and the peripatetic tendencies of the men who undertake this type of work, but a central registry to collect the medical and other relevant confidential information about these men has now been established by the Medical Research Council in the University of Newcastle upon Tyne, England.

SUMMARY

1. A radiographic investigation of a group of 241 men who had worked in compressed air at pressures up to 35 pounds per square inch gauge on the construction of tunnels under the River Clyde showed that forty-seven men (19 per cent) had one or more lesions of aseptic necrosis of bone.

2. The radiological lesions have been classified as juxta-articular, which may lead to pain and limitation of movement, and head, neck and shaft lesions, which are usually symptomless. In 10 per cent of the men the lesions were juxta-articular and therefore potentially disabling. The treatment of juxta-articular lesions is described and reviewed.

3. The environmental factors associated with the occurrence of aseptic necrosis of bone, the radiological and histological appearances, and the pathogenesis of the lesions are discussed. Bone lesions were found to be related directly to the number of times a man had been decompressed, to the height of pressure at which he had worked and to attacks of bends for which treatment was given.

4. When the histological and radiographic appearances of aseptic necrosis of bone in compressed air workers are compared it is clear that a radiograph may not always reveal the full extent of the lesion, and some lesions may not show up at all. The cause of the necrosis is obscure because experimental and direct evidence of bone infarction by gas bubbles is lacking.

5. The currently accepted decompression procedures and treatment of bends used in civil engineering practice, do not prevent the occurrence of aseptic necrosis of bone in compressed air workers.

6. It is suggested that periodic radiological examination of the bones of compressed air workers should be carried out and the results correlated with other information about the men and the contracts on which they have worked in order to elucidate the causative factors in aseptic necrosis of bone. A central registry has been set up by the Medical Research Council in the University of Newcastle upon Tyne to fulfil this function.

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# DECOMPRESSION SICKNESS DURING CONSTRUCTION OF THE DARTFORD TUNNEL

BY

F. CAMPBELL GOLDING[1], P. GRIFFITHS[2], H. V. HEMPLEMAN[3], W. D. M. PATON[4], and D. N. WALDER[5]

*A Report by the Dartford Decompression Sickness Panel of the Medical Research Council.*

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A clinical, radiological and statistical survey has been made of decompression sickness during the construction of the Dartford Tunnel. Over a period of two years, 1,200 men were employed on eight-hour shifts at pressures up to 28 pounds per square inch (p.s.i.). There were 689 cases of decompression sickness out of 122,000 compressions, an incidence of 0·56%.

The majority of cases (94·9%) were simple "bends". The remainder (5·1%) exhibited signs and symptoms other than pain and were more serious. All cases were successfully treated and no fatality or permanent disability occurred. In two serious cases, cysts in the lungs were discovered. It is suggested that these gave rise to air embolism when the subjects were decompressed, and pulmonary changes may contribute more than hitherto believed to the pathogenesis of bends. Some other clinical features are described, including "skin-mottling" and an association between bends and the site of an injury. The bends rate is higher for the back shift (3 p.m. to 11 p.m.) and the night shift (11 p.m. to 7 a.m.) than for the day shift. In the treatment of decompression sickness it appears to be more satisfactory to use the minimum pressure required for relief of symptoms followed by slow decompression with occasional "soaks", than to attempt to drive the causative bubbles into solution with high pressures.

During the contract the decompression tables recently prescribed by the Ministry of Labour were used. Evidence was obtained that they could be made safer, and that the two main assumptions on which they are based (that sickness will not occur at pressures below 18 p.s.i., and that a man saturates in four hours) may be incorrect. It is desirable to test tables based on 15 p.s.i. and eight-hour saturation. The existence of acclimatization to pressure was confirmed; it is such that the bends rate may fall in two to three weeks to 0·1% of the incidence on the first day of exposure. Acclimatization is lost again, with a "half-time" of about seven days, if a man is away from work.

A study of bone damage in compressed air work has been started. In certain radiographs, abnormalities have been seen which may represent an early stage of caisson disease of bone.

The new tunnel between Kent and Essex under the Thames at Dartford is part of a four miles road link between A2, the London-Rochester road, and A13, the Barking-Southend road. It is situated 14 miles down river from the Blackwall Tunnel, until now the most easterly point at which it has been possible to cross the Thames by road. The river at Dartford is half a mile wide, so that the total length of the tunnel, including the sloping approaches at each end, will be approximately one mile. The tunnel lies about 20 ft. below the existing bed of the river in strata which consist of soft blue peaty clay overlying gravel which in turn overlies solid chalk. The preliminary pilot tunnel was completed in 1938, and the present contract for the full tunnel was let in 1956. It has an internal diameter of 28 ft. 2 in. and will accommodate two 10 ft. 6 in. traffic lanes with 16 ft. headroom, and be able to take double decker buses.

When constructing such tunnels, situated only a short distance underneath the river bed, it is necessary to use compressed air within the workings in order to keep out the water which would otherwise percolate through the surrounding strata and flood the tunnel. The pressure required to keep the tunnel

Address: [1] X-ray Department, Middlesex Hospital.
[2] Royston, Bayleys Hill, Sevenoaks, Kent.
[3] R.N. Physiological Laboratory, Alverstoke.
[4] Department of Pharmacology, Oxford.
[5] University Department of Surgery, Newcastle on Tyne.

dry varies according to the type of strata through which the tunnel is passing, and also with the depth of the river which at this point is tidal. In this project compressed air at pressures up to 28 pounds per square inch (p.s.i.) has been necessary.

The use of compressed air results in exposing the men who build the tunnel to the risk of decompression sickness. The risk can be minimized by taking certain precautions which have been laid down by the Minister of Labour and National Service in the Work in Compressed Air Special Regulations, 1958.

In spite of adherence to the prescribed precautions, however, a number of cases of decompression sickness still occur, and it is because of this that the present investigation has been carried out.

### *Arrangement of Workings*

First two vertical shafts were sunk, one on each bank of the river, 2,832 ft. apart. From both of these, tunnelling was then begun towards the centre of the river.

A few months before these under-river tunnels from the two sides met, tunnelling under compressed air was started in a landward direction from the bottom of the Kent shafts, working towards the surface portal; about 200 ft. had been completed at the time of the junction.

All this work has had to be carried out in compressed air, which was first used on the Kent side in April 1957, and on the Essex side in September 1957. Owing to the slightly different nature of the ground on the two sides, pressures up to 28 p.s.i. have been used on the Kent side, but only up to 21 p.s.i. on the Essex side.

About six months before the tunnel across the river was completed, the pressure on the two sides was equalized.

**Decompression Air Locks.**—In order to get men and materials in and out of the tunnel whilst maintaining the pressure within, it was necessary to build air locks at both entrances to the workings. These air locks were situated at the bottom of the shafts in a short access tunnel; on each side of the river there was a man lock 12 ft. diameter by 33 ft. long (this was fitted with benches and could hold 50 men), and a material lock 7 ft. diameter by 28 ft. long. Heaters (two of 5 Kw. capacity) were fitted in the man lock to minimize discomfort when the temperature suddenly fell during the rapid phase of decompression. The locks were at all times controlled by a trained lock keeper, who was also responsible for keeping records of all persons entering and leaving the tunnel and ensuring that they received the correct decompression.

***Medical Air Locks.***—On each side of the river, situated at the medical centres, each within 100 yards of the top of the shafts, were two medical recompression chambers (each 7 ft. diameter and 14 ft. long). They were fully equipped with air lock entrances so that the doctor in charge and medical attendants could enter and leave during a recompression if it was necessary to examine or treat the patient, and so that food, books and other things could be passed in and out without interfering with the recompression.

**Population at Risk and Working Shifts.**—Over a period of two years (April, 1957 to April, 1959) 1,200 men have worked in compressed air on this contract, with between 250 and 320 on the active list at any one time. This has involved 122,000 compressions, of which 119,000 were at pressures over 16 p.s.i. Of the men, 1,060 were shift workers and 140 non-shift workers.

Throughout the duration of the compressed air work, a shift system has been in operation. Three shifts of approximately 25-30 men per shift are worked during the 24 hours, the men spending eight hours in the compressed air, followed by whatever period of time is necessary in the man lock to ensure proper decompression under the prevailing circumstances. In addition to the shift workers, there was a group of men (engineers, electricians, carpenters, fitters) entering and leaving the tunnel to perform tasks, the duration of which did not coincide with that of the regular shifts, who also had to be decompressed according to their exposure to compressed air.

### *Clinical Data*

**Definition.**—It is first necessary to define what, for the purposes of this paper, should be regarded as decompression sickness. Many men suffer minor pains ("niggles") after decompression but these are too indefinite for quantitative study. Therefore only those cases with symptoms sufficiently severe to bring the man back for treatment have been counted as decompression sickness, and they were, in fact, always recompressed.

**Classification of Cases.**—There were 685 cases of decompression sickness. It was found that they could be divided into two types: Type 1, or simple "bends", which accounted for 650 of the total and Type 2, more serious and more complicated, of which there were 35.

TYPE 1 CASES.—In these the complaint was one of pain, usually described as being in or around a joint. In 85% the lower limbs only were affected; in 7%, upper limbs only; in 8% both upper and

lower limbs. The pain varied in intensity from a "nagging ache" to a very severe pain. It started on the average about three hours after decompression, but the time of onset varied considerably, from immediately after decompression to 12 hours later. Ninety-two per cent of the cases had worked shifts of eight hours or longer; 3% had worked for four hours only.

About half the cases responded quickly to recompression, but the remainder needed to be kept above working pressure for periods up to one hour before relief of pain was obtained. The most difficult case was that of a miner (Case 499) who had to be recompressed 10 times in all before he obtained complete relief of pains in the shoulders. On 12 occasions men suffering from the bends went back to work in the tunnel, without first reporting for medical recompression, and were not relieved of their symptoms; they had to be brought out from the tunnel and recompressed to a higher pressure in the medical lock in order to get relief.

Sometimes there was a history of bruising, sprain, or excessive use of the part of the body in which the bends pain arose. In 29 cases out of 502 (6%), over a period of 19 months, the evidence was sufficiently definite to be entered on the case sheet. In one case (Case 288) a man bruised his head in the tunnel, causing a small haematoma. Ten hours after decompression he returned from his home to the medical centre (a journey of 25 miles) with acute pain in the haematoma; on recompression the pain went at 10 p.s.i. and did not return. Among fitters, who frequently work in cramped or kneeling positions, the bends incidence was approximately 50% higher than among other workers. After a mild electric shock, one man (Case 348) suffered bends in the affected arm and shoulder. Some workers attributed their attacks to such causes as tiredness, lack of sleep or change of occupation in the tunnel involving the excessive use of muscles not "in training". Age does not seem to be important: as an example, two men who gave the wrong age and were found to be over 50 worked two years as labourers without trouble. The average age of Type 1 cases was 30 years.

TYPE 2 CASES.—These have been defined as patients presenting with symptoms other than pain or with abnormal physical signs. A summary of the presenting signs and symptoms in these cases is as follows: 26 with vertigo, 15 with signs of "shock" (pale, clammy, thready pulse, hypotension), six with visual symptoms, five with paralysis of limbs, five with epigastric pain, four with dyspnoea, three with speech defects, one with epileptiform attack, one with signs suggesting a cardiac lesion and one who collapsed and was unconscious on leaving the decompression lock. In addition to these 35 cases some men volunteered information about symptoms for which they had not requested treatment: 10 men reported brief attacks of "shortness of breath" on the way home, and two had visual symptoms within two hours of decompression.

The Type 2 cases always start early: six cases started either during the final stages of decompression or at its end; 26 cases started within one hour of the end of decompression. One case occurred six hours after decompression. The average time of onset was approximately 50 min. after decompression. The average age of the Type 2 cases was 36 years, somewhat higher than that of Type 1 cases.

No obvious predisposing cause was found; long exposure to pressure was not essential, for 11 cases had been exposed for five hours or less. In no case was the attack due to faulty decompression.

In general these cases reacted to therapeutic recompression more dramatically than did Type 1 cases; improvement usually began at comparatively low pressures, often considerably below working pressure (Table 1).

TABLE 1

COMPARISON OF SALIENT FEATURES OF TYPE 1 AND TYPE 2 CASES

| | Type 1 | Type 2 |
|---|---|---|
| Symptoms | Limb or joint pain | Diverse |
| Latency of onset | 0-12 hours from end of decompression<br>Mean three hours | Before end of decompression to six hours after<br>Mean 50 minutes |
| Response to decompression | Good but sometimes slow | Dramatic, sometime at quite low pressure |
| Age | Mean 30 years | Mean 36 years |
| Predisposing factors | Injury, fatigue, ischemia, long exposure | Lung cyst<br>Long exposure not necessary |
| No. of cases | 650 | 35 |

The following case histories illustrate some of the features mentioned:

### Case Histories

**Case 23.**—This man, after working for eight hours at 21 p.s.i. fainted in the man lock during decompression with his shift, but recovered immediately. He was kept under observation for two hours and then allowed to go home apparently fit. Paralysis of legs and bladder came on gradually during the night, and it was 12 hours after decompression before treatment began. Relief of symptoms by recompression was successful, although a pressure much higher than working pressure was needed. Great difficulty was experienced in returning this patient to atmospheric pressure; despite the use of very slow decompression with periods of prolonged equilibration

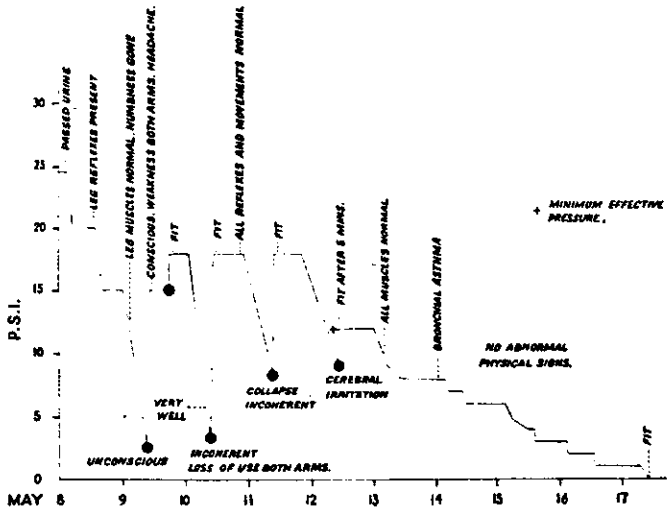



FIG. 1.—Diagram of the therapeutic recompression of Case 23, presenting with retention of urine and loss of reflexes in both legs, after an eight-hour shift at 21 p.s.i. The filled circles denote the pressure at which symptoms or signs recurred. (In medical lock 9¼ days.)

at intermediate pressures (the so-called "soaks") and of oxygen inhalation, it was nine and a half days before he could be released from pressure without a return of symptoms. Fig. 1 shows his treatment diagrammatically. Especially remarkable was the manner in which paralysis of the lower or upper limbs returned within 2 lb. of atmospheric pressure in spite of lowering the pressure at a rate of only 1½ lb. per hour, and later recurred with a rate three times slower. The only physical abnormality detected at subsequent medical examination was the cyst at the base of the right lung mentioned elsewhere in this paper.

**Case 268.**—An engineer aged 55 fell unconscious on leaving the man lock, after only three-quarters of an hour at 26 p.s.i. He was recompressed immediately in the man lock and kept at 26 p.s.i. When he recovered consciousness 20 minutes later he could move neither arms nor legs; all reflexes were exaggerated and plantar responses extensor. Thirty minutes later he was free of symptoms and had normal reflexes. He was very slowly decompressed and quickly transferred to the medical lock where further recompression and decompression treatment was completed. Both ear drums were damaged during the initial emergency recompression, but they healed quickly without disability. Subsequent investigation showed him to be a fit man, but radiological investigation of his chest revealed a cyst at the base of the right lung.

**Case 341.**—An engineer aged 48 collapsed with signs of "shock" 15 minutes after an exposure of one hour at 26 p.s.i. He recovered quickly on recompression and no other ill effects were detected. Later, a radiograph of his chest (AP) appeared normal.

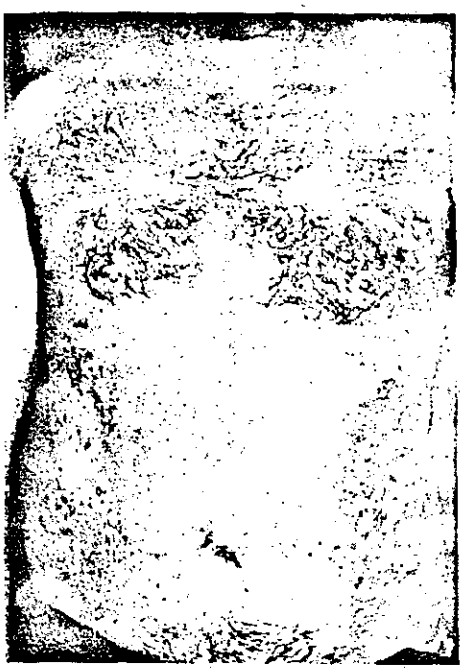
Both these engineers had been exposed repeatedly to compressed air for many years without previous trouble.

**Case 9.**—A chargehand fitter aged 41 had "staggers", and was apparently cured by treatment in the medical lock. One hour later, while still under observation, he collapsed unconscious, with a pulse rate of 40. Within five minutes of recompression he was conscious and well, with a pulse rate of 78, and no further trouble was experienced. With this man, also, an AP chest radiograph was normal.

**Skin Mottling.**—An interesting sign seen in some subjects after decompression is the occurrence of a purplish patchy discolouration of the skin, known as "mottling" (Fig. 2). This disappears on local pressure, returning when pressure is released. The area most commonly affected was the upper abdomen but occasionally it was seen spreading to the back and down the limbs.

Faint mottling was often seen over the upper abdomen during routine inspection, but unless associated with symptoms, was ignored. Some authorities consider the occurrence of skin mottling to be an indication of grave prognostic significance and therefore any man with severe mottling, with or without other symptoms, was either forbidden to work in compressed air, or limited as to time and pressure.

Twenty-two men showed extensive mottling and of these, 15 were obese. In 15 cases, there were other symptoms requiring recompression; in seven cases, the men reported the mottling but had no symptoms other than skin irritation. One fitter (Case 126) who used a hammer for four hours at 24 p.s.i. within an hour of decompression had a



IG. 2.—Photograph of mottling of the trunk after normal decompression of a shift worker from a pressure of 26 p.s.i.

ymptomless deep purple discolouration over the right shoulder and chest, covering almost exactly the muscles most used in hammering.

**Cases Occurring among Men exposed to Pressures less than 18 p.s.i.**—Since bends are usually supposed to be rare at pressures less than 18 p.s.i., some details of those occurring at Dartford require mention. There were 45 cases, 41 being Type 1, and the remaining four Type 2. Table 2 shows the pressures at which they occurred. Of the Type 1 series, one man had worked only four hours; three others had worked 10 hours or more. The Type 2 cases had all worked eight-hour shifts.

TABLE 2

CASES OF DECOMPRESSION SICKNESS AT PRESSURES LESS THAN 18 p.s.i.

| Pressure (p.s.i.) | Type 1 Cases | Type 2 Cases |
|---|---|---|
| 16 | — | 1 |
| 16½ | 6 | 1 |
| 17 | 23 | — |
| 17½ | 12 | 2 |

The occurrence of cases, both non-serious and serious, at these low pressures, raised the question of the accuracy of the pressure gauges. All pressures were recorded on three separate large scale gauges which were calibrated regularly by the makers, Messrs. Elliott Bros. At no time were errors more than 0·5 p.s.i. detected and they were always such that the recorded pressure was higher than the true pressure.

### Radiological Studies

The construction of a tunnel under the Thames at Dartford presented an opportunity to carry out a radiological survey on men working in compressed air. This was made possible by the loan of radiographic apparatus from the Royal Air Force and facilitated by the cooperation of the contractors. The apparatus was installed in the medical centre, close to the shaft when the tunnel was about half-way to completion. The original intention was to radiograph the limbs of those men who had suffered an attack of bends, in order to determine the incidence of aseptic necrosis in bone, but this objective was later extended to include some workers who had escaped a frank attack of bends but had had minor symptoms described as niggles, or had suffered from mottling of the skin. Coincident with this survey, two examples of severe decompression sickness were encountered. A radiograph of the chest showed that both men had lung cysts. At this time no relationship had been established, either by other investigators or by ourselves, between disease of the lungs and these major attacks, but after these events a radiograph of the chest was taken of all men starting to work in compressed air.

**Bone and Joint Lesions.**—The literature contains many examples of bone and joint lesions attributed to decompression sickness. Nearly all these were patients who attended hospital because they complained of symptoms. The extent to which bone changes occur without symptoms has hardly been explored. The lesions in bones and joints consist of sclerotic changes in the medulla which often terminate as "lakes" in the bone, and a varying degree of destruction of articular surfaces, the predominant feature being sclerosis. The radiology of aseptic necrosis has been described many times and does not require review here.

Radiographs were taken of the shoulders, hip joints and knee joints, including a large part of the diaphysis, in each case. In the early part of the survey only experienced compressed-air workers were examined, men who had had one or more attacks of bends. There were 83 men in this group and none of them complained of symptoms.

TABLE 3

BONE SCLEROSIS IN COMPRESSED AIR WORKERS

| Age | Period of Employment in Compressed Air (years) | Maximum Pressure Worked (p.s.i.) | Number of Attacks of Bends Experienced | *Radiological Findings: Sites of Sclerosis* |
|---|---|---|---|---|
| 43 | 22 | 40 | 6 | Right shoulder upper shaft |
| 61 | 31 | 40 | Many | Femora lower shaft<br>Tibiae upper shaft probably |
| 40 | 12 | 40 | 3 attacks of staggers and chokes | Femora lower shaft<br>Tibiae upper shaft probably<br>*Right humerus at joint* |
| 40 | 10 | 46 | 6 | Right femur-joint at hip<br>Left femur lower shaft probably |
| 34 | 5 | 42 | 1 | Right femur lower shaft<br>Left femur doubtful lower shaft |
| 43 | 8 | 40 | 7 | Femora lower shaft<br>Left humerus at joint<br>Right humerus probably at joint |
| 28 | 2 | 28 | 5 | *Femur upper shaft* |
| 37 | 1 | 28 | None | Right humerus upper shaft |
| 38 | 3 | 40 | None | Left humerus joint |
| 36 | 10 | 28 | None | Right femur upper shaft |
| 30 | 1½ | 28 | 5 | Right femur—joint at hip |
| 30 | 3½ | 28 | 2 | Femora lower shaft<br>Left femur—joint at hip |
| 21 | 1½ | 28 | 1 | Left femur at hip joint |

An analysis of these 13 cases showed that the medulla of the shaft of long bones was affected in 19 instances, of which five were designated as highly probable, but not certain, involvement. The joints were involved in eight instances; in one of these the diagnosis might have been questioned. The films which were regarded as doubtful are not included. Of the 83 men who had had an attack of the bends, 10 had demonstrable changes in the bones. Of the 20 men who had not had an attack of bends, three showed demonstrable changes in bones.

Towards the end of the investigation it was decided to examine men who had never had an attack of bends, it being thought possible they might show radiological changes; it is already known that medullary infarcts, when the joint is unaffected, are symptomless. Unfortunately, as many workers had left, there was at this time only a small group of 20 men who had worked for varying periods in compressed air without an attack of bends. Of these men, three showed some evidence of early infarction (see Table 3). No comparable population exists from whom control radiographs could be obtained; but the lesions recorded are such as had never occurred in routine hospital radiological work.

*It was expected that a routine antero-posterior* film would give all the information that was required to establish a diagnosis. This expectation was based on the frank abnormalities which have been reported in the literature. It was soon realized that lateral films were necessary to confirm the diagnosis in many cases, since minor variations in texture were discovered which might have been disregarded without the lateral projection.

Two results emerged: (1) Labourers who have worked for years in compressed air, and are still working without symptoms, may show evidence of aseptic necrosis in bones and joints; (2) Aseptic necrosis may be found in the absence of a history of bends for which treatment has been sought.

**Pulmonary disease.**—In two men (Cases 23 and 268) lung cysts were found by radiological examination (Fig. 3). In Case 23, there were two thin-walled cavities in the right lower zone of the lungs, measuring 1·5 in. in diameter, and not containing fluid. In Case 268, there was a single cyst, again in the right lower zone, 1·5 in. diameter; it contained a fluid level, indicating that it communicated with a bronchus and that the bronchus was partly occluded.

Although it must be supposed that these cysts were the cause of the sickness of the two men the evidence is only circumstantial. The mechanism by which they could do so is sufficiently clear. A partial occlusion of a bronchus could become complete at any time. Should this occur during decompression, the cyst must expand when the ambient pressure falls. This would lead, at least, to an abnormal gas exchange through the wall of the cyst, and possibly to rupture of the wall and discharge of gas into venous channels. A process of this sort would account for the peculiarities of Case 23, *especially the fact that the rate of* lowering of pressure during the recompression had to be far slower than is needed in conventional therapeutic decompression. This is intelligible if the problem were the elimination of free gas from a closed cystic space, *rather than the elimination of dissolved gas* from a tissue perfused by circulating blood. But the problem remains as to why, if the men have had the cysts for some time, they did not encounter trouble earlier; or, if the cysts were a result of damage to the lung, how such *well defined cavities were produced*, quite unlike the rents observed with lungs burst by raised intrapulmonary pressures.

These pressure effects in the lung are analogous

to those which cause lesions in the middle ear when the Eustachian tube is blocked. The comparison suggests that complete blocking of minor bronchi in acute bronchitis or chronic bronchitis and emphysema might lead to decompression sickness and might even be a factor in the large variation of weekly bends incidence among labourers under constant working conditions. This would imply that patients with bronchitis and emphysema are not good risks for work in compressed air, and has prompted a further exploration of the radiological and physiological state of the respiratory tract in compressed air workers. A great advance in the prevention of decompression sicknesss, particularly of its major calamities, might be made if it were possible to radiograph the lungs of a patient in the decompression chamber during the attack.

Such cases present a therapeutic problem. In the first place, the cyst cavities, being organized structures, cannot be made to disappear by high pressure or by prolonged treatment, as can a bubble. Secondly, it is usually supposed that bubble formation will not occur in the body until a large pressure change is experienced, but in the event of occlusion of a bronchus small pressure changes are likely to cause trouble. It is advisable that in any atypical or serious case of decompression sickness the possibility of a cyst or of occlusion of a bronchus be borne in mind and two general principles followed: extremely slow rates of therapeutic decompression should be used and, should symptoms recur, no attempt must be made to dissolve a bubble by recompressing the patient to high pressures; the pressure should be raised just sufficiently high to relieve the symptoms. When this has been achieved, the slow decompression can be resumed.

FIG. 3a

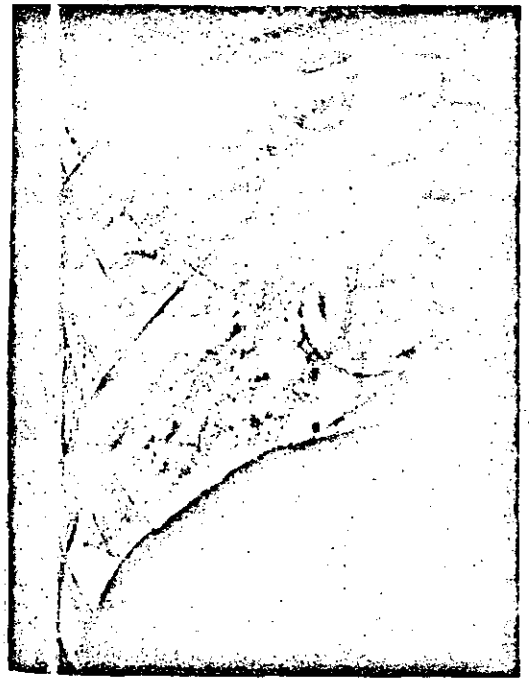


FIG. 3a.—Chest radiograph of Case 23. There are two cysts, one partly concealed by the right border of the heart: no fluid levels.

FIG. 3b

FIG. 3b.—Chest radiograph of Case 268. There is a cyst in right lower zone, containing a fluid level.

## Statistical Analysis of Some Factors in Decompression Sickness

The number of cases of decompression sickness per 100 compressions will be called the "bends percentage". Table 4 summarizes the general bends rate over the whole period of the contract.

TABLE 4
INCIDENCE OF DECOMPRESSION SICKNESS

| Pressure (p.s.i.) | | Compressions | Bends | % |
|---|---|---|---|---|
| *Kent Side* | | | | |
| 0-16 | All exposures | 530 | nil | 0 |
| 16-18 | All exposures | 810 | 7 | 0·86 |
| 18-28 | Over 4 hours | 55,900 | 576 | 1·03 |
| | Under 4 hours | 14,500 | 7 | 0·05 |
| *Essex Side* | | | | |
| 0-16 | All exposures | 1,320 | nil | 0 |
| 16-18 | Over 4 hours | 17,500 | 40 | 0·23 |
| | Under 4 hours | 6,250 | nil | 0 |
| 18-21 | Over 4 hours | 16,800 | 47 | 0·28 |
| | Under 4 hours | 5,900 | nil | 0 |
| *Caissons* | | | | |
| 0-23 | Up to 12 hours | 2,400 (decanted) | 8 | 0·33 |

For detailed analysis, the weekly bends incidence for the Kent side workings over the first 68 weeks of the contract was used. The incidence, plotted in Fig. 4a, varied considerably, from nil to 2·64%, with a modal value of 0·5-1·0%. It bore little direct relation to the pressure in the workings (Fig. 4b). The average bends percentage for the whole of this particular period, in this part of the workings where the tunnelling was hardest, was 0·98%. This is a very creditable figure for the earlier part of a contract; but there are indications that it could be improved.

**Variation in Susceptibility.**—It was obvious that some men have more than their share of bends. The frequency with which men were attacked is shown in Table 5. This shows the way in which a relatively small group of men are responsible for quite a large proportion of the bends. As an example, if the 12 men with five or more bends were to be eliminated then the total number of bends would fall to 310, and bring the average percentage over this 68-week period from 0·98% to 0·77%; if 43 men (about 4% of the working force) with three or more bends were eliminated, the bends incidence would be halved. A further point is that 20% of the total population of workmen had one or more attacks of the bends. Thus it is possible to judge the success of present procedures from contrasting points of view. For an individual worker the risk of an attack of bends at some time during his work in compressed air is quite high (20%): but from the medical aspect the bends percentage, *i.e.*, the number of bends per 100 compressions, is satisfactorily low (1%).

**Decompression Schedule** (as described in the Work in Compressed Air Special Regulations 1958).

Although the present decompression procedure affords considerable protection against bends we obtained evidence that it could be usefully revised, as regards two fundamental assumptions on which the calculations are based.

(1) In preparing the official decompression tables it has been assumed that 18 p.s.i. represents a safe threshold pressure below which negligible trouble would occur. This turned out to be untrue. In the first few weeks on the Kent side, while the pressure was rising from 10 p.s.i. to 18 p.s.i., the average weekly incidence rose steadily to over 0·8% and eight cases of bends occurred. This was sufficiently serious to call for a modified decompression schedule: to provide increased protection the slow phase of all decompressions was lengthened to 10 minutes per lb. Men working at pressures from 16 to 18 p.s.i. were decompressed as though they had worked at 18 to 20 p.s.i. Even with this revised threshold pressure, 28 bends (0·2%) occurred in the Essex workings over a period of six months although the pressure never exceeded 17½ p.s.i. It appears, therefore, that even 16 p.s.i. is above the threshold pressure for absolute safety.

Another sign that the usual assumptions are inadequate appeared when the incidence on the Essex side was compared with that on the Kent side for a similar period; on the Kent side, the incidence was about four times greater, about 1·0%. It is true that the pressure was much higher on the Kent side; but if the decompression tables were properly constructed, the protection should be equal at all working pressures.

(2) In calculating the present decompression routine, it has been assumed that four hours at some pressure is sufficient to ensure full saturation of the relevant body tissues to that pressure. In the decompression tables this assumption gives rise to decompression times which increase as duration of work increases until a four-hour exposure is reached.

TABLE 5
DISTRIBUTION OF BENDS OVER 68-WEEK PERIOD ON KENT SIDE

| Number of bends per man | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 20 |
|---|---|---|---|---|---|---|---|---|---|---|
| Number of men | 817 | 118 | 43 | 18 | 13 | 5 | 1 | 4 | 1 | 1 |
| Number of bends per group | 0 | 118 | 86 | 54 | 52 | 25 | 6 | 28 | 8 | 20 |

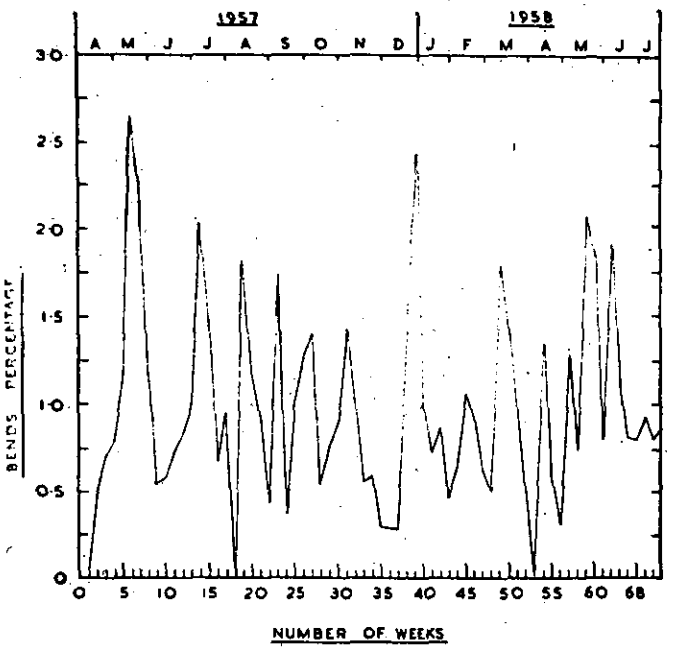



FIG. 4a.—Graph of the weekly bends percentage on the Kent side.

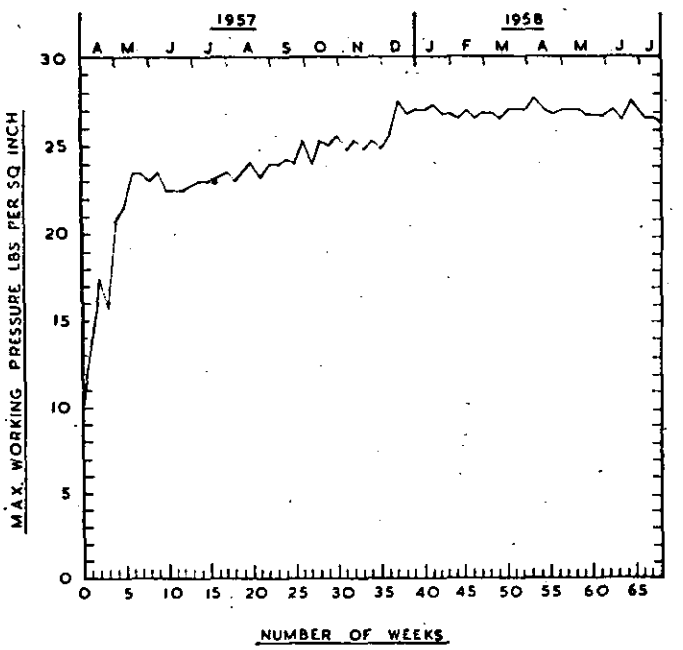



FIG. 4b.—Graph of the maximum weekly working pressure (p.s.i.).

TABLE 6
VARIATION IN BENDS INCIDENCE WITH NATURE AND DURATION OF WORKING PERIOD

| | Day Shift (7 a.m.-3 p.m.) | Back Shift (3 p.m.-11 p.m.) | Night Shift (11 p.m.-7 a.m.) | Total |
|---|---|---|---|---|
| Number of compressions over four hours | 12,943 | 7,905 | 8,174 | 29,022 |
| Number of compressions under four hours | 8,198 | 2,645 | 410 | 11,253 |
| Bends percentage (over four hours) | 1·13 | 1·78 | 1·28 | 1·35 |
| Bends percentage (under four hours) | 0·02 | 0·02 | 0·00 | 0·03 |
| Overall percentage | 0·70 | 1·34 | 1·22 | 0·98 |

All periods of work longer than four hours have, at present, the same decompression time. If this was a correct procedure, the risk of periods of work, four hours or less in duration, should be of the same order as periods of work greater than four hours duration. Table 6 shows an analysis of the experience over the 68-week period on the Kent side; it is quite clear ($p<0.001$) that the risk is far greater with the longer exposure.

This table also brings out two other important points. The group of men exposed for four hours or more constitute the shift working population; it can be seen that they carry the greatest part of the bends risk. Further, there is a distinct tendency for the back shift to be the most hazardous ($\chi^2 = 37$, d.f. = 2, $p<0.001$). This tendency persists even if the shift workers alone are considered ($\chi^2 = 16$, d.f. = 2, $p<0.001$).

**Acclimatization.**—The existence of a marked decline in bends incidence with the number of shifts worked was established in an earlier report (Paton and Walder, 1954). The present undertaking gave an opportunity to confirm and extend these findings. The ordinary shift workers proved to be an unsuitable group for this investigation; the reason was that the presence of alternative compressed air work in the district made it difficult to be certain that the new starters at Dartford were new starters at compressed air work. The employment of 22 steel erectors, who had never entered compressed air until they commenced work at Dartford, provided, however, a remarkable opportunity for examining this question. These men were all quite fit, and they were well used to the type of job which they performed in the tunnel. They were followed for a period of time of over one month, during which the pressure was relatively constant. The number of attacks of bends versus the number of shifts is shown in the histogram (Fig. 5). There is a large decline in the bends incidence with the passage of time; the data are well fitted ($r = 0.97$) by the regression line $\log_{10}$ (number of bends) = 1·16 − 0·42 (number of compressions) giving a half time of $7\pm4$ compressions ($p = 0.05$).

It was also found that working at low pressures for a few days does not appear to confer any measurable benefit on men subsequently introduced to higher pressures. This can be seen from Fig. 5 where a progressive rise of pressure caused an increase in the number of bends; but once the steady maximum level had been reached there was quite a marked fall in bends incidence very similar to that in Fig. 5, where no one had had previous experience of air work.

The confirmation of the existence of acclimatization to air work led naturally to the question of how long the acclimatization persisted when air work ceased. To answer this question the complete histories of a large number of men were scanned to see when an attack of bends occurred on returning to work after a period of absence. The week-ends gave a large number of two-day lapses in regular

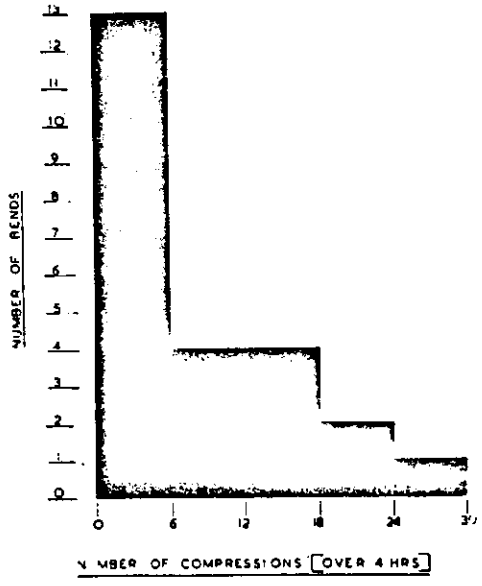



FIG. 5.—Graph of the number of bends occurring in a group of 22 steel erectors, for exposures over four hours, in relation to the number of compressions to which they had been exposed: showing the development of acclimatization.

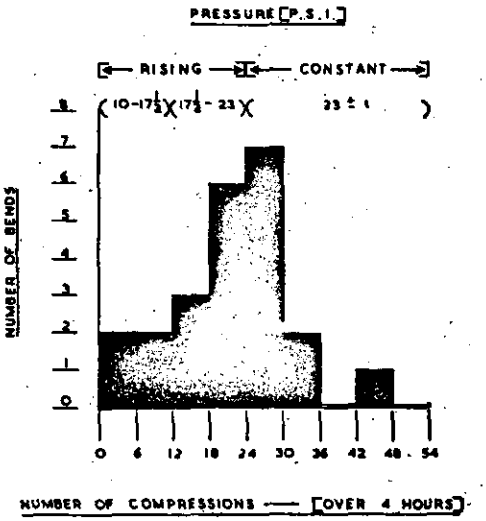



FIG. 6.—Graph of the number of bends occurring in relation to the number of compressions experienced, during a period when the pressure rose from 10 to 23 p.s.i., and then remained constant. Acclimatization did not begin until the pressure stabilized, showing that exposure to low pressures does not protect against exposure to higher pressures.

working, and holidays and strikes gave a large number of lapses of 10 days or over. Unfortunately, few figures accumulated for intermediate periods of time. Fig. 7 shows that whenever a man was away for a period exceeding 10 days then his chance of obtaining a bend on returning to work was very much greater than if he had been away for only two days. The two-day figure is represented by 14 bends and the over-10-day figure by 24 bends, the difference between them is highly significant. The intermediate points, whilst not contradicting the general trend do not permit any further quantitative statements to be made.

The existence of processes of acclimatization and "de-acclimatization" can now be seen to account for a great deal of the apparent randomness in the attacks of bends. The magnitude of the contribution of acclimatization and de-acclimatization may be judged by assuming that some procedure had been evolved to introduce new starters safely to compressed air work and to ensure that no bend occurred in the first three shifts after a period away from work of 10 days or more. In this eventuality the total number of bends over the 68-weeks period would drop to 170 and the overall percentage from 0·98% to 0·42%. The possibility of safely introducing men to higher pressures by first working them at lower pressures has already been shown to fail (Fig. 6). The time spent at the lower pressure appears to be quite irrelevant; thus there are nine cases of men who spent several months free from discomfort at 17 p.s.i. but when transferred to working at 27 p.s.i. had an attack of bends in the first few shifts at the new pressure. There remains the possibility of introducing men to compressed air working by gradually increasing the time worked at pressure. Since the half-time of the acclimatizing process is about seven days any such method would need to be quite prolonged in order to give useful protection. Unfortunately, there is no evidence from the present workings to indicate whether such a procedure would meet with success.

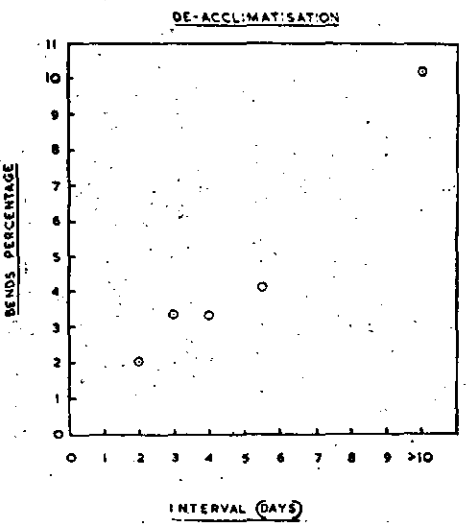



FIG. 7.—Graph of the increase in bends percentage against the duration of a period away from work under pressure.

Climatic Conditions.—During the construction of the Tyne Tunnel, Paton and Walder (1954) failed to find any connexion between the external climatic conditions prevailing and the bends rate. It was thought that the internal environment of the Dartford Tunnel should be investigated.

The most striking finding is the constancy of the internal environment of the tunnel. This appears to be quite independent of the external climatic conditions. Observations were made from September, 1957 to August, 1958 a period including

great changes in the outside weather conditions. Yet the air temperature ranged only from 55 to 69°F. and the relative humidity between 97% and 99%. Considerable difficulty was experienced in measuring the wind velocity in the tunnel, because Kata-thermometer readings are inaccurate when made in compressed air, but the movement of titanium tetrachloride clouds and soap bubbles in the tunnel suggested that the wind velocity was of the order of 5 ft./min. At first sight it is surprising that men can do hard and prolonged physical work in an environment which is 97% saturated but calculation of the "corrected effective temperature" shows this to be well within the accepted limits of comfort. No relationship could be demonstrated between the internal environment of the tunnel and the bends rate.

### Methods of Treatment

All cases were treated by recompression: the methods used were modified during the course of the contract, and were adapted to the nature of the case.

Type 1 Cases.—The majority of cases were compressed to 2-3 lb. above the working pressure and, after being free of symptoms for 10 minutes were decompressed in the usual way, as though for an exposure of more than four hours. If the patient was not free of symptoms after one hour at 3 lb. above working pressure, a higher pressure was used. On two occasions it was necessary to use 10 lb. above working pressure. The pressure at which fast decompression ceased and the slow phase commenced was, in every case, based on the highest pressure to which the man had been exposed in the previous 24 hours—either in the working chamber or medical lock. With this decompression time, however, a third of the cases required one or more further recompressions. For all cases after the first 50, the slow phase of the decompression was therefore lengthened from 9 min./lb. to 15 min./lb.; even so one in 10 required further recompression.

In 56 cases the pressure was raised, not as just described, to a few pounds above working pressure, but only to the pressure required to make the patient symptom-free; after 10 minutes at this pressure, routine decompression was carried out. The average "minimum effective pressure" required was 8 lb. below working pressure. The results were very satisfactory, only one case requiring a second recompression. The use of the minimum effective pressure was also found satisfactory when recompressing a second time; in these cases the man was kept at the requisite pressure for half an hour before decompressing.

About 25% of the men had a "residual soreness" at the end of treatment. There is a marked difference between this soreness and the pain of "bends" and the patient is always aware of the difference. Heat treatment (exposure to the radiations of an infra-red lamp) was found to be beneficial for this residual soreness as also was the use of tablets of aspirin or tab. codein co., B.P. In all cases the patient was considered to be free from the pain of "bends" at the end of treatment. If it was considered that, because of time spent in medical lock under treatment, the man had had insufficient sleep since his last shift, he was advised to miss a shift.

Type 2 Cases.—All cases were treated by immediate recompression. Initial recompression was always to working pressure, higher pressures being used when necessary to remove symptoms. The "effective pressure" was maintained for half an hour after all signs and symptoms had gone before decompression was commenced. The decompression was slow, and the patient was recompressed at once if signs or symptoms returned. For the first four cases the rate of decompression was 10 min./lb. After the fourth case (23) a period of soaking of one to four hours at 12 or 15 lb. was added during the slow decompression. After the 19th case (306) a more prolonged course of treatment was used for all subsequent Type 2 cases. This treatment was as follows: The effective pressure was maintained for half an hour after all signs and symptoms had gone. The patient was then decompressed to 12 p.s.i. at 15 min./lb. and "soaked" (*i.e.*, maintained) at 12 lb. for four hours. Decompression was then continued at the rate of 1 lb. every half hour, "soaking" for one and a half hours at 8 lb., one hour at 4 lb., and one hour at 2 lb. Although this method may take 15-20 hours no additional recompressions have been necessary after its use. Any man who suffered a Type 2 attack of bends was either forbidden to go into compressed air again or strictly limited as to maximum permissible compression pressure and duration of exposure.

### *Discussion*

In principle, decompression sickness should be a totally preventable disease. In fact, it is extremely difficult to eliminate. In assessing the incidence of sickness on this contract particular attention must be paid to two factors. The first is the number of compressions which take place at pressures where a risk exists. Often at the beginning of a working, only trivial pressures are used; yet recording each exposure as a "compression" may serve to lower enormously the overall bends rate. Without information as to the history of the pressure changes in the working, an overall bends rate can be almost

meaningless (see, for instance, Kooperstein and Schuman, 1957); it is desirable to know the rate for pressures above 16 or 18 p.s.i.; and, on large contracts, the number of deaths or of cases of permanent disability are important. The second factor is that of shift length. A common safeguard, used especially in the United States, is to shorten the time spent by each shift in compressed air as pressure rises. Thus a regime may be used which consists, for instance, of two spells of one and a half hours each in compressed air separated by an interval of three hours, which is very wasteful of manpower, but appears safe. The incidence of bends has ranged from about 0·05% to 1% with this type of regime (Norrie, 1934; Boulton, 1942; Levy, 1922; Keays, 1909; Kooperstein and Schuman, 1957). Deaths and permanent paraplegia have still, however, been recorded.

It may be that a procedure of this sort offers advantages. But the recent regulations agreed by the Ministry of Labour and the Institution of Civil Engineers in this country lowered the assumed "safe" working pressures from 22 lb. to 18 lb., and allowed shifts of eight hours or more; and exposures of this length have been used on this contract. A bends incidence, over the whole undertaking, of less than 2% has been regarded as satisfactory by the Institution of Civil Engineers. Reports of undertakings comparable with that discussed here are somewhat scanty. During the construction of a caisson (Lewis and Paton, 1957) an overall incidence of 4% was recorded. At the Tyne Tunnel (Paton and Walder, 1954) for pressures over 18 p.s.i. it was 0·87%, with three cases of paraplegia. In the Dartford pilot tunnel built in 1937-8, the overall incidence was 0·9%. It is satisfactory, therefore, that despite the large number of compressions (119,000) at a pressure of over 16 p.s.i. and up to 28 p.s.i. there has been no fatal case, no permanent disability and an overall incidence of 0·55% (over 18 p.s.i. 0·93%). The presence of a full-time doctor on the site (an unusual feature in such contracts) has ensured that all serious cases were properly treated. It may also have inspired a willingness by the men to return for treatment even in mild cases of bends, thus raising the recorded bends incidence.

Despite this satisfactory record, the occurrence of 650 cases of bends underlines the extent of the failure to abolish the disease. In planning a further attack on the problem of reducing the incidence of bends the first requirement is as full an account as possible of the natural history of the condition. For this reason alone, the confirmation that a process of acclimatization exists, and the further discovery that acclimatization is lost in a week or two if work under pressure ceases, is valuable; for without this knowledge it would be nearly impossible to reach a correct interpretation of the success or otherwise of particular decompression procedures. The cause of acclimatization and its loss remains obscure; it might be that the nuclei available for bubble-formation become used up (Harvey, 1951); or that the nerve endings responding to the painful stimulus produced in "bends" become adapted. The suggestion advanced by Paton and Walder (1954), that it followed an acclimatization to muscular exercise in general cannot be held, now that we know that work at a lower pressure does not acclimatize to work at a higher pressure. If acclimatization could be deliberately induced, without harm, and retained, this alone could lower the bends rate by a large factor; but no means of doing this can yet be indicated.

An obvious possibility for lessening the incidence of the disease is the elimination of susceptible subjects. Unfortunately at present there exists no means of identifying such men, save by seeing whether they get bends. Once employed, they are often willing to continue employment, with its high rates of pay, despite continuing occasional attacks. Our observations on lung pathology suggest that further investigations should be made into the possible relationship between the susceptibility to decompression sickness and lung lesions of a kind hitherto disregarded. This is being attempted.

A further scope for improvement is by modification of the decompression procedures. This has the troublesome feature that any improvement so far envisaged will lengthen the time the men are on the site, without increasing their useful working time. It is quite clear that two assumptions of current decompression theory, *viz.*, that work in compressed air below 18 p.s.i. is absolutely safe, and that a man is fully saturated with nitrogen at four hours, are wrong. The question in this context simply becomes that of balancing an acceptable incidence of bends against a tolerable decompression time. There is lacking, however, any knowledge of what the incidence would be for an assumed safe pressure of 15 p.s.i., and full saturation time of eight hours; to know this would greatly assist the balancing of the issues. A further complication arises where bends follows some sort of injury; it may be that the site of an injury would give rise to pain on decompression at much lower pressures than normal.

Even if minor bends cannot be eliminated in the immediate future, the prospect seems more hopeful as regards the more important serious cases. The two cases we have described, who proved to have cysts in the lungs, exhibited a sequence of events which has occurred in serious cases elsewhere. Further, the character of these attacks and their

severity are such that it is difficult to believe that the mechanism of their production is similar to the harmless limb pains of bends. A large potentially valvular airspace, however, could account for massive air embolism under changing pressure and we suspect that a good many other serious cases may have been due to a mechanism of this type. Routine chest radiographs should serve to eliminate men with such lung cysts from the population at risk (unless the cyst actually arises during a decompression).

The treatment of decompression sickness has also been studied. Two general approaches may be made to the problem: in the first (as in the U.S. Schedule for therapeutic recompression), one may choose high pressures in the hope of compressing any bubbles present and securing their rapid solution; the second approach is to keep the therapeutic pressure as low as possible, so as to minimize any contribution which absorption of nitrogen during the recompression itself may make to recurrence of the lesion. On the whole our experience has supported the second approach; the need for subsequent recompression has been least when compression to the lowest effective pressure was used.

We are most indebted to Mr. J. Kell of Mott, Hay & Anderson, and to Mr. R. H. Falkiner of Messrs. Edmund Nuttall, Sons & Co. Ltd., and to Mr. E. Ll. Earp, O.B.E., contractor's agent, for their helpful cooperation; to the Air Ministry for the loan of the radiographic apparatus; and to Dr. R. C. Norton of the M.R.C. Head Office, for discussion and advice.

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THE TWELFTH UNDERSEA
MEDICAL SOCIETY WORKSHOP

# "EARLY DIAGNOSIS OF DECOMPRESSION SICKNESS"

UMS ANNUAL SCIENTIFIC MEETING
Toronto, Canada
12 May - 1977

Surgeon Commander Ramsay Pearson, RN
Chairman and Rapporteur

UNDERSEA MEDICAL SOCIETY, INC.
9650 Rockville Pike
Bethesda, Maryland 20014

# W O R K S H O P

on

# EARLY DIAGNOSIS OF DECOMPRESSION SICKNESS

held on

Friday, 13 May, 1977.
Toronto, Canada
(preceding the UMS Annual Scientific Meeting)

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Surgeon Commander Ramsay Pearson, RN
Chairman and Rapporteur

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# EARLY DIAGNOSIS OF DYSBARIC OSTEONECROSIS

BY

P.J. GREGG AND D.N. WALDER

Newcastle-upon-Tyne, England

At the present time radiography remains the only accepted means of confirming the diagnosis of lesions-producing symptoms and, what is more important, detecting the presence of symptomless lesions. It is unsatisfactory because (1) there may be a long delay between the causative insult and the appearance of a recognizable abnormality on the radiograph, (2) some lesions of bone necrosis may never become apparent on the radiograph, and (3) radiology only demonstrates a fraction of the total lesion.

There has been an urgent need for a sensitive indicator of bone and/or marrow damage induced by exposure to pressure. Not only may this allow a much earlier diagnosis of osteonecrosis to be made than is possible at present, but also it may allow the damage to be related to a specific exposure to pressure. The latter would be of great value in validating present-day decompression schedules and in experiments designed to develop new decompression schedules which would not result in bone and marrow necrosis.

Study of the pathology of dysbaric osteonecrosis reveals certain features which are of importance in this context. First, in a region where bone necrosis has occurred there is also marrow necrosis. Second, there is often new living bone deposited on the surface of dead trabeculae, presumably as a result of a reactive or repair process.

For the purposes of our investigations bone and marrow necrosis was produced in adult female N.Z.W. rabbits by introducing a saline suspension of glass microspheres (50-70 μm diameter) into the right external iliac artery so as to result in embolization of the right femur. This model was used because not only are persistent gas bubble emboli simulated within the circulation, but also the exact time of the insult can be determined.

Three possible biochemical indicators have been studied: serum alkaline phosphatase, serum ferritin and urinary hydroxyproline excretion.

Because biochemical changes do not indicate the site of the damage bone scintigraphy was investigated as another possible sensitive indicator.

1. Serum alkaline phosphatase

Bone alkaline phosphatase originates mainly in functioning osteoblasts. An increase in serum alkaline phosphatase activity may result from and therefore reflect osteoblastic proliferation or increased activity.

Study of the pathology of caisson disease of bone shows that one characteristic of the lesions is the new living-bone formation which often occurs on the surface of the dead trabeculae. Whether the associated osteoblastic activity is vigorous enough to cause a detectable change in serum alkaline phosphatase activity and therefore constitute a possible biochemical means of detecting this repair stage of bone necrosis is not known. For this reason an investigation of serum alkaline phosphatase activity following the experimental production of bone necrosis in rabbits was carried out.

Bone and marrow necrosis was produced in 9 adult female N.Z.W. rabbits by the method described.

Blood samples were obtained from a marginal ear vein (care being taken to avoid haemolysis) on each of three days before operation, and weekly for six weeks and then on alternate weeks for a further six weeks after operation.

The blood was centrifuged, within one hour of withdrawal, the serum collected by pipetting and an estimation of serum alkaline phosphatase activity performed within 24 hours.

Serum alkaline phosphatase activity was measured using a Clinicard TM Alkaline Phosphatase Chemistry Item 32300. The results were obtained as a direct reading in units per litre on a Clinicard 368 Analyser. The animals were killed 12 weeks after operation.

The range of preoperative alkaline phosphatase activity was found to be 10-39 u/l (Mean 23.3; S.D. 3.81). At no time during the 12 weeks following operation did the serum alkaline phosphatase activity differ significantly from the preoperative mean ($p>0.05$, Student paired-t test).

Macroscopic and microscopic examination of the excised femora revealed bone and/or marrow necrosis in each of the nine animals used. Microscopic examination revealed the presence of areas of dead bone, recognized by the characteristic absence of osteocytes from the lacunae of bone. These areas of avascular necrosis of bone were usually associated with evidence of a surrounding reaction or attempt at repair in the nature of new-woven bone formation.

2. Urinary hydroxyproline excretion

It has been suggested that since bone necrosis is associated with an increased turnover of collagen, the excretion of hydroxyproline - an imino acid found almost exclusively in collagen - is likely to be altered (2). This has been investigated by (8) using the rabbit model already described. They found that a significant rise in total hydroxyproline excretion occurred within a few days of the injection for those rabbits in which there was later shown to be histological evidence of bone necrosis. This indication occurred long before there was any radiographic change.

They suggested that urinary hydroxyproline estimations might be used to give an early indication of bone necrosis in man.

Unfortunately, urinary hydroxyproline excretion is affected markedly by the constituents of the diet, and it would not be feasible to keep all men on a constant diet to overcome this problem. This is a serious drawback to the possible use of this method for the surveillance of those men at risk.

3. Serum Ferritin

Ferritin is the major iron-storage protein in the body.

Unlike the other iron-storage complex haemosiderin, ferritin is water soluble. Measurements of nonheme iron concentrations indicate a particularly large amount in the liver, spleen and bone marrow (5).

Recently ferritin has been found to be present in the serum of man with the use of a sensitive immunoradiometric assay (1). The serum concentration exhibits little diurnal of daily fluctuation in health (7).

Recently there have been demonstrated (3) rises in the serum ferritin levels following paracetamol overdosage. In the latter cases the serum ferritin levels correlated well with the amount of cell death seen in liver biopsy specimens. It is assumed therefore that ferritin leaks out of damaged liver cells and gains entry into the circulation. Whether an increase in serum ferritin concentration accompanies marrow damage has been investigated (4).

Marrow necrosis was produced in adult female N.Z.W. rabbits by the method described. There were seven rabbits in the experimental group and in addition there was a control group of six rabbits.

Serum ferritin concentration was measured by a method based on the immunoradiometric assay technique described by Addison (1).

The reference range for rabbit serum ferritin concentration was calculated to be 2.4 - 31.0 µg/l with a mean of 11.0 µg/l (S.D. ± 9.49; S.E.M. ± 2.63).

All rabbits receiving microspheres had serum ferritin levels outside the reference range within 48 hours of operation. Peak levels were obtained in five animals within 24 - 48 hours but in the remaining two animals the levels were still rising 96 hours after operation. In none of the control (injection of saline only) rabbits did the serum ferritin level deviate from the reference range and the mean daily change was only ± 19%. There was a statistically significant difference ($p<0.05$) between the serum ferritin concentration of rabbits receiving microspheres and the serum ferritin concentration of control rabbits on each of the four days after operation (Student unpaired-t test).

Examination of the excised right femora of rabbits receiving microshperes revealed macroscopic and/or microscopic evidence of marrow infarction within the bones of all animals.

4. Bone scintigraphy

Bone scintigraphy has now an established role in the early detection of malignant secondary deposits in bone before they can be diagnosed by radiography.

The pathological basis for the abnormal bone scintigram is thought to be as follows. Regardless of whether the secondary malignant deposit forms or destroys bone, it induces much reactive new-bone formation. It is thought that the bone-seeking tracer is deposited in increased amounts in the osteoid tissue which is produced during this reactive new-bone formation.

This increased concentration of radioactive tracer at the site of a secondary deposit in bone can be detected by the external counter and appears as a 'hot-spot' on the scintigram.

Study of the pathology of caisson disease of bone has shown that, probably as a result of revascularization and attempted repair, new-bone formation takes place on the surface of the dead trabeculae without prior resorption of the latter. In theory therefore it may be possible, using bone-scintigraphy, to detect this new-bone formation at an earlier stage than is possible by radiography.

Bone and marrow necrosis was produced in 14 rabbits by the method described. Bone scintigrams of both femora were performed before operation and 3 and 12 weeks after operation. Radiographs of both femora were performed immediately after operation, to establish a base line, and at three-weekly intervals thereafter for 12 weeks. Following the bone scintigram 12 weeks after operation the animals were killed and the femora excised for macroscopic and microscopic examination.

Each animal was given an intravenous injection of approximately 5mCi of $Tc^{99m}$-labelled Osteoscan (Proctor and Gamble) into a marginal ear vein and imaging of the bones was performed 4 - 6 hours later using a gamma camera (Ohio Nuclear, Series 100) fitted with a pinhole collimator with a 4mm aperture.

Radiographs were obtained using a Watson MX4 X-ray unit and Ilford Rapid R X-ray film in conjunction with Ilford Fast Tungstate Intensifying screens.

Of the scintigrams performed 3 weeks after operation on the 14 animals, 12 showed abnormalities (in the nature of 'hot-

spots') at a time when radiography revealed no abnormalities; one scintigram was normal and one was suspected to be abnormal. On repeating the scintigraphic examination 12 weeks after operation, 9 scintigrams were still abnormal, one scintigram was still normal, two had become normal and one previously suspected to be abnormal was now definitely abnormal. One of the original 14 animals (whose scintigram was abnormal 3 weeks after operation) had died. Radiography at this stage revealed abnormalities in only 2 of the 13 remaining animals with one animal having suspected abnormalities.

There was a total of 27 areas depicted as abnormal either on the 3-week or the 12-week scintigram; of these bone necrosis was confirmed in all of them on microscopic examination. In nearly all of the areas of bone necrosis there was microscopic evidence of new living appositional bone formation which may be the pathological basis of the positive scintigram.

Discussion and Conclusions

Measurement of the serum alkaline phosphatase activity does not appear to be a sensitive enough indicator of the osteoblastic activity associated with regions of bone and marrow necrosis to be of any value in the early diagnosis of this condition.

It would appear that the concentration of serum ferritin may increase as a result of marrow necrosis and that this change may be observed as early as 24 - 48 hours after the causative insult.

Attention must be drawn to the fact that the marrow of rabbits, even when mature, is much more cellular in all regions of the femur than the fatty marrow present in most regions of the adult human femur. It may be that the concentration of ferritin is much greater in haemopoietic marrow and that infarction of the fatty marrow of human femora would not result in any observable change in serum ferritin concentration. However, it must also be pointed out that some haemopoietic marrow is nearly always present in the upper ends of the femur and humerus which are the sites of the important and potentially disabling juxta-articular lesions.

There are several important advantages of this method as a possible early indicator of caisson disease of bone. Because it is thought that the rise in serum concentration results from the release of ferritin from damaged cells the method is not dependent on revascularization and the establishment of a repair

process which perhaps may not always occur. Because it may be possible to detect marrow damage as early as 24 - 48 hours after the causative insult it may be possible, using this method, to relate the damage to a specific exposure to pressure. To do so would be of great value in validating presently-used decompression schedules and in experiments designed to produce decompression tables which would result in the complete elimination of bone and marrow damage. Study of the pathology of this condition suggests that where bone necrosis occurs so also does marrow necrosis and therefore the bone damage may be indirectly detected by this method. However, were marrow alone to be damaged, it is unlikely that it would be detected radiologically unless subsequent calcification were to occur in the infarct; it may however be detected by the change in serum ferritin concentration.

There are some disadvantages of this method for the early detection of caisson disease of bone. The most important disadvantage is that it will not detect the site of the damage. It also requires blood sampling of those men at risk which would have to be repeated after each exposure because the rise in serum concentration which may reflect marrow damage is probably short-lived, lasting only about four days.

For the successful use of this method in those men at risk one would have to ascertain that an increase in serum ferritin concentration does not occur merely as a result of exposure to pressure or the subsequent decompression. With reference to the latter one might argue that an increase in serum ferritin concentration might result from damage to the liver or spleen by circulating gas-bubble emboli; however, there is no evidence that this occurs at the present time.

The serum ferritin concentration does not exhibit diurnal or daily fluctuations in health, nor is it affected by diet. The assay requires only 0.1ml of serum which can be obtained from a finger-prick sample and which can be stored indefinitely until a large number of samples can be assayed at once. This method is therefore eminently suitable for the repetitive sampling of men at risk 'on site'. There is now available a semiautomatic immunoradiometric assay for serum ferritin (6); 200 samples can be analyzed in two half-days.

It is suggested that this method should now be used on a trial basis in those men at risk in order to refute or substantiate its possible usefulness as an early indicator of caisson disease of bone. With the exception of intercurrent infection, the other causes of a raised serum ferritin concentration are unlikely to confuse the picture in commercial divers who have to be passed medically fit annually in order to obtain certification.

Considering the results of radiographic examination of rabbits following the production of bone and marrow necrosis, in most cases there was no change in the radiographic appearance up to 3 months after the causative insult despite the presence of lesions which were already associated with a reactive or repair process (in many cases marked) in the nature of new-bone formation. This is further evidence of the inadequacy of radiography for the early detection of bone and marrow necrosis.

It was possible to detect regions of bone and marrow necrosis as early as 2-3 weeks after the causative insult by scintigraphic examination of the rabbit femora following the intravenous injection of $Tc^{99m}$-labelled Osteoscan. In most cases the abnormalities observed on the scintigram persisted for at least 12 weeks. There were no false positive scintigrams.

The advantages of this method when compared with the estimation of changes in serum ferritin concentration for the early diagnosis of bone and marrow necrosis are that it is possible to identify the site of the damage and also, because the abnormality appears to persist in most cases for 12 weeks at least it would not be necessary to examine the man at risk after every exposure. Permission has now been obtained from the Isotope Advisory Panel of the D.H.S.S. to carry out a limited trial of the value of this technique in the early detection of bone necrosis in those men exposed to the risk of developing caisson disease of bone.

The possible disadvantage of scintigraphy is that it appears that the presence of a reactive or repair process in the nature of new-bone formation may be an important factor in determining the presence of a 'hot-spot' on the scintigram; this may not always be present and would therefore probably lead to the lesion being missed. In this latter respect the estimation of changes in serum ferritin concentration would be a more satisfactory method.

In summary it is suggested that radiography has serious shortcomings in the early diagnosis of caisson disease of bone because of the long delay before the appearance of an abnormality. Two additional methods which have been investigated show promise i.e. scintigraphy using $Tc^{99m}$-labelled diphosphonate and the estimation of changes in serum ferritin concentration.

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Aus dem Zentralröntgeninstitut der Medizinischen Akademie Danzig
(Direktor: Prof. Dr. H. U. Albrecht)

# Veränderungen am Schultergelenk als Folge von Druckluftkrankung

Von K. Th. Grützmacher

Mit 2 Abbildungen

Bei den sog. Drucklufterkrankungen handelt es sich um bestimmte typische Krankheitserscheinungen bei Arbeitern, die unter erhöhtem Luftdruck arbeiten. Zahlreiche Untersuchungen und Beobachtungen haben das Wesen dieser *Druckluft- oder Caissonkrankheit* zu klären versucht und sind im Schrifttum niedergelegt.

*Bei den Caissonarbeitern* wird in einem Senkkasten gearbeitet, in den zur Verdrängung des Wassers Luft mit erhöhtem Druck eingepreßt wird. Diese Luft höheren Druckes gelangt durch die Atmung in den Körper und wird von den Gewebsflüssigkeiten absorbiert. Da eine Flüssigkeit um so mehr Gase aufnimmt, je stärker der auf ihr lastende Druck ist, kommt es allmählich zu einer völligen Sättigung des Organismus mit einer Gasmenge, die dem Partialdruck der umgebenden Luft entspricht. Außerdem findet noch eine selektive Absorption *des Luftstickstoffs statt. Dieser* speichert sich besonders in den Fetten und Lipoiden, die ungefähr 6mal soviel Stickstoff wie das übrige Körpergewebe *aufnehmen können.*

Die Erscheinungen der Caissonkrankheit treten nun nicht während des Aufenthaltes in komprimierter Luft, sondern erst beim oder nach dem Verlassen der mit Preßluft gefüllten Räume auf, während oder nach der sog. Dekompression. Die Erkrankung kommt dadurch zustande, daß in den mit verdichteter Luft gesättigten Organen beim Übergang zum Atmosphärendruck Gas frei wird und sich in Form von Luftblasen in den Geweben ansammelt. Das frei werdende Gas besteht *im* wesentlichen aus Stickstoff, der also von den im Körper absorbierten Gasen für die Entstehung der Dekompressionskrankheit in erster *Linie in Frage kommt.*

Um das Auftreten dieser Luftblasen zu vermeiden, darf die Dekompression nur langsam *durchgeführt* werden. Dadurch wird dem in den Geweben absorbierten Stickstoff Gelegenheit gegeben, auf dem Wege über die Lungen den Körper zu verlassen, ehe es zu einer Bildung von Luftblasen kommt. Diese frei werdenden Luftblasen lösen nun je nach ihrem Sitz verschiedene Krankheitssymptome aus. Am bekanntesten sind die starken Schmerzanfälle in den Extremitäten, die sog. „bends", und die sehr gefährlichen Erscheinungen der Apoplexie, Myelitis, Lungenembolie und des Menièreschen Symptomenkomplexes.

Unter ähnlichen Verhältnissen wie ein Caissonarbeiter arbeitet ein Taucher. Der Tauchapparat besteht aus *Helm und Gummianzug*, die beide wasserdicht miteinander verbunden sind. Die Atmungsluft wird dem Taucher durch Schläuche, die in den Helm münden, zugeführt und kann sich von hier aus über den Anzug verteilen. Es wird aber nur soviel Luft hinein gepumpt, daß sich in dem Gummianzug ein Luftmantel befindet, der dem Taucher ungefähr bis zur Brust reicht. Die eingepumpte Luft muß den auf ihr lastenden Wasserdruck kompensieren, so daß im Taucheranzug

immer ein der Tiefe entsprechender Druck herrscht. In 30 m Wassertiefe beträgt dieser Druck in Süßwasser 3 atü (4 Atm. absolut), in Seewasser entsprechend dem Salzgehalt etwas mehr.

Die Arbeit im Taucheranzug geht also praktisch unter denselben physiologischen Bedingungen wie im Caisson vor sich, und es können daher beim Taucher dieselben Dekompressionserscheinungen auftreten wie bei den Caissonarbeitern. Daher haben auch beim Tauchen ähnliche Verhaltungsmaßregeln und Verhütungsvorschriften Gültigkeit wie beim Arbeiten im Caisson. Der Taucher muß darauf achten, daß nach Abschluß seiner Arbeit der Luftdruck innerhalb seines Taucheranzuges langsam wieder bis zur Norm absinkt. Die Zeit, die für den Druckausgleich verwandt werden muß, hängt von der aufgesuchten Wassertiefe und der Dauer des Tauchens ab. Der Taucher muß aus

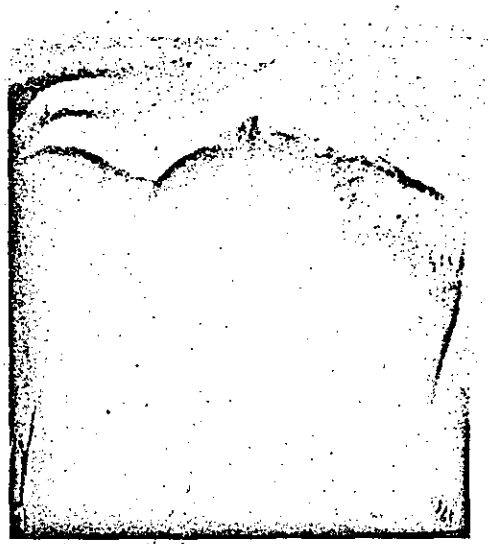

Abb. 1. März 1939.

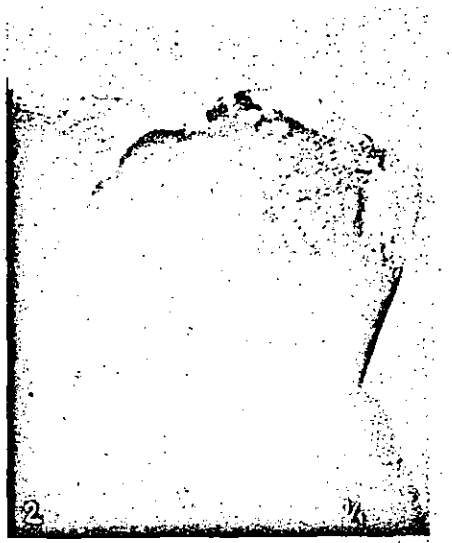

Abb. 2. Oktober 1940.

größeren Tiefen absatzweise und in eingeschalteten Pausen auftauchen, um das Auftreten von Dekompressionserscheinungen zu verhüten. Diese sind zu befürchten, wenn lange Zeit über 13 m getaucht wurde und danach das Auftauchen zu schnell erfolgte. Für den Fall, daß sich Anzeichen von Drucklufterkrankung bemerkbar machen, oder wenn zu schnell aufgetaucht wurde, finden sich an Bord von Taucherschiffen, insbesondere von Marinetaucherschiffen, Sanitätsschleusen, um den Taucher wieder unter erhöhten Druck setzen zu können

Bei Caissonarbeitern kommt es gehäuft zu chronischen Gelenkleiden. Von Bornstein und Plate wurden bereits 1905 erstmalig deformierende Gelenkveränderungen bei Caissonarbeitern beschrieben. Die von ihnen angeführten Röntgenbefunde zeigen aber lediglich das Bild einer Arthrosis deformans, ohne irgendwelche hiervon abweichenden, für eine Caissonkrankheit charakteristischen Symptome aufzuweisen. Seitdem ist im Schrifttum verschiedentlich angeführt, daß eine Arthrosis deformans als Folge langjähriger Caissonarbeit auftreten kann. Erst Christ teilt 1934 vier Fälle von Hüftgelenkserkrankungen mit, die ein ganz typisches, in dieser Form bisher nicht beschriebenes Krankheitsbild bieten. Bei seinen Fällen handelt es sich um Hüftgelenkserkrankungen, bei denen im Röntgenbild der Hüftgelenkkopf an mehreren Stellen der Kalotte rundliche Aufhellungen und strukturlose Knochenpartien zeigt. In einem Falle war der Kopf dadurch so zerstört worden, daß es zu einem teilweisen Einbrechen der Gelenkfläche in Form der

sog. Eierschalenfraktur gekommen war. Nach der Ansicht von Christ handelt es sich hierbei um das Auftreten von Resorptionsherden, die von subchondral gelegenen Knochennekrosen herrühren, die die Oberfläche des Hüftkopfes unterminieren und dadurch zu seinem Einbrechen führen können.

Im Zentralröntgeninstitut ergab sich die Gelegenheit, bei einem Taucher ganz gleichsinnige Gelenkveränderungen am Schultergelenk zu beobachten, wie sie von Christ beschrieben wurden. Es handelt sich dabei um folgenden **Fall.**

Bl., Otto, 37 Jahre alt. Früher nie ernstlich krank gewesen. Patient ist bereits von 1911—40, also jetzt seit 29 Jahren als Taucher tätig. Er hat im allgemeinen immer nur in geringen Wassertiefen bis zu 10 m getaucht. Am 9. 9. 1934 hat er aber in 32 m Wassertiefe gearbeitet. Er mußte wegen eines Defektes am Ventil innerhalb kürzester Zeit an die Oberfläche kommen. Anfangs bestanden keine Beschwerden. Einige Stunden nach dem Auftauchen kam es aber zu heftigsten Schmerzen in beiden Schultern, besonders in der rechten. Es handelte sich um einen typischen Anfall von „bends". Da es an Bord des Tauchschiffes eine Überdruckkammer, eine Sanitätsschleuse nicht gab, in die man den Patienten hätte wieder einschleusen können, wurde er in das Krankenhaus eingeliefert. Unter Verabfolgung von Analgetika ließen die Beschwerden im Laufe der nächsten Tage nach, so daß der Patient nach 3 Tagen wieder aus dem Krankenhaus entlassen werden konnte. Irgendeine Behinderung in den Schultergelenken hat vorerst nicht bestanden. Bei einer Untersuchung, die im März 1939 wegen neu aufgetretener stärkerer Beschwerden in den Schultergelenken vorgenommen wurde, fand sich bereits damals, daß die Beweglichkeit im rechten Schultergelenk eingeschränkt war. Die Hebung des Oberarms war nur bis zur Horizontalen möglich. Die Rotation war unbehindert. Dieser klinische Befund hat sich bis zu einer Nachuntersuchung im Oktober 1940 nicht wesentlich geändert.

Röntgenbefund vom März 1939: Das rechte Schultergelenk zeigt eine Deformation des Gelenkkopfes, der stark abgeflacht ist. Die Struktur des Knochens ist nicht einheitlich. Man erkennt einzelne Aufhellungen, die von verdichteten Bezirken umgeben sind. In der Nähe der Gelenkfläche ist der Knochen zerklüftet und sieht strukturlos aus. Die Gelenkkontur ist an einigen Stellen unterbrochen. Ein Einbruch der Gelenkfläche ist also bereits erfolgt. Dieser Befund erfuhr im Laufe der Zeit bis Oktober 1940 noch weitere Veränderungen. Die strukturlosen Knochenpartien grenzen sich noch stärker ab und machen den Eindruck von Sequestern. Der Einbruch der Gelenkfläche wird größer. Schließlich kommt es auch zur Sequestrierung ins Gelenk und damit zur Bildung eines größeren Defekts am Gelenkkopf. Geringe Veränderungen bestehen am rechten Schultergelenkkopf. Derselbe ist nur gering deformiert. Die gelenknahen Partien erscheinen deutlich verdichtet und sind von einzelnen Aufhellungslinien durchzogen. Dieser Befund ist im Laufe der Zeit stationär geblieben. Untersucht wurden außerdem sämtliche sonstigen Gelenke, an denen aber in keinem Falle ein pathologischer Befund erhoben werden konnte.

Wenn man sich die Entstehung der eben beschriebenen Veränderungen vor Augen hält, so ist das Krankheitsbild und das anatomische Bild ohne weiteres verständlich. Die Allgemeinansicht geht heute dahin, daß es sich bei derartigen Drucklufterkrankungen um die Folge von Gasembolien handelt. Derartige Embolien bedingen Ernährungsstörungen und rufen Nekrosen des Knochens hervor, die subchondral gelegen sind. Diese werden zum Teil resorbiert und unterminieren die Gelenkflächen, bis diese schließlich einbrechen. Dabei stoßen sich dann einzelne Sequester ins Gelenk ab. Der Röntgenbefund erinnert stark an die Perthessche Erkrankung der Hüftgelenke, der im wesentlichen die gleichen pathologisch-anatomischen Veränderungen zugrunde liegen. Im vorliegenden Falle bestanden aber keine Bedenken, die von uns beobachteten Gelenkveränderungen als die Folge einer Drucklufterkrankung anzusehen. Der Zusammenhang mit dem schweren Anfall von „bends" im Jahre 1934 ist gegeben. Früher haben nie Beschwerden in den Schultergelenken bestanden, so daß man eine angeborene Störung oder eine in der Jugend überstandene Epiphysenerkrankung ausschließen konnte. Ein Trauma wurde nicht angegeben. Außerdem wurde ein neurologischer Befund nicht erhoben. Eine Arthropathie auf dem Boden einer Tabes oder Syringomyelie kam also nicht in Frage. Neu ist nur, daß derartige Drucklufterkrankungen auch an Schultergelenken auftreten können, während sie bisher nur an den Hüftgelenken beobachtet wurden.

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**The final results of the 3-year X-ray survey of the sample of 383 naval clearance divers were: positive, 16; doubtful, 7; and negative, 360. (DHE)**

Surgeon Captain J A B Harrison
(*Royal Naval Hospital, Haslar, Gosport, Hampshire*)

## Aseptic Bone Necrosis in Naval Clearance Divers: Radiographic Findings

Before 1966 it was suspected that aseptic bone necrosis did occur in naval divers, but previous X-ray surveys had proved inconclusive and abortive. No documentary evidence existed of definite accepted radiological lesions and there was no knowledge of any possible incidence in the naval diving population.

A survey was undertaken in 1967, 1968 and 1969 to establish the presence and assess the incidence of aseptic bone necrosis in a sample of naval clearance divers. An interim report of our methods and techniques has been published (Elliott & Harrison 1970), but briefly we endeavoured to obtain standard high quality radiographs of the shoulders, hips and knees, and specific detailed standardized projections were laid down using eight exposures per diver X-rayed. At the end of the survey the films were double-read (F C Golding & JABH) and all discrepancies and doubtful results were reviewed by them in concert. At this stage the radiologists were unaware of the details of diving history of the cases whose X-rays they examined.

The criteria of radiological diagnosis were those adopted by the Medical Research Council Decompression Sickness Panel (McCallum *et al.* 1966) and now accepted on an international basis (Table 1). The lesions are well known in caisson workers and have been described by several workers (F C Golding, J K Davidson & P D Griffiths, MRC Decompression Sickness Panel, University of Newcastle, 1967, personal communication). The lesions in divers are similar and have been described (Elliott & Harrison

1970). More advanced lesions have been detected in other surveys of divers, some diving under largely uncontrolled conditions (Y Ohta 1969, personal communication). The early lesions are difficult to detect, requiring an educated eye. We have tried to eliminate observer error and subjective impression by double-reading and strict adherence to the described criteria of known lesions. Most of the lesions we have found are shaft lesions. The juxta-articular lesions have been less common in our sample of naval divers. The lesions have generally preceded symptoms.

On conclusion of our double-reading of the survey films we had established an incidence of 4·2% in the sample of clearance divers using the standard described survey views. At this stage three main tasks remained:

(1) Re-examination of the doubtful lesions, using special X-ray views of the suspected lesions, and employing tomography where necessary to try to eliminate these uncertainties.
(2) X-ray of a control sample of naval personnel not exposed to pressure in the age-rank distribution of the clearance diving population, in an effort to exclude possible differential diagnoses of the causes of aseptic bone necrosis.
(3) Discriminant analysis of the diving history in correlation with the X-ray findings.

It was decided that the re-examination of doubtful lesions must be carried out at either RNH Plymouth or RNH Haslar. In fact, 2 cases were X-rayed at Plymouth under the supervision of the radiologist there and 5 at Haslar; 2 have yet to be examined for that variety of reasons which those familiar with the Service environment will appreciate; and 2 are now civilians and have not yet attended Haslar for re-examination. This re-examination has been both revealing and unrewarding. Revealing, because it has convinced me personally that the most meticulous X-ray examination and display of those X-ray lesions, which to the educated eye appear doubtful, does not resolve one's doubts. The lesion is seen more clearly; it may be more easily shown to others and may appear more convincing to them. But only rarely does this process resolve one's doubts as to its nature. Perhaps this is why only 4 of the original 11 doubtful lesions have so far been reclassified; all these are now considered negative. But a further 4 have not as yet been re-examined by more detailed X-ray techniques than the survey views.

*Table 1*
**Early radiological parameters of aseptic bone necrosis**

| |
|---|
| *Juxta-articular* |
| (A1) Dense areas with intact articular cortex |
| (A2) Spherical segmental opacities |
| (A3) Linear opacity |
| (A4) Structural failures: (*a*) translucent subcortical band; (*b*) collapse of articular cortex; (*c*) sequestration of cortex |
| (A5) Secondary degenerative arthritis |
| *Head, neck and shaft* |
| (B1) Dense areas (*not* bone islands) |
| (B2) Irregular calcified areas |
| (B3) Translucent areas and cysts |
| (B4) Cortical thickening |

*Table 2*
**Aseptic bone necrosis: control sample of 100 naval personnel not exposed to pressure in age-rank distribution of a random sample of clearance divers**

| *Rank* | *Age-group* | *No. in sample* | *No. X-rayed to 30.1.71* |
|---|---|---|---|
| Lieutenant Commander | 31–47 | 6 | 2 |
| Lieutenant | 23–30 | 11 | 5 |
| | 34–45 | 4 | 3 |
| Sub-Lieutenant | 29–34 | 2 | 1 |
| Chief Petty Officer | 32–49 | 9 | 2 |
| Petty Officer | 25–39 | 28 | 15 |
| Leading Seaman | 20–33 | 20 | 16 |
| Able Seaman | –30 | 20 | 19 |

The final results of the 3-year X-ray survey of this sample of 383 naval clearance divers were: positive, 16; doubtful, 7; and negative, 360. During the three years 243 divers were X-rayed once, 121 twice, and 19 three or more times. In addition, 7 divers with doubtful lesions on the survey views have been X-rayed by tomography and using special views.

The generally accepted causes of aseptic bone necrosis include sickle cell anæmia, alkaptonuria, polyarteritis nodosa, syphilis, chronic pancreatitis, caisson disease, chronic alcoholism and corticosteroid therapy. Most of these can be readily eliminated and with one exception are unlikely in fit naval personnel. However, it was decided to X-ray a control sample. So far, only 63 of this balanced sample of 100 naval personnel, who meet the requirements of age, rank and non-exposure to pressure, have been induced to volunteer for X-ray. All cases X-rayed have been X-rayed at Haslar and examined by me (Table 2). No evidence of aseptic bone necrosis has been found, all being considered negative.

Meanwhile, of course, further X-ray views of the 383 naval clearance divers have continued on a routine 'annual' basis, and 144 have been re-X-rayed up to January 30, 1971. I think the change produced in our findings is probably the strongest confirmation of our results, techniques and methods. Three cases have moved from negative to doubtful, one from negative to positive and one from doubtful to positive. The results at January 30, 1971, were therefore: negative, 356; doubtful, 9; and positive, 18.

The 2 most recent positive cases are of some interest; Case 105 had been engaged in deep

*Table 3*

**Extract of classified results from series of 383 naval clearance divers (*see* Table 1)**

| *Case No.* | *Year of X-ray* | *Result* | *Humerus (head & shaft)* R | L | *Femur, upper* R | L | *Femur, lower* R | L | *Tibia (upper)* R | L |
|---|---|---|---|---|---|---|---|---|---|---|
| 46 | 1967 | − | − | − | − | − | − | ? | − | − |
| | 1971 | + | − | − | − | − | B2 | B2 | − | − |
| 105 | 1967 | ? | − | − | − | − | ?B2 | − | − | ?B2 |
| | 1971 | + | − | − | − | − | B2 | ?B2 | − | B2 |

− = negative. + = positive. ? = doubtful

trial dives prior to 1967, as indeed had most of our positive cases. Case 46, negative in 1967, has since then been engaged on trial dives with the US Navy (Table 3).

Finally we must attempt to discern some pattern in the distribution and ettology of these lesions of this clusive disease. Some tentative correlations between diving history and the X-ray lesions have already been made. Perhaps discriminant analysis will assist in detecting further correlations.

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# DYSBARIC OSTEONECROSIS IN DIVERS

## I. A Survey of 611 Selected U.S. Navy Divers

by

C.A. Harvey, CDR, MC, USN
and
R.L. Sphar, CAPT, MC, USN

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Approved and Released by:

R.L. Sphar, CAPT, MC, USN
Commanding Officer
NavSubMedRschLab

## ABSTRACT

The Naval Submarine Medical Research Laboratory is conducting a radiological survey to determine the prevalence of dysbaric osteonecrosis in U.S. Navy divers and to develop epidemiological data related to those aspects of the hyperbaric environment that contribute to the ultimate occurrence of the lesions. Twelve juxta-articular lesions and nine head, neck or shaft lesions have been identified in the extremities of fifteen divers who are radiologically positive cases of dysbaric osteonecrosis among 611 non-randomly selected divers surveyed. While the number of positive cases is too small to draw statistically reliable conclusions, certain trends are evident. Lesions were most common in the shoulders and in older divers. Saturation divers and all other helium divers had almost the same percentage of positive cases but air divers had a slightly lower percentage than either group. Data derived from an enlarging survey population should provide additional insight into the epidemiology of the condition.

## SUMMARY PAGE

### THE PROBLEM

To determine the prevalence of dysbaric osteonecrosis in U.S. Navy divers and to develop epidemiological data for insight into those aspects of the hyperbaric environment that contribute to the ultimate occurrence of dysbaric osteonecrosis.

### FINDINGS

Twelve juxta-articular lesions have been identified among 21 lesions observed in fifteen radiologically positive cases of dysbaric osteonecrosis observed in 611 non-randomly selected U.S. Navy divers. One symptomatic case of dysbaric osteonecrosis has been observed. Lesions tended to appear in older divers. Saturation divers and all other helium divers had almost the same percentage of positive cases but air divers had a slightly lower percentage than either group.

### APPLICATIONS

Based on statistically inadequate but strongly indicative data, diving as conducted in the U.S. Navy is related to a low prevalence of dysbaric osteonecrosis, and only rare symptomatic cases. An increased survey population is being obtained to provide additional insight into these preliminary observations.



### ADMINISTRATIVE INFORMATION

This investigation was conducted as part of Bureau of Medicine and Surgery Research Work Unit MF51.524.014-0004 - "Dysbaric Osteonecrosis in Navy Divers". The present report is No. 1 on this work unit. It was received for review on 19 February 1976, approved for publication on 24 February 1976 and designated as NavSubMedRschLab Report No. 832.

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# Decompression Sickness

## Volume 1

*The Biophysical Basis of Prevention and Treatment*

**B. A. Hills**
*Professor of Physiology and Chief*
*Hyperbaric Physiology Section of the Marine Biomedical Institute*
*University of Texas Medical Branch, Galveston*

*A Wiley–Interscience Publication*

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# Chapter 8

# Treatment and General Hyperbaric Limitations

The formulation of a decompression and the overall planning of a dive is not solely determined by the imminence of decompression sickness. There are factors which limit the rate of compression, the composition of the mixture breathed on the 'bottom' and then the use of agents such as oxygen for both prevention and treatment of bends. In addition, there are a number of hyperbaric phenomena which have been observed scientifically but are better discussed separately since it is not certain that they are responsible for the clinical effects or have any clinical manifestations at all. However, the most serious clinical consequences of diving, second only to neurologic and spinal decompression sickness, are those of dysbaric osteonecrosis ('bone rot'). Although it is not yet known how a dive can be modified to prevent it, or even whether it can be prevented at all, enough information is starting to accumulate to enable some prediction of its incidence to be made.

## Dysbaric Osteonecrosis

There is now little doubt that aseptic necrosis of bone can be caused by exposure to compressed air, since the incidence is several orders of magnitude higher in caisson workers and divers than in the normal population. In this text the view has been taken that this insidious occupational hazard is better considered alone, since it is not certain that it is the result of inadequate decompression that many assume it to be; while certain pathological studies indicate that bends and bone necrosis may result from different disease processes (Rozsahegyi, 1956). Large epidemiological surveys have been completed and the clinical course of dysbaric osteonecrosis is now quite well documented along with some comprehensive studies of the general pathology. However, the basic mechanism remains unknown and hence the means of prevention. This fact is not aided by the general lack of fundamental knowledge of the physiology of bone—a most complex organ—which in the past has all too often been viewed as just the mineral 'coathanger' for the physiological system.

### *Symptomatology*

Most of the standard clinical texts on dysbaric osteonecrosis immediately plunge the reader into the radiographic language of 'segmental and linear opacities', 'snow-caps', etc., needed to describe bone lesions. However, these are essentially irregularities from what is considered normal or non-pathological in an X-ray of that bone and require interpretation not only by qualified radiologists but by those radiologists familiar with the characteristics of long-bone surveys peculiar to divers and caisson workers. For the best descriptions of the early diagnosis of dysbaric osteonecrosis, the reader is therefore referred to the work of Golding *et al.* (1960), Davidson (1964), Harrison (1971, 1974), Fagan *et al.* (1974) and several reports published by the Decompression Panel of the Medical Research Council (MRC) in London (1966, 1971, 1974). For those seeking a more introductory text to the radiographic appear-

ance of bone lesions, the reader is referred to the superb atlas of high-quality X-rays and accompanying case histories produced by Griffiths at the MRC's Registry in Newcastle.

Lesions have been reported in the long bones of caisson workers almost from the time that X-ray machines were invented at the turn of the century. Essentially they are recognized as regions of abnormal opacity, those less dense than normal representing sequestration of mineral, while denser regions indicate mineral deposition—regrowth of new bone on to dead trebeculae which are the mineral 'skeletons' remaining after death of the cells. Hence radiographic evidence may be quite a late indication of the onset of osteonecrosis.

The disease follows no specific course and, when once initiated, may start or stop at any time related in no obvious way to any history of continuing exposure to compressed air. Lesions occur in both the shaft and the ends of the bones—particularly the long bones. Most remain asymptomatic but where they progress to any appreciable extent close beneath the articular surface of a joint (a juxta-articular lesion), the disease may cause the weight-bearing surface to collapse. This may occur slowly, when it is often incorrectly diagnosed as arthritis, or suddenly as in the case of the tunnel worker who has just started to lift a heavy beam or bag of tools as his job demands. Although some surgeons may go to enormous lengths to repair such damage (Jones, 1974) the majority of these manual workers remain disabled, while prostheses have a limited life—a major problem in a young tunnel worker or diver in which these are feasible. Detailed descriptions of the management of these cases include those of Walder (1974) and Barnes (1967).

*Incidence*

Massive epidemiological surveys of British caisson workers of which there are now some 1,500–2,000 registered with the MRC Registry, some followed for as long as 12 years, have indicated an overall incidence of radiographically identifiable lesions as about 20% (MRC, 1975). However, such lesions may be found in at least 50% of those men who have worked regularly in compressed air over a number of years. Of the total showing some form of aseptic osteonecrosis, this occurs in disabling juxta-articular sites in about 17% but sometimes up to 49% (Davidson and Griffiths, 1970) or even 71% (Nellen and Kindwall, 1972).

In divers, the overall incidence of radiographically identifiable bone lesions tends to vary more widely, ranging from 2% in the U.S. Navy (Peck, 1974) and 6% in the Royal Navy (Elliott and Harrison, 1970) up to 27% for commercial diving in the Gulf of Mexico (Fagan *et al.*, 1974). This probably reflects the amount of actual diving performed by these men since, for professionals with at least ten years in the industry, there are reports of incidences as high as 50% in Japan (Ohta and Shigeto, 1969) and 55% in Germany (Alnor, 1963). However, these figures should only be taken as a rough guide, since different diagnostic criteria could have been used by the radiologists employed in each survey.

*Features*

The major problem in elucidating the mechanism of dysbaric osteonecrosis is the delay in observing radiographic changes. It may be anywhere from several months to several years after his last dive that lesions are positively identified in a diver. Thus, if a man has had more than one hyperbaric exposure, no particular occasion can be singled out as responsible for initiating the disease process, unlike the case of a bend. It is not even known whether the correlation between the incidence of bone lesions and the number of exposures (MRC, 1966) is attributable to a cumulative effect of compressed air or the statistical chances of a single event occurring, i.e. the more times anyone takes the risk, the more likely he is to get caught. The second viewpoint (i.e. 'Russian roulette') would be favoured by the observation that of five non-diving submariners who performed a successful escape from the Royal Naval sub-

marine HMS *Poseidon* after it sank, three were found to have positive bone lesions when X-rayed ten years later (James, 1945). A single exposure to compressed air would appear sufficient to initiate the disease (Swain, 1942). On the other hand, the cumulative stand is favoured slightly by the observation that the incidence of bone necrosis was higher in tunnel workers on eight-hour shifts (18%) than in those who usually spent less than four hours in compressed air (11%) in the same tunnel but the numbers are not satistically significant (MRC, 1966). The increasing incidence with the number of exposures may be responsible for the apparent increase found in susceptibility with age (McCallum *et al.*, 1976), assuming that older men have spent more time working in compressed air.

The incidence increases not only with the number of exposures as already described but also with the exposure pressure. This is shown clearly by MRC (1966) statistics of tunnel workers where there is a positive correlation between the number of radiographically identifiable bone lesions and the maximum pressure of air in which each man has worked at some time in his career. The incidence seems to rise quite steeply on reaching 30 psi (67 fsw). In divers, the same trend seems to occur, although the smaller numbers involved make it harder to reach statistical significance. Royal Naval data collected by Elliott and Harrison (1971) indicate that few bone lesions, if any, occur in divers who have not exceeded 185 fsw upon air. However, two cases of disabling osteonecrosis have recently come to the attention of this author in divers who were engaged for a year or so on repetitive air diving to 80 fsw. It is very difficult to tell whether bone lesions can be caused by heliox exposures, since all caisson workers breathe air and all divers start their careers by diving on air.

*Sites*

Lesions occur predominantly in the head of the humerus and both ends of the femur (fig. 69); although there is some indication that the femoral head is less prone to the disease in divers (McCallum *et al.*, 1976). A feature of

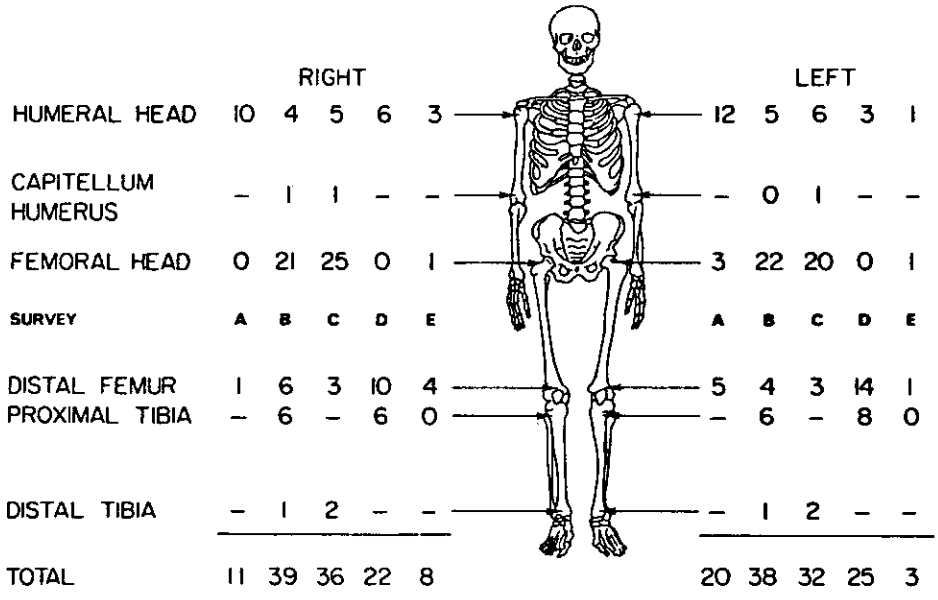


Fig. 69 A summary of the distribution of bone lesions found in five surveys: A: commercial divers (Fagan *et al.*, 1974), B: alcoholic patients (Jones, 1974), C: patients with hypercortisonism (Jones, 1974), D: naval divers (Harrison, 1974) and E: doubtful cases in naval divers (Harrison, 1974)

their distribution is the remarkable symmetry, unlike decompression sickness where bends occur predominantly in those limbs selectively exercised (p. 45). Not only does this occur overall but about half of the lesions detected occur bilaterally.

The lesions often follow no particular vascular distribution but those in the shaft tend to follow the contour of the bone, while those at the ends sometimes coincide with the old epiphyseal–metaphyseal plate (MRC, 1966). The general radiographic and microscopic picture seems to be compatible with post-fracture avascular osteonecrosis. Thus the mechanisms proposed are essentially aimed at explaining osseous ischaemia. However, the ischaemic episode would need to persist for at least 10–12 hours to initiate aseptic necrosis (Jones *et al.*, 1974). This rules out the transient changes in bone blood flow and intramedullary pressure induced directly by compression and decompression (fig. 70) as responsible for the dysbaric induction of the disease, infarction mechanisms providing more permanent means of locally interrupting the circulation. This suggests the same set of infarcting agents discussed in Chapter 3 in connection with the aetiology of decompression sickness. However, before passing on to mechanisms which assume an ischaemic episode in the pathogenesis of dysbaric osteonecrosis, it should be pointed out that death of the cells (osteocytes) is one of the few ways in which bone can manifest a physiological insult.

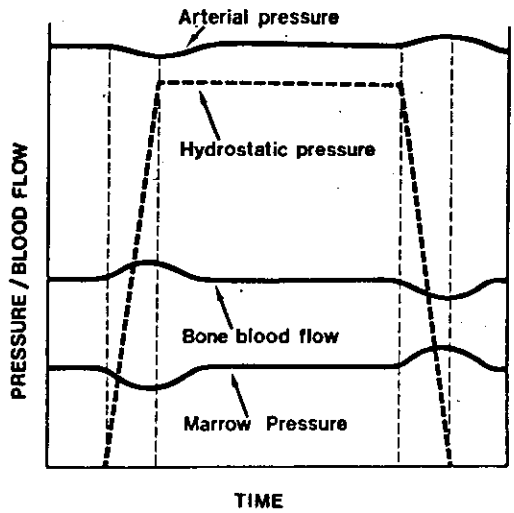


Fig. 70 Variation in the blood flow in the tibia of a dog and in the intramedullary pressure during the various phases of an exposure to compressed air at 45 p.s.i. (100'). Data from Harrelson and Hills (1970) and Hills and Straley (1972)

*Comparison with the bends*

If the same infarcting agents are causing both bends and bone lesions, then there should be a close correlation between the incidences of the two diseases. Moreover, this should also occur if bends were caused by extravascular gas as indicated in Chapter 3, since the decompressions depositing more gas in one site should also result in more bubbles in other sites including blood and hence more circulating emboli or their products of blood degradation or lipid release.

However, this does not appear to be the case in practice, where surveys of large numbers of caisson workers (MRC, 1966) have shown no statistically significant correlation between the incidence of bone lesions and the number of treatments requested for bends. Moreover, there is the case of two large civil engineering projects in Britain, using similar pressures and decompression schedules, where the incidence of bone lesions was greater in the construction of the Clyde Tunnel than in the Dartford Tunnel (19% to 10%) yet the incidence of bends was reversed (0·31% to 0·55%). Furthermore, in a group of 290 men with osteonecrosis, 36% had never complained of a bend (Walder, 1969) while in other groups (MRC, 1966) as many as 55% of those with bone lesions had no history of treatment for bends. Similar figures seem to apply to divers where Asahi *et al.* (1968) noted that in 15 with bone lesions out of 79 diving fishermen, 8 had never experienced the bends.

The only data indicating a correlation between bends and bone lesions has been presented by Elliott and Harrison (1970) on a relatively small number of Royal Naval

divers—a survey updated in many later papers by Elliott. However, taking the incidence of bone lesions in these men and their histories of treatments for decompression sickness from those data, both would appear to show more significant correlations with participation in 'experimental diving'. Moreover, if the divers are divided into those who have been engaged in 'experimental diving' and those who have not, then there is no correlation between bends and bone lesions in either group. Hence this could be another trap for the unwary; rather like attributing coronary artery disease to television because the incidence of this disease shows a very significant statistical correlation with the number of T.V. sets. These were shown not to be causally related but to be the result of a third factor (affluence) just as bends and bone lesions could result from experimental diving rather than from some common mechanism.

Another significant factor is the virtual absence of aseptic osteonecrosis in aviators, even though measurements of changes in general physiological parameters of bone, such as intramedullary pressure, show similar responses to both simulated altitude (Kalser *et al.*, 1951) and hyperbaric exposure (fig. 70). Allen *et al.* (1974) could find only two cases of disabling aseptic osteonecrosis in hypobaric personnel in their review of the aviation literature from 1945 to 1971. Moreover, Berry and Hekhuis (1960) found not a single lesion in anterior–posterior views of the humeri, radii, ulnae, femorae, tibiae and fibulae of 579 altitude-chamber men when X-rayed, even though approximately half of them had experienced acute decompression sickness. Furthermore, some cases of aerial bends can be most severe and even produce residual effects, yet do not induce aseptic necrosis of bone.

Hence dysbaric osteonecrosis would appear to be more dependent upon the absolute pressure than decompression sickness.

*Pathogenesis*

Despite the foregoing indications that bends and bone lesions are not causally related, most mechanisms which have been proposed for dysbaric osteonecrosis reflect those already put forward for decompression sickness, most involving vascular occlusion as described in Chapter 3. However, there is now a big difference in so far as it is not known whether recompression rapidly restores blood flow in a hypothetically occluded bone in the same way that it reverses limb pain. Hence lipid emboli and the other incompressible infarcting particles, particularly those produced by blood degradation, cannot be dismissed as the primary insult as readily as for decompression sickness.

Moreover, many of these are likely to be produced by the other disease conditions which tend to occur simultaneously with 'idiopathic' aseptic osteonecrosis, their accompanying blood disorders being succinctly described by Boettcher (1974). These predisposing factors include alcoholism (Axhausen, 1928; Vignon *et al.*, 1960), corticosteroid therapy (Pietrogrande and Mastromarino, 1957), sickle cell anaemia (Diggs, *et al.*, 1937; Chung and Ralston, 1969), rheumatoid arthritis and gout (Mauvoisin *et al.*, 1955), gouty arthritis (McCollum *et al.*, 1971), pancreatitis (Immelman *et al.*, 1964), Gaucher's disease (MRC, 1966) and following the transplant of kidneys (Jones *et al.*, 1965) but not of other organs. The bone lesions found in association with these disorders are virtually indistinguishable from those of dysbaric osteonecrosis (Jones, 1974), with the same tendency to occur bilaterally. It is therefore possible that the dysbaric-provoked mechanism is also responsible for one or more of these 'idiopathic' forms of the disease, in which case it would be dangerous to employ a caisson worker or diver with one of those disorders. There is a general feeling that the effects are additive but this writer could find no hard statistically significant data to support this statement; although it is common to take the precaution of not employing men as compressed-air workers who have a history of those potentially predisposing factors (Behnke and Jones, 1974).

*Mechanisms: remotely generated insult*

The assumption that aseptic necrosis of bone

s a result of inadequate decompression domi-
nates the mechanisms which have been proposed
so far, despite the lack of statistical correlation
and consequently these were the first to be
proposed in a list which includes:

1) *Gas emboli*: Bubbles have been implicated
n the pathogenesis of dysbaric osteonecrosis
since the first demonstration of bone lesions
n compressed-air workers (Bornstein and Plate,
1911). Occlusion of nutrient arteries by bubbles
s a theme reiterated by many later workers
and provides a simple concept still vigorously
defended (Smith, 1974). One of the major
pieces of evidence is the presence of large
numbers of intravascular bubbles known to
occur during many a bends-free decompression
(p. 146). However, these gas emboli detected
in *venous* blood would need to reach the
arterial system to cause vascular occlusion and
raises the old question of the effectiveness of
the lung as a bubble trap (p. 66). It is also
difficult to envisage bubbles randomly entering
the nutrient arteries to bones causing such
extensive areas of necrosis as Bornstein and
Plate found without lodging in other organs
where they would soon become manifest.

(2) *Extravascular gas*: This line of reasoning
led Kahlstrom *et al.* (1939) to include extra-
vascular gas as a means of obstructing bone
blood flow. The large volume of nitrogen
deposited from fatty marrow in which it is
so soluble might press upon blood vessels
tending to close them. This would certainly
explain the magnitude of the lesion, bilateral
symmetry and involvement of the humerus
and femur where the fat content of the marrow
is high (Rozsahegyi, 1956). Occlusion of blood
vessels by extravascular gas would be more
likely when it is mechanically 'contained'
in a structure as rigid as bone and where,
according to Nelson *et al.* (1960), vessel walls
are particularly thin. The hypothesis is also
highly compatible with the concept of peri-
vascular 'cuffs' of fluid proposed by Hills and
Straley (1972) to explain the opposing trends
found in intramedullary pressure and bone
blood flow on hyperbaric exposure (fig. 70)
and on switching to and from anaesthetic
gases. However, if the gas phase is responsible,
a better correlation of bone lesions with
bends would be expected and either intra-
vascular or extravascular bubbles would need
to persist for 10–12 hours to initiate necrosis.

(3) *Fat emboli*: Considerations of this factor
has led Jones *et al.* (1974) to propose that
dysbaric osteonecrosis is caused by infarction
by lipid emboli whose impaction into the
vascular bed would cause more than a transient
reduction in blood flow. It is well known that
fat emboli are produced by decompression
(p. 55) while disruption of femoral marrow
was thought to be the source (Clay, 1963).
However, such fatty droplets deposited into
the marrow circulation would need to occlude
the venous outlet or, once again, traverse the
lungs to reach the arterial system. Jones makes
the major point that bubbles could cause the
liver to release a shower of lipid emboli in the
same manner that *alcohol* can provoke a fatty
liver (Lynch *et al.*, 1959; Kimble, 1961).
Thus aseptic osteonecrosis induced by decom-
pression and by alcohol would have a largely
common aetiology. However, if fat were a
major factor, one would expect the incidence
of bone lesions to vary with obesity but unlike
decompression sickness (p. 41), such a correla-
tion is missing (MRC, 1971). Unfortunately,
by this hypothesis, it is also difficult to explain
the apparent absence of lipid infarction of other
organs and the failure to find bone lesions
caused by other disease processes known to
produce lipid emboli (McCallum, 1975) but,
once again, these would need to reach the
arterial system. However, there is the interesting
case reported by Bühlmann (1974) where,
at the autopsy of a subject who died six days
after a simulated dive, diffuse fat embolization
was revealed—not only of lungs but also of
brain, heart, kidneys and the muscular system.
The source of these emboli was a region of exten-
sive haemorrhage in the marrow of the distal
third of the left femur.

(4) *Blood clots*: The need for emboli deposited
from other organs to reach the arterial system
is largely avoided in the next type of mechanism
related to the many blood disorders which can

occur during decompression. The debris can form into various potential infarcting agents or the general sludging can reduce the circulation to inadequate levels, particularly in organs such as bone which have few means, if any, of signalling ischaemia let alone responding to such feed-back by adjusting vasomotor tone. Potential infarcting agents include Swindle's red cell agglutinates proposed as a mechanism for decompression sickness by End (p. 49) and the microthrombi of platelets and red cell aggregates (Philp *et al.*, 1971). However, this mechanism suffers from the same criticism of other infarction hypotheses that it is difficult to explain the symmetry of dysbaric osteonecrosis, the absence of infarction of other organs and the failure of most other disease conditions producing those disorders to cause osteonecrosis.

(5) *Increased blood viscosity*: The increase in blood viscosity produced by decompression (Guest *et al.*, 1974) has led these authors to suggest this as a source of the ischaemic episode initiating the necrosis. The relative inability of the vasculature to respond to the higher resistance to flow of this sludged blood would therefore make bone a prime target but it is difficult to know whether the flow reduction would be large enough and last long enough. The viscosity increase is attributable to the known haemoconcentration on decompression (p. 51) but Guest *et al.* do not specify where the water goes or what moves it, a large proportion apparently going to the lungs. One possible driving force is osmosis induced by the higher gas concentration in tissue during that phase of the dive (p. 213) but the tendency for such shifts to persist for long periods (Hong *et al.*, 1976) indicates that the true explanation is likely to be physiological rather than physical.

*Time course*

However, in all of the mechanisms proposed so far, the ischaemic episode would need to occur at the time of decompression or within a short period thereafter, the longest delay recorded of any circulation-related phenomenon being three days for the drop in platelet level and rise in creatine phosphokinase (Martin and Nichols, 1972). Thus the time course of dysbaric osteonecrosis would seem altogether too long since, after the ischaemic episode, aseptic necrosis should proceed just as it would in the same bone post-fracture and become radiographically identifiable several weeks and not several months or even years after the last exposure (the minimum period is about 3½ months—Walder, 1974). Although this is a very important point in differentiating between mechanisms, this statement is made from a collection of published comments (e.g. MRC, 1966) and discussions with radiologists but the clinical evidence is still rather fuzzy, due largely to the risk involved in taking long bone X-rays in men any more frequently than once a year. There is the odd case quoted in the literature where necrosis of the femur could not be identified until 9½ months post-fracture, (Stewart, 1933) but these seem to be the exceptions rather than the rule. Hence it would appear that either dysbaric osteonecrosis is not ischaemically mediated or there is a long induction period in producing the ischaemia, in which case it is more likely to be induced locally.

*Mechanisms: local insult*

This line of argument has tended to focus more attention on more subtle forms of insult likely to be generated within bone itself and has provided the following mechanisms to continue the original list:

(6) *Oxidation of collagen*: Sobell (1971) has shown changes in the collagen of rats exposed to oxygen partial pressures in excess of normal and has gone on to point out how such changes could influence the deposition of hydroxyapatite upon the collagen matrix in forming bone, implying that this could be a factor in dysbaric osteonecrosis. There is little doubt that mineralization is very sensitive to a number of factors, an excellent introduction to this complex process being found in the monograph written by Neuman and Neuman (1958). One of the

controversies in this field concerns the provision of nuclei for the regulated precipitation of mineral from solution in which it is supersaturated under normal conditions—even in plasma (Strates and Neuman, 1958). Glimcher and Krane (1968) review the cases for homogeneous nucleation (p. 78) versus heterogeneous nucleation where the collagen provides the sites for the deposition of hydroxyapatite as needed, their evidence tending to favour the second approach. All of this refers to air breathing at normal atmospheric pressure, so that it is quite conceivable that a change in the molecular structure of collagen, such as cross-linking adjacent polymer chains by oxygen, could totally disorganize the mineralization process. Since this is very slow, it could take months or years for the results of incorrectly seeded crystals to become manifest. However, if oxygen were the agent responsible for dysbaric osteonecrosis, one would expect to find aseptic necrosis of bone in subjects who had received oxygen therapy, since their exposure to oxygen even at normal pressure is appreciably greater than needed to provoke the collagen changes seen in Sobell's rats.

(7) *Carbon dioxide*: Another possible insult to the normal biochemical processes in bone could occur if the pH were reduced by exogenous means. Bone resorption occurs if the pH is reduced by the generation of lactate and citrate ions within the osteocyte among other factors (Raisz, 1970). Certainly a fall in pH is associated with bone resorption (Neuman and Neuman, 1957) just as a piece of bone demineralizes when dropped into acid *in vitro* (Deiss, 1974). Hence it is tempting to speculate that an elevated level of carbon dioxide might do the same. Lung disorders are occasionally cited as associated with 'idiopathic' aseptic osteonecrosis (Davidson, 1964). The diver or tunnel worker who proves to be a carbon dioxide retainer under pressure (p. 206) may be prone to this disease. This could not only explain the absence of bone lesions in aviators but the high incidence in the five submariners who did not escape from HMS *Poseidon* until several hours after the accident (James, 1945), during which time they would probably have become hypercapnic. This mechanism could also offer a possible explanation for the variation in the incidence of bone lesions between tunnel projects, carbon dioxide released from the earth of the diggings being something characteristic of that particular site.

(8) *Gas-induced osmosis*: The mineralization process is highly regulated under normal conditions and particularly sensitive to water content (Neuman and Neuman, 1958) so that any fluid shift could disorganize this finely balanced process. One means of effecting this shift is by osmosis induced by the transient imbalance of inert gases as they are taken up or eliminated by bone during compression or the rapid initial phase of decompression (Hills, 1970e, 1972a). Rapid compression can cause fluid shifts *around* bone as evidenced by 'dry joints' (p. 206), while articular cartilage has been shown to be an effective osmotic membrane for nitrogen in solution (Hills, 1971e). These shifts could also occur *within* bone, in which case compression should produce the same effect as switching the inert gas to one which is more osmotically potent (nitrous oxide), while the return to normal air breathing should correspond to decompression. These are in agreement with recordings of two of the simplest parameters to monitor—bone blood flow and intramedullary pressure (Harrelson and Hills, 1970; Hills and Straley, 1972).

Hills (1970e) goes on to speculate that one way by which intra-osseous fluid shifts could induce aseptic necrosis would arise if the dissolved minerals did not permeate the osmotically active membrane as readily as the displaced water. Their normal supersaturation would then be increased to a degree at which they would seed spontaneously, as described for bubbles (p. 78), thus forming *homogeneous* nuclei rather than waiting for a heterogeneous site to occur. Hence the regulation of mineralization would break down and the nuclei formed would continue to grow under the normal state of supersaturation, even without further diving, eventually to produce crystals in the undesirable places where they could occlude

blood vessels or cause other embarrassment to the osteocytes. It is necessary to remove no more than 5% of water from normal plasma to initiate spontaneous mineral deposition (Hills, 1973a) whereas the shift needed to initiate crystallization may be less on days when a diver's diet has elevated his natural level of mineral supersaturation.

This hypothesis is not only compatible with the time course of dysbaric osteonecrosis but with its bilateral incidence and the tendency to occur idiopathically after kidney transplant (i.e. dehydration concentrating minerals) and with excessive alcohol—a potent osmotic agent, mild diuretic and an agent for 'salting out' dissolved minerals. The maximum rate of pressure change is another factor unique to each tunnel project, depending upon the size of the lock and its valves, compression rates estimated for six U.K. tunnels lying in the same order as the incidence of osteonecrosis but not of the bends rate.

In addition to the foregoing mechanisms, McCallum (1975) also suggests that nitrogen could prove toxic to bone cells but the biochemical evidence on which this possibility is based (Deiss *et al.*, 1962) actually refers to a means by which hypoxia can inhibit the biosynthesis of collagen.

*Prevention*

It must be remembered that each of the eight possible mechanisms listed above is hypothetical and none may prove to be correct in the final analysis. If the primary cause is bubbles (1 and 2), or the results of their presence in the form of fat emboli (3) or microthrombi (4), then the same means of preventing bends should also be effective in preventing dysbaric osteonecrosis, viz. more adequate decompression. However, appreciable increases in total decompression time introduced in the tunnel projects carefully followed on large numbers of men by the MRC (1971) have failed to show any improvement in the incidence of dysbaric osteonecrosis. Enough time has now elapsed for any improvement to be detected. These changes have been more effective in reducing gas separation and its effects, since the incidence of bends has been reduced appreciably; so there is good reason to look beyond the popular mechanisms (1 to 4) for the cause. The time course for the disease is also difficult to interpret by these infarction approaches and by the rheological mechanism (5). This and the *local* mechanisms (6, 7 and 8) can all explain bilateral symmetry, the absence of bone lesions in aviators, while all of these except the oxygen hypothesis (6) are compatible with potentiation of the disease by alcohol.

Of the remaining mechanisms to which there are no obvious incompatibilities with the principal features of the disease, the following implications can be drawn.

(a) The carbon dioxide mechanism (7), if correct, would emphasize clean air and good ventilation and switching to heliox where possible to minimize carbon dioxide retention. Modification of the decompression would have no effect.

(b) A mechanism based on gas-induced osmosis, either directly (8) or indirectly (5), would implicate rapid change of pressure as the cause, whether undertaken during the first phase of decompression or during compression (8). In this connection it is interesting to see bone lesions arising in submariners undergoing escape training (Elliott, 1974) where compression and decompression are both very rapid and carbon dioxide build-up cannot be invoked; while slow compression (20 ft/min) has yielded a low incidence of bone necrosis (Sealey, 1974) but for quite moderate exposures. Rapid compression has again been implicated in recent studies on small animals (Chryssanthou, 1975) and adds support for the suggestion of *compression* tables (Hills, 1970e, 1972a).

Hence, if dysbaric osteonecrosis is not simply another symptom of inadequate decompression as most believe it to be, then the answer to its prevention could lie in keeping body carbon dioxide to normal levels, or in changing pressure much more slowly than usual, either

in compressing or in decompressing to the first stop. However, none of these factors may hold the answer; while the final outcome could well prove that the disease can be initiated by several mechanisms.

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# LATE BONE LESIONS IN CAISSON DISEASE

## THREE CASES IN SUBMARINE PERSONNEL

C. C. MICHAEL JAMES, FRCS E
CAPTAIN RAMC ; LATELY SURGICAL REGISTRAR, PARK PREWETT EMS HOSPITAL, BASINGSTOKE

CAISSON disease, otherwise called compressed air illness, decompression illness, or commonly, "the bends," is a condition from which divers and other workers in high atmospheric pressure suffer when returned too quickly to a lower pressure. The main symptom is severe muscle pains. These are due to the release of the dissolved gases which come out of solution in the blood and tissues as a result of their lowered partial pressures. The gases are oxygen, carbon dioxide, and nitrogen ; the two former are removed very rapidly, the first by reabsorption, the second by exhalation in the lungs. Nitrogen is relatively insoluble and therefore collects as minute bubbles of gas, coalescing to form larger bubbles which constitute nitrogen emboli. The absorptive powers for nitrogen of various tissues and substances have been calculated ; fats and lipoids are five to six times more absorptive than blood, and they, along with water, are the chief solvents of nitrogen. The carbon-dioxide content of the blood also affects the severity of compressed air illness (End, quoted by Dudley, 1936).

### BONE LESIONS

The lesion is essentially the result of infarction. According to Quadri (quoted by Coley and Moore 1940) immediate lesions occur most frequently in the skin, muscular and articular tissues, internal ear, and central nervous system in descending order of frequency.

Bone and joint lesions, by their nature, are not noticed for some time after the accident and have only been reported in recent years. They are commonest in the hips and shoulders. It is always the cancellous tissue

near the ends of the long bones which is affected. The high fat and lipoid content of bone-marrow and the blood-supply at the bone ends without good collateral circulation all tend to produce nitrogen emboli and slow elimination.

The subsequent infarction causes aseptic necrosis; attempts are made at repair by gradual osteoclasis, organisation, and eventual recalcification. The lesions seen in later years are the result of incomplete repair; the infarcts are not completely reorganised and reossified, they remain as " cystic " areas of dead bone, persisting in structure but without nuclear staining or signs of osteoclastic activity, surrounded by a layer of fibrosis and new bone. Arthritis follows as a result of this absorption and attempted repair in or near the epiphysis of weight-bearing long bones with collapse of the articular surface. Kahlstrom, Burton, and Phemister (1939), Phemister (1940), and Swain (1942) have reported cases which were examined post mortem.

The X-ray appearances are described by Coley and Moore. Infarction presents as a cyst-like area of irregularly increased density in cancellous bone, normally surrounded by a thin band of calcification on the outside of which is a variable amount of normal appearing medulla. The articular changes resemble arthritis deformans. These appearances are compatible with the pathology; there is a central area of dead bone, whose irregular outline is due to the partial replacement by new bone and new marrow, surrounded by a band of calcification. Small areas can be replaced entirely by dense new bone.

Treatment is essentially preventive—i.e., recompression followed by slow decompression.

### CASE-HISTORIES

In 1931, HM Submarine *Poseidon* sank in 120 feet of water after a collision. Five of the crew escaped and survived using the Davis apparatus, and three of them have since been examined. They all suffered in varying degree from the " bends " immediately or shortly after arriving at the surface.

When the submarine went to the bottom the survivors were all in the bows, and before escaping had to wait while the compartment was filled with water to equalise the pressures within and without the vessel. When these pressures were equal, a hatch could be opened

outwards to allow the men to rise to the surface. In the present instance, two men escaped after 2½ hours under this increasing pressure and the rest after 3 hours. It seems that during this period the air in the submarine could not escape but was gradually compressed. No recompression treatment was performed.

When examined 12 years after the accident 3 of the 5 survivors all showed bone lesions ; the other 2 survivors could not be traced.

CASE 1.—Aged 27 at time of accident. Was 2½ hours in submarine under increasing pressure. He had generalised body pains 5–10 minutes after arriving at the surface ; these lasted for about a fortnight getting steadily less severe. He was kept 7 days in bed ; the pain left the buttock region last, and was felt for a further period on moving the hips.

In 1942 he was physically normal but had an obvious anxiety state. He had been discharged from the Navy in 1933 after a nervous breakdown. He still suffers from headaches and nightmares.

*X-ray findings.*—Left shoulder (fig. 1): In the region of the anatomical neck there is a rounded area of decreased density demarcated by a thin layer of sclerosis less well marked inferiorly. Right shoulder, hips, and elbows appear normal.

CASE 2.—Aged 27 at time of accident. Was 3 hours in submarine under increasing pressure. When the accident occurred he struggled violently for several minutes without success to open a sea-cock to flood the compartment. Almost immediately on arriving at the surface he felt very severe pain in his limbs. Since 1932 he had pain in both hips increasing in severity with passage of time, and in 1934 was treated for this in hospital, after tonsillectomy, by radiant heat and massage.

In 1942 he was invalided out of the Navy. He was complaining of continuous pain in both hips, right more than left, which radiated occasionally down the back of the thighs to the knees, and was worse on exercise after resting. There was pronounced limitation of all hip movements with much pain ; lumbar lordosis and bilateral hip flexion deformity were well marked. All other joints were normal. No history of previous illness affecting the hips or of any trauma at any time was obtained.

*X-ray findings.*—Both hips show advanced arthritis deformans (fig. 2a and b). There are many cystic spaces with hypercalcified margins in the acetabulum and head

and neck of femur. There is partial collapse of the femoral heads and it is evident that this has occurred by fracture of the hypercalcified margin of several "cystic" areas, the sclerosed bone being so dense as to resemble sequestra. Mottling extends into the diaphysis of the right femur but is poorly defined there. Shoulders show typical cystic areas with surrounding calcification situated in the head of the humerus, more definite on left side (fig. 2c). Knees and elbows normal.

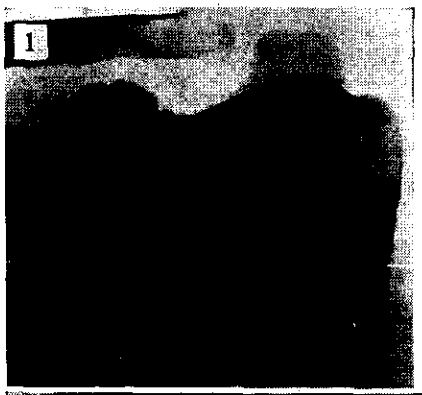
CASE 3.—Aged 29 at time of accident. Was 3 hours in submarine under increasing pressure. He had pain in left arm and shoulder only, which came on about an hour after arriving at the surface.

When examined in 1942 he had no symptoms and said he was perfectly fit. He never suffered from rheumatism. All joints were painless and had a full range of movement. There was well-marked crepitus in the left shoulder but he was not aware of this. He is still serving in the Royal Navy.

*X-ray findings.*—Left hip: One fairly well-marked cystic area either in the head of the femur near the fovea or in the acetabulum. Suggestion of several small cystic areas in the left ischiopubic ramus as compared with the right. *Left shoulder* (fig. 3): Near the articular surface of the head of the humerus there is an area of irregularly increased density surrounding a small rarefied oblong space, similar to those described by Coley and Moore. This lesion is probably similar to that in Swain's case, affecting the articular cartilage. In the region of the anatomical neck there is an irregular line of increased density separating the normal trabeculation of the head from a localised area of decreased density fading into the medulla of the shaft. *Elbows* and *right shoulder* and *hip* appear normal.

## DISCUSSION

The exact cause of the infarction is not yet decided. Phemister's experiments on dogs (Kahlstrom, Burton, and Phemister, 1939) demonstrate that air embolus is not the only cause of this infarction in bone. His experimental air emboli failed to produce any change in bone in spite of the fact that 2 dogs died of air embolism in a few hours, and 4 others developed complete or partial paralysis of the hind limbs. According to End (quoted by Dudley, 1941–42) compression in animals increases normal physiological intravascular agglutination of erythrocytes; and Swindle (1937) has shown that increased carbon dioxide also tends to increase this agglutination. A combination of these two factors together with the stasis resulting



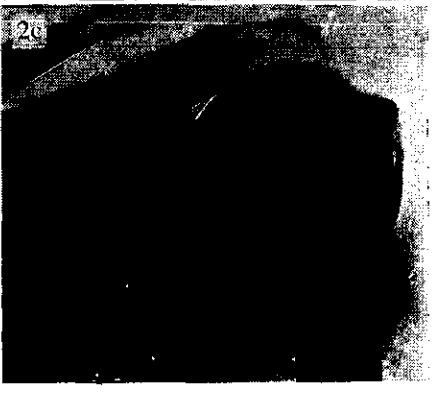


Fig. 1 (Case 1) : left shoulder.
Fig. 2 (Case 2) : (a) right hip ; (b) left hip ; (c) left shoulder.
Fig. 3 (Case 3) : left shoulder.

from nitrogen embolism and the mechanical effect of gas-distended blood-vessels blocking venous return in a rigid bone tube is most probably the main cause of the infarction.

End (1938) found in practice that ingestion of sodium bicarbonate by divers decreased the frequency of attacks of " the bends " in experimental deep dives.

Taylor (1944) has an interesting discussion on the causation of bone infarction and aseptic necrosis. He quotes several cases where lesions similar to those described in this paper are found without any history of, or possible exposure to, compressed air illness, but all in an older age-group.

The cases reported in this paper are of interest because the men all suffered from their original caisson disease under the same conditions on the same occasion 12 years ago ; they are of similar age and yet in one of them the lesions are much more severe than in the others. No lesions in tissues other than bones and joints were evident.

The severity of the lesions in case 2 seems to be related to this man's effort to open the sea-cock. One of his companions said that he fought for several minutes to open the sea-cock and almost exhausted himself by his struggles. Jenkinson (1940) points out that the rate of tissue saturation by nitrogen is slower where there is a meagre circulation of blood, as in ligaments and joints. Consequently it might be expected that in case 2 the increased circulatory rate during the recovery period following his strenuous activity would tend to permit more rapid absorption of the gases while the pressure was increasing, and more complete distribution through the body. The increasing atmospheric carbon dioxide would also make the lesion more severe.

Several writers on caisson disease have doubted whether the bone lesions ever develop after a single over-rapid decompression. This doubt is removed by these three cases, since there is no suggestion that any of them suffered from caisson disease at any other time.

Coley and Moore (1940) say that the bone lesion is always situated in the diaphysis, and may or may not also involve the epiphysis and secondarily the joint. Although they were not looked for especially in the present 3 cases, no lesions were apparent in the parts of the shafts of the long bones seen in the radiograms. The blood-supply is so good in the diaphysis that one

would expect gas emboli to be removed rapidly and any damage done to be completely obliterated. The fact that there was a lesion in the head of the left humerus in each of these three cases, whereas the right humerus was affected in only one, may be significant; this might be due to the mode of origin of the left subclavian artery as opposed to the right.

These cases bear out Jenkinson's statement (1940): ". . . How important it is that the submarine compartment or chamber should be quickly flooded in order to minimise the time under pressure." Because it took 2¼–3 hours to flood the compartment in the *Poseidon*, these men were highly saturated with nitrogen and in consequence their lesions were irreversible. The lesions were probably made worse by the increased carbon-dioxide concentration in the air and this should be remembered when methods for preserving life in submarine accidents are being considered.

It would appear that these are the first cases to be reported of caisson disease of bone in Naval personnel.

SUMMARY

Three men were examined 12 years after suffering from a single severe attack of "the bends" as a result of being trapped in a submarine at a depth of 120 feet. They had had to wait for 2¼–3 hours under increasing pressure before escaping by the Davis apparatus.

They were of similar age and experienced the same conditions, but the bone lesions were much more gross in one case, probably because this man made strenuous efforts to open a stop-cock.

On radiological examination all three men showed small rounded areas of rarefaction surrounded by a thin shell of hypercalcification in the ends of the long bones, confirming the pathology of infarction followed by aseptic necrosis and incomplete repair. In the severe case the heads of both femora had partially collapsed, resulting in well-marked osteo-arthritis deformans.

The possible causes of this bone infarction are discussed and mention made of similar lesions without a history of exposure to rapid decompression.

The duration of high pressure conditions and the carbon-dioxide content of the atmosphere are important factors in the production of bone lesions in caisson disease.

I have to thank the Medical Director-General of the Royal Navy, and the Medical Superintendent of Park Prewett Hospital for permission to publish these cases; also Mr. V. H. Ellis for his advice and interest, and the late Mr. R. H. Jocelyn Swan, under whose care case 2 was admitted, for his encouragement.

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# ASEPTIC NECROSIS OF BONE

## I. Infarction of Bones in Caisson Disease Resulting in Encapsulated and Calcified Areas in Diaphyses and in Arthritis Deformans

S. C. KAHLSTROM, M.D., Bath, New York, and C. C. BURTON, M.D., F.A.C.S., Dayton, Ohio
D. B. PHEMISTER, M.D., F.A.C.S., Chicago, Illinois

CAISSON disease is the result of injury to tissues by nitrogen bubbles liberated when the body, which in compressed air has absorbed an excess of nitrogen, is too rapidly removed from the decompression chamber. This explanation was first offered by Paul Bert in 1871 and it has been substantiated by the studies of Heller, Mager and Schrotter, Boycott, Damant and Haldane, Bornstein (6, 7), and others.

The amount of nitrogen absorbed varies with the duration and height of the pressure and with the different types of tissues. According to Bornstein, nitrogen saturation for a given pressure is not complete for 7 to 10 hours. Boycott, Damant, and Haldane estimated that there is practically complete saturation for man at high pressures in 5 hours. Bohr and Henriques showed that 100 cubic centimeters of shed blood absorbs at body temperature and one atmosphere pressure 1.2 cubic centimeters of nitrogen and at 4 atmospheres 4.8 cubic centimeters. As to the different types of tissues, fat has been found to absorb the largest amount of nitrogen. Vernon reported that at body temperature and atmospheric pressure, fats (lard, olive oil, cod liver oil) dissolve more than five times as much nitrogen as an equal volume of water or blood plasma. He attributed the special tendency of the fat or lipoid containing tissues, such as subcutaneous tissues, spinal cord and nerves, to suffer injury in caisson disease to this great solubility. Attention was called to the large amount of fat in the marrow of some bones but no mention was made of known lesions of the bones in caisson disease.

It has also been found (Bornstein) that the less active the circulation of a tissue the more slowly it absorbs nitrogen and in turn, the more slowly is the gas removed from it by the circulation when the increased pressure is reduced; consequently the greater the likelihood of gas bubble formation in it. The nitrogen has been found to damage the tissues most extensively by producing embolism but it also damages by the pressure of gas bubbles extravascularly.

Dr. Kahlstrom and Dr. Burton, from the U. S. Veterans Administration.
Dr. Phemister, from the Department of Surgery of The University of Chicago.
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Acute symptoms of caisson disease appearing a few minutes to hours after too rapid exit from the chamber are referable most frequently to the spinal cord, internal ears, brain, subcutaneous tissues, and the limbs. The commonest complaints are severe pains, especially in the abdomen ("bends") and in the extremities, ringing in the ears with or without impairment of hearing, hemorrhages in the skin and mucous membranes, bluish mottled discoloration and induration of the skin and subcutaneous tissues, and in some cases, paralysis in the extremities. Severe cases may cause cerebral or pulmonary embolic symptoms and death may be an early result. Prompt recompression usually ameliorates and sometimes completely relieves the symptoms. Chronic lesions sometimes result from caisson disease, the most important being impairment of hearing, paralysis from spinal cord damage, and disturbances of the bones and joints.

Pains in the extremities in the early stages have often been referred to as in the joints, particularly the hips, less often the knees, ankles, and shoulders. In most instances, they clear up but in some cases symptoms and signs similar to those of chronic deforming arthritis have continued. Chronic pains in the course of the bones have also been present in some cases.

Bornstein and Plate and independently Bassoe were the first to describe joint lesions in caisson disease. Bornstein and Plate in 1911 reported 3 cases in which symptoms and signs were present resembling chronic arthritis. A shoulder was involved in one case, one hip in another, and both hips in the third case. Roentgenograms of the hips revealed mottled changes in density in the head of the bone with flattening of its articular surface, irregularity and slight narrowing of cartilage space, and marginal lipping. The findings were considered those of arthritis deformans but they thought that the lesion was due to nitrogen bubbles in the bone bordering on the joint and not to nitrogen in the joint. No more detailed definition of the lesion was attempted.

In his report on the late manifestations of compressed air diseases Bassoe described deforming changes in the joints and also changes in the bones away from the joints. There were 2 cases of involvement of the hip, 1 of 11 and the other of 13 years' standing, in which roentgenologically the head showed mottling and flattening and there was narrowing of cartilage space and lipping which led to a diagnosis of arthritis deformans. In another case there was a similar change in the head of the humerus and lipping of the glenoid margins.

Twynam, in 1888, reported the case of a man who had severe symptoms of caisson disease with pain and swelling above the right knee and 2 months from the onset abscess formation which was drained. Later on there was another painful swelling about the right trochanter which was drained and sinuses persisted for 2 years, at which time amputation was performed through the lower third of the femur. The entire shaft of the femur was found to be necrotic and there was involucrum one-third of an inch thick surrounding it. This appears to have been a case of massive necrosis of the shaft of the femur with secondary infection which resulted in a picture resembling closely that of pyogenic osteomyelitis.

Chronic changes in the cancellous bone away from the joints was noted roentgenologically by Bassoe three times, once in the upper and once in the lower diaphysis of the tibia and once in the lower epiphysis of the fibula. There were mottled areas of absorption and irregular lines of new bone formation. No definite interpretation was made of these bone changes, and there were no reproductions of the roentgenograms in the article. Fortunately, the roentgenograms of the tibial lesions have been preserved and with Dr. Bassoe's permission they were compared with roentgenograms showing tibial lesions in some of the cases here reported and found to be quite similar.

A number of reports have since been made of the joint changes in caisson disease. Plate in 1928 reported a case and considered the change to be analogous to arthritis deformans. Burkhardt classified caisson lesions of the joints under the category of arthritis deformans but considered the primary lesion most likely in the adjacent bone. Christ in 1934 published a very comprehensive review

of the literature with a report of 4 cases involving the hip joint in one of which the lesion was bilateral. Symptoms were of relatively short duration, ranging from 4 to 18 months. All had worked from 3 to 4 years in compressed air. In all 4 cases the head of the femur roentgenologically showed scattered areas of reduced density, mixed usually with blurred areas of normal to slightly increased density. There was a variable amount of irregularity of the shadow of the articular cortex and slight flattening of the weight bearing surface of the head in each case. The cartilage space was little narrowed and the acetabulum little changed. Slight marginal lipping of the head was present in 3 cases. Christ concluded that nitrogen gas embolism had occurred in the vessels of the head of the femur producing subchondral necrosis of bone. This was followed by spotted absorption of the necrotic bone with irregularity and sinking in of the articular surface. He mentioned gas bubble formation in the bone but considered it unlikely despite the presence of fat in the medullary canal and the sluggish circulation of the bone marrow.

No case has been reported in the literature in which pathological examination has been made of the bone and joint changes except the grossly examined infected bone which was reported by Twynam.

## CASE REPORTS

Four cases of caisson disease with extensive changes in the skeleton have been studied clinically and roentgenologically. One case came to autopsy and in another a biopsy was performed on the involved head of the femur. Extensive lesions were revealed in diaphyses and in epiphyses of certain bones with changes in the joints, all of which appeared to be the result of massive aseptic necrosis of bone secondary to interruption of its blood supply by the liberated nitrogen gas.

CASE 1. Necrosis of epiphyses with secondary deforming arthritis and massive necrosis of shafts of long bones in caisson disease of 35 years' standing.

A 61 year old white male has been a member of the Veterans' Administration Facility, Bath, New York, intermittently since 1930. His chief complaint is pain and limitation of motion in the hips and to a less extent in the left shoulder and knees. He has also had varicose veins of both legs for many years with swelling, pruritus, and repeated attacks of thrombophlebitis.

Fig. 1. Case 1. Deforming arthritis of both hips and loose body, *a*.

The complaint referable to the joints dates back to an attack of caisson disease in about 1901 when he worked on the construction of the Cleveland Water Works tunnel. He was incapacitated for 6 or 7 days due to the severe pains experienced in the arms, hips, and legs. He never completely recovered and by 1907 he limped, favoring the left leg. By 1917 he had adopted the use of a cane and by 1930 his hips were so troublesome that he gave up his trade, that of a gunsmith. He has had a chronic cough most of the time for 5 years and during the past 2 months it has been severe and productive. Roentgenograms of the chest taken at intervals since 1933 show no lung change until 1936, when an infiltrative process was revealed extending into the right upper lobe from the right hilum.

Past history reveals no joint disturbance whatsoever before the occurrence of the caisson disease. There is no history of other illnesses of consequence.

*Physical examination.* Patient is an obese elderly man in fair general condition. He walks with a marked limp favoring the left leg and with the aid of a cane. Regional examination is essentially negative aside from the chest, left shoulder, spine, and lower extremities. There is dullness and impaired breath sounds are present over the right upper lobe, especially posteriorly. There is a rather conspicuous atrophy of the muscles about the left shoulder. Elevation of the left arm is limited to about 90 degrees. There is a definite scoliosis of the dorsolumbar region with convexity to the right. There is practically no abduction of either hip and considerable limitation of both rotation and flexion of both hips. Motion in the knees and ankles is practically normal. There are varicosities and scars from old varicose vein operations in both legs. The lower left leg is slightly swollen. Reflexes are present in both upper and lower extremities.

*Laboratory findings.* Laboratory examinations revea inegative blood Wassermann and Kahn tests: blood calcium and phosphorus, normal; normal white count; red blood cells, 4,000,000. Urine shows albumin with occasional hyaline and granular casts.

Roentgenograms were made of the entire skeleton. The hips showed very extensive changes most marked on the left side (Fig. 1). There is marked flattening of the femoral heads with a narrowing of

Fig. 2. Case 1. Central necrotic area in shaft of left femur with calcified and ossified zone of demarcation.

the cartilage spaces and marginal lipping, especially on the right side. There are scattered areas of reduced density in the subarticular portions of the femoral heads and acetabula, interspersed with areas of increased density.

Anteroposterior and lateral roentgenograms of the lower three-fourths of the left femur reveal an oblong area of altered density in the medullary region beginning 2½ centimeters above the condyles and extending upward for a distance of 18 centimeters (Fig. 2). It occupies almost the entire width of the medullary cavity below and tapers off irregularly above. It is surrounded by a narrow irregular zone of increased density most marked along the mesial and posterior sides. The density of the interior is mottled, being slightly increased in most of its extent as compared with that of the normally appearing cancellous bone below the lesion. The shadow of the cortex surrounding this area shows slightly longitudinal streaking, but the shaft is not increased in thickness.

A roentgenogram of the right femur shows a similar area in the same region (Fig. 3). The area is 10 centimeters long and is 4.5 centimeters broad at the lower end in the anteroposterior view. There is a narrow dense zone about the periphery in almost its entire extent. Just beyond its upper limit there is a separate island 1 centimeter in diameter, with a dense zone about its periphery. There is a dense streak within, 3 centimeters above the lower end in the anteroposterior view and another crossing the involved area transversely 10 centimeters above the lower end seen in the lateral view. The cortex surrounding the area is longitudinally streaked in places and appears slightly irregular in outline in the anteroposterior view. There is a dense island in the external condyle of femur. These areas in the femurs are interpreted to represent masses of old aseptic dead bone that have had a calcareous capsule laid down about them.

A roentgenogram of the left shoulder joint and humerus shows extensive changes, those in humerus tapering downward for a distance of 20 centimeters (Fig. 4). There is a slight flattening of the articular cortex and slight bony overgrowth at the lower margin of the head of the humerus. There is a dense shadow resembling an osteophyte or loose body at the upper margin of the glenoid and another mesial to the surgical neck of the humerus just below the glenoid margin. There is a mottled increased density in the mesial portion of the upper end of the shaft extending to the anatomical neck and into the upper portion of greater tuberosity. There is an oval area 7 centimeters long extending downward in the shaft of the humerus with a zone of increased density about its periphery, most marked at the upper and lower ends. The interior of this area is somewhat mottled in appearance and there is a faint network of increased density extending down the medullary canal from this.

A roentgenogram of the left tibia shows irregular lines of sharply increased density extending slightly obliquely across the shaft in the medullary region 12 centimeters below the knee joint (Fig. 5). There is also an island of slightly increased density in the mesial portion of the upper end of the shaft about 1.5 centimeters in diameter though hazy in outline. There is a narrow transverse line partly traversing the medullary region about 7 centimeters above the lower end of the shaft of the tibia, which has the appearance of an old growth arrest line. Roentgenograms of the lower thoracic and lumbar spine reveal the end stage changes of moderate adolescent scoliosis without any evidence of lesions in the bones of the type seen in the humerus, femurs, and tibia.

Roentgenograms of the chest, including the cervical spine, reveal no changes in the clavicles and none in the spine and ribs except those resultant from scoliosis. There is a large area of increased density in the region of the right upper lobe which is sharply outlined.

The lung condition was diagnosed as bronchiogenic carcinoma. The patient's chest symptoms fluctuated during the next few months but the cough continued. He gradually lost strength and developed edema of the dependent portions with increased non-

Fig. 3.

Fig. 3. Case 1. Central necrotic area in the shaft of the left femur. The calcified and ossified zone of demarcation and the calcified necrotic island in the external condyle, *x*, are clearly shown.

Fig. 4.

Fig. 4. Case 1. Loose bodies in shoulder joint and walled off necrotic area in upper half of humerus.

Fig. 5.

Fig. 5. Case 1. Sclerosed patches in upper diaphysis of tibia.

protein nitrogen of the blood and died December 5, 1937.

*Autopsy.* At autopsy the following anatomical diagnoses were made: bronchiogenic carcinoma of the right lung with extension into the superior vena cava; chronic nephritis; cardiac hypertrophy and dilatation; arteriosclerosis, most marked in aorta; duodenal ulcer (five small ulcers); cholelithiasis; cicatrices and pigmentation of legs; scoliosis, ancient; infarcts, ancient, massive, in shafts of both femurs and left humerus and minimal in shaft of left tibia; arthritis, chronic, deforming, of hips and left shoulder secondary to necrosis of heads of femurs and humerus; osteocartilaginous loose bodies in left shoulder and right hip.

The entire right upper lung lobe was involved in carcinoma originating in the bronchus. It penetrated and largely blocked the superior vena cava near its termination. No distinct tumor metastases were found. The heart was moderately hypertrophied but the coronary vessels were patent and smooth throughout. The heart valves appeared normal. There were no signs of infarcts, old or recent, in heart muscle, kidneys, spleen, or brain.

*Skeletal structures.* There was marked right lumbar scoliosis with conspicuous articular proliferation. The trunk bones otherwise showed no outward changes. The right sixth rib was removed and sectioned. No abnormalities were seen. The left scapula and humerus, both innominate bones, both femurs, and the left tibia were removed. When the left shoulder was opened marked villous proliferation of the synovial membrane and thickening of the capsule were noted. It contained seven osteocartilaginous loose bodies ranging from 1 to 2 centimeters in diameter, some of which were flattened and nodular. The articular cartilage of the glenoid was somewhat frayed but there was no marginal lipping or change in the underlying bone. Roentgenograms showed the same changes in the bones as were present at the examination on admission.

*Left humerus.* The head of the humerus was flattened and its articular surface rough with marked proliferation of the surrounding borders. The articular cartilage was markedly thinned and in places entirely wanting. Section of the humerus (Fig. 6) showed 2 cystic areas in the head containing necrotic and gelatinous material. The proximal half of the shaft presented an irregular circumscribed area of necrosis of the medullary portion. It measured 17.5 centimeters in length and varied in width from 20 millimeters in the proximal portion to 4 millimeters in the distal portion. It was surrounded

Fig. 6. Case 1. Central necrotic area in upper half of diaphysis of left humerus. Deforming arthritis in humeral head and 7 osteocartilaginous loose bodies in shoulder joint.

by a dense wall which varied greatly in thickness at different levels, being thickest at the upper and lower limits. The center contained brownish to grayish friable débris and there were calcareous bridges crossing its middle portion. The cortex of the upper half of the shaft was approximately normal in appearance, but there was an irregular zone of cancellous bone of increased density between it and the wall of the central necrotic area. The lower half of the humerus and the elbow joint were normal.

The capsule of the left hip was somewhat thickened and the synovia showed moderate villous arthritis with lymphocytic infiltration. The femoral head was markedly flattened, devoid of articular cartilage and surrounded by marginal osteophytes. There was destruction of articular cartilage of the glenoid which was changed in shape to fit the altered head, and there was a long osteophyte extending outward from the superior margin of the acetabulum. There was also a marginal osteophyte in the region of the cotyloid notch. An osteocartilaginous body was attached by a pedicle to the inferior portion of the capsule.


Fig. 7. Case 1. Section of femurs showing remnants of infarcts in lower half and resolved but deformed femoral heads. Partly calcified, incompletely resolved area of necrosis at *a*.

Coronal sections were made of the left femur (Fig. 7) and left innominate bone passing through the hip joint. The acetabular portion of the innominate bone showed marked sclerosis with a few scattered cystic areas in its mesial portion. The bone away from the acetabular region was normal in appearance.

The shaft of the left femur was normal to external appearance. The cut surface of the flattened head showed it to consist of irregular dense bone surrounding cystic areas beneath the articular surface and extending into the proximal portion of the neck. Osteophytosis was most marked at the lower margin. The remaining portion of the neck and upper half of shaft of the femur appeared normal. The distal half of the shaft contained an incapsulated area of necrotic grayish friable débris measuring 15 centimeters in length and varying in width approximately from 4 millimeters at its upper end to 25 millimeters at its lower end, which extended to within 2 centimeters of the epiphysis. It was surrounded by a dark hard zone varying from ⅓ to ½ centimeter in thickness. There were areas of cancellous bone and calcareous deposit within the necrotic débris. The cortex surrounding the necrotic area was approximately normal in appearance but there was sclerosed cancellous bone about the dense capsule. The lower epiphysis, articular surface of the femur, and the lining of the knee were normal in appearance.

*The right hip.* The capsule of the right hip was also thickened and there were many villi springing

Fig. 8. Case 1. Coronal section of posterior portion of external condyle of right femur, showing calcified necrotic area.

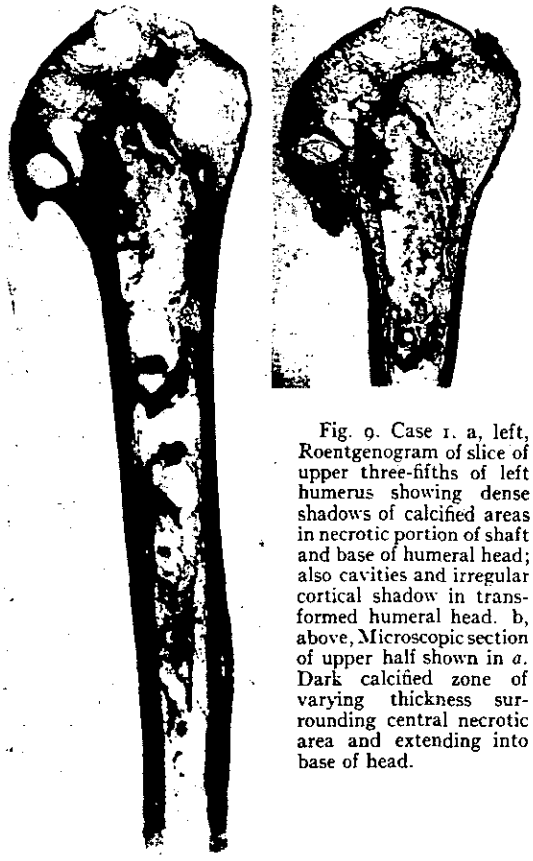

Fig. 9. Case 1. a, left, Roentgenogram of slice of upper three-fifths of left humerus showing dense shadows of calcified areas in necrotic portion of shaft and base of humeral head; also cavities and irregular cortical shadow in transformed humeral head. b, above, Microscopic section of upper half shown in *a*. Dark calcified zone of varying thickness surrounding central necrotic area and extending into base of head.

from the synovial lining. The head was flattened and conical in shape although less pronounced than on the left side. There was an osteocartilaginous body attached by a thin pedicle to the inferior portion of the capsule. Articular cartilages were destroyed on the superior surface of head and opposing surface of the acetabulum and there were marginal osteophytes on both head and acetabulum.

Coronal sections were made of the right femur (Fig. 7) and iliac bone extending through the acetabulum. Section of the acetabulum showed sclerosis of the bone bordering on the articulation to a depth of 1 to 2 centimeters and two cavities ½ and ⅓ centimeter in diameter in the weight-bearing region. One was filled with fibrous tissue and one with fluid (Fig. 12). There were also marginal osteophytes. The bone away from the acetabulum was normal in appearance. Section of the femur showed loss of articular cartilage on the weight-bearing portion of the head, with only a thin layer along the inferior portion. The underlying cancellous bone was sclerotic and contained several small cavities, some filled with fibrous tissue and some with fluid. A yellowish dark area at the base of the upper part of the neck of the femur appeared to be calcified infarct. The cortex and medullary portions of the shaft from there down to the middle had a normal appearance. In the lower half of the shaft there was a necrotic area with a dense surrounding zone of demarcation of approximately the same size and location as that seen in the left femur. The roentgenogram revealed a dense mottled area in the posterior part of the external condyle of the right femur. A section through this region (Fig. 8) revealed a yellowish, hard, amorphous blotchy area averaging 1½ centimeters in diameter which also looked like a necrotic calcified region. The epiphysis otherwise and the knee joint were normal in appearance.

The left tibia was normal in external appearance. On section a mottled, grayish yellow, blotchy streak was found in the medullary cavity of the shaft 10 centimeters below the upper end of the bone. There was also an irregular area of slight sclerosis in the cancellous bone of the lateral portion 2 centimeters below the epiphyseal line.

Slices ½ to 1 centimeter thick were cut from the upper three-fifths of the left humerus, the left glenoid, the upper two-fifths of the left tibia, the entire length of the femurs and the acetabula and iliac bones. Roentgenograms of the slices brought out sharply the dense zones of demarcation about the necrotic areas and the blotchy areas of increased density irregularly distributed within them, also the subarticular sclerosis and cavities in the femoral and humeral heads. Large microscopic sections were prepared of the slices of bone, also sections were made of the villous linings of the shoulder and hip joints and of one of the loose bodies which were present in the shoulder.

1 2 3

Fig. 10. Case 1. Section of wall about necrotic area in Figure 9, b, showing: 1, necrotic bone and marrow with calcareous islands; 2, fibrosed, calcified and partly ossified wall; 3, surrounding living cancellous bone and marrow.

Figure 9 shows the appearance of the roentgenogram of the slice cut from the humerus and of a microscopic section of the upper half of the slice. Under the microscope the central region of the shaft was found to consist of necrotic cancellous bone and marrow with blotchy areas of calcification. About the upper and lower limits of the necrotic area there was a broad layer of heavily calcified connective tissue and débris. Along the sides the zone of demarcation was much narrower. The lateral wall consisted of a narrow zone of calcified tissue in its upper three-fourths and of uncalcified dense fibrous tissue in its lower fourth. There was also an uncalcified fibrous wall along the lower two-thirds of the mesial wall. Surrounding this zone were living cancellous bone and fatty marrow. A microscopic section of the calcified lateral wall is shown in Figure 10. The internal portion consisted of small trabeculæ with empty lacunæ and of necrotic marrow. The outlines of the dead fat cells were remarkably well preserved. They were generally filled with an albuminous substance (edema *ex vacuo*). There were in places large and small calcareous granules. The zone of demarcation consisted of fibrous tissue which was extensively calcified and in places had been transformed into bone. It incorporated some dead trabeculæ which had not yet been absorbed and replaced by new bone. Outside of this was living cancellous bone and fatty marrow. The humeral head was flattened and contained three cystic areas —two in its lower part and one in its upper part. They were filled partly with a coagulum and partly with fibrous tissue. The joint surface of the superior and lateral portion of the head was covered with normal articular cartilage and underlying cortex. The rest of the head was covered with an incomplete thin layer of fibrocartilage and the articular cortex was bare and sclerosed in places. There was an osteophyte at the lower limit of the articular surface and a notch at the junction of the normal and transformed articular surfaces at the top of the head.

Fig. 11. Case 1. Roentgenogram of slice of right femur and acetabulum showing arthritis deformans and walled off infarct in lower half of femoral shaft.

Numerous villi sprang from the synovia. At the base of the head in its upper portion a partly transformed calcified necrotic zone separated it from the greater tuberosity.

The changes in the head are best explainable on the basis of a massive necrosis of all except its superior and lateral portion with death of overlying articular cartilage. The subsequent changes have consisted in gradual invasion, absorption, and replacement of the necrotic portion by cancellous bone and cystic cavities, and calcified tissue at its base. The dead articular cartilage has been partly replaced by an incomplete layer of thin fibro-

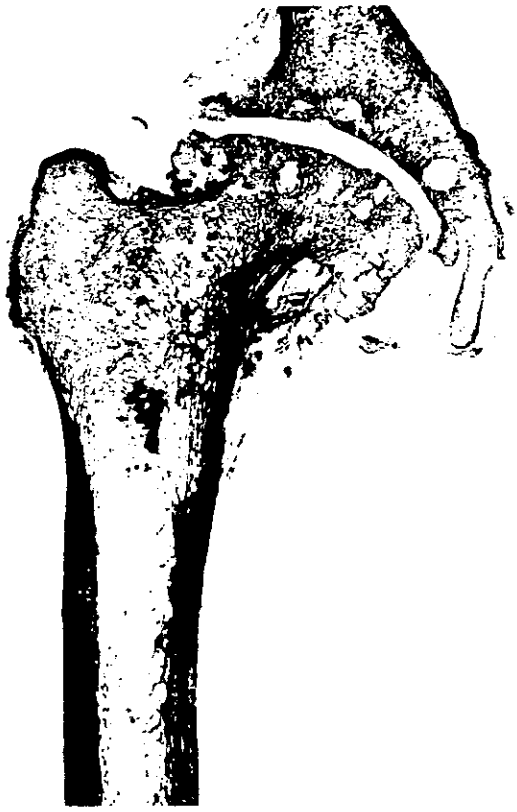

Fig. 12. Case 1. Microscopic section of the upper portion of the right femur and of the acetabulum showing deforming arthritis.

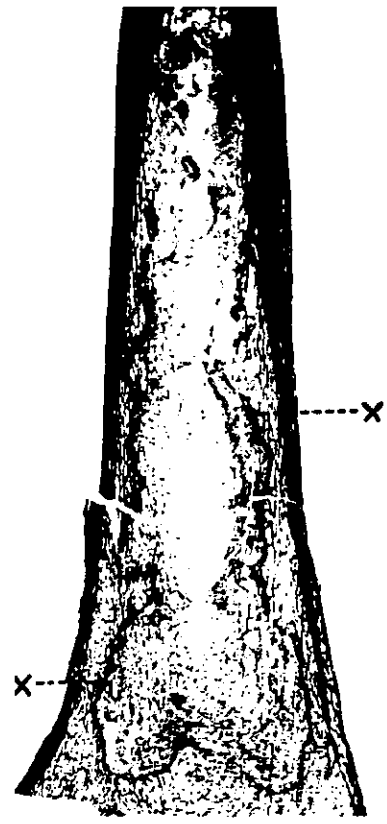


Fig. 13. Case 1. Microscopic section of lower half of shaft of right femur showing central necrotic area and calcified zone, *x*, about its periphery.

cartilage. These changes gave rise secondarily to villous synovitis and osteocartilaginous loose bodies. A section of one of the loose bodies showed it to consist of a center of calcified fibrocartilage and an outer portion of irregularly laminated fibrocartilage and calcified cartilage

Figure 11 is a roentgenogram of coronal slices of the right femur and acetabulum and Figure 12 a microscopic section of the upper portion of the femur and acetabulum.

The changes in the head of the femur and acetabulum were similar to those in the head of the humerus. Microscopically, the articular surfaces on both sides of the joint were covered by an irregular layer of fibrocartilage. In places it was incomplete and bare sclerosed bone with fibrous marrow bordered on the joint. There were subchondral cavities filled with fibrous tissue or with coagulum and there was marked osteophyte formation at the limits of the articular surfaces. The synovia showed a villous arthritis and there was a small island of bone imbedded in capsule at the inferior portion of the joint. At the base of the neck both mesially and laterally there were irregular islands of calcified fibrous marrow indicative of ancient bone necrosis. The head presented the picture of ancient aseptic necrosis with secondary collapse, invasion, and transformation similar to that which has been observed following intracapsular fracture of the neck with necrosis of the head, bony union of the fracture and subsequent weight bearing.

The rest of the upper diaphysis showed no change.

Microscopic examination of a section of the lower half of the shaft of the right femur (Fig. 13) revealed a central area of necrosis of cancellous bone and marrow with a small amount of granular calcification similar to that seen in the upper diaphysis of the humerus. The dead trabeculæ were unaltered in form as can be seen in Figure 12. There was a surrounding narrow zone of demarcation of calcified and partly ossified connective tissue. In places the connective tissue had grown for short distances into the necrotic zone, and in the upper limits were broad bands and islands of calcified tissue. There was a surrounding zone of living trabeculated bone and marrow, except at the upper end where the calcified

a b c

Fig. 14. Case 1. Wall of necrotic area: a, Necrotic bone and marrow within; b, calcified fibrous zone of demarcation; c, surrounding living cancellous bone and marrow. ×25.

wall merged with the compact cortex laterally. Figures 14 and 15 show the microscopic appearance of the zone of demarcation.

The articular cartilage and synovial lining of the knee joint were normal, which would indicate that the necrotic lesion did not primarily reach the articular surface of the joint. A microscopic section of the yellowish dense area in the posterior part of the external condyle showed it to consist in its deeper portions of old dead bone with cancellous spaces filled with a partly calcified sparsely cellular connective tissue. In its peripheral portion were living bony trabeculæ and the lesion was surrounded by living cancellous bone and fatty marrow. Microscopic examination of the yellowish dense area in the upper third of the shaft of the left tibia showed a picture similar to that in the external condyle of the femur. These were obviously old areas of necrosis with fibrous invasion, calcification, and incomplete replacement by new bone. The one in the condyle of the femur appeared to be an infarct which arose separate from that in the diaphysis.

CASE 2. L. O'B., aged 37 years, was admitted to the Veterans' Administration, Dayton, Ohio, in June, 1934, because of pain and stiffness in both hips of 4 years' duration. He states that in 1930 while working in a caisson there was leakage of gas from a neighboring plant and the crew was hurriedly taken out without gradual decompression. The patient developed the "bends" and was placed in a recompressor. On removal the attacks recurred so that he was returned to the recompressor and kept for 1 day. He was sent to a hospital with bleeding from the ears, nose, and mouth, and delirium which necessitated restraint. Ecchymoses developed in the skin of various parts of the body. He has had pain in the hips and legs from the time of admission to the hospital to the present although in diminishing severity, also some pain and stiffness in the shoulders. In 1931 he went into compressed air again to see if it

a b c

Fig. 15. Case 1. High power view of zone of demarcation. a, Necrotic border; b, calcified zone; c, surrounding living bone.

would benefit his hips. He thought the pressure affected his heart and the joints were not benefited. The pain and stiffness in the hips have advanced to a point where he has had to discontinue all work.

*Past history.* He was a steam fitter before being a caisson worker. He has had the usual diseases of childhood, and smallpox, influenza, and pneumonia; gonorrhea in 1923. He denies having syphilis. No history of joint trouble was elicited before the onset of the caisson disease. He suffers from headaches and attacks of dizziness. He smokes and drinks alcoholics moderately.

*Physical examination.* The patient is short, stocky, and somewhat overweight. He walks carefully with a waddling gait. Regional examination is essentially negative aside from the hips and shoulders. There is slight limitation of motion in both shoulders, more marked in the left. Motion in the hips is limited in all directions to about one-half normal and forced motion is painful. There is normal range of motion in the ankles and knees.

*Laboratory findings.* Basal metabolic rate was −10; blood Wassermann and Kahn, negative. Cytology and chemistry of blood, analyses including calcium, phosphorus, and uric acid, were within normal limits.

Roentgenograms were taken of the hips (Fig. 16). The head of the left femur showed a large spherical area of mottled density in the weight-bearing portion, including the joint surface and extending to the junction with the neck. It was separated from the surrounding bone by a broad zone of reduced density and its articular surface was depressed 3 to 4 millimeters. The rest of the articular surface of the head and that of the acetabulum appeared even in outline, and the cartilage space was of normal width. The mesial and inferior portions of the head were slightly increased in density and there was haziness and slight increase in density of the bone surrounding the demarcated spherical area, and extending downward into the adjacent portion of neck.

The right femur showed a similar area in the same region of the head which was larger, more dense, and

Fig. 16.


Fig. 17.

Fig. 16. Case 2. Necrosis of heads of femurs in caisson disease of 4 years' duration with sequestration of superior portions from weight bearing.

Fig. 17. Case 2. Left shoulder. Large portion of head of humerus shows irregular reduction in density with zone of increased density about it.

less demarcated from the surrounding head by the zone of reduced density. Its articular surface was dense, smooth, and depressed mesially where it extended to the fovea. The bone of the head and neck surrounding the demarcated area was somewhat mottled and increased in density. The shadow of articular cortex of acetabulum was intact and the cartilage space of the joint was approximately normal in width.

Roentgenograms of the shoulder showed blotchy reduction in density with a surrounding zone of increased density in the head of each humerus, more marked in the left (Fig. 17).

The diagnosis was made of caisson disease producing large areas of aseptic necrosis in the heads of the femurs, which, as a result of too much weight bearing, had been separated from the surrounding living bone. A biopsy was performed of the left hip by Dr. Walker. The cartilage looked pale. With a gouge some bone was removed from the neck of the femur. Aerobic and anaerobic cultures and guinea pig inoculations for tuberculosis gave negative results. Evidently the lesion of the head was not entered as microscopic sections of the bone removed showed atrophic living bone with an increase of fat and in some places of fibroblasts in the marrow spaces.

The patient remained in the institution with little change in his condition. February 9, 1935, a roentgenogram of the hips showed slight progression of the disease, the separated area of the head of the right femur being slightly more depressed. May 1, 1935, because of continued pain in the right hip an operation was performed at which cartilage and necrotic bone were removed, reducing the head to about one-fourth its normal size. Microscopic sections were made of a piece of the excised head. It contained bony trabeculæ, the lacunæ of which were entirely devoid of cells. The marrow spaces were partly filled with white fibrous connective tissue much of which was necrotic and in places the bone was being eroded along its surface. The microscopic picture was that of aseptic necrosis of bone with subsequent invasion and partial absorption by connective tissue. The patient after a few months walked in a caliper splint but the joint continued to be weak and painful and he was unable to work. A roentgenogram of the left hip taken 3 years after the first showed only slight progression of the process.

CASE 3. B. W., male, aged 54 years, was admitted to the University of Chicago Clinics, January 3, 1938, because of spastic paralysis in the lower extremities. In 1908 while working at bridge construction he came out of a caisson of 40 pounds' pressure in 5 minutes. Twenty minutes later he suffered severe pains in the abdomen, arms, and legs, and was removed to a hospital. There he developed in addition paralysis of the lower extremities and bladder and was confined for 4 months. The pains gradually disappeared but the limbs remained weak and became spastic.

Since 5 months after the injury the patient had walked with a cane but always with great difficulty. Sexual impotence had been present since the injury. He had had no pains in the limbs until 2 years ago since which time there had been frequently a dull ache, especially at night, over the lower half of the right tibia.

*Past history.* Patient could not recall any case of illness before accident in 1908; no history of venereal infection.

*Physical examination* revealed a well nourished male, weight 200 pounds; blood pressure, 150/90. Regional examination aside from the lower extremities was essentially normal, except for the right pupil which was slightly larger than the left and both pupils reacted sluggishly to light. He walked slowly with a spastic gait. Both lower extremities were spastic and movements of the joints were carried out with difficulty. The patellar and Achilles reflexes were exaggerated and clonus was easily incited. The hip, knee, and ankle joints showed no palpable changes but motion was restricted in them due to the spasticity. There was hypesthesia and marked dimi-

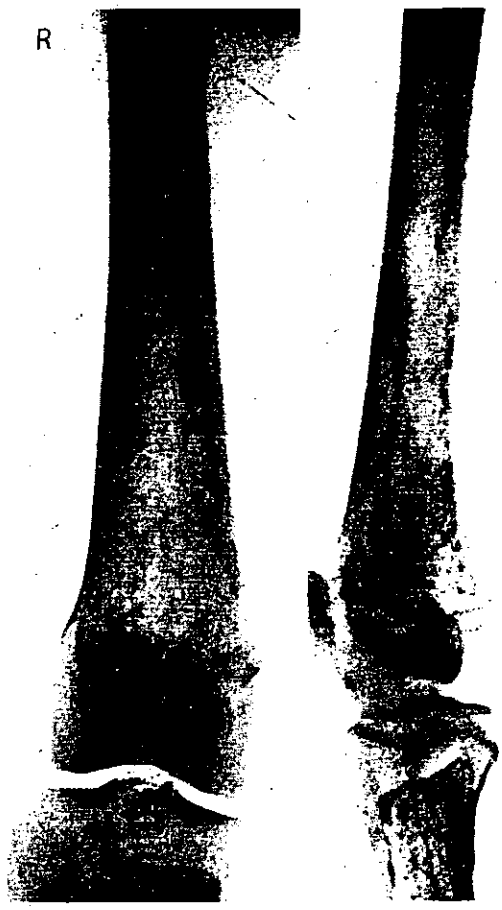


Fig. 18. Case 3. Walled off zones of increased density within shafts of right femur and tibia.

Fig. 19, left. Case 3. Demarcated dense zones in upper portions of right tibia and fibula.

Fig. 20, right. Case 3. Right tibia and fibula. Lower metaphysis involved in tibia and free in fibula.

nution in tactile sense below the knees. Blood Wassermann 4 plus, Kahn 3 plus.

Roentgenograms were made of the entire skeleton. Areas of increased density were revealed within the shafts of the lower ends of the femurs, the upper ends of the fibulas, and the upper and lower ends of the tibias. In the right femur the lower three-fifths of the shaft was involved. There was a dense irregular zone of demarcation at the junction of the cancellous and cortical bone of the metaphysis and irregularly along the walls of the medullary cavity above (Fig. 18). A similar condition was seen in the upper third of the shaft of the right tibia and in the upper metaphysis of the right fibula (Fig. 19). There was a similar dense blotchy area in the lower end of the right tibia 6 centimeters long beginning 1½ centimeters above the epiphyseal line (Fig. 20). In the left femur the involvement began just above the lower epiphysis and extended upward throughout three-fifths of the shaft (Fig. 21). The lesions in the left tibia and fibula resembled those of the right (Figs. 22 and 23). The left humerus showed a pointed area of increased density in the region of the lesser tubercle. There was no change in the head of the humerus or shoulder joint (Fig. 24). Roentgenograms of the rest of the skeleton revealed no abnormal changes. It was particularly noteworthy that the heads of the femurs and hip joints were uninvolved.

*Diagnosis.* The condition was diagnosed as a late stage of caisson disease with spastic paraplegia of the lower extremities and areas of incompletely resolved and calcified aseptic necrosis of the femurs, tibias, fibulas, and left humerus. Lues was diagnosed because of the positive Wassermann and Kahn tests and the sluggishness and inequality of pupils. But the roentgenographic appearance of the bone lesions

Fig. 21.

Fig. 22.

Fig. 21. Case 3. Demarcated zone and dense areas within shaft of left femur.

Fig. 22. Case 3. Upper end left tibia. Involved area densest about periphery. Involved fibula equally dense throughout.

Fig. 23. Case 3. Both ends left tibia and upper end of fibula involved.

Fig. 23.

was like that of Case 1 and very different from that seen in bone syphilis. No treatment was advised for the caisson disease but treatment was recommended for the lues.

CASE 4. L. P., male, aged 55 years, entered the University of Chicago Clinics, April 11, 1938, because of long-standing stiffness and pains in the hips, knees, and shoulders. In February, 1917, the patient worked for 8 hours in a caisson with pressure of 20 pounds. He came out in 4 minutes and 30 minutes later developed severe pains in the abdomen, legs, and arms. He had hemoptysis and hematemesis and was very ill for several days. He gradually improved and in 3 months was able to work but still had pains in both upper and lower extremities. Five months after the accident he had to give up work because of stiffness and soreness in the hips. These symptoms have persisted and he has gotten around with increasing difficulty. Pain and stiffness in the shoulder have also continued. Swelling developed in the lower legs and the skin became discolored with the development of leg ulcers. He has been unable to do any kind of work for several years.

*Past history* disclosed the usual diseases of childhood and gonorrhea at 19 years.

*Physical examination* revealed a well nourished male who moved about with great difficulty. Regional examination was essentially negative aside from the extremities. There was limitation of elevation of the arms to about 90 degrees and forced motions caused pain in the shoulders; marked

Fig. 24. Case 3. Blotchy dense area in metaphysis of humerus. Head and shoulder joint unchanged.

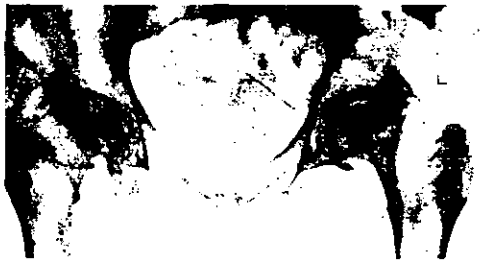

Fig. 25. Case 4. Left hip deformed with sequestrum at top of flattened transformed femoral head. In right hip are noted osteophytes and mottled density of head.

limitation of motion in all directions in both hips; knee and ankle motion was slightly limited.

Moderate swelling of the lower half of the legs was noted and also brawny induration, pigmentation, and small ulceration of the skin were present. Little muscle weakness was found in the legs and forearms. The reflexes were normal throughout. No disturbance of sensation of the skin was noted in any part of the body. Blood pressure was 130/76. Urine and blood examinations were essentially negative. Wassermann and Kahn tests were negative.

Roentgenograms were made of the entire skeleton. Extreme deformity of both hips was noted, more marked in the left (Fig. 25). The head of the left femur was flattened and the underlying bone was irregularly increased in density. The depressed dense area at the middle of the top appeared to be a detached piece of necrotic cortex such as is often seen in the collapsed femoral head that is necrotic following traumatic dislocation of the hip, fracture of the neck of femur, slipped epiphysis or Legg-Perthes' disease. The cartilage space of the joint was narrowed and there was marked osteophyte formation at the acetabular margins. The right hip showed narrowing of the cartilage space of the joint, increased density, and mottling of the head of the femur and lipping of the lower articular margins of the head and of the upper margin of the acetabulum. There was a half-moon shaped shadow of blotchy increased density in the upper portion of the head of the left humerus bordering on the articular surface which was irregular in this region (Fig. 26). The greatest increase in density was at the junction of head and neck and there was a narrow, irregular streak of increased density extending downward for approximately 3 centimeters into the shaft. The right humerus showed a similarly situated area of increased density which was more uniform and the articular surface of the area was somewhat irregular and flattened. The process did not extend into the shaft of the humerus.

Somewhat hazily outlined areas of increased density were apparent in the interior of the diaphyses of the lower ends of the femurs, both ends of the tibias and questionably the proximal ends of the fibulas, as seen in Figures 27, 28, and 29. The appearance differed from that of the corresponding


Fig. 26. Case 4. Mottled increased density in head of each humerus with extension into metaphysis of left.

leg bones in Cases 1 and 3 in that dense lines of demarcation had not yet formed about the periphery of the lesions. The epiphyses of all three bones were free of involvement and no changes appeared in the joint spaces.

A *diagnosis* was made of caisson disease with necrosis and partial replacement by new bone and partial calcification in the heads of the humeruses and femurs and necrosis with less complete reorganization and calcification in the diaphyses of femurs and tibias.

In view of the similarity of roentgenographic changes in the bones and joints in the 4 cases and of the established nature of the pathology in Cases 1 and 2, the evidence appears to be conclusive that the primary lesion is an accumulation of nitrogen gas in the bones—whether intravascular or extravascular will be discussed later—with interference of circulation and a resultant massive aseptic necrosis. In the head of femur or humerus the necrotic lesions may break down and be invaded and eventually replaced by new bone or fibrous tissue. Invasion of portions of the epiphysis may be followed by calcification and arrested transformation, especially in portions of the epiphysis away from the articular surface. Involvement of articular cortex and cartilage leads to the slow development of arthritis deformans with or without osteocartilaginous loose bodies. These changes are in keeping with those seen in the head of the femur and hip joint years after interruption of blood supply of the head of femur as by slipped epiphysis, certain cases of traumatic disloca-


Fig. 27.

Fig. 28.

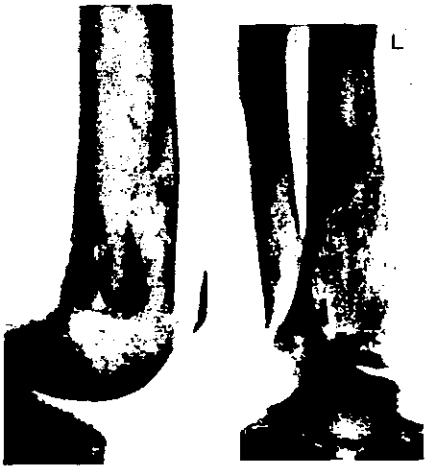


Fig. 29.

Fig. 27. Case 4. Central involved areas in shafts of right femur, tibia, and fibula hazy in outline and slightly increased in density.

Fig. 28. Case 4. Hazily outlined central increased density in shaft of femur, greatest in metaphysis.

Fig. 29. Case 4. *Blotchy dense areas in medullary canal and metaphysis of tibia.*

tion of the hip, fracture of the neck of the femur followed by bony union (Phemister) and idiopathic necrosis in adults (Chandler).

The lesions in the shafts are remarkable in that they are much more numerous and extensive than in any case of bland infarction or aseptic necrosis of bone found reported. The necrosis was of the interior of the diaphysis in all instances and because of the long time that had elapsed since the initial lesion it was difficult to know how much if any of the internal portion of cortex was involved. Creeping invasion and substitution of the dead bone by new bone may have reduced materially the size of the necrotic area before the process came to a standstill with calcification of the surrounding fibrous zone. Preservation of circulation to the cortex would tend to guard against the occurrence of pathological fracture but the presence of central necrosis producing weakness of bone would set up a reparative stimulus leading to creeping replacement of some of the dead bone by new bone. Once the diaphysis is sufficiently strong to support the part, the stimulus for substitution would come to a standstill and the remaining portion become incapsulated. One reason why these large diaphyseal lesions have not been heretofore recognized may be the slightness or absence of associated symptoms and the failure of occurrence of pathological fractures. On the other hand, the pains in the limbs during both early and later stages are doubtless due in some cases to the bone necrosis.

It is difficult to state whether the lesions in the bones produced by the nitrogen gas were the result of nitrogen embolism or of nitrogen accumulation within the medullary cavity and direct compression of blood vessels and other tissues or a combination of the two. Lesions of the soft parts are known to be produced by both methods. Points in favor of nitrogen embolism are: (1) The lesions were frequent (in three cases) in the heads of femurs where end arteries are known to be frequently found; (2) the metaphyses of the lower end of the femur and of upper end of fibula and both ends of tibia were affected in some cases while their epiphyses escaped,

which would favor embolism of the branches of their nutrient arteries. Points against the embolic theory are: (1) The enormous size and symmetrical distribution of the necrotic areas. With such extensive infarction of the bones produced by embolism, similar infarction of the spleen and kidneys might be expected and this was not found at autopsy in Case 1. Also, in the presence of such extensive embolism of bones, death might be expected to result from embolism of soft parts supplied by end arteries as brain, lungs, kidneys, intestine, etc. (2) Absence of involvement of the bones of the trunk.

In favor of the local pressure on blood vessels and other tissues of nitrogen gas accumulated in the medullary cavities is the limitation of the process to the extremity bones. The extremity bones are rich in fatty marrow while the trunk bones which have higher temperatures than the extremity bones (Huggins and Blocksom) contain hematopoietic marrow. Since fats and lipoids are known to absorb approximately five times as much nitrogen as other tissues, more nitrogen should be liberated within the extremity bones than within the trunk bones in caisson disease. Bornstein drew attention to the fact that the sluggishness of circulation in the bone marrow would mean less rapid removal of the gas from the bone marrow than from other tissues and consequently greater likelihood of necrosis from prolonged pressure. Larsen has shown that when a hydrostatic pressure of 180 centimeters or more is maintained in the medullary canal of the femur of the dog, by means of an infusion flask connected with a cannula passing through the cortex, massive diaphyseal necrosis of the medullary tissues and the cortex takes place.

Experience in the treatment of aseptic necrosis of the head of the femur in fractures of the neck with bony union, Legg-Perthes' disease, and slipped epiphysis indicates that the best possible management of any form of necrosing lesion of the head of the femur (including caisson disease necrosis) is prolonged abstinence from weight bearing, thus permitting reorganization of the necrotic area, and if possible replacement by new bone with the avoidance of collapse of the head.

## ANIMAL EXPERIMENTS

A search of the literature on experimental caisson disease failed to reveal a report of examination of the skeleton for evidences of lesions produced by liberated nitrogen gas.

### *Experiments on Dogs*

One of us (D.B.P.) in the department of surgery of the University of Chicago attempted to produce bone necrosis on seven dogs by arterial air embolism in the following manner: The dogs were anesthetized with ether and the head lowered in extreme Trendelenburg position. Aseptic technique was used and the right femoral artery was exposed and ligated. An arterial clamp was applied 1 inch above and the artery was opened near the ligature. A ureteral catheter, large enough to fill the artery, was introduced and, after removal of the clamp, pushed upward until its tip was in the aorta just above the bifurcation. Air varying in amounts from 6.7 to 12 cubic centimeters per kilogram body weight was then slowly injected. The air passing into the arteries produced crepitation in the lower extremities. After the wounds were closed the surviving animals were left in the Trendelenburg position for 3 hours to decrease the amount of air embolism in heart, lungs, and brain and to prolong that in the lower extremities.

### *Protocols of Experiments*

Seven cubic centimeters per kilogram body weight injected in one dog caused paralysis in the hind legs; death in 7 days. The femurs and tibias were split longitudinally and no gross changes were observed. Microscopic sections of upper end of left femur showed no abnormalities.

Eight cubic centimeters per kilogram body weight injected in one dog caused partial paralysis of hind legs. Infection developed in the operative wound and killed the dog in 8 days. Bones of both hind limbs were split open. No gross evidence of necrosis was seen anywhere.

Ten cubic centimeters per kilogram body weight injected in one dog produced partial paralysis in the hind legs which slowly improved to some extent. Death occurred from distemper in 78 days. The bones of the hind legs were removed, roentgenographed, and split open. A microscopic section was made of the upper end of the femur. No x-ray, gross, or microscopic change was found.

Ten cubic centimeters per kilogram body weight injected into one dog produced complete paralysis

and contractures of the hind limbs. Animal was sacrificed in 155 days. The spinal cord was examined by Dr. Cloward. It showed marked degeneration in distribution of anterior spinal artery of lumbosacral region. The muscles of the hind limbs were dissected from the skeleton. In places they were pale and shrunken, especially the adductors. Microscopic sections showed extensive-scattered replacement by fat. The bones of the hind limbs were roentgenographed, split open, and the left femoral head was sectioned for microscopic study. No changes were found aside from slight atrophy.

Twelve cubic centimeters per kilogram body weight injected in one dog caused death in 10 minutes from embolism.

Ten cubic centimeters per kilogram body weight injected in another animal caused death over night from embolism.

Six and seven-tenths cubic centimeters per kilogram body weight injected in one dog caused no symptoms afterward. Animal was sacrificed in 94 days. The bones of the hind limbs were roentgenographed and split and microscopic sections were made of the head of left femur. No pathological changes were found in the bones.

The absence of necrosis in the bones of the 4 dogs whose hind limbs were partly or completely paralyzed by the air embolism may possibly be considered as evidence favoring the view that the bone lesions in caisson disease are due rather to gas liberated in the medullary cavity under sufficient pressure to asphyxiate the tissues than to embolism.

## SUMMARY

The literature of skeletal lesions of caisson disease is reviewed.

Four cases of caisson disease of long standing in adult males are reported in which there was evidence that multiple infarction of large to small portions of long bones occurred as a result of damage by liberated nitrogen gas. All cases were studied clinically and roentgenologically, and the diagnosis was confirmed in one case by autopsy and in another by biopsy.

Late changes in the necrotic areas varied with the location and duration of involvement.

When the necrotic bone was situated in the epiphyses and bordered on joints, varying amounts of collapse of the weight-bearing portions, invasion and replacement by new bone, and calcification of non-substituted portions were noted. Articular cartilage overlying involved areas broke down and was replaced by fibrocartilage and more or less extensive arthritis deformans was established, accompanied in some instances by the formation of osteocartilaginous loose bodies. Support is furnished for the theory that arthritis deformans may be due to vascular blockage and necrosis of bone underlying articular cartilage.

When the necrotic bone was situated in the diaphyses or in epiphyses away from the articular surfaces, collapse did not occur and there was evidence of some invasion and replacement by new bone, as judged by the presence of irregular cancellous living bone surrounding and even penetrating the persistent areas. Complete replacement of some of the smaller areas had probably come about. But in the case of large areas replacement after advancing to the point of restoring approximately normal strength to the bone, came to a standstill as shown by repeated roentgenographic studies at long intervals, and the fibrous wall about them became more or less extensively calcified and ossified. Small necrotic areas were found, as one in the femoral condyle, invaded by connective tissue and extensively calcified. Scattered calcification also took place to some extent in the large central uninvaded encapsulated areas.

The encapsulated and calcified areas of necrosis in the diaphyses produced characteristic pictures in roentgenograms.

Uncertainty prevails as to whether the necrosis was produced by nitrogen gas obstruction of end arteries of the bones by embolism or by direct pressure on blood vessels and other tissues after liberation from solution in the fat of the bone marrow or in some other unexplained way. The facts that the long bones of the extremities, which are rich in fatty marrow, were the only bones involved, that fat absorbs relatively very large amounts of nitrogen and that nitrogen bubbles would be absorbed slowly from the marrow tissues because of the known sluggishness of the intra-osseous circulation, favor the theory of direct pressure of the gas on vessels and other tissues within the bone. But the extensive involvement of the diaphyses in some cases without involvement of epiphyses, and the involvement of the epiphyses, especially of the head of the femur, without involvement of

diaphyses or without continuity of involved regions in epiphysis and diaphysis are points in favor of infarction produced by nitrogen gas embolism or some other form of intravascular obstruction. Experimental air embolism of the lower limbs of dogs failed to produce bone necrosis.

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# BONE LESIONS IN DIVERS

YOSHIMI OHTA and HITOSHI MATSUNAGA, KITAKYUSHU, JAPAN

*From the Kyushu Labour-Accident Hospital Divers Disease Panel, Kitakyushu**

Avascular or aseptic necrosis of bone is often seen in compressed air workers and in divers. Twynam first reported this type of bone necrosis in 1888, but his report was later discarded because the condition he described was not, by definition, aseptic necrosis of bone, but due rather to osteomyelitis.

The radiographic appearances of avascular necrosis of bone in compressed air workers were described by Bornstein and Plate (1911) and Bassoe (1913), followed by many authors chiefly in Europe and America. The descriptions by Kahlstrom, Burton and Phemister (1939), Taylor (1944) and Bucky (1959) are often cited in Japan. An investigation during the construction of the Dartford tunnel by the Medical Research Council Decompression Sickness Panel in Britain (Golding, Griffiths, Hempleman, Paton and Walder 1960) and a recent report from the Clyde tunnels (McCallum, Walder, Barnes, Catto, Davidson, Fryer, Golding and Paton 1966) were fully descriptive of the disorder in compressed air workers.

These reports concerned only caisson workers, and there have been few reports of avascular necrosis of bone in divers. Single cases or small series have been presented by Sartor (1947), Herget (1948), Dale (1952), Ronald (1953), Pirastu and Perra (1960) and Kirjakov (1964). In general, in Europe and America aseptic necrosis of bone appears to be much less frequent in divers than in compressed air workers, as Walder has pointed out. On the contrary, in Japan there have been few reports of aseptic necrosis of bone in compressed air workers despite a large number of major public engineering works. The lesions in divers, on the other hand, have been reported by several Japanese authors. Kimura, Ono and Taguchi (1959) reported eight affected out of twenty-one divers, and Kinoshita and his associates reported osteoarthritis in thirteen cases in 1959 and in three additional cases in 1961. In 1965 Nagai and Ibata also described forty-six cases of bone necrosis among sixty divers, an incidence of 77 per cent.

This report is based on a survey carried out at a coastal village where the male population consists mainly of divers. It covered a period of three years, and we presented an interim report in Japanese in 1966. Here the authors will discuss only the statistical evaluation and the radiographic changes, not the clinical features, pathology or treatment.

## THE MODE OF LIFE OF THE DIVERS

In a village called Ohura on the shore of the Ariake Sea off northern Kyushu, about 400 divers, active or retired, live with their families. Their diving technique has been handed down from one generation to another. Nearly all the men of the community begin diving at the age of sixteen or seventeen after they have completed their compulsory education, and most of them are professional divers from the age of eighteen. They usually retire from this work in their fifties.

The main purpose of the diving is to collect the expensive shell-fish *Atrina Japonica*, widely used in Japanese and Chinese dishes. The fishing season extends over the five winter months from November to March. Except during stormy weather, the men dive ten to thirty metres from early morning to sunset, with a break of one hour at noon. The usual time on the sea bed is four hours in the morning and four in the afternoon. Outside the fishing season the

* The members of the Panel are Professor T. Amako (Chairman), Dr Y. Ohta, Dr H. Matsunaga, Dr O. Shigeto, Dr H. Hayashi, Dr D. Matsumoto, Dr T. Torisu and Dr M. Kawashima.

men dive to collect other kinds of shell-fish at a depth of thirty to sixty metres, to salvage objects at a depth of twenty to seventy metres or more, or to perform structural work at ten to thirty metres. They can therefore be said to dive almost all the year round.

On our first visit these divers knew nothing of physiological problems or correct methods of ascent and were completely ignorant of regulations and recompression chambers; each year three to five men died from accidents or from decompression sickness. "The bends" were very common; they almost ignored them, thinking them unavoidable and treating them with baths and by drinking alcohol. Experience had taught the divers to attempt treatment of severe bends or paralysis by recompression in the sea, but this usually failed. Some indeed froze to death.

Since the survey started Government officers have explained the official regulations and have instructed the men particularly with regard to correct decompression during ascent. In consequence the incidence of attacks of the bends has decreased remarkably.

## THE INVESTIGATION

Between 1966 and 1968 the men were examined in February of each year. A total of 301 divers out of about 400 agreed to cooperate. There were difficulties, because on the day for examination some would be away from home and others refused examination for one reason or another. In all, forty-three divers were examined on three occasions and 144 were examined twice or more. We thought these numbers would enable us to reach some conclusions.

For each diver a record was made of his past medical history, diving experience, and attacks of the bends. It was difficult to obtain precise information concerning each diver's individual experience because the men kept no records and their memories were unreliable. Accordingly we accepted the men's statements with regard to maximum working depth but ignored their statements concerning exposure times, decompression procedures and water temperatures. The clinical examination included an electrocardiograph, a chest radiograph, tests of pulmonary function, blood pressure reading, urine tests, physical measurements and radiological examination of bones. Radiographs were taken of the shoulders, hips and knees, the films being examined by three orthopaedic surgeons and thoroughly reviewed again a few months later.

The radiographic appearances of bone were divided into three groups: 1) definite—clear evidence of avascular necrosis; 2) questionable—necessary to re-examine; and 3) none—no evidence of avascular necrosis. Definite cases were further classified into either "juxta-articular lesions" or "head, neck and shaft lesions" according to the classification adopted by the Medical Research Council Decompression Sickness Panel.

## FINDINGS

Of 301 divers who agreed to be examined, 152 (50·5 per cent) had avascular necrosis of bone. Sixteen other men had doubtful bone changes but these were ignored.

**Juxta-articular lesions**—Forty-four men had seventy-five juxta-articular lesions. Thirty-five men had forty-eight lesions of the head of the humerus; thirteen men had bilateral lesions, nine men had the left side only affected and thirteen the right side. Nineteen men had twenty-seven lesions of the head of the femur; eight men had bilateral lesions, five had the left side and six had the right side only affected.

As in all other reports, the surface of the knee joint was never involved.

**Head, neck and shaft lesions**—These were more frequent in the lower limbs (171 lesions) than in the upper limbs (seventy-eight lesions). There were twelve tibial and 159 femoral lesions.

**Age groups** (Table I)—With increasing age there was a rise in the incidence of bone lesions ($p<0·01$), particularly over the age of thirty.

**Duration of diving experience** (Table II)—It was possible to show an association between the

duration of diving experience and the incidence of bone lesions ($p<0.01$). The men with over ten years' experience of diving were highly affected.

**Site of bone lesions** (Table III).—The lesions were seen most frequently in the upper humerus, followed by the lower and upper femur and the upper tibia in that order. There was a significant difference in the proportions of bone lesions in the upper humerus compared with those in the upper femur and tibia, but no significant difference between those in either end of the femur.

TABLE I

THE INCIDENCE OF BONE LESIONS RELATED TO AGE

| Age (*years*) | Number of men | Number with bone lesions | Number with no bone lesion |
|---|---|---|---|
| 16 to 19 . | 19 | 3 | 16 |
| 20 to 29 . | 141 | 49 | 92 |
| 30 to 39 . | 91 | 62 | 29 |
| 40 to 49 . | 36 | 28 | 8 |
| 50 and over | 14 | 10 | 4 |
| Totals . | 301 | 152 | 149 |

TABLE II

THE INCIDENCE OF BONE LESIONS IN RELATION TO YEARS OF DIVING

| Duration of diving (*years*) | Number of men | Number with bone lesions | Number with no bone lesion |
|---|---|---|---|
| 0 to 4 . | 88 | 19 | 69 |
| 5 to 9 . | 92 | 42 (12)* | 50 |
| 10 to 14 . | 48 | 34 (4) | 14 |
| 15 to 19 . | 39 | 29 (12) | 10 |
| 20 to 24 . | 23 | 19 (11) | 4 |
| 25 and over . | 11 | 9 (5) | 2 |
| Totals . | 301 | 152 (44) | 149 |

* Number of men with juxta-articular lesions in brackets.

There were sixty men (39·5 per cent) with a solitary lesion and ninety-two men (60·5 per cent) with multiple lesions. Lesions of the upper humerus and femur were more frequently unilateral than bilateral, but were not significantly more numerous on the right side than on the left. The incidence of lesions in the lower femur was equal in bilateral and unilateral cases but in the latter the lesions were more frequent on the right side.

**Bone lesions and decompression sickness.** *Bone lesions and the bends* (Table IV).—There was a significant difference ($p<0.01$) between the incidence of bone lesions in the men with and without a previous history of bends.

*Bone lesions and previous complete or incomplete paraplegia caused by decompression sickness* (Table V).—It was not possible to show a significant association ($p>0.01$). We found forty-eight divers who either were suffering, or had suffered, from complete or incomplete spinal

paraplegia due to Type II decompression sickness. In forty-two of the forty-eight men (87.5 per cent) the paraplegia followed dives to deeper than 30 metres. The remaining six men were affected after diving to between 20 and 30 metres and soon recovered completely. There were no cases of paraplegia following dives to less than 20 metres.

*Type of bone lesion and the bends*—Of forty-four men with juxta-articular lesions, forty-one (93 per cent) had experienced attacks of the bends somewhere in the body. On the other hand, of 108 men with head, neck and shaft lesions, eighty-one (75 per cent) had experienced the bends. These figures had no statistical significance.

TABLE III
THE SITE OF THE BONE LESIONS

| Site | Side | Cases | Totals |
|---|---|---|---|
| Upper humerus 92 (35)* | Left | 32 (9)* | 92 cases, 126 sites |
| | Right | 26 (13) | |
| | Bilateral | 34 (13) | |
| Upper femur 58 (19) | Left | 21 (5) | 58 cases, 76 sites |
| | Right | 19 (6) | |
| | Bilateral | 18 (8) | |
| Lower femur 72 | Left | 12 | 72 cases, 110 sites |
| | Right | 22 | |
| | Bilateral | 38 | |
| Upper tibia 9 | Left | 5 | 9 cases, 12 sites |
| | Right | 1 | |
| | Bilateral | 3 | |

* Juxta-articular lesions.

TABLE IV
BONE LESIONS AND THE BENDS

| History | Number with bone lesions | Number without bone lesions | Totals |
|---|---|---|---|
| Bends | 122 (41)* | 84 | 206 |
| No bends | 30 (3) | 65 | 95 |
| Totals | 152 | 149 | 301 |

* Juxta-articular lesions.

*Site of the bends and site of bone lesions*—We found no significant relationship. The lesions occurred at the same site in 135 men (43 per cent) and at a different site in 177 men (57 per cent).

**Bone lesions and maximum depth of diving** (Table VI)—In general, the incidence of bone lesions increased in proportion to the depth of diving. In the men who worked in the shallow sea at less than 10 metres there were no bone lesions. In the men who dived up to 20 metres there were no true bone lesions, though possibly very slight bone changes. There was a significantly higher incidence of bone lesions in the men who usually dived over 30 metres compared with those who dived to less than that ($p<0.01$).

RADIOGRAPHIC APPEARANCES OF AVASCULAR NECROSIS OF BONE IN DIVERS

These are indistinguishable radiologically from those in compressed air workers and from other causes. Therefore the diagnostic standards for compressed air workers can be applied to divers. The Medical Research Council Decompression Sickness Panel in Britain has presented the classification shown in Table VII, which we used initially because it was convenient and had been accepted. Later, however, the authors found a need for modification with regard to juxta-articular lesions, as shown in Table VIII.

*Points of difference between the two classifications—M.R.C. and O.M.*—Firstly, in the present series, the typical "Dense areas with an intact articular cortex" (M.R.C.) was seen in only

TABLE V

BONE LESIONS AND PARAPLEGIA

| History | Number with bone lesions | Number without bone lesions | Totals |
|---|---|---|---|
| Paraplegia . | 31 | 17 | 48 |
| No paraplegia | 121 | 132 | 253 |
| Totals . | 152 | 149 | 301 |

TABLE VI

BONE LESIONS IN RELATION TO DEPTH OF DIVING

| Maximum depth of diving *(metres)* | Number of men with *bone lesions* | Number of men without *bone lesions* | Totals |
|---|---|---|---|
| Up to 9 . | 0 | 8 | 8 |
| 10 to 19 . | 7 | 28 | 35 |
| 20 to 29 . | 42 (5)* | 50 | 92 |
| 30 to 39 . | 40 (12) | 35 | 75 |
| 40 to 49 . | 29 (12) | 16 | 45 |
| 50 and over | 34 (15) | 12 | 46 |
| Totals . | 152 (44) | 149 | 301 |

* Juxta-articular lesions.

two cases involving the humeral head, and one of these changed to "Mass opacities" (O.M.) two years later. Also, three out of ten cases with lesions in the head of the femur classified as "Dense areas" (M.R.C.) had become "Juxta-articular lesions" one or two years later.

Bone has a three-dimensional structure and is projected two-dimensionally on a plain radiograph. Therefore the appearances change according to the direction of the projection. For example, a small dense area adjacent to an intact articular cortex shown in a film is naturally classified as a "Dense area with intact articular cortex", A1 (M.R.C.). However, this small dense area may appear to be about the centre of the head and away from the articular cortex on another film taken from a different angle. On this occasion it may be recorded as a "Dense area", B1 (M.R.C.), unless the real location of the lesion is confirmed by tomography or other methods. For this reason, the authors put the cases with "Dense areas with an intact articular cortex", A1 (M.R.C.), into the group of "Dense area of head lesions", B1 (M.R.C. and O.M.).

Secondly, in the femoral head the authors include U-shaped increased linear density of bone into "Linear opacity", A3 (M.R.C.). Out of three cases diagnosed as linear opacity of the femoral head in this series two showed U-shaped increased linear density without any destruction of the articular cortex.

Thirdly, in the authors' classification a new category of "Mass opacities" has been included. The lesion does not involve the articular cortex, but consists of patches of increased density disseminated widely over almost all the area of the head, and in the neck.

TABLE VII

M.R.C. CLASSIFICATION

| | |
|---|---|
| **Juxta-articular lesions** | |
| Dense areas with an intact articular cortex | (A1) |
| Spherical segmental opacities | (A2) |
| Linear opacity | (A3) |
| **Structural failure** | |
| Transradiant subcortical band | (A4a) |
| Collapse of the articular cortex | (A4b) |
| Sequestration of part of the cortex | (A4c) |
| **Osteoarthritis** | (A5) |
| **Head, neck and shaft lesions** | |
| Dense areas | (B1) |
| Irregular calcified areas | (B2) |
| Transradiant areas and cysts | (B3) |

TABLE VIII

OHTA AND MATSUNAGA'S CLASSIFICATION

| | |
|---|---|
| **Juxta-articular lesions** | |
| **Intact articular cortex** | |
| Segmental opacities | (A1) |
| Linear opacity | (A2) |
| Mass opacities | (A3) |
| **Structural failure** | |
| Sequestration of the cortex | (A4) |
| Collapse of the cortex | (A5) |
| **Osteoarthritis** | (A6) |
| **Head, neck and shaft lesions** | |
| Dense areas | (B1) |
| Irregular calcified areas | (B2) |
| Transradiant areas and cysts | (B3) |

Fourthly, although structural failure is divided into three groups in the M.R.C. classification, we have put it into two groups. In this series there were only three cases that might be classified as "Transradiant subcortical band", A4a (M.R.C.), and these could primarily fall into the category of "Sequestration of part of the cortex", A4c (M.R.C.). Therefore we have called both of them "Sequestration of the cortex", A4 (O.M.).

Finally, for the sake of convenience, in our classification each category has been given a single letter (A or B) and a single number (1 to 6).

## RADIOGRAPHIC APPEARANCES IN DIVERS

**Juxta-articular lesions**—In the survey forty-four men of 301 divers (14·6 per cent) fell into this group. For the purposes of this discussion we have also included nineteen divers not from Ohura found with juxta-articular lesions. These sixty-three men were divided according to the sites of lesions as follows: fifty men had lesions of the upper humerus, fifteen on the right, twelve on the left and twenty-three on both sides; thirty men had lesions of the upper femur, eight on the right, seven on the left and fifteen on both sides.

Tables IX and X record the radiographic appearances by our classification. Table IX summarises the juxta-articular lesions found in 144 divers at Ohura who were examined twice or more. The headings I, II and III indicate the radiographic findings of the first, second and third survey respectively, and the yearly changes can be followed.

Table X records the men with juxta-articular lesions who had only one radiographic examination.

*Segmental opacities* (A1)—These were more frequent in the humerus (thirty-five cases with forty-one lesions) (Fig. 1) than in the femur (eight cases with thirteen lesions).

*Linear opacity* (A2)—This type of bone lesion as defined in the M.R.C. classification was seen in six men, who had six lesions in the humeral heads (Fig. 2) and one in the femoral head. In the femoral head a U-shaped linear opacity with an area of decreased density between it and the articular cortex was sometimes seen (Fig. 3). Two examples of this were classified as cases of linear opacity.

TABLE IX

SITE AND TYPE OF THE JUXTA-ARTICULAR LESIONS FOUND IN THIRTY-TWO DIVERS RADIOGRAPHED TWICE OR MORE

| Case number | Upper humerus | | | | | | Upper femur | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Right | | | Left | | | Right | | | Left | | |
| | I | II | III | I | II | III | I | II | III | I | II | III |
| 1 | no | ? | A1 | no | A1 | A1 | no | no | no | no | no | no |
| 2 | no | no | no | ? | ? | A1 | no | no | no | A1 | A1 | A1 |
| 3 | no | no | no | no | no | no | ? | A3 | A3 | no | no | no |
| 4 | A1 | — | A1 | A1 | — | A1 | A3 | — | A3 | A3 | — | A3 |
| 5 | A2 | A2 | A4 | ? | ? | A1 | no | no | no | no | no | no |
| 6 | — | A4 | A5 | — | no | no | — | no | no | — | no | no |
| 7 | ? | — | A4 | A1 | — | A1 | no | — | no | no | — | no |
| 8 | A1 | A1 | A1 | A2 | A5 | A5 | no | no | no | A2 | A5 | A6 |
| 9 | no | — | no | no | — | no | no | — | A2 | no | — | no |
| 10 | no | — | no | no | — | no | no | — | A3 | B1 | — | A3 |
| 11 | — | A1 | A3 | — | B1 | B1 | — | no | A3 | — | no | no |
| 12 | — | A1 | A1 | — | no | A1 | — | no | no | — | no | no |
| 13 | no | ? | A1 | no | A2 | A2 | no | no | no | no | no | no |
| 14 | no | no | no | ? | ? | A2 | no | no | no | no | no | no |
| 15 | A1 | — | A1 | A1 | — | A1 | no | — | no | no | — | no |
| 16 | no | — | no | A1 | — | A1 | no | — | no | no | — | no |
| 17 | no | — | no | no | — | no | A6 | — | A6 | A6 | — | A6 |
| 18 | — | ? | A1 | — | no | no | — | no | no | — | no | no |
| 19 | A1 | — | A1 | no | — | no | no | — | A1 | no | — | no |
| 20 | no | ? | A2 | no | no | no | no | no | no | no | no | no |
| 21 | no | no | — | A3 | A3 | — | no | no | — | no | no | — |
| 22 | no | — | A4 | no | — | no | no | — | no | no | — | no |
| 23 | no | no | no | no | no | no | no | no | no | A2 | A2 | A5 |
| 24 | no | no | no | no | no | no | no | no | A3 | B1 | B1 | A3 |
| 25 | A3 | — | A3 | B1 | — | A3 | no | — | no | no | — | no |
| 26 | no | — | no | no | — | no | no | — | no | no | — | A4 |
| 27 | no | no | no | A1 | A1 | A1 | no | no | no | no | no | no |
| 28 | no | A1 | A1 | no | no | no | no | no | no | no | no | no |
| 29 | no | no | no | no | no | no | no | no | A1 | no | no | A1 |
| 30 | — | A5 | A5 | — | no | no | — | B1 | A1 | — | A1 | A1 |
| 31 | — | no | A1 | — | A2 | A4 | — | no | no | — | no | no |
| 32 | — | A5 | A5 | — | A1 | A1 | — | no | no | — | no | no |

*Mass opacities* (A3)—The affected area of the humeral or femoral head termed "mass opacities" is usually greater than in the case of "segmental opacities" (Fig. 4). It includes almost the whole of the head, extending over most of the neck and sometimes to the shaft. Mass opacities show patches of varying density. Mass opacities were seen in the humeral heads in seven men with eight lesions and in the femoral heads in nine men with twelve lesions.

*Sequestration of the cortex* (A4)—In this series "Sequestration of the cortex" (Fig. 5) includes both "Transradiant subcortical band" and "Sequestration of part of the cortex" of the M.R.C. classification. We found such lesions in thirteen men, fourteen in the humeral heads and one in a femoral head. Among these men the lesion called "Transradiant subcortical band" (M.R.C.) was seen twice in the humeral head and once in the femoral head. In the sequestration cases the remaining part of the head showed remarkably increased density, occasionally with a sharply defined edge.

TABLE X

SITE AND TYPE OF LESION IN TWELVE DIVERS RADIOGRAPHED ONLY ONCE IN THE SURVEY

| Case number | Upper humerus | | Upper femur | |
|---|---|---|---|---|
| | Right | Left | Right | Left |
| 1 | no | A1 | no | A3 |
| 2 | A5 | A1 | no | A1 |
| 3 | A1 | A1 | no | no |
| 4 | A3 | no | no | no |
| 5 | no | no | A6 | no |
| 6 | no | A1 | no | no |
| 7 | no | A1 | A1 | A6 |
| 8 | A1 | no | no | no |
| 9 | A5 | no | no | no |
| 10 | A1 | no | no | no |
| 11 | A1 | no | A3 | A3 |
| 12 | no | A3 | no | no |

*Collapse of the articular cortex* (A5)—All cases in our survey were unilateral, seven in the humeral head (Fig. 6) and four in the femoral head (Fig. 7).

*Osteoarthritis* (A6)—Fourteen hip joints and one shoulder joint were affected (Fig. 8).

**Head, neck and shaft lesions**

*Dense areas* (B1)—These are dense areas with an intact articular surface (Fig. 9)—the "dense areas" of the M.R.C. classification. Occasionally dense areas due to aseptic necrosis are indistinguishable from bone islands seen in normal radiographs, so any cases where the diagnosis was in doubt have been excluded.

These lesions were found at the upper ends of the humerus, femur and tibia. Forty-nine lesions were seen in the humerus, twenty-five on the left and twenty-four on the right; ten lesions in the femur, seven on the left and three on the right; and three lesions in the tibia, two on the left and one on the right. No lesion was seen in the lower femur.

*Irregular calcified areas* (B2)—These lesions were not found in the upper humerus or femur but affected the lower femur (Fig. 10) (105 lesions, forty-seven on the left and fifty-eight on the right) and upper tibia (eight lesions, five on the left and three on the right).

YEARLY CHANGES IN RADIOGRAPHIC APPEARANCES

Changes in bone structure over a period of one to three years could be followed in 144 men who were examined at least twice during the three-year survey.

FIG. 1

Figure 1—Juxta-articular lesion. Segmental opacity.

FIG. 2

Figure 2—Juxta-articular lesion. Linear opacity

FIG. 3

Figure 3—Juxta-articular lesion. U-shaped increased linear density of bone.

FIG. 4

Figure 4—Juxta-articular lesion. Mass opacities.

*Men examined at all three surveys*—Forty-three men were examined on all three occasions (Table XI). Twenty-two men had normal radiographs at the first examination; three of these men had bone lesions on the second survey, segmental opacities in one humeral head in two men and in both in the third.

Another man with irregular calcified areas in both femoral shafts but no juxta-articula lesion had mass opacities in the right femoral head a year later; these appearances were unchanged at the third examination.

FIG. 5

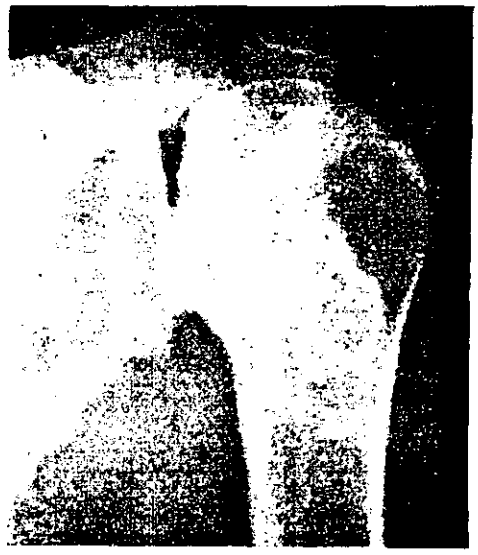

FIG. 6

Figure 5—Juxta-articular lesion. Sequestration of the cortex. Figure 6—Juxta-articular lesion. Sequelae of sequestration of the cortex.

FIG. 7

FIG. 8

Figure 7—Juxta-articular lesion. Collapse of the cortex. Figure 8—Juxta-articular lesion. Osteoarthritis.

Five men with normal radiographs at the first and second surveys showed lesions at the third survey. Two had segmental opacities in both humeral heads, one had mass opacities in both femoral heads and irregular calcified areas in both femoral shafts, one had a collapsed

articular cortex in the left femoral head, and the fifth had transradiant areas in the right femoral neck (Fig. 11). In addition one other man, who showed only calcified areas in the right femoral shaft and a cyst in the humeral neck at the first and second surveys, had by the third survey developed segmental opacities in both femoral heads.

FIG. 9
Head, neck and shaft lesion. Dense areas.

FIG. 10

FIG. 11

Figure 10—Head, neck and shaft lesion. Irregular calcified area. Figure 11—Head, neck and shaft lesion. Transradiant areas.

*Men examined at first and third surveys*—Thirty-one men were examined at the first and third surveys (Table XII). Twenty-one men showed bone lesions at the first survey but two appeared normal at the third survey. This was because head, neck and shaft lesions had disappeared

in six cases by the time of the third survey, while the number of men with juxta-articular lesions had increased from seven to eleven. Of these four additional men, one had segmental opacities in the right femoral head, one had mass opacities in both femoral heads, one had mass opacities in one femoral head, and one had sequestration of the cortex in the right humeral head.

TABLE XI

MEN EXAMINED AT ALL THREE SURVEYS

| | First | Second | Third |
|---|---|---|---|
| With bone lesion | 21 (3)* | 24 (7) | 29 (12) |
| No bone lesion | 22 | 19 | 14 |

* Juxta-articular lesions.

TABLE XII

MEN EXAMINED ONLY AT FIRST AND THIRD SURVEYS

| | First | Third |
|---|---|---|
| With bone lesion | 21 (7) | 19 (11) |
| No bone lesion | 10 | 12 |

On the other hand six men with transradiant areas and cysts at the initial survey—in the right humeral neck in one man, in both humeri in two men, in the neck of the left femur in two men, and in both femoral necks in one man—showed no bone lesions two years later. The initial films were carefully re-examined and the "lesions" showed either absence of, or very slight, marginal sclerosis.

*Men examined at first and second surveys*—In this group of forty-nine men no changes were seen over the period of a year (Table XIII).

*Men examined at second and third surveys*—Again in this group of twenty-one men no changes were seen (Table XIV).

TABLE XIII

MEN EXAMINED ONLY AT FIRST AND SECOND SURVEYS

| | First | Second |
|---|---|---|
| With bone lesion | 21 (1) | 21 (1) |
| No bone lesion | 28 | 28 |

TABLE XIV

MEN EXAMINED ONLY AT SECOND AND THIRD SURVEYS

| | Second | Third |
|---|---|---|
| With bone lesion | 13 (6) | 13 (6) |
| No bone lesion | 8 | 8 |

TABLE XV

YEARLY CHANGES IN JUXTA-ARTICULAR LESIONS

| Radiological appearance | Upper humerus | | | Upper femur | |
|---|---|---|---|---|---|
| | Not changed | Changed | | Not changed | Changed |
| Segmental opacities (A1) | 13 | 1 | (A1→A3) | 2 | 0 |
| Linear opacity (A2) | 1 | 3 | A2→A2→A4<br>A2→A5→A5<br>A2→A4 | 0 | 2 A2→A5→A6<br>A2→A5→A5 |
| Mass opacities (A3) | 2 | 0 | | 3 | 0 |
| Sequestration (A4) | 0 | 1 | (A4→A5) | 0 | 0 |
| Collapse (A5) | 2 | 0 | | 0 | 0 |
| Dense areas (B1) | | 1* | (B1→A3) | | 3 B1→A3<br>B1→B1→A3<br>B1→A1 |

* Dense areas with an intact articular cortex.

**Yearly changes of juxta-articular lesions**—The yearly changes in appearance of the juxta-articular lesions, which clinically and radiologically are the most important, are summarised in Table XV. In the whole series there was no instance of "segmental opacities" advancing to "structural failure of the articular cortex". However, of six lesions classified as "linear opacity", five developed structural failure (Figs. 12 to 14).

FIG. 12 FIG. 13 FIG. 14

Juxta-articular lesion. Figure 12—Rarefied area bounded by linear opacity at the first survey. Figure 13—The same case one year later. Figure 14—The same case two years later.

In three instances lesions first classified as "dense areas" at the proximal end of the femur appeared later to be typical juxta-articular lesions. These may have been originally juxta-articular but diagnosed simply as dense areas because the density was not clearly defined.

## DISCUSSION

Estimates of the incidence of avascular necrosis of bone in divers varies widely in the literature. From Europe, Herget in 1948 reported bone lesions in thirteen of forty-seven divers (28 per cent). From Japan there have been several reports on the incidence—38 per cent by Kimura *et al.* in 1959, 60 per cent by Kinoshita *et al.* in 1963, and 76·6 per cent by Nagai and Ibata in 1965. These figures vary according to the diving history of the men concerned. From the present investigation we believe that the incidence of bone necrosis increases in proportion to both the length of diving experience and the working depth.

In the present series juxta-articular lesions were seen only in men who had had over five years of diving and who had dived deeper than twenty metres. The general incidence of bone necrosis was low among men who had a short diving history or had worked at depths less than twenty metres. The incidence clearly depends upon various combinations of these two factors.

In the whole survey 301 of the 400 divers were examined radiologically and lesions were found in 152 (50·5 per cent). Of these 152 men, thirty-five (23 per cent) had juxta-articular lesions of the humeral head and nineteen (12·5 per cent) of the femoral head, figures which are extremely high compared with the 6 per cent and 4 per cent respectively found in compressed air workers on the Clyde Tunnel.

## SUMMARY

1. A three-year survey of avascular necrosis of bone has been carried out in a community of some 400 professional divers for shell-fish who had used no modern technique of decompression.

2. Of 301 divers radiographed, 152 (50·5 per cent) had bone lesions.
3. The incidence of bone necrosis increased in proportion to the length of diving experience, being highest in men with over ten years' experience.
4. The incidence was also higher in men who usually dived deeper than thirty metres.
5. There was a high incidence in men with a history of the bends but no significant relationship between the sites of the bends and those of the lesions.
6. Bone lesions were more frequently multiple than solitary.
7. The upper end of the humerus was significantly more affected than the upper end of the femur or tibia, but not significantly more than the lower end of the femur.
8. At the upper ends of the humerus and femur the lesions were more frequently unilateral than bilateral.

The expenses of this investigation were defrayed by the Workmens Compensation Board and the Kyushu Labour-Accident Hospital. We also wish to express our thanks to the orthopaedic staff of that Hospital for their cooperation.

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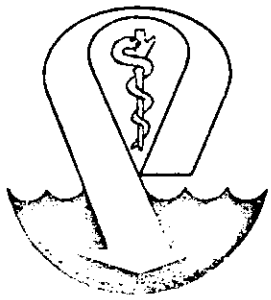


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Post Office Box 398
Avalon, California 90704

Program Chairman:
ANDREW A. PILMANIS, Ph.D.
Phone: (213) - 746-6792

# HISTOPATHOLOGY OF ASEPTIC BONE NECROSIS IN MINIATURE SWINE

K.H. Smith, P.J. Stegall and T.W. Huang, Virginia Mason Research Center, 1000 Seneca Street, Seattle, Washington 98101, U.S.A.

Dysbaric osteonecrosis was produced in miniature swine by repeated exposure to 60 fsw for 6 hours followed by decompression at the rate of 30 fpm.

Histopathologically the most prominent finding was extensive hyaline thrombosis of small vessels in the Haversian canals of cortical bone. This was associated with cortical bone necrosis. Subsequent reparative attempt of bone led to resorption of necrotic bone, deposition of new lamellar bone on inner surface of widened Haversian canals, and subendosteal new bone formation. The osteons appeared disorganized and separated by necrotic interstitial bone plates.

Within the tubular bones was extensive necrosis of cancellous bone and fatty marrow. The latter resulted in lakes of fat surrounded by foamy histiocytes and giant cells. Necrotic areas showed extensive osteoclastic activity and reactive new bone formation. Hemorrhage, hemosiderin-laden macrophages and prominent fibrosis were present in the necrotic foci. There were many medium-sized muscular arteries exhibiting concentric intimal thickening and narrowing of lumens as a result of myointimal cell proliferation and accumulation of collagen. The endothelial cells of the affected arteries were inordinately prominent.

Bony trabeculae revealed abnormal cement lines characterized by numerous cement lines intersecting at sharp angles, and scalloping patterns. Occasional osteoclastic and osteoblastic (osteoplastic) activities were noted.

The epiphysial plate invariably showed foci of necrosis accompanied by fraying of cartilage and calcification. Occasional hyaline thrombi in capillaries were appreciated.

## PRINCE ALFRED HOSPITAL, SYDNEY, NEW SOUTH WALES.

### A CASE OF CAISSON DISEASE.

(By G. E. TWYNAM, M.R.C.S.E., Assistant-Surgeon.)

G. H., a strong, healthy man, weighing 14 stone 3 lbs., went to work for the first time in the cylinder at the Iron Cove Bridge on March 6th, 1882, at 9.30 A.M., and came out again at 12.30 P.M. During this time he was working under a pressure of 60 lbs. to the square inch, or four atmospheres.

Whilst in the cylinder he seemed well, and especially did not notice the pain in the ears so often complained of. At 12.30 P.M. he came up into the airlock, and in three minutes the pressure was reduced to the ordinary atmosphere. He left, and shortly after, on the way home, felt a severe pain in the right elbow joint as though he had been struck on the ulnar nerve. Within half an hour his right knee suddenly gave way, and he fell, and in a few minutes became semi-conscious.

In this state he was taken home, when very acute pain set in in both knees and both elbows, but there was no marked swelling in the joints. At 6 P.M. he was almost pulseless and quite chilled. For two days his face was very swollen, and he spat blood slightly for three or four days after the accident; it then ceased, but began again within the month with cough and night sweats. He had shifting pains in various parts of the body for seven days after the accident. From a week to a fortnight after the commencement of the attack the pain suddenly left the other joints and concentrated itself in the right knee, which began to swell and contract. A month later the limb was forcibly straightened under chloroform by Dr. Shewen, and secured on a back splint. Within fourteen days an abscess in the popliteal space appeared, which afterwards proved to be connected with another some inches higher up at the back of the thigh. These were opened early in July and drained, when another swelling with but slight pain was discovered in front of the right trochanter. This was aspirated twice, and about two pints of fluid in all drawn off. The abscess cavity was afterwards drained, and finally in August laid open, when a sinus was discovered leading up to the groin, of which the end was never reached by a probe. At this time the leg again contracted, and remained so during the patient's voyage home to England.

In April, 1883, thirteen months after the injury, he was seen by an eminent surgeon in London, who failed to discover diseased bone, but advised the leg being straightened on a MacIntyre's splint, which was done in nineteen days. He left England May 19th, 1883; during the voyage the leg contracted again, and remained so until I saw him for the first time in November, 1884. He then had two or three sinuses on the outer side of the thigh and one in the popliteal space. I enlarged two old openings, scraped out the sinuses, and followed one beneath the femoral vessels to the inner side of the leg, and up into the pelvis, but could not touch dead bone. This, to my regret, did him no real benefit, for the sinuses continued to discharge, and I saw nothing of him for a year, until October, 1885, when he appeared at the out-patient department of the Prince Alfred Hospital. Dead bone was then detected in the popliteal space, and he was advised to come in.

On October 21st, under chloroform, the sinus was explored, and a probe passed through the condyles.

On October 23th, I amputated by anterior and posterior flaps through the lower third of the femur. On section, the bone looked anything but healthy, being of a greenish colour in the medullary canal and cancellous part, with a smell of sulphuretted hydrogen. I should at once have removed it higher up had I not promised not to do so; however, I scraped out the sinuses near the trochanter thoroughly.

He made a good recovery, his temperature only once reaching 101° F., and that on the second night after operation. He was discharged at the end of November with a sinus at the point of the stump, the old sinus by the trochanter still discharging a little thin pus. He continued thus until the beginning of January, when he came to be examined again. I then found necrosis when probing the upper sinus, and consequently recommended the removal of the remainder of the femur, as bare bone could be felt at the point of the stump also.

On January 13th, 1886, using a strong india-rubber tube as tourniquet, applied in figure of eight round the limb and pelvis, and held in position by bandages, I removed the bone by Furneaux Jordan's method.

At first the patient was very low, but under opium and brandy he rallied, and the dressings were changed for the first time on the second day. Two openings on the face of the stump were still discharging at the time he left the hospital.

In June, 1886, I found a roughness at the end of one sinus which had not closed. Some new bone deposited from the portions of periosteum left behind; two stout silk ligatures were removed, and afterwards a painful nerve end was excised by Dr. MacCormick when I had left for England. This left him a very good stump or pad, and he has since gained weight considerably, and now weighs 12 stone, 5 pounds.

An examination of the bone after removal showed that the periosteum surrounding the whole bone from end to end was about a third of an inch thick, with a layer of new bone under it closely applied to the old shaft. The compact layer of the old shaft was pale and necrosed, but the cancellous part and medulla were stuffed full of a green coloured fatty material like putty, which no doubt was the original medulla, changed probably by effusion of blood into it. The decomposition of this gave the peculiar colour noticed on section. The surrounding tissues were matted together, and the openings of the sinuses were in such situations that the bone could not be reached by a probe.

REMARKS BY MR. TWYNAM.—The most interesting point of the whole case lies in its causation; for this I must refer you to the Croonian lectures for 1881 by the late Dr. Moxon. Some of his conclusions are, shortly:—1. Having given the anatomical uses of the cerebro-spinal fluid, he goes on to prove that the human brain is capable of withstanding enormous intra-cranial pressure without real damage, provided asphyxia or strangulation be not present. 2. The real danger to the nervous system depends on the pressure being too rapidly removed. 3. Further on he shows how paraplegia is dependent on the poor blood supply of the spinal cord, especially the corda equina, in consequence of the great length and small calibre of the spinal arteries. Through the cervical dorsal portions of the cord these arteries are reinforced by small branches which pass in on the nerves, but in the corda equina, such as there are, are long and very small. When the pressure is removed rapidly there is a great rush of blood into the tissues of the surface of the body. The spinal cord then being very poorly supplied with blood is in a state of marked anæmia, and I may remind you that anæmia in other cases is an early stage of "white softening," as met with in ordinary paraplegia.

This, then, Dr. Moxon considers the reason why so many men who have been subjected to great pressure have suffered from paraplegia. But there is one factor in this description of which he makes no direct mention as influencing the anæmic state, and which seems to me likely to have considerable bearing on the prevention of these particular symptoms; namely, the prolonged extraordinary pressure of the cerebro-spinal fluid on the cord. It is true that in the earlier part of his anatomical description he shows that as the brain fills with blood, the cerebro-spinal fluid is driven out to press on the cord, and that whilst the brain is gorged with blood the men are lively and work well. One more anatomical fact: in the cord the cavity of the arachnoid is larger below than it is above. Possibly the anæmic condition of the lower end of the cord may in part be produced by the pressure of this fluid, when we consider the hydrostatic relation of the long column of fluid pressing the blood out of the tissues of the cord. Under ordinary atmospheric pressure this effect is not sufficient to damage the cord, as it is met by the emptying of the vessels in the loose tissues surrounding the dura mater. But with the increased blood-pressure in the brain, representing the power, and the lower end of the cord the body to be compressed—lying as it does in that part of the cylinder where the diameter is the larger, and therefore the pressure is the greater—an anæmic condition is produced, and the longer this is continued, the worse for the workman, hence the value of the "short spells," which have been found to be the best preventitive under these circumstances. Certain it is that a too long continuance in the air chamber was almost invariably followed by exhaustion and paralysis during the sinking of the caissons for the bridge at St. Louis, whilst this paraplegic condition does not seem to have been met with in any of those who remained under two hours in the cylinder.

If the pressure be taken off at once, instead of the circulation generally being evenly supported by the atmospheric pressure being reduced by degrees, the blood will rush into those parts of the system which have not such long arteries, and into those favoured by gravitation, as shown by Dr. Moxon—so continuing the anæmia. Whereas, if the pressure be taken off gradually, there is more likelihood of all the vessels getting their fair share of nourishment.

With regard to the limb in question, the medullary cavity answers in some degree to the cranium; as the compact bone takes the surface pressure from the medulla, but it had no means for the regulation of its contents, similar to the cerebro-spinal fluid, and I think it highly probable that under the great pressure of the circulation some vessels gave way, and this was the origin of the thrombosis which led to the destruction of the bone, and so to a condition such as Sir James Paget calls "quiet necrosis."

One more point regarding those cases: May not the pains so commonly noticed in the joints be due to an engorgement of the synovial membranes, similar to that found in early joint disease?

[The patient was exhibited at a meeting of the medical section of the Royal Society of New South Wales.]