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CLINICAL SPACE MEDICINE

A PROSPECTIVE LOOK AT MEDICAL PROBLEMS FROM HAZARDS OF SPACE OPERATIONS

by Douglas E. Busby

Prepared by
LOVELACE FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH
Albuquerque, N. Mex.
for

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Prepared under Contract No. NASr-115 by
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"In truth, we advance far by the harmonious assembling of facts made known by many observers and writers."

Charles H. Mayo, 1918

PREFACE

Many real and potential hazards will face astronauts* during operations in space. Some of these hazards might be of little medical significance; others might produce serious medical problems.

In this report, an attempt is made to describe the characteristics and suggest the management in space of possible medical problems which might arise from hazards of space operations; attention will therefore not be given to possible naturally-occurring diseases. Writing is oriented to missions during which, due to the time required to return to Earth, the diagnosis and interim treatment of medical problems will have to be carried out in space. Therefore it is assumed in this report that diagnostic and treatment facilities will be available, and that advanced spacecraft concerned will provide a "shirtsleeve" environment in which multidisciplined crews, including medically-trained personnel, will be able to live in reasonable comfort.

To lay the groundwork of Clinical Space Medicine, a field in which very little has been written and no experience gained to date, this report covers more than just the clinical manifestations, diagnosis, and treatment of possible medical problems in space. Wherever necessary, various hazards of space operations are defined and analysed in order to determine their possible medical effects. The pathophysiologic characteristics of medical problems are discussed, frequently in detail, to provide the rationale for the prevention and treatment of the problems in space. Many pertinent basic medical facts are stated not only to refresh memories of physicians not actively engaged in the practice of medicine, but also to familiarize non-medical readers, such as design engineers and operations analysts with the cause, natural history and performance impairment to be expected of each medical problem. An effort is also made to provide a substantial bibliography for workers in Clinical Space Medicine and to identify areas of research which will contribute to this field.

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*"a traveller in interplanetary space" (Webster's New International Dictionary, Second Edition, 1934)

This report focuses on the primary goals of Clinical Space Medicine - namely to prevent the occurrence of medical problems in space and to restore an astronaut who is suffering from a medical problem to an optimum functional capability as quickly as possible. It is conceivable, however, that an astronaut might have to forego definitive treatment temporarily while he performs a task vital to mission safety or success. During this period of time, his symptoms might be alleviated with supportive measures.

The first five chapters of this report are concerned with the various effects of decompression an astronaut could suffer. Medical problems which could result from thermal stresses are discussed in Chapters 6 and 7. Possible medical consequences of weightlessness are considered in Chapters 8, 9 and 10, and those of "particles" travelling in space in Chapters 11 and 12. Various traumatic injuries receive attention in Chapters 13 and 14. Medical problems produced by carbon dioxide, which will always be the major gaseous contaminant of space atmospheres, are reviewed in Chapter 15. Since the risks of oxygen toxicity and chronic exposure to trace atmospheric contaminants should be virtually eliminated in advanced space systems, these medical problem areas will not be discussed in this report. Finally, Chapter 16 gives consideration to the general aspects of the diagnosis and treatment of medical problems in space

I am most grateful to Drs. A. H. Schwichtenberg, E. M. Roth and T. M. Fraser of the Department of Aerospace Medicine, The Lovelace Foundation for Medical Education and Research, for their many constructiv comments which greatly assisted me in the preparation of this report. The many contributions of Dr. U. C. Luft of the Department of Physiology are also acknowledged. Gratitude is also expressed to my secretaries, Mrs. J. H. Rigler and Mrs. J. J. Whalon, and to our Chief Document Librarian, Mrs. J. Wilson, and her staff for their immense help.

D. E. B.

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CHAPTER 1

ACUTE HYPOXIA

A rapid unforeseen loss of the atmospheric pressure in a spacecraft cabin or space suit, leading to manifestations of acute hypoxia, possibly ebullism (Chapter 2) and explosive decompression injuries (Chapter 3), will undoubtedly always be a major hazard facing astronauts during operations in space. Any number of causes of such a critical event are conceivable. Considered foremost is penetrating damage to a space suit, possibly from contact with rugged terrain on a lunar or planetary surface, a pointed tool, a sharp projection from the spacecraft exterior, or a meteoroid. Decompression of the spacecraft cabin might result from a structural failure due to an excessive spacecraft docking or landing impact, or from penetration of a cabin wall by a meteoroid. Other possible causes of acute hypoxia include an accidental disconnect or failure of a pressure valve in a life support system, and an emergency decompression for fire extinguishment or for removal of a toxic atmospheric contaminant. Finally, acute hypoxia could result from depletion of oxygen supplied by a portable life support system, or from the purging of a spacecraft cabin atmosphere with carbon dioxide or inert gas to extinguish a fire.

In this chapter, an attempt is made to present aspects of acute hypoxia considered pertinent to the space situation. Under separate headings are discussed the sequence of clinical events which would occur during a severe acute hypoxic exposure in space, various measures which might be used in resuscitating a hypoxic astronaut, the so-called "oxygen paradox", and the characteristics and management in space of the sequelae of hypoxia - posthypoxic cerebral edema and delayed post-hypoxic encephalopathy.

Clinical Events in Acute Hypoxia

In their excellent review of the literature on hypoxia, Van Liere and Stickney [96] made note of the fact that all tissues of the body are immediately affected to some degree when a rapid significant reduction of

the partial pressure of inspired oxygen occurs. However the remarkable intolerance of the central nervous system, especially the brain to oxygen deprivation, accounts for the earliest and most striking manifestations of acute hypoxia [8].

If an astronaut should suffer acute hypoxia, he could lose "useful consciousness" after a latent period of several seconds to many minutes. The term "useful consciousness" has been used to define that period during which purposeful acts can still be performed [98]. It is noted that the slower the onset of hypoxia, the more specific must be the definition of the performance degradation which reflects loss of "useful consciousness" [78].

A hypoxic astronaut's "time of useful consciousness" will depend upon the rate of reduction and the final level of the partial pressure of oxygen in his ambient atmosphere. During this period, the astronaut should be able to function normally, so that if he recognizes the cause of a hypoxic event, he should be capable of initiating a life-saving emergency measure or declaring his situation to other members of the crew. Once beyond the "time of useful consciousness", however, he could either enter a brief "prodromal period", which is usually characterized by a high degree of helplessness, or suddenly lapse into unconsciousness.

The results of numerous decompression studies indicate that the "time of useful consciousness" of an astronaut who is rapidly decompressed to a relatively low partial pressure of oxygen should be reasonably predictable [4, 5, 7, 10, 22, 41, 66, 67, 76, 78, 101] It is noted that there is a marked variation in individual susceptibility to acute hypoxia, except at relatively high altitudes [7]. Data on the mean "times of useful consciousness" following rapid decompressions of humans who are breathing either air or oxygen throughout decompression are shown in Figure 1.1. The curves in this figure demonstrate that:

> -the "time of useful consciousness" becomes shorter with increasing altitude until a minimum time is reached. From data cited by Luft (64, 66), this time appears to vary from about 10 to 15 seconds. It is reached at about 46,000 feet (106 mm Hg or 2.04 psia) when air is breathed throughout decompression,

or about 52,000 feet (79 mm Hg or 1.53 psia) when oxygen is breathed throughout decompression [93]. Notably, the "time of useful consciousness" remains unchanged for decompressions above 52,000 feet whatever the concentration of oxygen in the inspired gas might be.

-below 50,000 feet, the use of pure oxygen delays the onset of unconsciousness considerably, so that in decompressions to 45,000 feet breathing oxygen, "useful consciousness" may be fully maintained for many minutes while breathing air under the same circumstances leaves little more than 10 seconds for emergency action. The difference in shape between the two curves can be attributed to the presence of nitrogen in the air-breathing decompressions.

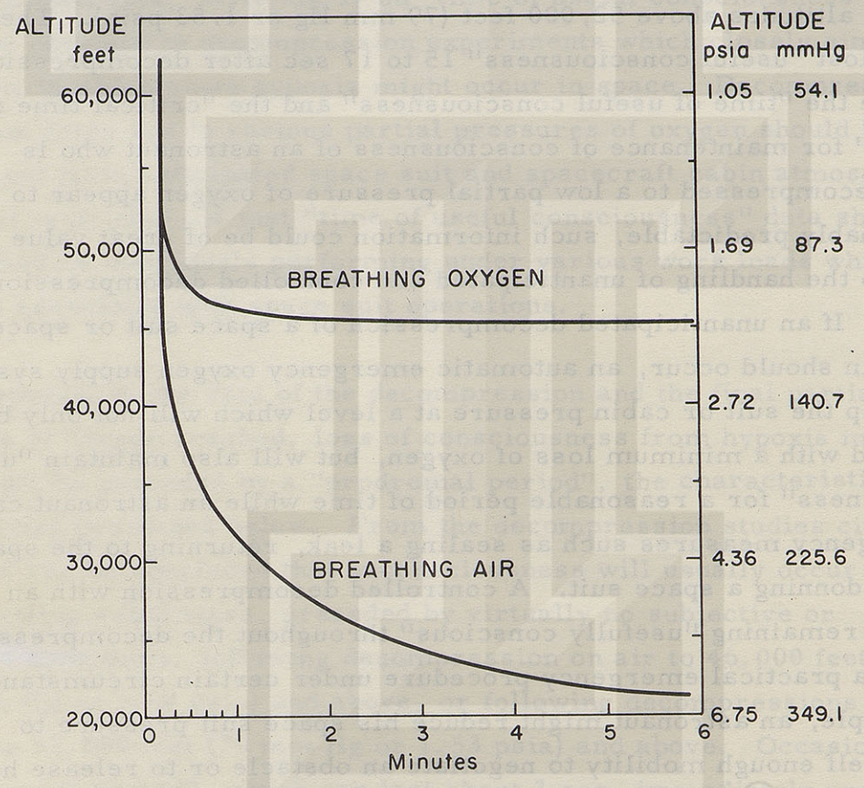

Figure 1.1 "Times of useful consciousness" on exposure to various high altitudes after rapid decompression, accomplished in less than one second, from sea level breathing 100 percent oxygen.

(After Luft [65]).

Decompression studies have also demonstrated that there is a "critical time of exposure" within which an individual must recommence breathing an adequate partial pressure of oxygen if "useful consciousness" is to be continuously preserved [3, 4, 66, 76]. This time apparently also reaches a minimum with increasing altitude. Bryan and Leach [10] found that oxygen had to be given within 7 sec to subjects decompressed from 8,000 feet (564 mm Hg or 10.91 psia) to 40,000 feet (141 mm Hg or 2.72 psia) in 2.5 sec in order to preserve continuous consciousness. The average "time of useful consciousness" in their studies was 15 sec. Luft and co-workers [66], noted that the "critical time of exposure" should not exceed 5 to 6 sec in rapid decompressions (2 sec) to altitudes above 52,000 feet (79 mm Hg or 1.53 psia). Their subjects lost "useful consciousness" 15 to 17 sec after decompression.

Since the "time of useful consciousness" and the "critical time of exposure" for maintenance of consciousness of an astronaut who is rapidly decompressed to a low partial pressure of oxygen appear to be reasonably predictable, such information could be of great value if applied to the handling of unanticipated and controlled decompressions in space. If an unanticipated decompression of a space suit or spacecraft cabin should occur, an automatic emergency oxygen supply system might keep the suit or cabin pressure at a level which will not only be associated with a minimum loss of oxygen, but will also maintain "useful consciousness" for a reasonable period of time while an astronaut carries out emergency measures such as sealing a leak, returning to the spacecraft, or donning a space suit. A controlled decompression with an astronaut remaining "usefully conscious" throughout the decompression might be a practical emergency procedure under certain circumstances. For example, an astronaut might reduce his space suit pressure to give himself enough mobility to negotiate an obstacle or to release himself from a trapped situation. A controlled reduction of the cabin pressure might be used to dump into space most of an atmosphere accidentally contaminated with chemically-active particles and droplets. This measure might also be used for extinguishing a fire and, secondarily, for its cooling effect and removal of noxious fumes from the cabin

atmosphere. It must be noted, however, that rapid permanent extinguishment of a fire can be attained only by decompressing to a vacuum until the temperature of a burning system is below ignition temperature. Thus an astronaut, who will undoubtedly not have time to don a space suit prior to decompression for fire extinguishment, may experience the consequences of both hypoxia and ebullism (Chapter 2). If the spacecraft cabin atmosphere contains an inert gas, he will be subjected to a risk of decompression sickness (Chapter 4). It is assumed that if any controlled decompression produces a loss of consciousness, recompression will be programmed to occur within a time period sufficient to prevent sequelae of hypoxia and possibly ebullism.

Additional data, particularly on "time of useful consciousness", should be obtained in decompression experiments which closely simulate situations in which acute hypoxia might occur in space. Decompressions at various rates and to various partial pressures of oxygen should be carried out from anticipated space suit and spacecraft cabin atmospheres. Finally it is pointed out that "time of useful consciousness" data should be obtained on individuals performing under various work loads which could be associated with space suit operations.

Depending on the rate of the decompression and the final partial pressure of oxygen reached, loss of consciousness from hypoxia may or may not be preceded by a "prodromal period", the characteristics of which are presented below. From the decompression studies cited above, it can be concluded that unconsciousness will usually occur with startling suddenness, preceded by virtually no subjective or objective symptoms, following decompression on air to 46,000 feet (106 mm Hg or 2.04 psia) and above, or following decompressions on oxygen to 52,000 feet (79 mm Hg or 1.53 psia) and above. Occasionally, a "prodromal period", which can last about 3 sec, immediately precedes loss of consciousness following such decompressions. This relatively short period is characterized by amnesia and uncoordinated or clonic movements.

As the rate of decompression decreases or the final partial pressure

of oxygen increases, the "prodromal period" will increase in duration. The common, well documented manifestations of hypoxia at this point are predominantly due to central nervous system malfunction, characterized by aberrations of mental function, such as errors in and loss of interpretation and judgment, overconfidence, confusion, euphoria, drowsiness, paranoia and amnesia, and of neuromuscular activity, such as incoordination and clonic movements (41, 64, 67, 72).

The question arises as to whether manifestations of acute hypoxia, especially during a relatively prolonged prodromal period, could be recognized by an astronaut exposed to hypoxic conditions. If so, he might possibly be able to initiate appropriate emergency measures or signal the incident to other members of the crew. Classically, most individuals are unable to recognize subjectively any manifestations of acute hypoxia. On repeated hypoxic exposures and with adequate training, some do learn to recognize hypoxia if it comes on slowly. However, it is apparent that such a capability cannot be relied upon during operations in space, especially if hypoxia is of rapid onset or the attention of an astronaut is focused on a seemingly more important matter at the time of a hypoxic event. Therefore, even though astronauts should be well trained in this area, primary reliance will have to be placed on devices which sense and adequately warn of changes of the partial pressure of oxygin in spacecraft cabin and space suit atmospheres and, wherever possible, command the restoration of an adequate oxygen tension.

As part of a hypoxia indoctrination program, it is advisable for an astronaut to observe carefully the response of each fellow astronaut to hypoxia. Since many individuals exhibit a stereotyped response, such as euphoria, paranoia and drowsiness, to a lowered partial pressure of inspired oxygen, the knowledge of any manifestations which characterize an astronaut's response to hypoxia might be of some value in recognizing and possibly in distinguishing it from other causes of central nervous system malfunction, such as acute carbon dioxide toxicity, hypothermia and hyperthermia. Even though cyanosis is a reasonably good sign of hypoxia, this sign will be difficult to monitor visually during space suit operations. Devices which sense and warn of the occurrence

of cyanosis might be considered, but these should be ancillary to those which monitor partial pressure of atmospheric oxygen.

If exposure of an unconscious astronaut to a low partial pressure of oxygen continues, vital systems of his body will quite rapidly cease to function normally. Respiration usually fails early. Although peripheral circulatory collapse usually coincides with or soon follows cessation of respiration, some degree of cardiac activity may continue for a prolonged period of time. It is readily apparent that the times at which these events occur are related to the partial pressure of oxygen to which an individual is exposed. Data on humans from which these times might be predicted are sparse, for in human decompression experiments, exposures to low partial pressures of oxygen are stopped when consciousness is lost. Studies of prolonged accidental hypoxic events have yielded only very rough estimations of the durations of such events.

If deprived of oxygen, man has no mechanism which will enable him to survive more than a very few minutes. It is a well established fact that serious permanent damage of brain tissues begins to occur about 4 minutes after arrested cerebral circulation [84, 88]. This time might be somewhat increased in cases where the cardiovascular system continues to function, and so continues to supply glucose and other nutrients to and remove toxic metabolites from the brain [19].

Cessation of respiration frequently occurred at the same time as loss of consciousness during a decompression study in which human subjects were decompressed in less than one second from 33,000 feet (196 mm Hg or 3.80 psia) to about 55,000 feet (69 mm Hg or 1.33 psia) while breathing oxygen [11]. On the other hand, this event did not occur in similar studies in which individuals were exposed to altitude until consciousness was lost [3, 43, 101]. If one assumes that exposure to a very low partial pressure of oxygen is essentially equivalent to a sudden circulatory arrest, respiration will cease within one minute after the exposure, cessation being preceded by stertorous periodic breathing [16, 43, 84].

It is extremely difficult to establish exact times to death for various

acute hypoxic exposures [69]. One study of hypoxic fatalities, in bomber aircrews, estimated that after onset of exposure 22 deaths apparently occurred between 5 and 15 minutes, and 4 deaths in less than 5 minutes [11]. It is noted that all these fatalities occurred at altitudes of less than 32,000 feet (206 mm Hg or 3.98 psia). Another study of 75 hypoxic fatalities at similar altitudes reported that the exact duration of exposure was known in only 6 cases, being less than 3 minutes in 4 cases and from 5 to 6 minutes in the other two [57]. Lewis and Haymaker [57] have noted that times to death appear to be much the same above certain altitudes. This may be due in part to the fact that once breathing stops, death occurs within a few minutes irrespective of the low partial pressure of oxygen to which an individual is exposed. Hence support of an astronaut's respiration would be indicated if it does not return to normal immediately after he is exposed to an adequate partial pressure of oxygen.

Events which will occur as a hypoxic individual progresses slowly through the unconscious period to death are similar to those occurring during deepening anesthesia [16, 43, 54, 84]. One who is lightly unconscious might be very difficult to manage. Restlessness, hyperirritability and rigidity are characteristic. Convulsions and vomiting commonly occur. As unconsciousness deepens, generalized flaccidity gradually appears. Respiration becomes irregular, stertorous and finally ceases. The pupils dilate. The pulse usually responds to severe hypoxia by becoming slower. Blood pressure increases initially, then decreases as both peripheral and central circulatory mechanisms fail.

Resuscitation

As quickly as possible, an astronaut unconscious from hypoxia must be exposed to as high a partial pressure of oxygen as can be attained. The importance of recompression as a resuscitative measure should be emphasized, particularly if a hypoxic astronaut is in a state of apnea. Recompression *per se* is equivalent to a deep inspiration [65]. An adequate airway must be assured by measures appropriate to the situation, such as positioning the head with the neck in extension or inserting an oral

endotracheal airway, if these specialized techniques can be carried out in space. If breathing does not start within or remains highly irregular a few seconds after oxygen is restored, artificial respiration should be commenced, using techniques such as exhaled air ventilation or intermittent positive pressure oxygen administration by mask [75]. Most individuals breathe unassisted, if they are to survive hypoxia, within the first minute after the restoration of oxygen. Continued irregular breathing will be associated with a high probability of severe brain damage, and hence a poor prognosis for survival.

Other than the restoration of oxygen, initial resuscitative measures which might be applied to any hypoxic individual will be determined by the conditions under which the hypoxic exposure occurred and by sound clinical judgment. A vasopressor drug, such as metaraminol, might be administered parenterally if hypotension continues beyond the immediate resuscitative period. The frequent administration of sodium bicarbonate and calcium gluconate solution intravenously are also considered primary drugs for use in this situation [34]. Unless "shock" might be due in part to hypovolemia, the administration of a blood volume expander should not be required following a purely hypoxic exposure. Gordon [34] believes that the early use of an intravenous rapid-acting cardiac glycoside, such as digoxin, to improve cardiac function is contraindicated except in situations where there is definite evidence of cardiac decompensation. Of interest in this respect is the report by Webb and Haymaker [57] pointing out that pulmonary edema was one of the most common post mortem findings in fatalities from acute hypoxia at altitude (69 of 74 cases examined). Moreover, Holmstrom [42] points out that survivors of an acute hypoxic exposure at altitude not infrequently develop pulmonary edema as a serious clinical complication which requires special medical attention, particularly in cases with delayed recovery. One wonders, therefore, whether the routine prophylactic administration of an intravenous cardiac glycoside might be indicated for individuals who suffer a moderate to severe hypoxic exposure. By improving cardiac function, such a measure would combat pulmonary edema and assist in providing required rapid tissue

reoxygenation. This area does appear to require study.

Situations where resuscitative measures will be delayed, hampered and even impossible to carry out in space are easily envisaged. Other than possibly restoring an adequate partial pressure of oxygen in the space suit, artificial respiration, if required, will probably not be accomplished until the suit helmet is removed after a hypoxic astronaut is brought back into a pressurized spacecraft or airlock.

Resuscitation should be attempted on any hypoxic individual in whom there is any chance of cardiac activity or if dilated pupils respond to light, for even if his respiration has ceased, there will be no immediat indication as to how much initial irreversible brain damage has occurred The level of cardiac activity can be monitored initially by palpation especially of the carotid pulse, since it is more accessible merely by removing the space suit helmet and since other pulses, such as the radial brachial and femoral pulses, might be inaccessible because of space suit and clothing. As well, the carotid pulse persists when the peripheral pulses are no longer palpable [34]. When possible, cardiac activity might also be monitored by cardiac auscultation, blood pressure recording and, if possible on board the spacecraft, by electrocardiography. Gordon [34] has suggested that external cardiac compression, or cardiopulmonary resuscitation be instituted if the heart is functioning but the systemic arterial pressure is under 50 mm Hg.

The duration that resuscitative measures should be carried out will also be determined by sound clinical judgment. If vital signs such as respiration, pupillary reaction to light, and response to painful stimuli do not appear and continue to improve, prognosis for survival is poor.

Depending mainly on the duration and severity of his hypoxia, an unconscious individual being resuscitated might regain full consciousness rapidly, or remain in a state characterized by impaired mental and motor function, or some level of unconsciousness, for a period of minute to many days, or permanently. A secondary, often fatal deterioration of consciousness can occur either within hours of a hypoxic exposure without full consciousness having been regained, or within several days after a seemingly complete but prolonged recovery from a severe exposu

These neurologic sequelae are attributed to reversible and irreversible hypoxic brain damage which results not only from the low partial pressure of oxygen at the time of exposure, but apparently also from the cerebral edema which follows severe hypoxia. Therefore, if full consciousness is not restored immediately by initial resuscitative measures discussed above, attention must be given to minimizing permanent brain damage by measures directed at cerebral edema. This is an area to be discussed below in detail.

Finally, it should be pointed out that Balke and co-workers [3] have reported that a measurable reduction in work capacity, associated with subjective symptoms of fatigue, occurred in subjects who returned to near sea level conditions after they were exposed to air at an altitude of 16,000 feet (412 mm Hg or 7.96 psia) for over 3 hours. This raises the question as to when an astronaut, who has apparently recovered completely from a hypoxic exposure, should be started back on activity associated with high work loads, unless absolutely necessary.

The "Oxygen Paradox"

Most individuals (about 85 percent in one series) who are still in a mildly hypoxic state can apparently experience a continued, often accelerated deterioration of consciousness for usually 15 to 30 seconds after they start breathing an adequate partial pressure of oxygen [26, 35, 55, 77]. This event is most likely to occur if pure oxygen is restored rapidly just before the onset of severe hypoxic manifestations; it is not in evidence after loss of consciousness [26, 77]. The question as to whether or not exertion or fatigue might be aggravating remains unanswered [35].

The cause of this apparently normal reaction to reoxygenation is unknown. The temporary decrease and even cessation of breathing frequently observed on reoxygenation may promote continuance of existing cerebral hypoxia until adequately oxygenated blood reaches brain tissues [6, 35]. Constriction of cerebral vessels possibly from the hypocapnia associated with hypoxia or from elevation of the arterial oxygen tension on reoxygenation does not appear to be a mechanism involved in producing

this response to reoxygenation [77]. A frequently observed, temporary vasodepressor response to reoxygenation, thought from animal studies as possibly being due to the release of a transiently-acting vasodilator substance, may contribute causally [12, 35].

A few individuals studied (2 of 180 in one series) are predisposed to suffer a severe disturbance of consciousness under the same reoxygenation circumstances as described above [77]. The clinical picture presented by this truly paradoxical action of oxygen, or so-called "oxygen paradox", varies considerably between individuals, but is constant from episode to episode in the same individual [27, 77]. This reaction, which usually lasts from 15 to 30 seconds in duration, is most likely to occur after exercise or a prolonged hypoxic exposure [74, 77]. Typical examples of this phenomenon are a narcoleptic episode with a marked decrease of muscle tonus, an abrupt short-lasting hypertonia of skeletal muscles, an episode of peculiar hyperkineses and a sudden loss of consciousness as in an epileptic attack [77].

The cause of the "oxygen paradox" is unknown. There appears to be no characteristic physiologic or pathologic features, including narcoleptic or epileptic tendencies, which distinguish individuals prone to this reaction from those not prone [35, 77]. The degree of reaction is reportedly enhanced by hyperventilation, but not significantly altered by the addition of carbon dioxide to the inspired air [77]. Mechanisms mentioned for the reaction to reoxygenation discussed above may play a causative role.

Possible serious implications of the "oxygen paradox" occurring in an operational space situation are readily apparent. Accordingly, the elimination of astronaut candidates in whom this reaction can be demonstrated is considered mandatory.

Posthypoxic Cerebral Edema

Although there has been a great deal of writing in the area of acute hypoxia in the past, only in recent years has attention been focused on the posthypoxic state and, in particular, on posthypoxic cerebral edema

the major sequela of acute hypoxia. It has become a generally accepted fact that even though irreversible damage of brain tissues can occur at the time of an acute hypoxic event, such damage can, on occasion, be minor as compared to that caused by posthypoxic swelling, or edema of these tissues. The following discussion deals briefly with the pathophysiology, clinical manifestations, diagnosis and treatment of posthypoxic cerebral edema. Greater detail on various aspects of this syndrome is provided in reviews by Allison [1], Cope [16], Harley [36], Sadove and co-workers [88], Wyant [104], and others [21, 61, 62, 84].

Pathophysiology

Edema can occur in any body tissue which is subjected to an abnormally low partial pressure of oxygen for a sufficient period of time [104]. Because of their remarkable sensitivity to a reduced oxygen supply, the brain tissues appear to be the most prone to become edematous following such an exposure [84].

Cerebral edema has been demonstrated in experiments in which animals were subjected either to low partial pressures of oxygen or circulatory arrest [13, 23, 24, 48, 63, 99]. It was observed in about one-third of the high altitude human hypoxic fatalities reported by Lewis and Haymaker [57]. Perhaps the best indication of edema being by far the major factor in causing the posthypoxic clinical manifestations to be described below has been the clinical improvement in both animals and man resulting from the use of tissue dehydrating agents directed at reducing this edema [2, 16, 20, 32, 37, 47, 49, 73, 82, 85, 88, 89].

Until recently, the pathophysiologic mechanisms involved in producing posthypoxic cerebral edema have been similarly stated by many investigators [16, 48, 61, 62, 84]. Hypoxia was thought to cause primarily an increase in the permeability of brain capillaries, which then allowed leakage of plasma protein from them. The consequent rise in intercellular osmotic pressure could then draw fluid out of blood vessels, leading to the formation of intercellular edema. The edema fluid would

act as a physical barrier, interfering with the passage of oxygen across the intercellular space to reversibly damaged brain cells. Intracellular edema was also thought to occur from an excessive passage of sodium and chloride ions, and hence water into cells which are functionally altered from hypoxia (16, 62, 71, 84). It was also postulated that once the cerebrospinal fluid allows for maximum expansion of the brain in its rigid bony casing, brain tissues would not only be mechanically compressed, but also have their perfusion, and hence oxygen supply diminished. Since these various effects of edema result in further hypoxic damage, the vicious circle of "hypoxia-edema-more hypoxia" would become established. The recurrence of a decreased oxygen supply could then be sufficient to inflict a final insult upon brain cells, converting reversible into irreversible damage. Thus it is understandable how brain damage, which is initially limited in degree, can assume fatal proportions or progress on to some degree of temporary or permanent decerebration of an individual when it would appear that the crisis at the time of an acute hypoxic exposure has passed.

Another mechanism might also be involved to some degree in the formation of posthypoxic cerebral edema. Studies utilizing the electron microscope have shown that glial cells in the brain swell markedly when the brain is subjected to such edema causing factors as hypoxia, hypotonic perfusion, toxic chemical agents and cold (36, 38, 44, 56, 59, 60, 79, 83). As discussed in a number of recent reviews, glial cells appear to give nutritive support to neurons and participate in the blood-brain barrier (36, 52, 68, 79, 83). The high metabolic activity associated with these and possibly other functions of glia would make these cells also highly susceptible to hypoxia, and hence would give reason for the glial edema observed after a hypoxic exposure.

It is readily apparent from the vast literature in this area that much research on hypoxia remains to be done to elucidate clearly the mechanisms involved in producing posthypoxic cerebral edema. Hopefully, such continuing research will yield optimum methods of combating this edema

therapeutically in space.

Permanent histopathologic changes in brain tissue following a hypoxic exposure have been comprehensively reviewed by Courville [18], Yant and co-workers [105], and others [40, 45]. Since most of these changes are irreversible, they are not pertinent to the treatment of posthypoxic cerebral edema. It is pointed out that the majority of the clinical residues of hypoxia correlate with damage seen in the cerebral cortex, cerebellar cortex and pyramidal nuclei.

Clinical Manifestations

Posthypoxic clinical manifestations, which have in most circumstances been attributed to cerebral edema, can vary considerably. They may appear up to several hours after either an apparently normal or a partial recovery from an acute hypoxic exposure [2, 16, 84]. On the one extreme, symptoms apparently from only mild edema are experienced for a few hours [20, 97]. They include headache, nausea with or without vomiting, drowsiness, emotional instability, and impairment of judgment, insight and logic. It is important to note that an astronaut in this state might be unable to perform required operational tasks.

On the other extreme is the clinical picture associated with more severe cerebral edema. It is characterized by coma, with signs depending on the depth of the coma [2, 16, 17, 49, 84, 89]. Respiration may be stertorous or gasping. Pronounced sweating of the face and neck is common, and marked hyperthermia may occur early. The pupils are usually equal in size and dilated. The eyes may be open and staring, and a coarse nystagmus may be present. Restlessness, twitching movements of the limbs and actual convulsions are signs which often appear as coma deepens. Decerebrate rigidity is characteristic of deep coma. The pre-terminal events of posthypoxic cerebral edema include an increase in pulse rate, flaccidity, loss of deep tendon reflexes, hyperthermia and Cheyne-Stokes respiration.

Maximum recovery from posthypoxic cerebral edema, if left untreated,

may take hours to many days [50, 97]. For some time, then, an astronaut could be a serious management problem, being unable to fulfill his own needs while in the comatose state. Even after return of consciousness, there could be a prolonged period of altered mental functioning, which could make him a potential danger to the mission or a useless member of the crew. It must also be remembered that some degree of incomplete recovery might occur. Cases of permanent hypoxic brain damage are well documented in the literature [17, 18, 50, 57, 84]. Coma can be permanent, with the affected individual usually dying soon from intercurrent infection or aspiration, unless rigorous supportive care is given. Residual motor involvement usually takes the form of impairment of fine coordination, spasticity or athetosis. Common mental sequelae are impairment of judgment, insight and logic, and emotional instability. It is considered reasonable to assume that any degree of permanent brain damage will affect the astronaut's highly developed skills.

It must be remembered that some degree of irreversible brain damage can occur in the pre-edematous stage of an acute hypoxic exposure. To this damage could be added that caused by cerebral edema resulting in serious mental and motor impairment of an astronaut. It is also possible for the initial irreversible brain damage to be sufficient to produce impairment in spite of measures which might adequately control posthypoxic cerebral edema. The literature seems to support the view that if an astronaut has a severe hypoxic exposure and remains deeply comatose from the time oxygen is restored, no early decision can be given as to what his prognosis for recovery might be. A failure to respond adequately to therapy in the immediate period after a hypoxic exposure would be a strong indication of permanent brain damage.

Diagnosis

For the most part, the diagnosis of posthypoxic cerebral edema should be obvious, especially if a deterioration of consciousness follows within a few hours what appears to be progressive recovery from an a

hypoxic exposure. The major identifying feature of cerebral edema, if the astronaut remains in a semi-conscious or unconscious state after restoration of oxygen, will be a deterioration in his condition.

It is possible that posthypoxic cerebral edema might have to be distinguished from air embolic phenomena associated with decompression sickness (Chapter 4) or resulting from lung disruption due to explosive decompression (Chapter 3), meteoroid blast (Chapter 12), or trauma (Chapter 14). Cerebral concussion, acute subdural hematoma, and internal hemorrhage (Chapter 14), might also conceivably enter into the differential diagnosis. It is apparent that the history and physical examination, finding in particular localizing signs characteristic of the above conditions, should distinguish these conditions from posthypoxic cerebral edema. The thought should still be kept in mind, however, that as the result of a decompression event, air embolism and post-hypoxic cerebral edema could occur together.

Treatment

In the light of the foregoing discussion of the pathophysiology of posthypoxic cerebral edema, it would appear that any measure directed at breaking the vicious circle of "hypoxic-edema-more hypoxia" would be an effective form of treatment of posthypoxic cerebral edema. With this principle in mind, Sadove and co-workers [88] in 1953 reported success with dehydration therapy in humans suffering from posthypoxic cerebral edema. Their treatment entailed either repeated intravenous injections of a 50 percent glucose solution or the continuous intravenous administration of a 25 percent glucose solution. These investigators found that posthypoxic coma markedly lightened soon after each administration of hypertonic glucose. However, after a time coma returned although to a lesser depth than pre-treatment. The improvement phase was attributed to an initial net loss of water from brain tissues into the hyperosmotic intravascular compartment. The rebound phase was thought due to a rapid return of water along with glucose, which passed in excess from the intravascular compartment, so to swell the intercellular and intracellular compartments. It was thought, therefore, that agents

which are of larger molecular size and hence have a greater tendency to remain in the intravascular compartment would be more effective than hypertonic glucose in producing cerebral dehydration. Several more effective agents suggested were concentrated human serum albumin, plasma expanders such as dextran and polyvinylpyrrolidone and quadruple-concentrated plasma.

In the past 14 years, a number of dehydrating agents, or so-called osmotic diuretics, have been used successfully in the treatment of posthypoxic cerebral edema. Experiments on animals have shown that urea and mannitol are effective in decreasing brain volume, increasing cerebral blood flow, decreasing cerebrospinal fluid pressure and producing clinical improvement of this syndrome (9, 13, 32, 33, 37, 47, 73, 82, 102). Success in treating humans has been reported for sucrose, albumin, urea and mannitol (2, 16, 51, 81, 84, 85, 89, Of all the dehydrating agents used in the past, mannitol would appear be the most appropriate for the treatment of posthypoxic cerebral edema in space. In animal and human experiments, which studied the cerebrospinal fluid pressure responses to intravenous equimolar dose of hypertonic urea and mannitol, it has been shown that urea produces a greater decline of this pressure, but the mannitol effect lasts longer 82, 91, 102). Furthermore, it was noted that although a secondary rise of cerebrospinal fluid pressure occurred after the administration of both of these agents, this rebound effect was much greater with urea. These findings correlate well with human clinical results, for mannitol appears to be not only more effective than urea and other dehydrating agents mentioned above in reducing the cerebral edema, but is also much less likely to produce rebound (48, 51, 84, 85). The clinical usefulness of mannitol has been attributed to the fact that it possesses the many properties desirable for a dehydrating agent, for it is non-toxic, is not significantly metabolized or stored in the b remains almost entirely outside of the intracellular compartment, an is excreted rapidly by the kidneys (21, 25, 85, 91, 102). Since mann is not reabsorbed in significant amounts from the renal tubules, it acts as an osmotic diuretic. This characteristic accounts for the we

known usefulness of this drug in preventing acute renal tubular necrosis from a variety of causes. A practical advantage of mannitol is the fact that it is easily dissolved in the concentration recommended for injection. Therefore, it is apparent that a strong case can be made for using mannitol in the treatment of posthypoxic cerebral edema in space. However, this view must be substantiated as this drug receives greater clinical usage with time.

Mannitol is administered in various concentrations (e.g., 20 percent solution) only by the intravenous route. Doses of up to 200 gm spread over a 24 hour period have been used safely [39, 51]. Because of the high urinary output which will accompany the administration of this agent to a comatose astronaut, his urinary bladder should be catheterized.

What should be the indication for and the time of administration of a cerebral dehydrating agent to an astronaut who has suffered an acute hypoxic exposure? From past experience, it appears that cerebral edema should be assumed responsible for some of the neurologic manifestations which occur up to several hours after exposure. Theoretically and clinically, a dehydrating agent should be administered for both preventive and therapeutic purposes. Such an agent should be given to an astronaut, who shows an inadequate neurologic response to oxygen, as soon as there is clinical evidence of adequate cardiovascular function.

Hypothermia has been markedly effective when used experimentally for the treatment of posthypoxic cerebral edema in animals [9, 85, 103, 106]. This measure, usually combined with dehydration therapy, has reportedly been highly beneficial in treating this syndrome in humans [36, 61, 84, 88, 89, 95, 100, 103]. Reasons for its efficacy, as given by Harley [36] and Wolfe [104], center on the improved balance between oxygen availability and demand in cooled, edematous brain tissues. Hyperpyrexia, which in itself can produce permanent brain damage, is prevented. Even in normal individuals, hypothermia reduces brain volume and intracranial pressure [27]. Thus, according to the more

recent concept of the cause of posthypoxic cerebral edema, hypothermia minimizes damage of brain elements, including the glial cells, and any associated edema.

The level of hypothermia recommended for the treatment of post-hypoxic cerebral edema has been between 30° C (86° F) and 32° C (89.6° [36, 104]. The importance of controlling shivering, which can detrimentally increase cerebral oxygen consumption, has been emphasized [36]. As is used even today, suppression of shivering would be possible with chlorpromazine.

Although hypothermia would apparently be of great value in the treatment of posthypoxic cerebral edema in space, therapeutic hypothermia might be operationally impossible in the foreseeable future. It is conceivable, however, that adequate total body cooling might be attained with a water-cooled space suit.

Finally, it should be mentioned that corticosteroids and corticosteroid-antihistamine combinations have been employed with great success in the relief of the edema and signs and symptoms associated with brain tumors [14, 28, 30, 31, 44, 53, 58, 70]. In animal studies, these agents have also reduced edema of cerebral tissues induced by toxic agents and cold [60, 87, 94]. Such drugs appear to combat edema formation primarily by reducing capillary leakage. However, their value in the treatment of posthypoxic cerebral edema remain to be determined.

Various supportive measures are required in treating an astronaut who is suffering from posthypoxic cerebral edema. Measures to assure adequate oxygenation may include continuing his exposure to 100 percent oxygen, assisting his ventilation, maintaining a clear airwa by measures mentioned above, and removing secretions from his respiratory tract. Provided there is no chance of serious respiratory depression, a sedative such as sodium phenobarbital might be required for controlling mental and motor manifestations, including convulsions, associated with posthypoxic cerebral edema. An oral or systemic tran-

quilizing drug, such as chlorpromazine, might also be of benefit in this situation. Intravenous fluids and electrolytes might be needed not only for feeding a comatose astronaut, but also for restoring his blood volume and electrolyte losses if dehydration therapy is carried out. Since gastric dilatation often accompanies the onset of cerebral edema, oral feeding should be withheld for the immediate posthypoxic period. Nasogastric intubation might be required for relieving this condition; it can also be used for feeding a comatose astronaut. Catheterization of the urinary bladder might be required, especially if a cerebral dehydrating agent is administered. A broad spectrum antibiotic might be given prophylactically for secondary respiratory and urinary tract infection if the period of coma is prolonged.

Delayed Posthypoxic Encephalopathy

Delayed posthypoxic encephalopathy is a serious neurologic deterioration which occurs several days following a seemingly normal clinical recovery from an acute hypoxic exposure. This problem is fortunately a very rare consequence of acute hypoxia, for Shillito and co-workers [92] discovered that only 13 cases of delayed posthypoxic encephalopathy occurred in 21,000 cases of carbon monoxide poisoning. Hence it will only be briefly discussed here.

A clear clinical picture of delayed posthypoxic encephalopathy has been presented in reviews by Plum [80] and Shillito [92] and their respective co-workers. The hypoxic exposure is usually severe, with most individuals awakening from posthypoxic coma within 24 hours and resuming full activity in 4 or 5 days. A clinically normal period of 2 to 10 days, and occasionally longer, follows. Then, abruptly, these individuals become irritable, apathetic, and confused. Some are agitated or manic. Motor control is usually clumsy, and diffuse skeletal muscle spasticity may develop. This neurologic deterioration may progress to coma and death, or be arrested at any level. Some individuals

recover to full health over a period of many months.

Extensive cerebral hemispheric demyelination, with no predilection for perivascular regions, appears to be the major pathologic abnormality common to all cases of delayed posthypoxic encephalopathy. Cerebral edema or swelling is absent as is damage to nerve cell bodies and axons.

The cause of this condition is not known. Although cerebral demyelination has followed hypoxia in several experimental studies, this paradox of extensive demyelination coupled with neuronal preservation has rarely been seen in such studies [80]. Recent findings would support the hypothesis that injury to the glia, which appear to be not only involved in the production and maintenance of myelin but also highly sensitive to oxygen lack, are responsible for this delayed consequence of hypoxia [36, 68].

Unfortunately there are no clinical signs which predict delayed posthypoxic encephalopathy before it occurs. The history of a hypoxic exposure and the diffuse findings with long latency described above should distinguish this syndrome from other conditions, such as psychiatric disease and chronic subdural hematoma.

Since the etiology of posthypoxic cerebral encephalopathy is unknown, it is possible to make no more than empirical suggestions for its treatment. This syndrome appears to occur for no defined reason after an individual recovers and resumes full activity after a severe hypoxic exposure, so that it might be wise to restrict the physical activity of an astronaut in such a situation as much as possible for many days. Once neurologic deterioration occurs, only the supportive forms of therapy discussed previously for posthypoxic cerebral edema can be suggested at this time.

1. All
2. Arg
3. Bal
4. Ban
5. Bar
6. Bill
7. Bloc
8. Boko
9. Brie
10. Brya
11. Burc
12. Burfo
13. Clase

REFERENCES

1. Allison, R. S., Discussion on the Clinical Consequences of Cerebral Anoxia. Proc. Roy. Soc. Med., 49:609-614, 1956.

2. Argent, D. E., Cope, D. H. P., Cerebral Hypoxia: Aetiology and Treatment. Brit. Med. J., 1:593-598, 1956.

3. Balke, B., Grillo, G. P., Konecci, E. G., Luft, U. C., Gas Exchange and Cardiovascular Functions at Rest and in Exercise Under the Effects of Extrinsic and Intrinsic Fatigue Factors. U. S. Air Force Sch. Aviation Med., Randolph Field, Texas, Proj. 21-1201-0014, Rept. No. 1, 1953.

4. Bancroft, R. W., Simmons, D. G., Rapid Decompressions Up to 60,000 Feet Wearing the Standard Oxygen Mask. Aerospace Med., 35:203-211, 1964.

5. Barron, C. I., Cook, T. J., Effects of Variable Decompressions to 45,000 Feet. Aerospace Med., 36:425-430, 1965.

6. Billings, C. E., Personal Communication. The Ohio State University, Columbus, Ohio, 1966.

7. Blockley, W. B., Hanifan, D. T., An Analysis of the Oxygen Protection Problem at Flight Altitudes Between 40,000 and 50,000 Feet. WEBB-955-FR, Webb Associates, Yellow Springs, Ohio, 1961.

8. Bokonjic, N., Stagnant Anoxia and Carbon Monoxide Poisoning. Electroenceph. Clin. Neurophysiol., Suppl. 21, 1963.

9. Brient, B. W., Zimmerman, J. M., King, T. G., The Effect of Prolonged Hypothermia and Mannitol Infusion Upon the Neurologic Sequelae of Total Cerebral Ischemia. Surg. Forum, 16:407-408, 1965.

10. Bryan, C. A., Leach, W. G., Physiologic Effects of Cabin Pressure Failure in High Altitude Passenger Aircraft. Aerospace Med., 31:267-275, 1960.

11. Burchell, H. B., Masland, R. L., Vital Statistics: Anoxia! Air Surg. Bull., 1:5-7, 1944.

12. Burford, R. G., Gowdey, C. W., Vasodepressor Effect of Reoxygenation. Aerospace Med., 37:1114-1120, 1966.

13. Clasen, R. A., Cooke, P. M., Pandolfi, S., et al, An Evaluation of Intravenous Hypertonic Urea in Experimental Cerebral Edema. AF-SAM-TDR-64-18, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1964.

14. Clasen, R. A., Cooke, P. M., Pandolfi, S., et al, Steroid-antihistaminic Therapy in Cerebral Edema. Arch. Neurol., 13:584-592, 1965.

15. Cole, F., Use of Human Serum Albumin in Cerebral Edema Following Cardiac Arrest. J.A.M.A., 147:1563-1564, 1951.

16. Cope, D. H. P., Dehydration Therapy in Cerebral Hypoxia. Proc. Roy. Soc. Med., 53:678-681, 1960.

17. Courville, C. B., The Pathogenesis of Necrosis of the Cerebral Gray Matter Following Nitrous Oxide Anesthesia. Ann. Surg., 107:371-379, 1938.

18. Courville, C. B., Residual Changes in the Brain Incident to Anoxia Under General Anesthesia: Report of a Case with a Survival Period of Six Years. Anesth. Analg., 39:361-368, 1960.

19. Dawes, G. S., Comments About Brain Circulation, Oxygen Supply and Anoxic Survival, in Selective Vulnerability of the Brain in Hypoxemia: A Symposium, J. P. Schade, W. H. McMenemey, (eds.). Oxford, Blackwell, 1963, pp. 37-40.

20. Dietz, H. W., Lower-Nephron Nephrosis Following Acute Hypoxia. J. Occup. Med., 4:490-491, 1962.

21. Dominguez, R., Cocoran, A. C., Page, I. H., Mannitol: Kinetics of Distribution, Excretion and Utilization in Human Beings. J. Lab. Clin. Med., 32:1192-1202, 1947.

22. Donaldson, R. T., Carter, E. T., Billings, C. E. Jr., Hitchcock, F. A., Acute Hypoxia During Rapid Decompression and Emergency Descent in a Commercial Jet Aircraft. Aerospace Med., 31:842-851, 1960.

23. Edstrom, R. F. S., Essex, H. E., Swelling of Damaged Brain Tissue. Neurology, 5:490-493, 1955.

24. Edstrom, R. F. S., Essex, H. E., Swelling of the Brain Induced by Anoxia. Neurology, 6:118-124, 1956.

25. Elkington, J. R., The Volume Distribution of Mannitol as a Measure of the Volume of Extracellular Fluid, with a Study of the Mannitol Method. J. Clin. Invest., 26:1088-1097, 1947.

26. Ernsting, J., Gedye, J. L., McHardy, G. J. R., Further Observations on Brief Profound Anoxia. J. Physiol., 155: 3P-5P, 1961.

27. Fraser, T. M., Personal Communication. Lovelace Foundation

for Medical Education and Research, Albuquerque, New Mexico, 1965.

28. French, L. A., The Use of Steroids for Control of Cerebral Edema. Clin. Neurosurg., 10:212-223, 1964.

29. French, L. A., The Use of Steroids in the Treatment of Cerebral Edema. Bull. N. Y. Acad. Med., 42:301-311, 1966.

30. French, L. A., Galacich, J. H., The Use of Corticosteroids for the Control of Cerebral Edema. J. Neurol. Neurosurg. Psychiat., 26:556, 1963.

31. Gårde, A., Experiences with Dexamethazone Treatment of Intracranial Pressure Caused by Brain Tumours. Acta Neurol. Scand., 41:Suppl.13:439-443, 1965.

32. Goldstein, S. L., Himwich, W. A., Knapp, F. M., Rovine, B. W., Effects of Urea and Other Dehydrating Agents Upon Dog Brain. J. Neurosurg., 21:672-677, 1964.

33. Goluboff, B., Shenkin, H. A., Haft, H., The Effects of Mannitol and Urea on Cerebral Hemodynamics and Cerebrospinal Fluid Pressure. Neurology, 14:891-898, 1964.

34. Gordon, A., Personal Communication. Lovelace Clinic, Albuquerque, New Mexico, 1967.

35. Grandpierre, R., Franck, C., The Paradoxical Action of Oxygen. J. Aviat. Med., 23:181-185, 1952.

36. Harley, H. R. S., The Use of Hypothermia and Dehydration in the Treatment of Severe Cerebral Hypoxia. Brit. J. Anesth., 36:581-590, 1964.

37. Harper, A. M., Bell, R. A., The Failure of Intravenous Urea to Alter the Blood Flow Through the Cerebral Cortex. J. Neurol. Neurosurg. Psychiat., 26:69-70, 1963.

38. Herschkowitz, N., MacGillivray, B. B., Cumings, J. N., Biochemical and Electrophysiological Studies in Experimental Cerebral Oedema. Brain, 88:557-584, 1965.

39. Hill, K., Reduction in Intraocular Pressure by Means of Osmotic Agents. Curr. Med. Digest, 32:48-50, 1965.

40. Hoff, E. C., Grenell, R. G., Fulton, J. F., Histopathology of the Central Nervous System After Exposure to High Altitudes, Hypoglycemia and Other Conditions Associated with Central Anoxia. Medicine, 24:161-217, 1945.

41. Hoffman, C. E., Clark, R. T., Jr., Brown, E. B., Jr., Blood Oxygen Saturations and Duration of Consciousness in Anoxia at High Altitudes. Amer. J. Physiol., 145:685-692, 1946.

42. Holmstrom, F. M. G., Personal Communication. U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1967.

43. Horvath, S. M., Dill, D. B., Corwin, W., Effects on Man of Severe Oxygen Lack. Amer. J. Physiol., 138:659-668, 1943.

44. Ibrahim, M. Z., Morgan, R. S., Adams, C. W. M., Histochemistry of the Neuroglia and Myelin in Experimental Cerebral Oedema. J. Neurol. Neurosurg. Psychiat., 28:91-98, 1965.

45. Jacob, H., CNS Tissue and Cellular Pathology in Hypoxaemic States, in Selective Vulnerability of the Brain in Hypoxaemia: A Symposium, J. P. Schade, W. H. McMenemey, (eds.). Oxford, Blackwell, 1963, pp. 153-163.

46. Johnson, J. A., Use of Betamethazone in Reduction of Cerebral Edema. Milit. Med., 131:44-47, 1966.

47. Joyner, J., Freeman, L. W., Urea and Spinal Cord Trauma. Neurology, 13:69-72, 1963.

48. Kaupp, H. A. Jr., Lazarus, R. E., Wetzel, N., Starzl, T. E., The Role of Cerebral Edema in Ischemic Cerebral Neuropathy After Cardiac Arrest in Dogs and Monkeys and Its Treatment with Hypertonic Urea. Surgery, 48:404-410, 1960.

49. King, R. B., Webster, I. W., A Case of Recovery from Drowning and Prolonged Anoxia. Med. J. Aust., 1:919-920, 1964.

50. Kossmann, C. E., Severe Anoxic Anoxia: Follow-up Report of a Case with Recovery. J. Aviat. Med., 18:465-470, 1947.

51. Krantz, J. C., Jr., Mannitol Therapy - Current Status. Curr. Med. Digest, 30:41-42, 1963.

52. Kuffler, S. W., Nicholls, J. G., The Physiology of the Neuroglial Cells. Ergebn. Physiol., 57:1-90, 1966.

53. Kullberg, G., West, K. A., Influence of Corticosteroids on the Ventricular Fluid Pressure. Acta Neurol. Scand., 41: Suppl. 13:445-452, 1965.

54. Lamb, L. E., Cardiovascular Considerations, in Aerospace Medicine, H. G. Armstrong, (ed.). Baltimore, Williams & Wilk

Co., 1961, pp. 422-423.

55. Latham, F., Studies on the Oxygen Paradox. FPRC-705, Royal Air Force Inst. of Aviation Med., Farnborough, England, 1948.

56. Lee, J.C., Bakay, L., Ultrastructural Changes in the Edematous Central Nervous System. II. Cold-Induced Edema. Arch. Neurol., 14:36-49, 1966.

57. Lewis, R. B., Haymaker, W., High Altitude Hypoxia: Observations at Autopsy in Seventy-Five Cases and an Analysis of the Causes of the Hypoxia. J. Aviat. Med., 19:306-336, 1948.

58. Long, D. M., The Response of Human Cerebral Edema to Glucosteroid Administration: An Electron Microscopic Study. Neurology, 16:521-528, 1966.

59. Long, D. M., Hartmann, J. F., French, L. A., The Ultrastructure of Human Cerebral Edema. J. Neuropath. Exp. Neurol., 25:373-395, 1966.

60. Long, D. M., Hartmann, J. F., French, L. A., The Response of Experimental Cerebral Edema to Glucosteroid Administration. J. Neurosurg., 24:843-854, 1966.

61. Lucas, B. G. B., Cerebral Anoxia. Amer. Heart J., 60:838-840, 1960.

62. Lucas, B. G. B., Some Observations on Anoxia. Anesthesiology, 12:762-766, 1951.

63. Lucas, B. G. B., Strangeways, D. H., The Effect of Intermittent Anoxia on the Brain. J. Path. Bact., 64:265-271, 1952.

64. Luft, U. C., Aviation Physiology - The Effects of Altitude, in Handbook of Physiology, Section 3, Respiration, Vol. II. American Physiological Society, Washington, D. C., 1965, pp. 1099-1145.

65. Luft, U. C., Personal Communication. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico, 1967.

66. Luft, U. C., Clamann, H. G., Optiz, E., The Latency of Hypoxia on Exposure to Altitude Above 50,000 Feet. J. Aviat. Med., 22:217-222, 1951.

67. Luft, U. C., Noell, W. K., Manifestations of Brief Instantaneous Anoxia in Man. J. Appl. Physiol., 8:444-454, 1956.

68. Luse, S. A., Harris, B., Brain Ultrastructure in Hydration and Dehydration. Arch. Neurol., 4:139-152, 1961.

69. Mason, J. K., Aviation Accident Pathology: A Study of Fatalities, London, Butterworth, 1962, pp. 211-215, 332-345.

70. Matson, D. D., Treatment of Cerebral Swelling. New Eng. J. Med. 272:626-628, 1965.

71. McDowell, R. J. S., Asphyxia and the Electrolytic Balance. Proc. Roy. Soc. Med., 45:747-748, 1952.

72. McFarland, R. A., Anoxia: Its Effects on the Physiology and Biochemistry of the Brain and on Behavior, in The Biology of Mental Health and Disease. New York, Paul B. Hoeber, Inc. 1952, pp. 335-355.

73. McQueen, J. D., Jeanes, L. D., Dehydration and Rehydration of the Brain with Hypertonic Urea and Mannitol. J. Neurosurg. 21:118-128, 1964.

74. Mebane, J. C., Neuropsychiatry in Aviation, in Aerospace Medicine, H. G. Armstrong, (ed.). Baltimore, Williams & Wilkins Co., 1961, pp. 443-466.

75. National Academy of Sciences- National Research Council Ad Hoc Committee on Cardiopulmonary Resuscitation of the Division of Medical Sciences, Cardiopulmonary Resuscitation. J.A.M.A., 198:372-379, 1966.

76. Nicholas, N. C., Wamsley, J. R., Bancroft, R. W., Decompressi Tests for the B-58 Escape Capsule System. Aerospace Med., 35:341-345, 1964.

77. Noell, W., The Posthypoxic Paradox Effect, in German Aviation Medicine in World War II, U. S. Government Printing Office, Washington, D. C., 1950, Vol. I, pp. 487-492.

78. O'Connor, W. F., Scow, J., Pendergrass, G., Hypoxia and Performance Decrement. FAA-AM-66-15, Federal Aviation Agency Office of Aviation Medicine, Washington, D. C., 1966.

79. Pappius, H. M., Dayes, L. A., Hypertonic Urea: Its Effect on the Distribution of Water and Electrolytes in Normal and Edematous Brain Tissues. Arch. Neurol., 13:395-402, 1965.

80. Plum, F., Posner, J. B., Hain, R. F., Delayed Neurological Deterioration After Anoxia. Arch. Intern. Med., 110: 18-25, 1962.

81. Raison, J. C. A., Cerebral Oedema: Follow-On Treatment After Cardiac Resuscitation and Respiratory Crisis. Lancet, 2:984-985, 1957.

82. Reed, D. J., Woodbury, D. M., Effect of Hypertonic Urea on Cerebrospinal Fluid Pressure and Brain Volume. J. Physiol., 164:252-264, 1962.

83. Richardson, A. E., Some Clinical Aspects of Cerebral Oedema. Proc. Roy. Soc. Med., 58:604-606, 1965.

84. Robson, J. G., The Physiology and Pathology and Acute Hypoxia. Brit. J. Anaesth., 36:536-541, 1964.

85. Rosomoff, H. L., Shulman, K., Raynor, R., Grainger, W., Experimental Brain Injury and Delayed Hypothermia. Surg. Obstet. Gyn., 110:27-32, 1960.

86. Rossanda, M., Digiugno, G., Dorizzi, A., The Use of 20 Per Cent Mannitol in Neurosurgery and Neurosurgical Emergencies. Acta Neurochir., 12:586-604, 1965.

87. Rovit, R. L., Effects of Dexamethazone on Abnormal Permeability of the Blood Brain Barrier Following Cerebral Injury in Cats. Surg. Forum, 16:442-444, 1965.

88. Sadove, M. S., Wyant, G. M., Gittelson, L. A., The Acute Hypoxic Episode. Brit. Med. J., 2:255-257, 1953.

89. Sadove, M. S., Yon, M. K., Hollinger, P. H., et al, Severe Prolonged Cerebral Hypoxic Episode with Complete Recovery. J.A.M.A., 175:1102-1104, 1961.

90. Seldon, T. H., Faulconer, A., Jr., Courtin, R. F., Pino, D. M., Postanesthetic Encephalopathy: The Postulation of Cerebral Edema as a Basis for Rational Treatment. Mayo Clin. Proc., 24:370-374, 1949.

91. Shenkin, H. A., Goluboff, B., Haft, H., Further Observations on the Effects of Abruptly Increased Osmotic Pressure of Plasma on Cerebrospinal Fluid Pressure in Man. J. Neurosurg., 22:563-568, 1965.

92. Shillito, F. H., Drinker, C. K., Shaughnessy, T. J., The Problem of Nervous and Mental Sequelae in Carbon Monoxide Poisoning. J.A.M.A., 106:669-674, 1936.

93. Strughold, H., Basic Environmental Problems Relating Man and the Highest Regions of the Atmosphere as Seen by the Biologist, in Physics and Medicine of the Upper Atmosphere, C. S. White, O. O. Benson, Jr., (eds.). Albuquerque,

University of New Mexico Press, 1952, pp. 23-34.

94. Taylor, J. M., Prevention of Cerebral Oedema Induced by Triethyltin in Rabbits by Cortico-steroids. Nature, 204:891-892, 1964.

95. Toker, P., Delayed Postanoxic Encephalopathy. Anesthesiology, 24:398-399, 1963.

96. Van Liere, E. J., Stickney, J. C., Hypoxia. Chicago, University of Chicago Press, 1963.

97. Ward, R. L., Olson, O. C., Report of a Case of Severe Anoxic Anoxia with Recovery. J. Aviat. Med., 14:360-365, 1943.

98. Webster, A. P., Reynolds, O. E., cited by O'Connor, W. F., Scow, J., Pendergrass, G., (see ref. 78).

99. White, J. C., Verlot, M., Selverstone, B., Beecher, H. K., Changes in Brain Volume During Anesthesia: The Effects of Anoxia and Hypercapnia. Arch. Surg., 44:1-21, 1942.

100. Williams, G. R., Jr., Spencer, F. C., The Clinical Use of Hypothermia Following Cardiac Arrest. Ann. Surg., 148: 462-468, 1958.

101. Wilson, E., Comfort, W., Some Factors Affecting Time of Consciousness at High Altitude. AF-TR-5970, U. S. Air Force Air Materiel Command, Wright-Patterson Air Force Base, Dayton, Ohio, 1950.

102. Wise, B. L., Chater, N., Effect of Mannitol on Cerebrospinal Fluid Pressure. Arch. Neurol., 4:200-202, 1961.

103. Wolfe, K. B., Effect of Hypothermia on Cerebral Damage Resulting from Cardiac Arrest. Amer. J. Cardiol., 6:809-812, 1960.

104. Wyant, G. M., The Management of Acute Hypoxia. Canad. Anaesth. Soc. J., 7:374-378, 1960.

105. Yant, W. P., Chornyak, J., Schrenk, H. H., et al, Studies in Asphyxia. PHS-211, Public Health Service, U. S. Treasury Department, Washington, D. C., 1934.

106. Zimmerman, J. M., Spencer, F. C., The Influence of Hypothermia on Cerebral Injury Resulting from Circulatory Occlusion. Surg. Forum, 9:216-218, 1959.

CHAPTER 2

EBULLISM SYNDROME

Especially during extravehicular operations in space, astronauts will risk accidental exposure to an ambient pressure which is equal to or less than the effective vapor pressure of body fluids at body temperature. Such an exposure will lead to profuse evaporation and outgassing of these fluids, with the formation of vapor bubbles in tissues, blood vessels and body cavities. This phenomenon has been termed "ebullism" and its resulting clinical manifestations, the "ebullism syndrome" [22, 26]. For all practical purposes, ebullism can be expected to occur at ambient pressures of 47 mm Hg (63,000 ft) or less.

It must be kept in mind that an astronaut subjected to ebullism will also suffer from primary acute anoxia (Chapter 1). Moreover, injuries sustained during an "explosive" decompression (Chapter 3) could further complicate the clinical picture of an astronaut who has experienced a decompression event.

A discussion of the pathophysiology, clinical manifestations, diagnosis and treatment of the ebullism syndrome follows. For more detailed information on the general aspects of this syndrome, including the results of animal experimentation in this area, reference is made to a recent monograph by Roth [22]. Also pertinent are reviews by Luft [20], Ward [26], and others [2, 16, 28].

Pathophysiology

The ebullism syndrome as it could occur in an astronaut has not been described for man. Moreover, only in the past few years have manned orbital flights and the increasing use of man-rated space simulators necessitated experiments exposing animals to "space" in order to predict with a reasonable degree of confidence what effects such an exposure could have on astronauts [3, 4, 5, 7, 8, 9, 10, 11, 12, 18, 24]. There appears to be no reason to suggest why the results of such experi-

ments, particularly those with large primates, should not be reasonably but cautiously extrapolated to man.

Animal experiments have shown that ebullism does not occur uniformly throughout the body [7, 20, 23]. Vaporization and outgassing tend to occur at various places in the body, depending on such local factors as temperature, hydrostatic pressure, tissue elasticity, solute concentration, and the presence of gas nuclei [17]. These factors account for the early appearance of vapor bubbles at or even slightly above a total ambient atmospheric pressure of 47 mm Hg in sites such as the pleural cavity and in the large central venous channels. In the former site, the pressure is usually less than that of the ambient atmosphere and in the latter site, the hydrostatic pressure is minimum and temperature of the blood is maximum [11, 13, 17]. As would be expected, profuse vaporization from the warm moist membranes of the respiratory passages and ocular conjunctivae occurs at a total ambient pressure close to 47 mm Hg [11].

The most significant pathophysiologic events observed during ebullism appear to result from bubble formation within the cardiovascular system. Almost immediately after decompression to an ambient atmospheric pressure at which ebullism can occur, vapor bubbles form at the entrance of the great veins into the heart [7, 13]. Vaporization then rapidly progresses in a retrograde fashion through the venous system to the capillary level. Venous return is blocked by this "vascular vapor lock". This leads to a precipitous fall in cardiac output, a simultaneous reduction of the systemic arterial pressure, and the development of vapor bubbles in the arterial system and in the heart itself, including the coronary arteries [7, 15, 20]. Systemic arterial and venous pressures then approach equilibrium with that of water vapor [9]. Animal studies have demonstrated that the circulation virtually ceases completely within 10 to 15 seconds after explosive decompression to an ambient atmospheric pressure of 30 to 40 mm Hg and within 10 seconds after rapid decompression to near-vacuum [9, 10, 15]. Interestingly, these cardiovascular effects of ebullism contrast with the cardiovascular

effects of profound acute hypoxia per se, in that the cardiovascular pressure response to hypoxia is manifested by a transient fall in systemic arterial blood pressure followed by a rebound, then a gradual decline over several minutes due to hypoxic circulatory failure [14]. Hence the pathologic effect of ebullism, particularly on brain tissues, might be even more severe than the effect of profound acute hypoxia per se, for if cardiovascular ebullism occurs, the tissues will be deprived not only of oxygen but also of the supply of other circulating nutrients such as glucose and the removal of toxic metabolites such as carbon dioxide and lactic acid [27].

During an ebullism exposure, cardiac damage might result from stretching of the myocardium by expanding gas inside the heart, combined with the effects of fulminating anoxia [7]. These factors were cited to explain the markedly abnormal cardiac electrical activity frequently observed in dogs explosively decompressed to an ambient atmospheric pressure of 30 mm Hg, and the failure to resuscitate the dogs so exposed for over 3 minutes in duration [7]. They might also have been involved in producing the fatal cardiac arrhythmias observed in other animal exposures to near-vacuum [3, 4, 5, 9, 19, 24].

Profuse fluid vaporization from the moist membranes in the respiratory tract apparently can traumatize delicate lung tissues [3]. Water vapor, oxygen, carbon dioxide and nitrogen or other inert gases, if present in the atmosphere prior to decompression, pour out of the pulmonary blood and tissues and rapidly escape through the airways into the surrounding environment. Whether the widespread pulmonary edema, atelectasis, congestion and hemorrhage observed in animals following ebullism are due to a disruptive effect of escaping gases, to tissue cold injury from fluid vaporization or to some combination of these factors has not been determined. The severity of lung damage does increase with the rate of decompression and the duration of the ebullism exposure [3]. Interestingly, serious lung damage was not observed in dogs subjected to near-vacuum unless their exposure time exceeded 90 seconds [11, 12]. Denitrogenation, or the breathing of oxygen for a period of time prior to exposure also exercised a significant protective effect on the degree

of lung involvement [4, 5, 11, 12]. Finally, it is noted that the atelectasis observed in animals exposed to total ambient atmospheric pressures at which ebullism occurred might in part be attributed to a displacement of intra-alveolar gasses by fluid vapor, followed by collapse of vapor-filled spaces on recompression [20]. The vapor which forms in the pleural "space", and so partially collapses the lung, might also be an important factor in producing atelectasis [14].

Heat losses mainly from fluid vaporization in the respiratory tract and on the skin surface has diminished the lower esophageal temperature of animals decompressed to near-vacuum for survivable lengths of time by several degrees centigrade [9]. Lowered body temperature reduces the vapor pressure of body fluids as well as tissue metabolism. However it is not known whether this phenomenon would affect survival. No doubt the body cooling takes place mostly within the chest and at the skin surface. Because of cardiovascular vapor lock, cooled blood cannot circulate to highly oxygen-sensitive brain tissues until brain perfusion is restored after recompression. Since this blood would be an admixture of blood from cooled and uncooled parts of the body, it would probably not be cool enough to confer significant protection from hypoxia on brain tissues between the moment of recompression and the restoration of adequate brain tissue oxygenation. Finally, whether blood cooling from ebullism could ever be great enough in a human to produce fatal ventricular fibrillation (Chapter 7) remains to be determined.

Vaporization and outgassing at sites in the body other than those mentioned above appear to be of minor pathophysiologic significance. Projectile vomiting, defecation, lacrimation, salivation, and urination have been observed in animals at the time of exposure to ambient atmospheric pressures at which ebullism occurred [3, 4, 5, 7, 8, 13, 14, 15, 17, 18,

Most important from a clinical standpoint in the ebullism syndrome appears to be the consequences of the profound anoxic exposure combined with the damaging effects of intravascular, and possibly extravascular bubbles which might fail to reabsorb completely coincident with recompression. Roth [23] summarized his discussion of the dynamics of subcutaneous vapor pockets forming in ebullism by stating that there is firs

a rapid conversion of liquid water to the vapor phase. This phenomenon reaches a peak rate at about one minute and then probably continues on at a slower rate for several minutes. He noted that there is an original rush of carbon dioxide, nitrogen, and oxygen into the pocket, but that carbon dioxide gradually becomes the most abundant gas. Reference was made to the pressure data of Kemph and co-workers [17], who showed that by 60 seconds after decompression to an ambient atmospheric pressure at which ebullism occurs, these gases may make up to about 10 percent of the total pressure within subcutaneous vapor bubbles. If it is assumed that the diffusion of gases into and out of vapor bubbles within the cardiovascular system approximates the diffusion of gases into and out of subcutaneous vapor bubbles, then there is a likelihood that some intravascular bubbles might fail to reabsorb completely on recompression, especially if the pre-decompression ambient atmosphere contains an inert gas. The probability of this occurring will increase with the length of time that ebullism is experienced. These post-ebullism bubbles could then continue to act as emboli, and so inflict temporary and possibly permanent tissue damage. By blocking blood flow through such critical tissues as the heart, brain, and lungs, they could conceivably be the major contributor to post-recompression death.

The rate of decay of a post-ebullism bubble is determined by the same factors which control the rate of reabsorption of a bubble of decompression sickness (Chapter 4). Complicated theoretical considerations beyond the scope of this discussion indicate that post-ebullism bubbles will always contain higher levels of carbon dioxide and oxygen than inert gas, and hence should reabsorb much more rapidly than bubbles of decompression sickness [22]. It is noted that the rate of reabsorption of a post-ebullism bubble will vary inversely with the amount of inert gas in the bubble, and hence on the duration of the decompression exposure. Roth [22] has discussed the significance of various inert gases in the reabsorption of post-ebullism bubbles. He concluded that because of its low permeation coefficient in blood, neon in a bubble would be reabsorbed more rapidly and therefore would be a "safer" inert gas for an astronaut to have in his ambient atmosphere than nitrogen. It was also postulated that nitrogen

would be a "safer" gas than helium. He predicted, however, that the overall dependence of the ebullism syndrome on the type of inert gas used would be much less for this syndrome than for decompression sickness. The observation that animals recover less rapidly after a brief exposure to a total ambient pressure at which ebullism occurs than after a decompression episode at a partial pressure just below this level has been attributed primarily to the existence of post-ebullism bubbles (20).

The recovery of dogs, squirrel monkeys, and chimpanzees has been studied after their exposure to near-vacuum for varying periods of time (3, 4, 5, 7, 8, 9, 10, 18, 19, 24). Perhaps the experimental observations which might best be extrapolated to man are those on chimpanzees (18, 19). However, when extrapolating the following experimental observations to man it must be kept in mind that the functional capabilities of man are much higher than the chimpanzee. Thus man might suffer a severe loss of higher psychomotor functions with a degree of brain damage which would still allow a chimpanzee to function adequately. Several chimpanzees, denitrogenated by breathing pure oxygen for four hours prior to decompression, have tolerated exposures to ambient atmospheric pressures of less than 2 mm Hg for up to 210 seconds with a return of apparently normal psychophysiologic function after recompression. Manifestations during the period of recovery are not unlike those during a recovery from a severe acute hypoxic episode. The time for first purposeful movement to occur after recompression increases with the duration of exposure, being about five minutes for a 60 second exposure, 20 minutes for a 120 second exposure, and 40 minutes for a 150, 180 and 210 second exposures. Likewise, the time for apparently complete recovery of normal psychomotor functioning after recompression increases with the time of exposure, being about 90 minutes for a 60 second exposure and less than four hours for 120, 150, 180 and 210 second exposures. From the time of first purposeful movement until recovery, these chimpanzees demonstrated varying degrees of confusion, lag time in task performance, diminished perception of auditory and visual stimuli, and motor incoordination and rigidity. Whether or not personality changes could occur and persist for varying periods of time, or even permanently, after recovery from the more prolonged exposures

remains to be determined. It is apparent that such experiments must be carried out on a larger population, extending the duration of exposure beyond 210 seconds before a more complete picture of all the possible manifestations, both temporary and permanent, of the ebullism syndrome can be presented for the chimpanzee. If spacecraft cabin atmospheres are to contain inert gas, then these primates should also be decompressed while breathing such atmospheres in order to determine inert gas contribution to clinical effects which, as noted above, could be markedly augmented in such a situation by post-ebullism bubbles.

Experiments with animal species other than the chimpanzee would suggest that when as astronaut experiences ebullism beyond 150 seconds in duration, the period of temporary functional impairment will be increasingly prolonged and manifestations of permanent brain damage will appear and rapidly increase in severity, especially if the astronaut is decompressed from an atmosphere containing inert gas [3, 4, 5]. From autopsies on animals which did not survive ebullism and observation of animals which recovered, it appears that brain damage in the ebullism syndrome is more diffuse than focal in nature. Cerebral edema (Chapter 1) resulting from the combined effects of the acute anoxic exposure and under certain circumstances brain tissue hypoxia secondary to blockage of cerebral vessels by post-ebullism bubbles will no doubt play the major role in the production of temporary and permanent cerebral manifestations of the ebullism syndrome. Finally there is experimental evidence that one or more post-ebullism bubbles can produce nervous tissue damage of a more focal nature. One dog subjected to ebullism exhibited severe post-decompression paralysis which gradually recovered over a period of weeks [3, 4, 5]. Its spinal cord had numerous demyelinated lesions which seemed to be the result of gas bubble emboli [11, 12]. Another dog manifested severe post-decompression paralysis which slowly improved over a two month observation period. This time focal lesions were found in both the brain and spinal cord, especially in their white matter [8]. The predilection of white matter for such damage may be due to the fact that as compared to gray matter, it is not only less vascular but also has a greater solubility for nitrogen [8]. Intra- and possibly extravascular, or autochthonous

bubble formation have both been implicated in the production of this pathology.

Blockage of coronary arterial blood flow in an astronaut is considered a serious possible consequence of post-ebullism bubbles. Due to the cumulative effects of an inadequate myocardial blood supply, impaired cardiac function could manifest itself immediately after recompression, or from minutes to many hours thereafter. Permanent myocardial damage leading to some degree of chronic myocardial insufficiency might even be possible.

It is conceivable that by depriving vascular beds of an adequate blood supply, ebullism bubbles could produce such wide-spread vascular injury, leading to impaired vasomotor control and loss of plasma through damaged capillary walls, that circulatory collapse might occur. As in decompression sickness (Chapter 4), this might occur up to several hours after recompression. Myocardial insufficiency secondary to bubble emboli might or might not assist in producing "shock". As in decompression sickness, the lungs could well be the main site of this plasma loss, especially since vapor bubbles tend to form in the right side of the heart. Animals autopsied after ebullism have demonstrated marked pulmonary edema. The observations that the pulmonary edema is much less severe, and is associated with a lower mortality rate in those animals which denitrogen as compared to those that breathe air prior to decompression lend support for the prediction on the theory that inert gas can play a detrimental role in the ebullism syndrome (11, 12, 22).

Clinical Manifestations

The fact that the ebullism syndrome has not been described to date for man bears re-emphasis. Moreover, animal experimentation has yielded data for near-vacuum exposures lasting up to only 210 seconds. Therefore the predicted clinical manifestations of the ebullism syndrome in man must be based not only on such data but also, for exposures longer than 210 seconds, on theoretical considerations.

From the discussion of man's clinical response to acute hypoxia in Chapter 1, it is apparent that if an astronaut is suddenly exposed to an

ambient atmospheric pressure at which ebullism will occur, time of useful consciousness will be about 10 to 15 seconds. As shown in ebullism experiments, and also pointed out in Chapter 1, hypoxic manifestations should not appear if, after a one second or less time to altitude, recompression is accomplished within 4 to 5 seconds' of exposure [4, 5].

Loss of consciousness will be abrupt. The ensuing state of flaccid paralysis might be preceded by tonic and clonic seizures lasting up to several seconds in duration. Systemic arterial pressure will fall precipitously, probably within 15 seonds after decompression. Breathing will be arrested about the time consciousness is lost or within a few seconds thereafter.

Marked abdominal distension will occur immediately after being decompressed, and possibly promote vomiting, defecation and urination, which could create an extremely serious particle and droplet hazard in the weightless environment if the exposure is survived (Chapter 9). A striking swelling of the subcutaneous tissues, beginning in loose skin areas such as the eyelids, axillae, scrotum, and neck will be noticeable within 10 seconds after decompression. As exposure continues beyond this time, this swelling will extend rapidly, creeping into some adjacent areas and extending rapidly into others. Since man's skin is "tighter" than the skin of animals, it is likely that this swelling will be much less in humans than that seen in animal exposures.

In general, the rate of recovery of an astronaut after suffering the effects of ebullism will be determined by such factors as the duration of his decompression, the rate of recompression and whether or not air or oxygen is breathed during recompression. As might be expected, the shorter the exposure and the faster the rate recompression while breathing oxygen, the greater and less complicated the recovery of animals subjected to near-vacuum [4, 5].

If a recompressed astronaut survives the immediate effects of ebullism and resuscitative measures are not employed, it might take up to a minute or more for adequate respiration to return, depending on the duration of his decompression. Recompression will in essence be a first

breath. If an astronaut is recompressed with oxygen there need not be an urgent requirement for artificial respiration, for adequate apneic oxygenation of pulmonary blood can occur for a period of time without interference from carbon dioxide accumulation providing, of course, his airways are unobstructed. Respiration might remain irregular for several minutes. If longer, the probability of severe temporary and possibly permanent brain damage will be great.

A recompressed astronaut's cardiovascular function might also take up to several minutes to return to an adequate level. Failure to do so might be due mainly to myocardial insufficiency caused by bubble embolization to the coronary arteries. This clinical state is characterized by a persistent tachycardia, arterial hypotension and venous distension. As mentioned previously, impaired vasomotor control and plasma loss might conceivably contribute significantly to the production of circulatory collapse, which might occur up to several hours after recompression and possibly have fatal consequences.

If an astronaut who is suffering from the ebullism syndrome does not have the benefit of therapeutic measures other than recompression, his time to maximum recovery might take hours to days and even weeks. Since it is thought that prolongation of recovery would be due to cerebral edema, the psychomotor manifestations which an astronaut will present will be much the same as those described for post-hypoxic cerebral edema (Chapter 1). Although considered more unlikely following ebullism, focal reversible or irreversible damage of brain tissues might occur, the clinical picture from this being thought essentially the same as that described for decompression sickness (Chapter 4).

Finally it is considered possible that pulmonary atelectasis secondary to ebullism could be severe enough to produce inadequate pulmonary ventilation. This problem would be characterized by rapid shallow breathing and persistent cyanosis. Hypoxia and carbon dioxide retention secondary to atelectasis might lead to death. Persistent atelectasis favors pulmonary

infection, which could seriously complicate an astronaut's recovery from ebullism.

Diagnosis

The diagnosis of ebullism itself should be obvious. However certain manifestations of the ebullism syndrome which occur after recompression might only be diagnosed by history, physical examination, and the use of special diagnostic procedures. The crepitus of subcutaneous bubbles might possibly be felt after recompression in a surviving case of prolonged exposure. Deepening unconsciousness, prolonged unconsciousness or delayed deterioration of consciousness after recompressing an astronaut might be indicative of either cerebral edema or cardiovascular "shock". Tachycardia, arterial hypotension and venous distension might be diagnostic of cardiac failure. Rapid shallow breathing and persistent cyanosis might represent pulmonary atelectasis. If possible on-board the spacecraft, a hematocrit determination could be used to diagnose pulmonary atelectasis.

Treatment

Up to the present time, the treatment of the ebullism syndrome has not received attention. Experimentation is certainly warranted in this area to justify the use of specific therapeutic measures which are indicated by theoretical considerations. In addition, a number of resuscitative supportive measures should be available and administered as sound clinical judgment dictates.

The initial resuscitative measures which might be applied to an astronaut who has suffered ebullism are similar to those discussed in detail under acute hypoxia in Chapter 1. He should be exposed to as high a partial pressure of oxygen as possible. However, in order to minimize the risk of pulmonary atelectasis which accompanies the use of 100 percent oxygen at reduced pressures, it might be wise to switch him to an inert gas-oxygen mixture as soon as his cyanosis clears.

From theoretical considerations, it is conceivable that immediate recompression of an astronaut to hyperbaric levels to hasten the reab-

sorption of post-ebullism bubbles might be a highly effective measure in the treatment of the ebullism syndrome. The rationale of having a recompression facility available for the treatment of this syndrome as well as decompression sickness and other air embolic phenomena which might occur during space operations is discussed under the treatment of decompression sickness in Chapter 4. If an astronaut can be recompressed, it is thought that due to the relatively lower inert gas content of post-ebullism bubbles, an adequate clinical result might be attained at an even lower ambient pressure in the treatment of ebullism than in the treatment of decompression sickness. This will particularly be so if ebullism results from decompression of the space suit, for an astronaut will be breathing 100 percent oxygen and so releasing the inert gas of the spacecraft cabin atmosphere from his body tissues for a period of time before his ebullism exposure. Since the lower the partial pressure of nitrogen in the inspired gas, the greater is the reabsorption rate of bubbles which contain nitrogen, it would seem advisable to have an astronaut breathing 100 percent oxygen or another inert gas throughout the period of his hyperbaric recompression [14]. On the other hand, the tendency of a pure oxygen environment to produce pulmonary atelectasis must be kept in mind. It is noted that if 100 percent oxygen is breathed, the recompression pressure would have to be limited to the lower pressure range (up to 3 atmospheres absolute) to prevent oxygen toxicity.

Positioning a recompressed astronaut in the head-down, left lateral position to minimize the migration of air emboli into the coronary and brain vessels will obviously be of no therapeutic benefit in the weightless environment. This measure should be carried out, however, if ebullism has occurred under sub-gravity conditions. If manifestations of pulmonary atelectasis are in evidence, reinflation of his lungs should be attempted. Mouth-to-mouth breathing or intermittent positive pressure oxygen are suitable means by which this might be accomplished initially. If he is conscious and if residual pulmonary atelectasis is found still to be present, he might continue periodic pressure breathing or be encouraged to cough or breathe deeply at intervals.

An astronaut suffering from the ebullism syndrome who does not respond adequately to oxygen should be treated for cerebral edema according to the indications and measures discussed under post-hypoxic cerebral edema in Chapter 1. If undertaken, dehydration therapy should begin as soon as possible after his systemic arterial pressure is restored to an adequate level. Because of myocardial infarction and plasma loss, this factor may be more critical in the therapy of ebullism than in post-hypoxia per se.

Various forms of supportive therapy should be administered as indicated. An intravenous vasopressor, such as metaraminol, and a rapid-acting intravenous cardiac glycoside, such as digoxin, might be given until the systemic arterial pressure stabilizes. The cardiac glycoside might be continued indefinitely if it appears that myocardial damage has occurred. Other intravenous fluids might be given not only for the feeding of an unconscious or semiconscious astronaut, but also for restoring excessive fluid and electrolyte losses from dehydration therapy. Such fluids must be given with care if myocardial damage has occurred.

The question as to whether a pulmonary vasodilator could provide some relief of the clinical manifestations produced by post-ebullism bubbles trapped in the pulmonary circulation remains to be answered. Such an effect would depend to some degree on the ability of such a drug to release the vascular spasm at sites of bubble lodgment. Isoproterenol would be the drug of choice, not only for its pulmonary vasodilatory activity, but also for its positive inotropic and chronotropic actions [1, 6]. Since metaraminol is a pulmonary vasoconstrictor, the administration of this drug to restore systemic arterial pressure in this situation is debatable [1]. On the one hand, it might tend to counteract the effect of a pulmonary vasodilator or if a vasodilator is not given, might seriously jeapordize pulmonary blood flow already partially blocked by bubbles. On the other hand, metaraminol might have no further effect on pulmonary vessels already maximally vasoconstricted due to bubbles. Experimentation in this area therefore appears indicated.

Sedation with a drug, such as phenobarbital, might be required for controlling mental and motor manifestations, including convulsions, of the ebullism syndrome. Since gastric dilatation often accompanies cerebral edema, oral feeding should not be attempted in the immediate post-recompression period. Nasogastric intubation may be needed for relieving gastric dilatation and used later if required for feeding. Urinary bladder catheterization should be undertaken if an astronaut is semicomatose or comatose. Prophylactic antibiotic therapy should be rendered if some degree of pulmonary atelectasis persists or if an astronaut remains in coma for a prolonged period of time.

REFERENCES

1. Aviado, D. M., The Lung Circulation. New York, Pergamon Press, 1965, Vol. I, pp. 355-443.

2. Bancroft, R. W., Medical Aspects of Pressurized Equipment, in Aerospace Medicine, H. G. Armstrong, (ed.). Baltimore, Williams and Wilkins Co., 1961, pp. 209-210.

3. Bancroft, R. W., Physiological Responses to Near Vacuum. AF-SAM TR-66-301, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1966.

4. Bancroft, R. W., Dunn, J. E., II, A. Experimental Animal Decompressions to a Near-Vacuum Environment. AF-SAM-TR-65-48, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1965.

5. Bancroft, R. W., Dunn, J. E., II, Experimental Animal Decompressions to a Near-Vacuum Environment. Aerospace Med., 36:720-725, 1965.

6. Beckman, H., Drugs: Their Nature, Action and Use. Philadelphia, W. B. Saunders Co., 1958, p. 359.

7. Burch, B. H., Kemph, J. P., Vail, E. G., et al, Some Effects of Explosive Decompression and Subsequent Exposure to 30 mm Hg Upon the Hearts of Dogs. J. Aviat. Med., 23:159-167, 1952.

8. Casey, H. W., Bancroft, R. W., Cooke, J. P., Residual Pathologic Changes in the Central Nervous System of a Dog Following Rapid Decompression to 1 mm Hg. Aerospace Med., 37:713-718, 1966.

9. Cooke, J. P., Bancroft, R. W., Some Cardiovascular Responses in Anesthetized Dogs During Repeated Decompressions to Near-Vacuum. AF-SAM-TR-66-88, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1966.

10. Cooke, J. P., Bancroft, R. W., Heart Rate Response of Anesthetized and Unanesthetized Dogs to Noise and Near-Vacuum Decompression. Aerospace Med., 37:704-709, 1966.

11. Dunn, J. E. II, Bancroft, R. W., Haymaker, W., Foft, J. W., B. Experimental Animal Decompressions to a Less Than 2 mm Hg Absolute (Pathological Effects). AF-SAM-TR-65-48, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1965.

12. Dunn, J. E.,II, Bancroft, R. W., Haymaker, W., Foft, J. W., Experimental Animal Decompressions to Less than 2 mm Hg Absolute (Pathologic Effects). Aerospace Med., 36: 725-732, 1965.

13. Edelmann, A., Hitchcock, F. A., Observations on Dogs Exposed to an Ambient Pressure of 30 mm Hg. J. Appl. Physiol., 4:807-812, 1952.

14. Hitchcock, F. A., Studies in Explosive Decompression, Physiological and Pathological Effects. WADC-TR-53-191, Wright Air Development Center, Wright-Patterson AFB, Ohio, 1953.

15. Hitchcock, F. A., Kemph, J. P., The Boiling of Body Liquids at Extremely High Altitudes. J. Aviat. Med., 26:289-297, 1955.

16. Ivanov, P. N., Kuzentzov, A. G., Malkin, V. B., Popova, Y. O., Decompression Phenomena in the Human Body in Conditions of Extremely Low Atmospheric Pressure. Biophys, J., 5: 797-803, 1960.

17. Kemph, J. P., Burch, B. H., Beman, F. M., Hitchcock, F. A., Further Observations on Dogs Explosively Decompressed to an Ambient Pressure of 30 mm Hg. J. Aviat. Med., 25:107-112, 1954.

18. Koestler, A. G., The Effect on the Chimpanzee of Rapid Decompression to a Near Vacuum. NASA-CR-329, National Aeronautics and Space Administration, Washington, D. C., 1965.

19. Koestler, A. G., Personal Communication. 6571st Aeromedical Research Lab., Holloman AFB, Alamagordo, New Mexico, 1966.

20. Luft, U. C., Aviation Physiology - The Effects of Altitude, in Handbook of Physiology, Section 3: Respiration, Vol. II, American Physiological Society, Washington, D. C., 1965, pp. 1099-1145.

21, Reynolds, H. H., Personal Communication. 6571st Aeromedical Research Lab., Holloman AFB, Alamagordo, New Mexico, 1965.

22. Roth, E. M., Space-Cabin Atmospheres. Part III. Physiological Factors of Inert Gases. NASA-SP-117, National Aeronautics and Space Administration, Washington, D. C., 1967.

23. Roth, E. M., Personal Communication. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico, 1965.

24. Rumbaugh, D. M., Ternes, J. W., Learning-Set Performance of Squirrel Monkeys After a Rapid Decompression to Vacuum. Aerospace Med., 36:8-12, 1965.

25. Schubert, G., Bruener, A., Die Entstehung freier Gase in Blut und Geweben bei rascher Dekompression. Klin. Wschr., 18:988-990, 1939.

26. Ward, J. E., The True Nature of the Boiling of Body Fluids in Space. J. Aviat. Med., 27:429-439, 1956.

27. Weinberger, L. M., Gibbon, M. H., Gibbon, J. H., Jr., Temporary Arrest of the Circulation to the Central Nervous System. II. Pathologic Effects. Arch. Neurol. Psychiat., 43:961-986, 1940.

28. Wilson, C. L., Production of Gas in Human Tissues at Low Pressures. AF-SAM-61-105, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1961.

CHAPTER 3

"EXPLOSIVE"* DECOMPRESSION INJURIES

However remote the possibility might be, astronauts will always face the potential hazard of "explosive" decompression during space missions. Such an extremely rapid reduction of the ambient atmospheric pressure of a spacecraft cabin might be caused by penetration of the cabin wall by a large meteoroid or structural failure resulting from a landing accident on a moon or planet. The space suit might be accidentally perforated by accidental contact with sharp stationary objects or with tools and other movable extravehicular equipment during extravehicular operations.

Theoretical analyses of "explosive" decompression transients have been presented by Haber and Clamann [8] and others [12, 13, 15]. These analyses indicate that the possible injuries from an "explosive" decompression are determined by the change in absolute pressure, the ratio of the initial to the final ambient atmospheric pressure and the rate of decompression. It is important to remember that one of the main factors which determines the rate of decompression is the ratio of the volume (V) of the spacecraft or space suit to the effective area (A) of the decompression orifice. This ratio becomes the time characteristic (t_c) of decompression when the velocity of sound (C) is included in the relationship

$$t_c = \frac{V}{A \cdot C}$$

for the particular volume and decompression orifice under consideration. It is noted that the time characteristic is independent of pressure.

*It is noted that for thermodynamic reasons, the flow of gases through an opening in the spacecraft cabin wall or in the space suit cannot exceed the speed of sound. On the other hand, one of the physical characteristics of an explosion is that its air blast is supersonic. Therefore the term "explosive" decompression is actually a misnomer. However, it is commonly used to refer to extremely rapid decompressions occurring in less than one second (2).

During "explosive" decompression, an exposed astronaut might sustain injuries inflicted internally by the rapid expansion of gases in gas-containing organs such as the lungs. A variety of mechanical injuries (Chapter 14) might be inflicted externally not only by being displaced or being struck by displaced objects as the cabin air rushes toward the decompression orifice, but also by the factor causing the decompression. After "explosive" decompression, acute hypoxia (Chapter 1) and ebullism (Chapter 2) will probably be experienced.

This chapter is mainly concerned with the pathophysiology, clinical manifestations, diagnosis and treatment in space of possible internally inflicted, "explosive" decompression injuries. The most likely externally inflicted injuries are mentioned, but discussion of their treatment is reserved for Chapter 14.

Internally Inflicted Injuries

Pathophysiology

Since the solid and liquid constituents of the body are not deformed by changes of ambient atmospheric pressure, only those organs which contain appreciable amounts of free gas are immediately affected by "explosive" decompression. Whenever expanding intracorporeal gases cannot readily escape during an "explosive" decompression, they will exert pressure on surrounding tissues. Due to their fragile structure and the large amount of gas they contain, the lungs are more susceptible to injury by overpressure than the abdominal organs [13].

It has been established experimentally that if the intact mammalian lung-thorax system is permitted to expand passively, lung structure will disrupt at pressure differentials across the lungs and chest wall of about 80 mm Hg [1, 17]. This is in contrast to the pressure differentials of more than 150 mm Hg frequently tolerated in the act of coughing, during which active muscular effort actually reduces lung volume by compressing its gas content [13].

Fortunately the probability that an astronaut's respiratory passages

could be obstructed and hence overdistended by trapped intrapulmonary gases at the instant of an "explosive" decompression is very remote. Moreover, it appears that patent airways will allow adequate escape of expanding gases under all but the most extreme conditions [13]. These conditions can be fulfilled if the difference between the time characteristic of the spacecraft cabin or space suit and that of an astronaut's respiratory passages is such that a transient pressure differential of a sufficient magnitude builds up between the lung and ambient atmospheric pressures. Since the volume of the lungs varies with respiration, it is apparent that the time characteristic of the lungs also varies with the phase of expiration. The transthoracic pressure differential for patent airways would therefore be greatest when decompression occurs at the time of full inspiration.

The time characteristic of "explosive" decompression required for injury or death is unknown for humans [15]. The results of animal studies, reviewed by Luft [13], indicate that a cabin V/A ratio of about 1.2 (m^3/m^2), or a time characteristic of about 3 milliseconds, is associated with a 50 percent mortality. If such data can be reasonably extrapolated to man, only the apparently uncomplicated exposures of Sweeney [18], who had the cabin V/A ratio about 1 (m^3/m^2), have been within the expected lethal range. It has been noted, however, that even if these human decompressions occurred with the respiratory passages closed and the lungs at mid-respiratory volume, the change in ambient atmospheric pressure would have been insufficient, despite the low V/A ratio, for a critical overpressure of about 80 mm Hg to be produced in the lung [13]. Finally the point should be brought out that even though the rate of gas escape from the spacecraft cabin or space suit and from the lungs depends mainly on the molecular weight of the gas under consideration. The molecular weights of the various gases which are being considered for use as spacecraft cabin atmospheres are probably not of great significance in influencing the magnitude of the "explosive" decompression hazard.

In his discussion of lung injuries caused by "explosive" decompression with the respiratory passages patent, Luft [13] described three phases

of lung decompression. The first phase is under essentially isometric conditions, with no change in volume; it is due to the inertia in the system. This phase is probably associated with the highest transthoracic pressures. In the second phase, the transthoracic pressure is attenuated due to the expansion of the chest and the escape of gas through the airways. The third phase is again isometric. The chest is normally expanded until the overpressure is dissipated by the escape of gas through the trachea. Disruption of pulmonary tissues probably occurs to the greatest degree when these tissues reach their limits of tensile strength during the third phase. However, structural damage might also occur during the first and second phases. In these phases, the differences in acceleration of intrathoracic tissues under the impulsive pressure loading could result in disruptive lesions similar to those encountered in meteoroid blast (Chapter 12). Luft pointed to convincing experimental evidence that overdistension of the lungs and not the pressure pulse of the first and second phases per se is the mechanism primarily responsible for lung disruption. Animals given pneumothoraces have survived "explosive" decompressions which would have been absolutely fatal otherwise. This suggests but does not prove that distension is the critical factor [11]. The fact that surrounding an animal's trunk with an inelastic fabric or plaster cast markedly increases tolerance to "explosive" decompression further substantiates this view [4, 5, 14].

Although highly unlikely, it is possible that an "explosive" decompression might occur when an astronaut's respiratory passages are closed, such as during swallowing and breath holding. Lung injuries occurring under these circumstances will be caused by the same mechanisms as those above. However, injuries due to over distension of the lung will always be more serious than those due to the pressure pulse of the first and second phases of lung decompression [13]. The pressure gradient (ΔP_L) across the lungs and passively distended chest wall in this situation can be estimated from the following relationship derived by Luft [13].

$$\Delta P_L = \left[\frac{V_i}{V_{max}} (P_i - 47) \right] + 47 - P_f$$

V_i is defined as the lung volume prior to decompression, V_{max} as the maximum intact volume of the lungs, P_i as the initial ambient atmospheric pressure, and P_f as the final ambient atmospheric pressure which, in the space situation, would be zero. It is apparent from this equation that when the initial and final pressures of decompression are given, the volume of gas trapped in the lungs relative to their total capacity is the factor which determines the transpulmonic pressure gradient which could cause overdistension and disruption of lung tissues.

From the above equation, the pressure gradient which might exist across an astronaut's lungs and passively distended chest wall if an "explosive" decompression to a vacuum occurs while his respiratory passages are closed was calculated both for different ambient atmospheric pressures which are currently used in the spacecraft (7 psia and 5 psia) and space suit (3.7 psia), and three different lung volumes prior to decompression: full inspiration ($V_i/V_{max} = 1.0$), the normal end expiratory position ($V_i/V_{max} = 0.55$), and full expiration ($V_i/V_{max} = 0.25$). This data is presented in Table 3.1.

$\frac{V_i}{V_{max}}$	ΔP_L at P_i = 7.0 psia (362 mm Hg)	ΔP_L at P_i = 5.0 psia (259 mm Hg)	ΔP_L at P_i = 3.7 psia (191 mm Hg)
1.0	362 mm Hg	259 mm Hg	191 mm Hg
0.55	220 mm Hg	164 mm Hg	121 mm Hg
0.25	126 mm Hg	100 mm Hg	83 mm Hg

Table 3.1 Pressure gradients (ΔP_L) which might exist across an astronaut's lungs and passively distended chest wall if an "explosive" decompression in space occurs while his respiratory passages are closed. They are calculated for different ambient atmospheric pressures. (P_i) and lung volumes (V_i) prior to decompression to a vacuum ($P_f = 0$).

It is most interesting to note that all such pressure gradients under these conditions are over the previously stated critical level of about 80 mm Hg. Therefore an "explosive" decompression in space while an astronaut's respiratory passages are closed is considered a very great hazard from the standpoint of serious lung injury from overdistension.

The pathophysiologic effects of the pressure pulse and the lung overdistention which occur during an "explosive" decompression have been described by Hitchcock [9], Karstens [10], and others [2, 7, 13, 19]. Since these effects are similar to those produced by blast [3], discussion of this area is reserved for Chapter 12.

"Explosive" decompression does not appear to have a serious pathophysiologic effect on the gastrointestinal tract. The gastrointestinal tract of experimental animals decompressed from 523 mm Hg to 87 mm Hg in 15 milliseconds showed no gross pathology [6]. It has been difficult to produce actual disruption of the gastrointestinal tract in animal experiments, even with the most severe decompressions [4, 16, 19]. In humans, abdominal gas pains caused by "explosive" decompression has usually been no more severe than that resulting from slower decompressions through the same pressure range [2]. As pointed out in Chapter 12, severe gastrointestinal dilatation might itself elicit a severe bradycardia. An expanded stomach might displace the diaphragm upwards and so possibly embarrass respiration [2]. A temporary gastrointestinal ileus might conceivably occur secondary to severe dilatation.

Expanding air in the middle ears should escape without producing injury, even during the most severe "explosive" decompressions. This is also true for the escape of air from the sinus cavities, provided that the sinus passages are unobstructed [2].

Clinical Manifestations

Since the pathophysiologic effects of "explosive" decompression on the lung are similar to those produced by blast, it can be assumed that

the clinical manifestations associated with lung involvement would be the same in both situations. These manifestations are described in Chapter 12.

As mentioned above, injuries from the rapid expansion of gas in the gastrointestinal tract and middle ear and sinus cavities are not an expected result of "explosive" decompression. Gastrointestinal distension might be associated with severe pain. Through a vagal reflex elicited by the distension, faintness or syncope might occur. Gastric distension might displace the diaphragm upwards, and so possibly embarrass respiration during the decompression period. A period of gastrointestinal ileus might conceivably follow severe distension. Expanding gases in the gastrointestinal tract might cause projectile vomiting and defecation.

Diagnosis

The diagnosis of internally inflicted injuries of explosive decompression should in most cases be obvious from an astronaut's history and physical examination. Reference is made to the diagnosis of blast injuries to the lung in Chapter 12.

Treatment

The treatment of the consequences of lung injury due to "explosive" decompression would be the same as those outlined for blast in Chapter 12.

Although injuries from the expansion of gas in the gastrointestinal tract are not anticipated, it should be mentioned that the oral intake of foods and fluids should be restricted until there is reasonable assurance that gastrointestinal distension has not produced an ileus. If ileus occurs, especially if it is accompanied by vomiting, nasogastric suction might be required.

Externally Inflicted Injuries

From past experience, the most serious consequences resulting from the accidental "explosive" decompression of pressurized aircraft have been the few unfortunate incidents in which an individual located

in the direct vicinity of the opening has been physically blown out of the cabin with the blast of escaping air or has been severely injured by striking or by being struck by objects in the cabin [2]. The rush of air through communicating channels or narrow passageways is often sufficient to propel an object or person within these areas with projectile-like velocities. Thus it appears that injuries might be inflicted during an "explosive" decompression, especially if an astronaut is unrestrained and is either close to the decompression orifice or in a narrow passageway between parts of the spacecraft cabin, or if items of equipment or other materials in the spacecraft cabin become detached or fragmented at the moment of decompression. This missile hazard will be particularly great if the cause of the "explosive" decompression is a meteoroid penetration (Chapter 12). The role of spacecraft cabin volume in determining the magnitude of this hazard must be kept in mind, for the greater this volume, the greater the potential momentum of an astronaut's body and disrupted structures produced by decompression.

The principles of treatment of various externally inflicted injuries which could result from an "explosive" decompression are discussed in Chapter 14.

REFERENCES

1. Adams, B. H., Polak, I. B., Traumatic Lung Lesions Produced in Dogs by Simulating Submarine Escape. U. S. Naval Med. Bull., 31:18-20, 1933.

2. Bancroft, R. W., Medical Aspects of Pressurized Equipment, in Aerospace Medicine, H. G. Armstrong, (ed.). Baltimore, Williams and Wilkins Co., 1961, pp. 209-210.

3. Chiffelle, T. L., Personal Communication. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico, 1965.

4. Corey, E. L., An Experimental Study of Explosive Decompression Injury. Amer. J. Physiol., 150:607-612, 1947.

5. Döring, H., Hornberger, W., cited by Luft, U. C., (see ref. 13).

6. Edelmann, A., Whitehorn, W. V., Lein, A., Hitchcock, F. A., Pathological Lesions Produced by Explosive Decompression. J. Aviat. Med., 17:596-601, 1946.

7. Gunn, F. D., The Lung, in Pathology, W. A. D. Anderson, (ed.). St. Louis, C. V. Mosby Co., 1957, 3rd Ed., p. 647.

8. Haber, F., Clamann, H. G., Physics and Engineering of Rapid Decompression: A General Theory of Rapid Decompression. AF-SAM-21-1201-0008-3, U. S. Air Force Sch. Aviation Med., Randolph Field, Texas, 1953.

9. Hitchcock, F. A., Physiological and Pathological Effects of Explosive Decompression. J. Aviat. Med., 25:578-586, 1954.

10. Karstens, A. I., Trauma of Rapid Decompression. Amer. J. Surg., 93:741-746, 1957.

11. Kolder, H. J., Explosive Dekompression auf Unterdruck. Sitzungsber. Osterr. Akad. Wissensch. Smn., 165: 358-419, 1956.

12. Luft, U. C., Physiological Aspects of Pressure Cabins and Rapid Decompression, in Handbook of Respiratory Physiology, W. Boothby, (ed.). U. S. Air Force Sch. Aviation Med., Randolph Field, Texas, 1954, pp. 129-142.

13. Luft, U. C., Aviation Physiology - The Effects of Altitude, in Handbook of Physiology, Section 3, Respiration, Vol. II,

American Physiological Society, Washington, D. C., 1965, pp. 1099-1145.

14. Polak, B., Adams, H., Traumatic Air Embolism in Submarine Escape Training. U. S. Naval Med. Bull., 30:165-177, 1932.

15. Roth, E. M., Space-Cabin Atmospheres. Part III. Physiological Factors of Inert Gases. NASA-SP-117, National Aeronautics and Space Administration, Washington, D. C., 1966.

16. Sargent, F. T., Williams, R. D., The Effects of Explosive Decompression on the Gastrointestinal Tract: A preliminary report. J. Trauma, 4:618-623, 1964.

17. Schaefer, K. E., McNulty, W. P., Jr., Carey, C., Liebow, A. A., Mechanisms in Development of Interstitial Emphysema and Air Embolism on Decompression from Depth. J. Appl. Physiol., 13:15-29, 1958.

18. Sweeney, H. M., Explosive Decompression. Air Surg. Bull., 1:1-4, 1944.

19. Whitehorn, W. V., Lein, A., Edelmann, A., The General Tolerance and Cardiovascular Responses of Animals to Explosive Decompression. Amer. J. Physiol., 147:289-298, 1946.

CHAPTER 4

DECOMPRESSION SICKNESS

Past experience has indicated that astronauts may be exposed to a risk of decompression sickness during extravehicular operations which require decompression from an atmosphere containing an inert gas. Such a risk will also be present following an emergency or accidental decompression of an inert gas atmosphere to an ambient pressure at which death does not immediately result from acute hypoxia (Chapter 1) or the combined effects of acute hypoxia and ebullism (Chapter 2).

As will be pointed out in this chapter, analysis of the risk of decompression sickness suggests that the potential incidence of minor manifestations of decompression sickness is quite low, and of major manifestations extremely low. However, until ground simulator and space operational experience confirm this optimistic attitude, it remains advisable to consider and prepare for the treatment of decompression sickness, especially for missions during which there will be much extravehicular activity.

A detailed discussion of decompression sickness here would be redundant in the light of many excellent reviews which have covered all known aspects of this syndrome, particularly as it occurs following ascent to altitude [20, 44, 64, 65, 79, 81, 88, 89]. This brief presentation summarizes only those aspects of decompression sickness considered pertinent to the occurrence and treatment of it in space. Further detail in this area can be sought in the key literature cited.

Pathophysiology

The pathophysiology of decompression sickness has received detailed consideration by Adler [1, 2], Catchpole and Gersh [18], Clamann [20], Harvey [46], Haymaker and Johnston [47], Kern [59], Luft [64], Rait [79], Wittmer [89], and many others [3, 7, 14, 19, 22, 23, 44, 77, 80, 81]. The following discussion is mainly concerned with the basic mechanisms involved in the production of this syndrome and the risk of its occurrence

relative to the use of various inert gases which might be considered for use in spacecraft cabin atmospheres. More specific pathophysiologic mechanisms will be considered in the subsequent discussion of the clinical manifestations of decompression sickness.

Many theories have been advanced to explain the various manifestations of decompression sickness. Most investigators believe that this syndrome results from the pressure and volume effects of bubbles which appear in the blood and tissues of the body when the sum of the partial pressures of gases dissolved in the body fluids becomes sufficiently greater than that of the ambient atmosphere.

The literature pertinent to the formation and growth of bubbles formed in decompression sickness has been summarized by Roth [81] and others [3, 20, 33, 59, 64]. It is thought that bubbles most likely originate as water vapor cavities in areas where large local decreases in hydrostatic pressure can occur [81]. Such areas include moving joints, the insertions of contracting muscles, and vortices of turbulent zones of blood flow. It has also been suggested that a bubble might originate from a stable bubble nucleus formed in tiny hydrophobic niches in tissue structures [20, 21]. The occurrence of pressure pulses and the propagation of sound waves have even been postulated as mechanisms in initiating bubble formation [20].

Whatever focal event might be responsible for initiating bubble formation, an essential prerequisite must apparently be fulfilled before a bubble can persist and grow to a size at which it can exert pathophysiologic effects. The sum of the partial pressures of gases dissolved in the fluid surrounding a bubble must be sufficiently greater than the absolute pressure (hydrostatic pressure plus ambient atmospheric pressure) being exerted on the fluid. This pressure difference then favors bubble growth from diffusion of gases into the bubble. In this respect, the nitrogen (or other inert gas) in the atmosphere which is breathed prior to decompression becomes the major contributor to bubble growth, due to its high partial pressure as compared to other dissolved gases at the sites where bubbles tend to form and grow. In the absence of gaseous super-

saturation of the surrounding fluid, a bubble will eventually collapse, the dissolution of gases and water vapor in it being driven mainly by the surface tension of its wall.

The initial rate of growth of a decompression bubble is proportional to the total amounts of gases available at the liquid-vapor interface. Because carbon dioxide has a higher permeation coefficient than other gases, it is the main early constituent of bubbles formed at altitude. This appears to account for the greater propensity for decompression sickness when exercising at altitude, and possibly for the fact that most decompression symptoms which occur at altitude rapidly disappear following a relatively slight increase in the ambient atmospheric pressure [7, 11, 46, 51, 64, 81]. As a bubble continues to grow, both the amounts of gases in the fluid surrounding the bubble and the diffusion constants of these gases will determine the rate of bubble growth. In time, the relative proportions of gases in a bubble will become proportional to the partial pressures of these gases in the surrounding fluid medium [81].

The non-supersaturated blood which circulates through a tissue or past an intravascular site where a bubble is formed affects the growth rate as well as the peak size and rate of decay of the bubble. After decompression, the systemic venous blood, for all practical purposes, loses all of its supersaturated gas in passing through the lungs [15]. Accordingly, as soon as a bubble is formed it begins to compete for gases with surrounding supersaturated tissues which are in turn being perfused, and so desaturated, by non-supersaturated blood. The degree of support given to bubble growth by a tissue will therefore be directly proportional to the rate of gas desaturation of the tissue. This rate which will depend on the relative solubility of nitrogen or other inert gas in the tissue as compared to blood, on the rate of blood perfusion of the tissue and, apparently to a very minor degree, on the diffusibility of the gas through the tissue [56, 81]. Taking solubility and perfusion factors into account, it is obvious why poorly perfused adipose or fatty tissues, in which nitrogen has a high solubility, support bubble growth so well. A favorable situation for bubbles also exists in poorly perfused

tissues such as fibrous tissue, cartilage and bone.

The ultimate size which an expanding bubble can attain is determined by the distensibility of the medium surrounding the bubble. Loose tissues favor the growth of large bubbles, which are usually asymptomatic due to the low deformation pressures associated with their growth. On the other hand, tight tissues such as tendons and joint capsules limit growth of bubbles. Such bubbles reach maximum sizes rather quickly and are associated with high tissue deformation pressures which, by triggering of pain responses and reflex vasospasm, disrupting tissues, and compromising tissue blood flow, are apparently responsible for many of the manifestations of decompression sickness.

Roth [81] has assessed the role which various inert gases might play in determining the rate of pressure or volume rise of a bubble and, therefore, in determining the risks of decompression sickness. Such an evaluation is quite pertinent to the selection of suitable spacecraft atmospheres. It also assists in the determination of appropriate measures which an astronaut might take in an operational situation, prior to and while decompressing from an atmosphere containing an inert gas, in order to prevent the occurrence of decompression sickness. Helium, neon and nitrogen appear to be the most suitable gases to consider for use in spacecraft cabin atmospheres. In the light of both his theoretical predictions and available empirical data, Roth concluded in essence that:

> -theory and empirical data indicate that the potential incidence of the minor manifestations of decompression sickness after decompression from an atmosphere containing helium probably does not differ from that after decompression from an atmosphere containing nitrogen, assuming that the inert gas and oxygen compositions are similar in both atmospheres. Neon might be somewhat more favorable than either helium or nitrogen in reducing this incidence.
>
> -theory indicates more striking differences between the various inert gases as far as the potential incidence of the major manifestations of decompression sickness is concerned. Although the potential incidence of "chokes" should be about equal for nitrogen and helium, the potential incidence of cardiovascular

and neurologic manifestations should be much less for helium than for nitrogen. Roth noted, however, that evidence from diving experiments indicates a less distinct difference between these gases. On theoretical grounds, neon should yield the lowest incidence of these manifestations of decompression sickness.

-empirical data in this area is greatly needed.

Clinical Manifestations

The clinical manifestations of decompression sickness experienced by an astronaut would be similar to those of decompression sickness at altitude described by Adler [1, 2], Clamann [20], Ferris and Engel [36], Kern [59], Luft [64], Gribble [44], Roth [81], and McIver [70]. Reference is made to many clinical reports of cases of decompression sickness at altitude [9, 10, 17, 21, 26, 31, 38, 54, 65, 68, 71, 82, 87]. The pathologic findings in fatal cases have also been well documented [2, 10, 18, 26, 47, 65, 69, 76]. Reference is also made to differences in the clinical manifestations of decompression sickness between aviators and divers [44, 47, 59].

Decompression sickness occurs in aviators after an ascent from ground level conditions of about 760 mm Hg (14.7 psia) to ambient atmospheric pressures of apparently always less than about 380 mm Hg (7.3 psia, 18,000 ft.), and usually less than 320 mm Hg (6.2 psia, 22,000 ft.) [39, 59, 81]. It should be noted that the latent period, rate and peak frequency of clinical manifestations of decompression sickness appearing after ascent are primarily functions of altitude and physical activity. Theoretical predictions of Nims [75] were substantiated by Anthony and co-workers [4] who observed that even under the most predisposing circumstances, signs and symptoms of decompression sickness may not appear for at least 5 to 10 minutes after a decompression event. Their rate of onset was found to increase to a peak in about 20 to 40 minutes, and then to decline practically to zero 2 hours after decompression. It is interesting to note that the clinical manifestations of decompression sickness have been found to appear sooner when helium as opposed

to nitrogen is the diluent gas in the pre-decompression atmosphere [6]. It should be noted, however, that this observation was made in short term experiments so that some nitrogen might have remained in tissues from the original air exposure to conbribute to the production of "helium 'bends' ".

The marked influence which physical activity has on the rate of appearance of clinical manifestations of decompression sickness deserves emphasis here, especially in the light of the fact that extravehicular operations in space will be associated with strenuous physical activity. This relationship was studied intensively by Henry [51] who published data presented graphically in Figure 4.1.

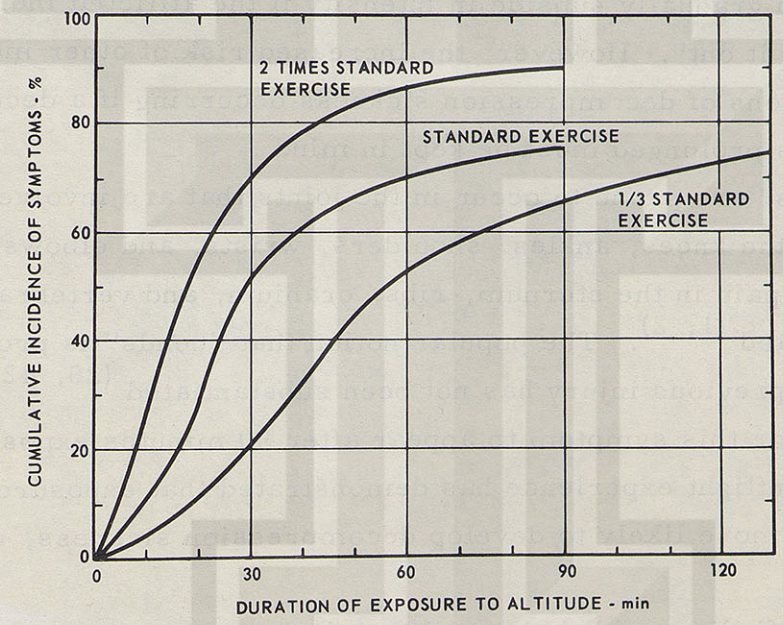

Figure 4.1 Effect of physical activity on appearance of clinical manifestations of decompression sickness at 38,000 feet. Standard exercise was 10 step-ups onto a 9 inch stool in 30 seconds, repeated every 5 minutes.

(After Henry [51], redrawn for Bioastronautics Data Book [74])

The clinical manifestations of decompression sickness in aviators fall into four categories - "bends", "chokes", skin manifestations, and

neurocirculatory manifestations.

"Bends"

"Bends" is the term used for most common clinical manifestations of decompression sickness. It is characterized by musculoskeletal discomfort which is usually described as a deep, poorly localized, waxing and waning, dull, gnawing pain which ranges in severity from mild discomfort to excruciating agony. "Bends" pain usually begins in the periarticular tissues, and then radiates distally along the bone shaft. Reflex weakness of the involved limb commonly occurs. "Bends" can be somewhat relieved by relaxing or applying pressure over the painful area. It may even gradually subside in intensity if the afflicted individual is able to "sit it out". However, the increased risk of other more serious manifestations of decompression sickness occurring if a decompression exposure is prolonged must be kept in mind.

"Bends" are prone to occur in the joints that are involved in motion, especially the knees, ankles, shoulders, wrists, and elbows. Instances of "bends" pain in the sternum, ribs, cranium, and vertebrae have also been reported [1, 2]. The popular notion that "bends" is prone to occur at sites of previous injury has not been substantiated [20, 42]. Notably, it is rare for this symptom to appear after 90 minutes exposure to altitude. Practical inflight experience has demonstrated that exposure to cold makes one more likely to develop decompression sickness, especially "bends".

X-ray findings of bubbles and the clinical pictures presented by individuals suffering from "bends" have in general correlated poorly [16, 36]. Bubbles with and without associated symptoms have been seen on x-ray in synovial spaces of joints, in bursae, and in vaginal sheaths of tendons [12, 36, 84]. They have apparently also been seen in fascial planes and connective tissue spaces in muscles, and in tissue spaces around blood vessels [55, 83]. Crepitation has also been felt along tendon sheaths in which gas bubbles were visualized by x-ray [36]. X-ray studies in animals have indicated that some of the thin radiolucent lines and more diffuse areas which have been attributed to extravascular bubbles

may actually be long, cylindrically-shaped intravascular bubbles [18]. The presence of bubbles in veins leading from exercising muscles also suggests that intravascular bubbles at muscular insertions could be a cause of "bends" [16, 18, 46].

It is a well known fact that on descent, "bends" almost invariably disappears completely. Of interest is the recent observation that "nitrogen 'bends' " were relieved at somewhat lower pressures than "helium 'bends' " [6]. Immediate reascent causes crepitus and x-ray findings to return, thus indicating that the bubbles are compressed but their contained gases are not completely redissolved until some time after descent [30, 36]. As the time period between exposures to decompression events lengthens, the time of onset and the progression of "bends" pain are slowed [83]. Re-exposure after 24 hours "on the ground" is apparently not accompanied by an increased "bends" susceptibility over that seen regularly [59]. Twinges of pain may occasionally be experienced in the affected part up to 5 days post-exposure. In very rare instances, signs and symptoms of mild inflammation may develop in the affected part and reach a peak intensity 12 to 36 hours post-exposure.

The marked influence which physical activity has on the occurrence of "bends" deserves further comment. It is noted that straining exercise is not only a factor in the location of "bends", but also a very important factor in influencing the incidence of "bends" and the speed it develops once altitude is reached [36, 43]. By the same token, strenuous physical activity has been shown to lower the altitude threshold for this manifestation by several thousand feet [20, 25, 37]. For example, such activity was found to increase the total number of "bends" incidents and shift the ratio of light to severe "bends" from 38,000 feet (155 mm Hg or 3.0 psia) to 28,000 feet (247 mm Hg or 4.8 psia) [20]. Increasing the frequency of exercise may decrease this threshold still further. Although the mechanism whereby muscular activity intensified the incidence and severity of these manifestations is still controversial, as mentioned previously, elevated local partial pressures of carbon dioxide and large mechanically induced negative pressures associated with

muscular action appear to be the major contributors to this intensification.

"Chokes"

"Chokes" is the next most common clinical manifestation of decompression sickness. It usually occurs after a longer exposure to altitude than that required for "bends". "Chokes" is an alarming peculiar form of substernal distress, characterized by chest pain, cough and respiratory distress, all of which are aggravated by deep inspiration or coughing. The appearance of this symptom complex is usually heralded by an inspiratory, substernal burning pain which is relieved by deep inspiration. This pain gradually increases in severity and is experienced during all phases of respiration. Paroxysms of non-productive coughing commence and become more and more frequent. Breathing becomes difficult and the affected individual experiences a sense of suffocation and apprehension. In late stages, cyanosis, syncope and "shock" can occur. The clinical manifestations of "chokes" are ameliorated by descent, but can persist for several hours depending on the period of time they are suffered at altitude. During this period, deep breathing can cause a recrudescence of symptoms.

Strangely, a fiery red mucosal lining in the pharynx and larynx if often seen in cases of "chokes". This sign can persist for many hours after descent. Auscultation, x-rays and electrocardiograms have never shown any very specific abnormalities in "chokes". Right heart dilatation has been seen in x-rays taken during "chokes" (16). Rales and x-ray findings of pulmonary congestion have been observed for a few hours after descent (59).

"Chokes" is currently thought to be due to a reflex phenomenon arising from irritation of the pulmonary tissues by gas emboli which obstruct blood flow through pulmonary arterioles and capillaries (81). Animal studies have supported this view (48, 63, 70, 72). In such studies, marked bubble formation on the venous side of the circulation following a decompression event was found to be associated with a rapid shallow respiration and pulmonary hypertension. Although quite variable, the clinical syndrome resulting from the intravenous injection of air in

humans often resembles "chokes" [81]. As will be discussed below, the possibility that fat emboli from disrupted adipose tissue can lodge in the pulmonary vessels, and so play a role in producing "chokes", remains controversial.

Skin Manifestations

The skin manifestations of decompression sickness are mild, usually occurring only after a relatively prolonged exposure to a decompression event [36]. They may occur in conjunction with or presage more serious manifestations of decompression sickness. It is notable that about 10 percent of those cases progressing to circulatory collapse present previous skin manifestations [81]. Four types of skin manifestations have been described.

1. A subjective cold sensation can be experienced during decompression. This sensation may or may not be due to decompression per se.
2. Tiny intracutaneous gas blebs can appear and produce an intense itching sensation which is usually referred to as "creeps". Prickling and burning sensations are also commonly associated with these blebs, which might in fact be gases trapped in the glands of the skin (81).
3. Subcutaneous emphysema rarely occurs. It is usually found on the forearms and thighs, where it can produce moderate pain and tenderness. Crepitus can be felt and gas can be seen on x-ray.
4. Actual skin lesions can occur. These lesions appear most frequently in individuals who are for some reason susceptible to "chokes". They are usually found on the chest, shoulders, and abdomen. A lesion first develops in a small skin area, then spreads out irregularly in all directions. In early stages it has a pale, mottled, cyanotic appearance. Later its center becomes erythematous and warm. Mild to moderate pain may occur at this stage; crepitus has not been found (81). During descent, this skin lesion becomes diffusely red and hot, and usually disappears about 3 to 5 minutes after descent. Four to 6 hours later, the lesion area again becomes tender. This

delayed response is maximal at 24 to 36 hours after descent, and can be associated with subcutaneous edema which may persist for several days.

It is probable that gas emboli in skin blood vessels is the cause of this clinical manifestation of decompression sickness. The mottled cyanotic appearance of the involved skin area is apparently due to the dilatation of superficial venules and capillaries adjacent to areas of severe vasoconstriction (81). This phenomenon can even result in petechial hemorrhages from damaged capillaries. Although subcutaneous fat is a source of these emboli, it has been suggested that emboli from this and other sources reach the cutaneous vessels at altitude by passing from the venous to the arterial side of the circulation through the large pulmonary arteriovenous shunts and in rare instances, through a patent foramen ovale (18). However, there is the possibility that gas emboli also form within the arterial system (81).

Neurocirculatory Manifestations

The cardiovascular and neurologic manifestations of decompression sickness have usually been described under this heading (1, 2, 10, 14, 36, 65, 68, 81). This is no doubt due to the fact that these manifestations often occur together and are the most serious, variable, poorly understood, rarely occurring manifestations of this syndrome.

Malette and co-workers (65) separated cases suffering from neurocirculatory manifestations of decompression sickness into two clinical categories. In one category, the signs and symptoms of disturbed cardiovascular function predominated. In the other, those of disturbed neurologic function predominated. At opposite ends of the scale were cases with only cardiovascular or with only neurologic manifestations. Between these extremes were various mixtures, with the clinical findings of the one or other category predominating. It is of interest to note that when these cases were arranged in this manner, no fatalities occurred in the group whose manifestations were only neurological (26, 65). On the other hand, when cardiovascular disturbances were part of the clinical picture, a very significant mortality rate existed.

A fall in systemic arterial blood pressure, often accompanied by a

marked bradycardia can occur at altitude. This reaction can be accompanied by the usual symptoms of arterial hypotension, such as pallor, perspiration, faintness and loss of consciousness. Hypotensive episodes reportedly occur in about 10 percent of severe "bends" and 25 percent of "chokes" cases, and can also be associated with decompression effects which are not usually classified as decompression sickness, such as gastrointestinal distension, aerosinusitis and aerotitis media [1, 20]. It should be noted that certain signs and symptoms similar to those due to, but not associated with hypotension, can occur at altitude [36, 59]. Hyperventilation is associated with manifestations such as paresthesias, lightheadedness, reduction in consciousness and tetany. Manifestations of acute hypoxia have been outlined in Chapter 1. Lightheadedness can be associated with the paroxysms of coughing and cyanosis due to "chokes". In such a case, actual loss of consciousness is rare.

Hypotensive episodes at altitude are usually relieved immediately by descent or within 30 minutes thereafter [59, 81]. Quite rarely, however, hypotension persists to a varying degree. In this case circulatory collapse, or the so-called delayed "shock" syndrome, frequently occurs in less than one hour to several hours after descent. Notably, this syndrome is most likely to appear in individuals who have experienced major manifestations of decompression sickness at altitude, especially severe "chokes". However it has arisen on rare occasions without any premonitory or minimal signs or symptoms of decompression sickness having occurred at altitude [81].

It appears that any one or more of a number of mechanisms might be the cause of hypotension at altitude. In all probability, the simple syncopal, or vasovagal reaction is the commonest mechanism. An explanation of the cause of syncope associated with "chokes" must take into account various factors, such as reflex bradycardia induced by the chest pain or by gas or other emboli in the pulmonary circulation, cardiac insufficiency due to extensive blockage of the pulmonary circulation by these emboli, and the peripheral vasodilatory effects of hypoxia and secondary hypercarbia which can occur with "chokes". Cases of

syncope at altitude have been associated with frank cardiac disturbances such as coronary occlusion, paroxysmal auricular fibrillation and bundle branch block [8]. A bubble or bubbles entering the coronary arterial system might well have been the cause of death in one of the cases of decompression sickness reported by Robie and co-workers [80]. Finally, it is conceivable that vasodepressor syncope might result from an autonomic imbalance caused by embolic damage of the central nervous system.

The delayed "shock" syndrome is characterized by a marked loss of plasma into the extravascular compartment, especially in the form of pulmonary edema and pleural effusion. It has been shown in recent animal experiments and assumed in the numerous human cases of the delayed "shock" syndrome cited above that death from hypovolemic "shock" can occur unless measures are taken immediately to supplement the diminishing blood volume [23, 24]. The basic mechanisms underlying this syndrome are, however, an enigma. The fact that it has been effectively treated by hyperbaric recompression supports the view that the shock is secondary to a scattering of air emboli throughout the body [10, 13, 21, 31, 32, 81]. As mentioned previously, bubbles formed in tissues at altitude might conceivably cross over from the venous to the arterial side of the circulation while an individual is at altitude. However, it is possible that this phenomenon would more likely occur during and after descent, when the bubbles have been made smaller. The probable routes of bubble passage are considered to be both well defined, anatomically normal shunts such as pulmonary arteriovenous anastomoses, bronchovenous shunts and large pleural capillaries, and pathologic shunts such as a patent foramen ovale [14, 18, 47, 65, 76, 89]. This cross-over concept becomes even more plausible when one takes into consideration the fact that high pulmonary arterial, and hence right heart pressures which can result from embolic blockage of the pulmonary circulation, would tend to drive bubbles through these shunts. It is also thought that bubbles can also be formed on the arterial side of the circulation [81].

The question arises as to why "shock" characteristically appears

some time after descent. As mentioned above, decrease in bubble size by descent may favor bubble cross-over. It has also been suggested that as a bubble gets smaller, it is more apt to migrate distally beyond collateral circulation points, and so produce ischemia [81]. As well, one must remember that decompression bubbles can persist for many hours before they are absorbed completely [33, 46]. These bubbles would then exert their damaging effects on blood vessels for some time, so that the clinical onset of "shock" from loss of plasma sufficient to produce this manifestation would be justifiably delayed. Finally, it should be noted that the marked loss of intravascular fluid into the lungs and pleural "space" might be due to the fact that the lungs act as a filter for emboli, and hence would be more likely to suffer more embolic damage than would be expected in other tissues.

The reason for the increased capillary permeability in the delayed "shock" syndrome is as yet to be defined. It is probable that tissue hypoxia from vessel blockage and irritative vasopasm induced by bubbles renders capillaries hyperpermeable. Since heparin appears to confer some protection on animals undergoing decompression, it has been suggested that bubbles promote platelet clumping, agglutination of erythrocytes and formation of plasma flocculates which lead to vascular thromboses [5, 41, 61]. Blockage of vessels by thrombi could then enhance the damaging effect of bubbles. In contrast to this success with heparin, however, a similar series of experiments failed to demonstrate any protective action of another anticoagulant, bishydroxycoumarin [41]. One explanation for this difference in findings is the possibility that heparin exerts its major protective effect though its antiproteolytic activity, which would tend to diminish the vasodilatory and injurious effects of the breakdown products of hypoxic tissues on vessel walls [5]. Another explanation centers on the observation that partially depolymerized hyaluronic acid (PDHA) has also had a protective action in decompressed animals. Interestingly, both heparin and PDHA have lipemia-clearing activity [41]. The possible implications of this are discussed below. Finally, it has been thought possible that biologically-active substances such as bradykinin, histamine, and sero-

tonin might be triggered in tissues by bubble expansion or blockage of blood flow, and so participate to some extent in the production not only of the delayed "shock" syndrome but also of other manifestations of decompression sickness [27, 60].

A not infrequent finding in fatal cases of decompression sickness has been the presence of microscopic fat emboli in the small arterial vessels and capillaries throughout the body, especially in the lungs [47, 65, 76, 80]. These emboli have also been demonstrated in animal decompression experiments [19, 22, 23]. The source and role of these emboli in the etiology of the delayed "shock" syndrome remains unclear [81]. Murray [73] has postulated that the high concentration of total circulating lipids associated with "shock", severe illness and trauma is due to the mobilization and subsequent aggregation of fat from body fat depots through increased activity of a hypothalamic "fat center". After finding more cholesterol in fat emboli than in depot fat in decompressed animals, LeQuire and co-workers [62] suggested that fat emboli of decompression sickness form primarily within the circulatory system as the result of physiochemical alterations induced by products of tissue damage and "shock", rather than by entering the circulatory system from fat depots disrupted by decompression bubbles. Further support for an intravascular aggregation of fat in decompression sickness has been given by the observations that heparin and PDHA, both of which have fat-clearing activity, confer significant protection on animals undergoing decompression [41].

In contrast to the views expressed above, Whiteley [86] could find no experimental evidence which would lend support for an intravascular aggregation of fat in decompression sickness. He postulated that fat enters the circulation at the site of tissue injury and that an injury itself can somehow modify the vascular bed, making it more sensitive to intravascular fat. Rait [79] has outlined a specific mechanism for the release of fat emboli from tissues into the circulation in decompression sickness. The presence of both fat emboli and a fatty liver in many of the fatal cases of decompression sickness studied suggested to him that a causal relationship existed between these findings. It appeared that a fatty liver

under decompression ideally fulfills the three requirements, stated by Harris [45], for fat embolism to occur. Firstly, a fatty liver contains a free, fluid, readily mobilizable fat. Secondly, the liver is essentially indistensible, so that intrahepatic tissue pressures higher than the hepatic venous pressure can develop as bubbles form in fatty hepatic cells. Thirdly, the liver possesses patent veins with open ends which do not collapse (sinusoidal system). Rait also noted that the presence of bone marrow emboli and, in some cases, fat emboli in fatalities from decompression sickness might also be explained by applying this mechanism to the bone marrow. Finally, he supported his fatty liver concept by pointing out that dietary management directed at reducing the prevalence of fatty liver in the Royal Australian Air Force has apparently accounted for the low incidence of the delayed "shock" syndrome in this group.

Intravascular fat could produce hypoxic tissue damage by interfering with blood flow. It could also hydrolyse into free fatty acids which would damage capillary endothelium, and so render it hyperpermeable. It is thought that the means by which fat emboli cross over from the venous to the arterial side of the circulation would be the same as that described above for bubbles, and that the lungs would again bear the brunt of embolic damage due to their filtering action. Also of interest is the fact that the circulatory collapse due to traumatic fat embolism is also a delayed phenomenon, if death does not occur immediately due to acute right ventricular failure secondary to blockage of pulmonary blood flow. This delay has been attributed to the time required for sufficient fatty acids to be released and subsequently exert their damaging effects [78].

Finally it should be pointed out that recent animal studies of Henn and Wünsche [49] might have shed some light on the roles of bubble and fat emboli in producing the delayed "shock" syndrome of decompression sickness. These investigators suggested that the time of ascent to altitude was critical in determining the type of emboli produced. Roth [81] has summarized the data from their experiments, which indicated that there might be both altitude and rate thresholds for the pro-

duction of fat emboli. A review of the literature on fatal cases of decompression sickness and two cases of their own in which fat emboli were found suggested that an ascent rate between 8 and 12 Km/min (26,400 to 37,000 ft/min) is the threshold for fat emboli in humans. Roth pointed out, however, that rates of 1000 to 1500 m/min (3000 to 4800 ft/min) have also been associated with fat emboli in humans [81]. Further investigation of this phenomenon is indicated.

The neurologic manifestations of decompression sickness are usually of a highly diversified but focal nature [59]. As pointed out above, they are frequently associated with other manifestations of decompression sickness. Those that develop at altitude are usually transitory, lasting minutes to a few hours after descent [20]. They can also appear at any time up to 12 hours after descent from altitude [81]. The most common neurologic manifestation is a homonomous, scintillating scotoma with sparing of central vision [87]. Other possible signs and symptoms include various hemipareses, monopareses, focal or generalized convulsions, aphasias, sensory disturbances and sensorial clouding [1, 20, 59, 81]. It is noted that such important signs as impairment of judgment and inability to assess the true nature of the situation can be pronounced [71]. Such manifestations can vary considerably before a stabilized clinical picture is established.

The disappearance of neurologic manifestations of decompression sickness is frequently followed by an intense throbbing headache on the side which is contralateral to the neurologic lesion. This headache has been occasionally experienced, however, without an antecedent neurologic event [59]. This headache is often associated with nausea, vomiting, prostration, photophobia, and increased pain on head movement. It usually lasts from one to 12 hours in duration.

Those neurologic manifestations with a delayed onset can take up to several weeks to disappear [20]. Reported cases of permanent neurologic sequelae of decompression sickness in aviators have been exceptionally rare, in contrast to such cases in divers [9, 20, 44, 59].

The electroencephalogram of individuals suffering from neurologic

manifestations of decompression sickness usually shows irregular slow waves at foci corresponding to neurologic findings [81]. It shows no abnormalities in those suffering from the headache described above, however.

It should be noted that the neurologic manifestations of decompression sickness do have to be distinguished from other neurologic signs and symptoms which can also occur at altitude. A convulsion can result from cerebral hypoxia accompanying a hypotensive episode or from a hypoxic exposure [59]. Weakness of an extremity simulating a neurologic lesion can be seen with "bends". As well, neurologic signs and symptoms can be caused by hypocapnia associated with hyperventilation.

The neurologic manifestations of decompression sickness are generally thought to be caused by focal hypoxia of brain tissue, not only from a blockage of blood flow, but also from local vasospasm induced by vascular irritation by bubbles [1, 90]. There is also the possibility that such manifestations might be caused by bubbles forming in cerebral veins and tissues. Interestingly, the incidence of spontaneous migraine is apparently higher in those individuals who develop a scotoma and headache associated with decompression sickness at altitude; similar electroencephalographic findings have been recorded in both instances [38, 59, 68]. This would lead one to speculate that bubbles might be preferentially generated at a turbulent site in the cerebral arterial tree, and hence tend to lodge in the same area of the occipital cortex after each altitude exposure [81]. Otherwise, the various mechanisms postulated for delayed "shock" syndrome have also been applied to the neurologic manifestations of decompression sickness. It is interesting to speculate that fat emboli might be the cause of at least some delayed neurologic manifestations, especially those which require a prolonged period for recovery or leave permanent sequelae.

Diagnosis

For the purpose of diagnosis, the requirement for thorough familiarity with the numerous recorded cases [2, 9, 10, 17, 18, 21, 26, 31, 38, 54,

65, 68, 71, 82, 85, 87) as well as the general aspects of decompression sickness cannot be overstressed. Any otherwise unexplainable sign or symptom which appears while an astronaut is in a decompression situation should be presumed to be a manifestation of decompression sickness. The strongest evidence supporting the occurrence of this syndrome would obviously be the relief or alteration of signs and symptoms by recompression.

Most important from a diagnostic standpoint are a detailed history, thorough physical examination and subsequent close observation of an astronaut who has experienced manifestations of decompression sickness such as severe "bends", "chokes", syncope and neurologic signs and symptoms while in a decompression situation, especially if signs and symptoms persist for some time after recompression. As noted above, the delayed "shock" syndrome is frequently preceded by such manifestations. Cardiovascular function should be monitored by repeatedly recording both pulse rate and systemic arterial blood pressure. Frequent recording of the hematocrit, if possible in space, should be undertaken to diagnose plasma loss. An electrocardiogram might be indicated if embolic myocardial damage is suspected. As mentioned previously, focal neurologic involvement in decompression sickness is usually associated with typical electroencephalographic abnormalities over the involved brain area.

Prevention

If an astronaut could be exposed for operational reasons or in an emergency to an ambient pressure at which decompression sickness can occur, the risk of this condition developing can be lessened by several means. Most apropos to the space situation is the selection of a suitable pressure and inert gas composition of the atmosphere from which and to which an astronaut can have a safe, rapid decompression. Another measure which would be feasible to undertake in space is preoxygenation.

The use of pure oxygen atmospheres in space would be the ideal preventive measure for decompression sickness. However, as Roth (81) pointed out in his recent assessment of atmospheres which have been

suggested for use in space, risks of fire and oxygen toxicity in particular mitigate against the use of pure oxygen as a spacecraft cabin atmosphere. On theoretical and empirical grounds, he predicted the risks of decompression sickness which would be present if an astronaut, who had been equilibrated with various 50 percent inert gas-oxygen mixtures in a spacecraft cabin at 7.0 psia (354 mm Hg) atmospheric pressure, is decompressed. He noted that rapid decompression from such an atmosphere, containing nitrogen as its inert gas, to a space suit atmosphere containing 100 percent oxygen at 3.5 psia (179 mm Hg) would be associated with a marked reduction in both the frequency and severity of "bends", as compared to a similar decompression from air at 14.7 psia (760 mm Hg). He predicted that the incidence of "bends" in a physically fit astronaut in equilibrium with such an atmosphere should be less than 7 percent if moderate exercise is performed, as was essentially the finding in human experiments [28, 29], and much less than one percent during piloting operations or while an astronaut is at rest. These values were about three times those predicted for decompression to 100 percent oxygen at 5.0 psia (258 mm Hg). Considering the risk of decompression sickness associated with other inert gases, Roth predicted that helium might be associated with a greater "bends" frequency than nitrogen. This appears to have been substantiated by recent experiments, which also showed that "helium 'bends' " appeared sooner than "nitrogen 'bends' " [6, 58]. Finally, Roth noted that there is theoretical evidence supporting neon as producing a much lower incidence of neurocirculatory manifestations, "chokes", and even "bends" than either nitrogen or helium. Others have arrived at similar conclusions using slightly different physical models [6].

Preoxygenation, or the continuous breathing of 100 percent oxygen for a period of time before decompression can be highly effective in preventing decompression sickness [6, 20, 28, 29, 58, 66, 67, 81]. Since this procedure must allow tissues which desaturate slowly to reach a "safe" level of dissolved nitrogen or other inert gas, the duration of preoxygenation is the major factor in determining its success. Even

if an astronaut has a short period of preoxygenation before decompression, the risk of suffering from decompression sickness will diminish. As well, the duration of decompression before signs and symptoms of decompression sickness appear will decrease [52, 57, 66, 67]. It should be noted that this latent period can be shortened somewhat if preoxygenation is accomplished while an individual is being decompressed, presumably due to the formation of silent bubbles at pre-"bends" altitudes [50, 58, 81]. Increase in age, physical conditioning, and physical activity during preoxygenation decrease the time required to accomplish an adequate preoxygenation [20, 64, 66, 81].

Preoxygenation rules for astronauts have also been suggested by Roth [81] in his detailed assessment of this area. He recommended a minimum of two or possibly three hours preoxygenation time for astronauts who have been breathing air at 14.7 psia (760 mm Hg) to equilibrate to the level of total body nitrogen in a 50 percent nitrogen-oxygen mixture in a spacecraft cabin at 7.0 psia (364 mm Hg) atmospheric pressure. He predicted that without preoxygenation, it would take an astronaut about 8 hours to equilibrate with this atmosphere. Whether preoxygenation should be carried out prior to decompressions from a 50 percent inert gas-oxygen mixture in a spacecraft cabin at 7.0 psia (364 mm Hg) atmospheric pressure to 100 percent oxygen at 3.5 psia (179 mm Hg) space suit atmosphere remains debatable, however, especially in the light of the low risk and mild clinical manifestations anticipated from such decompressions. When carried out for one-half hour in recent simulations of these space atmosphere exposures, this measure was quite effective in preventing "nitrogen 'bends' " but apparently was not effective in preventing "helium 'bends' ", although the symptoms of "helium 'bends' " had more of a tendency to disappear spontaneously when decompression exposures were continued [6]. It should be pointed out that these were short-term experiments, so that some nitrogen might have remained in tissues from the original air exposure, to contribute to the production of "helium 'bends' " following

decompression from the 50 percent helium-oxygen atmosphere at 7.0 psia.

Finally, it should be pointed out that an astronaut who experiences any manifestation of decompression sickness should be restricted, if possible, from being decompressed for at least 24 hours.

Treatment

Once a presumptive diagnosis of decompression sickness has been made, an afflicted astronaut should be recompressed as soon as possible to at least the atmospheric pressure with which he was equilibrated before decompression. "Bends" will in most instances completely disappear on recompression. If not, local pressure and massage over the involved joint areas may bring some relief. "Chokes" symptoms should be ameliorated, but might persist or recrudesce on deep breathing up to several hours after recompression. During this period, a suitable analgesic might be required for the relief of such symptoms. It does not appear to have been established whether the breathing of 100 percent oxygen is of greater value than the breathing of other gas mixtures in the relief of "chokes" symptoms.

The major aspects of the treatment of decompression sickness center on its cardiovascular and neurologic manifestations. The fact that little is known about the specific pathophysiologic mechanisms involved in producing these manifestations should be kept in mind. Accordingly, therapeutic measures suggested here may be inadequate as compared to those which might be used in the future.

Hyperbaric recompression has been used in aviation and diving with remarkable success in the treatment primarily of the delayed "shock" syndrome and the neurologic manifestations of decompression sickness, but also of "bends" and "chokes" not relieved by descent (10, 13, 17, 21, 31, 40). It is apparent that in order to be maximally effective, this measure must be commenced as soon as possible after its requirement is recognized. In the past, United States Air Force

authorities have recommended that aviators requiring recompression be taken to a maximum "depth" of 6 atmospheres absolute, and decompression from this pressure be carried out in accordance with the standard United States Navy diving tables for the treatment of decompression sickness and air embolism. However, there is now both rational and empirical justification for the use of a recompression profile to a maximum "depth" of 3 atmospheres absolute with oxygen being breathed during recompression [40, 71]. The theoretical bases for this are summarized in Table 4.1. It is pointed out that if experience justifies the use of such a profile for the treatment not only of manifestations of decompression sickness, but also possibly of other air embolic phenomena, the weight penalty associated with taking a recompression facility into space may be markedly diminished.

Characteristics	Standard Navy Treatment Tables	3 ATM. ABS. Oxygen Table
Maximal Pressure Applied	An amount of compression in excess of that needed for relief; limited by: Diminishing efficiency of added pressure to reduce bubble size; nitrogen narcosis; air density; heat of compression; risk of decompression sickness.	Limited by pressure-time aspects of O_2 toxicity risk and undefined retinal risk; Maximal bubble-ambient gradient for inert gas; Maximal efficiency of collateral circulation potential to supply compromised tissue foci.
Time of Exposure At Maximal Pressure	Pain unrelieved after 30 min. at depth not likely to be bends pain; symptoms persisting after 2 hr. probably herald residual tissue damage.	Not established; at least 1.5-2 hr.; Oxygen toxicity protection from interspersed air-breathing periods being investigated for man.
Indications to Begin Ascent	Expiration of 30 min. period or 30 min. plus time to relief on Table 4 of Standard Navy Table.	Establish that remission is complete; Remain an additional arbitrary period unless ended by O_2 exposure concern.
Pressure-time Ascent Pattern	Decompression to 60 ft. rapid, limited by decompression sickness risk; stage ascent pattern with rapid pressure changes; 30 ft/12 hr. stage prevents new bends.	No risk of decompression sickness from treatment, slow pressure changes of continuous ascent maximize inert-gas elimination gradient and least disturb bubble nuclei, or cavitation-prone turbulent streams.
Respired Air	Usually compressed air deeper than 60 ft.; gradient for N_2 elimination postponed until O_2 stops; O_2 needed to prevent bends in Table 4 attendants.	O_2 primarily, to supply tissues harmed by occlusive bubble emboli, to assist inert-gas elimination from bubbles; not required to avoid bends from the treatment.

Table 4.1 Summary of recompression method characteristics and their theoretical bases.

(After Goodman [40])

The question is raised as to whether or not to recommend the instal-

lation of a recompression facility on board future spacecraft for the treatment of decompression sickness, air-embolic phenomena associated with meteoroid penetration (Chapter 12), explosive decompression (Chapter 3), and the ebullism syndrome (Chapter 2). Assuming that suitable spacecraft cabin atmospheres will be selected, current predictions fortunately indicate that the probability of serious manifestations of decompression sickness occurring during space operations will be extremely low [81]. It is also thought that other unforeseen events which could result in serious manifestations due to bubble emboli are potentially rare. Therefore, in the light of the predicted rarity of serious clinical problems due to bubble embolic phenomena in space, transporting a recompression chamber into space does not appear justified at the present time. However, it is considered possible that in the future, recompression facilities such as reinforced, appropriately equipped air locks which offer a minimum weight penalty might be placed in spacecraft, and space, lunar and planetary stations when large-scale extravehicular operations are to be carried out and significant risks of such problems occurring are anticipated.

Any plasma loss associated with decompression sickness must be immediately replaced, using either plasma or another suitable plasma-expanding agent such as dextran. A vasopressor or intravenous saline solution would be inappropriate for treating impending or manifest "shock", but should be used until a plasma-expanding agent is made available or if such an agent is not available. The volume of plasma requiring replacement might be determined by calculating the static plasma deficit. If pulmonary edema is part of the clinical picture, it would be wise to administer a plasma-expanding agent slowly to avoid aggravation of this condition. Successful therapy of plasma loss is indicated by the level and stability of the pulse rate and systemic arterial pressure, by repeated determination of the hematocrit and by a steady urine output of at least 30 ml per hour.

The question arises as to whether or not mannitol or another suitable osmotic diuretic should be administered in conjunction with a

plasma-expanding agent to an astronaut who suffers the delayed "shock" syndrome. As pointed out in Chapter 1, mannitol has been used effectively for the prevention of acute renal failure from a variety of hypoxic factors, and for the treatment of post-hypoxic cerebral edema. Therefore it should be administered prophylactically for renal failure to an astronaut who progresses to the "shock" stage of the delayed "shock" syndrome. Also conceivable is the possibility that mannitol might be used effectively to reduce and possibly reverse the diffuse extravasation of plasma which is characteristic of this syndrome. By the same token, mannitol might even be an effective form of treatment for the neurologic manifestations of decompression by reducing the focal embolic brain edema which presumably accounts for such manifestations. It must be pointed out, however, that the possible usefulness of this or any other therapeutic agent in the therapy of decompression sickness remains to be established.

Total body hypothermia has apparently been effective in the treatment of the neurologic manifestations of decompression sickness [35]. As was pointed out in Chapter 1, hypothermia reduces tissue oxygen demand, assists in the control of cerebral edema, and controls the hyperpyrexia so often associated with severe brain damage. Although hypothermia might be a valuable therapeutic measure for neurologic manifestations and perhaps the delayed "shock" syndrome of decompression sickness, rendering an afflicted astronaut hypothermic might be impossible to accomplish in space in the foreseeable future. It is conceivable, however, that adequate total body cooling might be attained with a space suit water-cooled garment. Recommended hypothermic levels are given in Chapter 1. Suppression of shivering would be possible with chlorpromazine.

Most authorities have recommended that 100 percent oxygen at ground level ambient atmospheric pressure be administered as indicated to cases suffering from the delayed "shock" syndrome of decompression sickness [1, 31, 32, 53]. It has been suggested, however, that the cere-

bral vasoconstrictor effect of a high partial pressure of oxygen might in fact seriously compromise blood flow to brain tissue which has already been rendered ischemic by a combination of embolic blockage of blood flow and reflex irritative vasospasm [10, 90]. Because of its potent cerebral vasodilating action, 3.5 percent carbon dioxide has been added to high oxygen atmospheres, but the greater effectiveness of such gas mixtures over 100 percent oxygen in the treatment of the delayed "shock" syndrome, or even the neurologic manifestations of decompression sickness, remains to be proven [90]. Moreover, it should be remembered that currently proposed spacecraft cabin atmospheric pressures will not provide oxygen at a partial pressure which can significantly reduce cerebral blood flow. This would even be the case if an intravehicular astronaut is pressurized in his space suit.

Other therapeutic measures should be carried out as dictated by the particular case of decompression sickness. The intravenous administration of a rapid-acting cardiac glycoside, such as digoxin, might be considered if there is evidence of embolic myocardial damage or right heart strain secondary to embolic blockage of pulmonary blood flow or pulmonary edema. A sedative, such as phenobarbital, might be required to control an agitated astronaut. If an osmotic diuretic has been used, an electrolyte solution might be given intravenously to replace fluid and electrolytes, which are characteristically lost in excess as a result of osmotic therapy. Intravenous feeding might also be required. A clear airway must be insured by whatever means possible.

Finally, it should be mentioned that the potential usefulness of heparin in the treatment of decompression sickness remains to be determined. Whether or not this drug provided beneficial effects in animal decompression experiments through its anticoagulant, proteolytic or lipemia-clearing activity remains unanswered. The solution of this problem may lead not only to a better understanding of the basic mechanisms underlying the serious manifestations of decompression

sickness, but also to the possible discovery of agents which might be potentially useful in the treatment of decompression sickness in space.

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REFERENCES

1. Adler, H. F., Neurocirculatory Collapse at Altitude. Special Project, U. S. Air Force Sch. Aviation Med., Randolph Field, Texas, 1950.

2. Adler H. F., Dysbarism. AF-SAM-Rev-1-64, U. S. Air Force Sch. Aviation Med., Brooks AFB, Texas, 1964.

3. Andersen, H. R., A Historical Review of the Bubble Theory of the Etiology of Decompression Sickness as Related to High Altitude Exposure. AF-SAM-Rev-10-65, U. S. Air Force Sch. Aerospace Med., Brooks AFB, Texas, 1965.

4. Anthony, R. A., Clarke, R. W., Liberman, A., et al, Temperature and Decompression Sickness. NAS-NRC-CAM-136, National Academy of Sciences - National Research Council, Committee on Aviation Medicine, Washington, D. C., 1943.

5. Barthelemy, L., Blood Coagulation and Chemistry During Experimental Dives and the Treatment of Diving Accidents with Heparin. Proceedings Second Symposium on Underwater Physiology, NAS-NRC-1181, National Academy of Sciences - National Research Council, Washington, D. C., 1963, pp. 46-56.

6. Beard, S. E., Allen, T. H., McIver, R. G., Bancroft, R. W., Comparison of Helium and Nitrogen in Production of Bends in Simulated Orbital Flights. Aerospace Med., 38:331-337, 1967.

7. Behnke, A. R., A Review of the Physiologic and Clinical Data Pertaining to Decompression Sickness. NMRI-443-4, U. S. Naval Medical Research Inst., Bethesda, Maryland, 1947.

8. Behnke, A. R., Decompression Sickness Following Exposure to High Pressures, in Decompression Sickness, J. G. Fulton, (ed.). Philadelphia, W. B. Saunders Co., 1951, pp. 53-89.

9. Berry, C. A., Dysbarism: An Inflight Case and a Discussion of the Present Status. Aerospace Med., 32:107-112, 1961.

10. Berry, C. A., Smith, M. R., Recent U.S.A.F. Experience with Inflight Dysbarism. Aerospace Med., 33:995-1000, 1962.

11. Blinks, L. R., Twitty, V. C., Whitaker, D. M., Part II. Bubble Formation in Frogs and Rats, in Decompression Sickness, J. G. Fulton, (ed.). Philadelphia, W. B. Saunders Co., 1951, pp. 145-164.

12. Boothby, W. M., Lovelace, W. R., Benson, O. O., cited by Ferris, E. B., Jr., Engel, G. L., (see ref. 36).

13. Bratt, H. R., Report of a Case of Severe Dysbarism Treated with a Recompression Chamber. Aerospace Med., 33:358, 1962.

14. Brunner, F. P., Frick, P. G., Bühlmann, A. A., Post-Decompression Shock Due to Extravasation of Plasma. Lancet, 1:1071-1073, 1964.

15. Busby, D. E., Unpublished Observations. Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico, 1962.

16. Burkhardt, W. L., Adler, H., Thometz, A. F., A Roentgenographic Study of "Bends" and Chokes at Altitude. J. Aviat. Med., 17:462-477, 482, 1946.

17. Cannon, P., Gould, T. R., Treatment of Severe Decompression Sickness in Aviators. Brit. Med. J., 1:278-282, 1964.

18. Catchpole, H. R., Gersh, I., Pathogenetic Factors and Pathological Consequences of Decompression. Physiol. Rev., 27: 360-397, 1947.

19. Clay, J. R., Histopathology of Experimental Decompression Sickness. Aerospace Med., 34:1107-1110, 1963.

20. Clamann, H. G., Decompression Sickness, in Aerospace Medicine, H. G. Armstrong, (ed.). Baltimore, Williams and Wilkins, 1961, pp. 175-188.

21. Coburn, K. R., Gould, T. R., Young, J. M., Decompression Collapse Syndrome: Report of a Case with Successful Treatment by Compression to a Pressure in Excess of One Atmosphere. Aerospace Med., 33:1211-1215, 1962.

22. Cockett, A. T. K., Nakamura, R. M., Newer Concepts in the Pathophysiology of Experimental Dysbarism - Decompression Sickness. Amer. Surg., 30:447-451, 1964.

23. Cockett, A. T. K., Nakamura, R. M., Franks, J. J., Delayed Shock in Experimental Dysbarism. Surg. Forum, 14:7-8, 1963.

24. Cockett, A. T. K., Nakamura, R. M., Kado, R. T., Physiological Factors in Decompression Sickness. Arch. Environ. Health, 11:760-764, 1966.

25. Cook, S. F., Williams, O. L., Lyons, W. R., Lawrence, J. H., Comparison of Altitude and Exercise with Respect to Decompression. NAS-NRC-CAM-245, National Academy of Sciences -National Research Council, Committee on Aviation Medicine, Washington, D. C., 1944.

26. Cotes, F. L., Decompression Sickness with Post-Decompression Collapse. Flying Personnel Research Committee, Royal Air Force Institute of Aviation Medicine, Farnborough, England, 1953.

27. Cryssanthou, C., Kalberer, J.,Jr., Kooperstein, S., Antopol, W., Studies on Dysbarism. II. Influence of Bradykinin and "Bradykinin-Antagonists" on Decompression Sickness in Mice. Aerospace Med., 35:741-746, 1964.

28. Damato, M. J., Highly, F. M., Hendler, E., Michel, E. L., Rapid Decompression Hazards After Prolonged Exposure to 50 Per Cent Oxygen - 50 Per Cent Nitrogen Atmosphere. Aerospace Med., 34:1037-1040, 1963.

29. Damato, M. J., Kellett, G. L., Coburn, K. R., The Incidence of Aeroembolism Resulting from Rapid Decompression Following Exposure to a Mixed Gas Atmosphere at a Pressure of 380 mm Hg. NAEC-ACEL-529, U. S. Naval Air Engineering Center, Aerospace Crew Equipment Laboratory, Philadelphia, Pennsylvania, 1965.

30. Degner, E. A., Ikels, K. G., Allen, T. H., Dissolved Nitrogen and Bends in Oxygen-Nitrogen Mixtures During Exercise at Decreased Pressures. Aerospace Med., 36:418-425, 1965.

31. Donnell, A. J., Jr., Norton, C. P., Successful Use of the Recompression Chamber in Severe Decompression Sickness with Neurocirculatory Collapse: A Case Report. Aerospace Med., 31:1004-1009, 1960.

32. Downey, V. M., The Use of Overcompression in the Treatment of Decompression Sickness. Aerospace Med., 34:28-29, 1963.

33. Downey, V. M., Worley, T. W., Jr., Hackworth, R., Whitley, J. L., Studies on Bubbles in Human Serum Under Increased and Decreased Atmospheric Pressures. Aerospace Med., 34:116-118, 1963.

34. Epstein, P. S., Plesset, M. S., On the Stability of Gas Bubbles in Liquid-Gas Solutions. J. Chem. Phys., 18:1505-1509, 1950.