DIVING MEDICINE

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Second Edition

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Contents

Chapter 4

Mechanisms and Risks of Decompression

RICHARD D. VANN

Animal experiments by Paul Bert during the nineteenth century and autopsies of divers and caisson workers by Leonard Hill and others at the beginning of the twentieth century led to the conclusion that decompression sickness is caused by bubbles of inert gas in the blood and tissues.[1–5] The variety and severity of the symptoms depend upon bubble volume and location. Unconsciousness and death can result from bubbles in the brain, dyspnea from bubbles in the pulmonary arteries, and paralysis from bubbles in the spinal cord. The causes of the minor forms of decompression sickness are less clear, but muscle and joint pain appear to be due to bubbles in ligaments, fascia, periosteum, muscle spindles, and nerve sheaths. More recently, bubbles have been recognized to have biochemical as well as mechanical effects.[6]

DISSOLVED INERT GAS EXCHANGE

Perfusion-Limited Inert Gas Exchange

The first quantitative attempt to describe inert gas exchange was made in 1897 by Zuntz.[7] Zuntz assumed that cardiac output was distributed evenly throughout the body, nitrogen in blood mixed instantaneously with nitrogen in tissue, and nitrogen solubilities in blood and tissue were equal. With these assumptions, nitrogen exchange was completely determined by blood flow and tissue volume.

"Well-stirred" tissues of this nature are known as *perfusion limited*. Their gas exchange properties are defined by a characteristic *half-time* during which the difference between the arterial and tissue nitrogen tensions is reduced to half its initial value. This concept is illustrated in Figure 4–1 in which the x-axis is time in half-time units, and the y-axis is the difference in the arterial and tissue nitrogen tensions expressed as a percentage of the initial difference. At zero time, the nitrogen saturation is zero. After one half-time, tissue is half saturated, and after two half-times, it is three-quarters saturated. With each additional half-time, the dif-

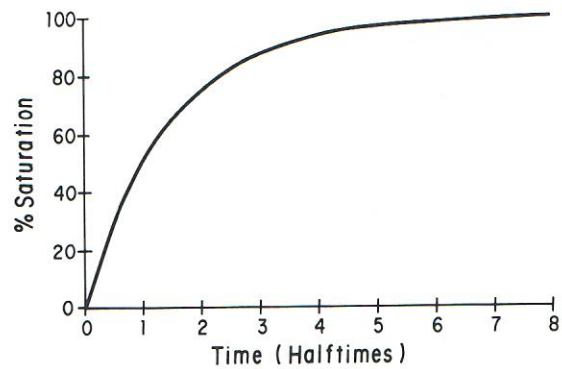

FIGURE 4–1. Percentage of nitrogen saturation in a well-stirred Haldane tissue as a function of time. Nitrogen saturation is expressed as the percentage difference between the arterial and tissue or venous tension. Time is in half-time units. The difference between the arterial and tissue tensions is reduced by half with each unit of time.

ference between the tissue and arterial tensions is reduced by half.

Using the same assumptions as Zuntz, Haldane estimated the total body half-time of nitrogen to be 23 min.[8] He pointed out, however, that there are tissues with shorter and longer half-times because blood flow is not evenly distributed, and nitrogen is more soluble in fat than in lean tissue. Haldane selected tissue half-times of 5, 10, 20, 40, and 75 min to represent the whole body.

Figure 4–2 shows the responses of these tissues to a 15-min dive at 168 fsw.[8] The x-axis is time in minutes, and the y-axis is the absolute pressure in atmospheres (ata). The solid line is the dive profile with decompression stages at 60, 40, 30, 20, and 10 feet of seawater (fsw). The dashed lines are the nitrogen tensions in the five tissues. The 5-min tissue responds rapidly to pressure change, while the 75-min tissue absorbs nitrogen slowly and retains it for a long time. According to Haldane's theory for safe decompression, bubble formation and decompression sickness could be avoided if no tissue tension were ever allowed to exceed twice the absolute pressure.

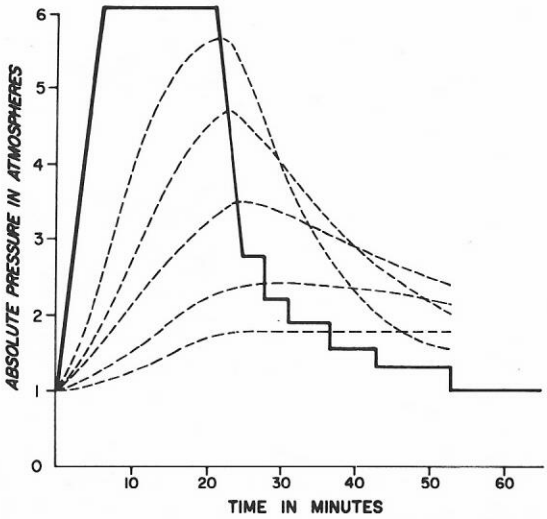

FIGURE 4–2. The responses of five Haldane tissues *(broken lines)* having 5-, 10-, 20-, 40-, and 75-min half-times to a 20-min dive at 168 fsw *(solid line)*. Decompression is conducted in stages according to the Haldane rule that no tissue tension should ever exceed twice the absolute pressure. (From Boycott AE, Damant GCC, Haldane JS: The prevention of compressed air illness. J Hyg 8:342–443, 1908, by permission of Cambridge University Press.)

Diffusion-Limited Inert Gas Exchange

Recent studies have demonstrated that except for avascular tissues such as bone or eye, perfusion is the primary determinant of dissolved inert gas exchange. Diffusion can have secondary effects, however, which make gas exchange slower than in well-stirred Haldane tissues.

Figure 4–3A shows inert gas diffusing between adjacent well-stirred tissues that are perfused at different rates or that have different inert gas solubilities.[9–13] Such intertissue diffusion might be significant in decompression, for example, where a slowly exchanging fat deposit acts as an inert gas reservoir for an adjacent rapidly exchanging lean tissue that is sensitive to decompression injury.

Figure 4–3B demonstrates how inert gas diffusing between adjacent arterioles and venules can be shunted around tissue. Arteriovenous diffusion shunts have been observed for oxygen[14–16] and would reduce the exchange rate of a highly diffusible gas like helium relative to a less diffusible gas like nitrogen.[17, 18]

Diffusion between closely spaced capillaries is generally so rapid that virtually no radial concentration gradients can exist. If the capillaries are very long, however, axial concentration gradients can develop in surrounding tissue because of the large longitudinal diffusion distances (Fig. 4–4). Such gradients act to reduce the rate of inert gas exchange.[19, 20]

UNDISSOLVED INERT GAS EXCHANGE

The Oxygen Window

Diffusion has only secondary effects on inert gas exchange as long as the gas remains dissolved. When bubbles form, however, inert gas becomes isolated from the circulation and cannot be removed by blood flow until it diffuses back into tissue. The speed of diffusion is determined by the difference between the nitrogen partial pressure in the bubble and the nitrogen tension in tissue. This difference is a direct result of the metabolic conversion of oxygen, a relatively insoluble gas, into carbon dioxide, which is some 21 times more soluble. Haldane understood this mechanism but did not need it in his theory for safe decompression, which assumed that decompression sickness and bubble formation occurred simultaneously.[8]

The effect of exchanging oxygen for carbon dioxide on dissolved gas tension is illustrated in

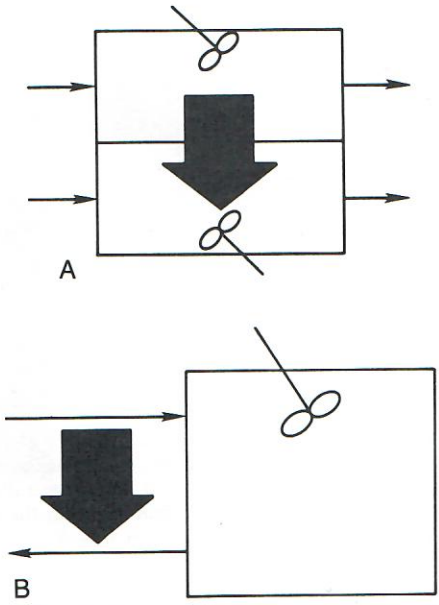

FIGURE 4–3. A, Inert gas diffusion between adjacent tissues that have different inert gas solubilities or perfusion rates. *B*, Inert gas diffusion between adjacent arterioles and venules. This causes a diffusion shunt that allows inert gas to bypass the tissue.

TABLE 4–1. Alveolar, Arterial, and Venous Gas Tensions

	Alveolar (torr)	Arterial (torr)	Venous (torr)
CO_2	40	40	45
O_2	104	95	40
H_2O	46	46	46
N_2	570	570	570
Total	760	751	701

Figure 4–5. The x-axis is dissolved gas tension in torr; the y-axis is gas content in ml gas per 1000 ml blood. The steeper line shows the relationship between carbon dioxide tension and content. The slope of this line is the carbon dioxide solubility. The other line represents the same relationship for oxygen. Its gradual slope reflects a lower oxygen solubility.

Suppose, as indicated by Point 1 in Figure 4–5, that the oxygen tension were 100 torr. This corresponds to an oxygen content of 3 ml oxygen per 1000 ml blood (Point 2). If each oxygen molecule were exchanged for a carbon dioxide molecule (Point 3), there would be no change in the dissolved gas volume, but the tension would fall to 4.7 torr (Point 4). This is because carbon dioxide is more soluble than oxygen.

The exchange of oxygen for carbon dioxide which occurs in tissue is illustrated in Table 4–1 for an air-equilibrated diver at sea level. In the lung, the sum of the alveolar partial pressures is normally near 760 torr. The sum of the arterial gas tensions is slightly less, largely because of ventilation-perfusion inequalities. Since the diver is equilibrated with atmospheric nitrogen, the alveolar, arterial, and venous nitrogen tensions are equal. Metabolism, however, causes the oxygen tension to fall from 95 torr in the arterial blood to 40 torr in the venous blood, while the arterial carbon dioxide rises from 40 torr to a venous level of 45 torr. The 55-torr fall in oxygen tension accompanied by the 5-torr rise in carbon dioxide tension are due to the solubility difference between oxygen and carbon dioxide with a small contribution from a respiratory quotient of less than one. Summing the venous tensions, the total dissolved gas tension is equal to 701 torr or 59 torr less than the absolute pressure.

The gas tensions in Table 4–1 are shown as bar graphs in Figure 4–6. The bar on the left presents gases in a diver's lungs at sea level. Dalton's law of partial pressures requires that the sum of these gases be 1 ata. The bar on the right represents the gases in the diver's tissues whose sum is less than 1 ata because of the oxygen for carbon dioxide exchange.

In Figure 4–7, the diver is breathing air at 33 fsw. The bar graphs on the left show the gases in his lungs and tissue upon arrival at depth. The oxygen and nitrogen partial pressures in his lungs have increased to make the sum of all gases equal to the absolute pressure of 2 ata, but his tissues have absorbed no additional nitrogen. The bar graphs on the right show the lungs and tissues after nitrogen equil-

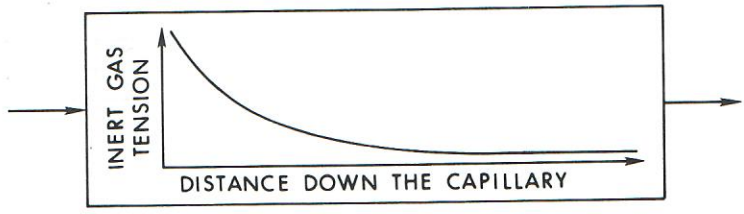

FIGURE 4–4. Inert gas concentration gradients in a tissue having long parallel capillaries. These gradients reduce the inert gas exchange rate and are the result of large axial diffusion distances.

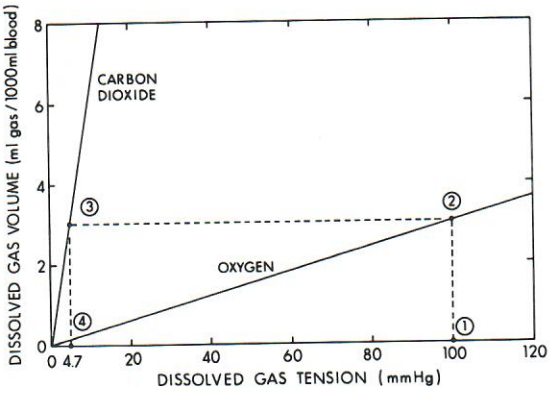

FIGURE 4–5. The effects of exchanging oxygen for carbon dioxide on dissolved gas tension. When oxygen is converted into carbon dioxide, the gas tension falls from 100 to 4.7 torr, but the dissolved gas volume or content remains unchanged because carbon dioxide is more soluble than oxygen.

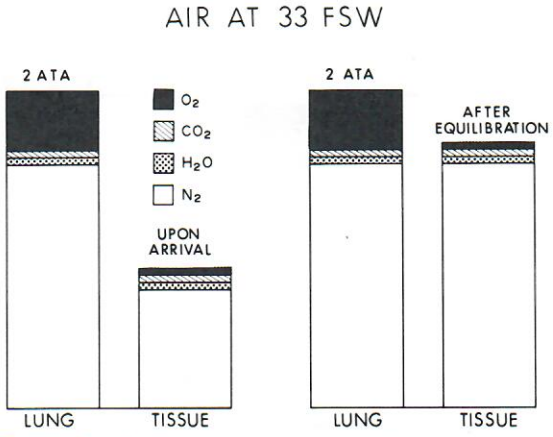

FIGURE 4–7. Gases in the lungs and tissues of an air breathing diver at 33 fsw. Initially, the tissue nitrogen tension is the same as in Figure 4–6, but after sufficient time at depth tissue nitrogen equilibrates with the 2 ata of air in the lung.

ibration. The tissue nitrogen tension now equals the alveolar nitrogen partial pressure.

Now, as shown in Figure 4–8, the diver returns to sea level, and bubbles form in his tissues. By Dalton's law, the sum of the partial pressures in the bubble is 1 ata. The water vapor pressure is constant, and the oxygen and carbon dioxide partial pressures are controlled to tissue levels. Since the nitrogen tension in tissue is elevated, nitrogen diffuses both into the bubble and into the blood. Nitrogen that diffuses into the blood and remains dissolved is carried to the lungs and is eliminated harmlessly, but nitrogen diffusing into the bubble causes it to expand.

Expanding bubbles may cause clinical decompression sickness. If so, the diver is placed on 100 per cent oxygen and is recompressed to 60 fsw where the absolute pressure is 2.82 ata in the bubble and lung (Fig. 4–9). Metabolism soon returns the oxygen and carbon dioxide in the bubble to their tissue levels. This raises the nitrogen partial pressure in the bubble, and nitrogen diffuses rapidly out of the bubble because of the large concentration gradient. Momsen[9] called this gradient the *partial pressure vacancy*; Hills[21] called it the *inherent unsaturation*; and Behnke[22, 23] called it the *oxygen window*.

Diffusion Gradients Around Bubbles

Figure 4–10 shows the effects of the oxygen window upon the concentration gradients of oxygen, nitrogen, or helium around a bubble.[24]

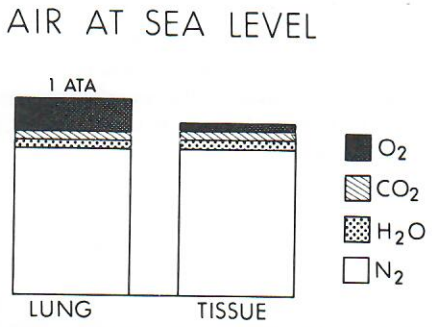

FIGURE 4–6. Gases in the lungs and tissues of an air breathing diver at sea level. The metabolic exchange of oxygen for carbon dioxide results in a total tissue gas tension that is less than the ambient pressure. This difference is the *oxygen window*.

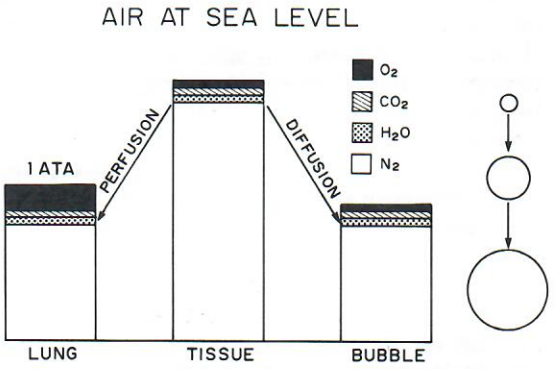

FIGURE 4–8. Bubble formation and growth after decompression from 33 fsw to sea level. The bubble grows by inward diffusion of supersaturated nitrogen from tissue. Dissolved nitrogen also is carried to the lungs by the circulation.

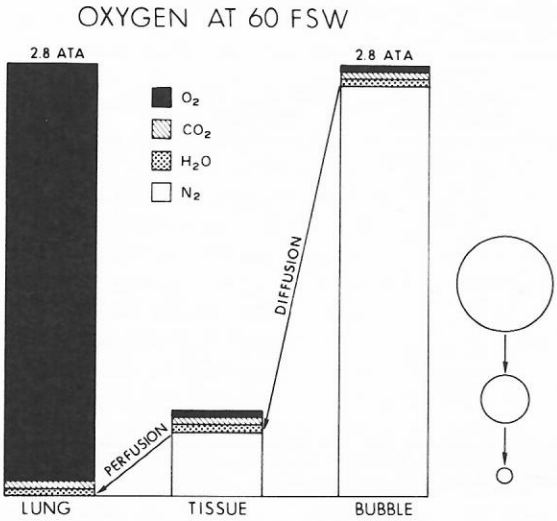

FIGURE 4–9. A diver who develops decompression sickness and is recompressed to 60 fsw while breathing 100 per cent oxygen. The sum of the partial pressures of all gases in the bubble increases to 2.82 ata, but outward diffusion of excess oxygen and carbon dioxide reduces their partial pressures to tissue levels. Since oxygen, carbon dioxide, and water vapor are controlled to their tissue values, the nitrogen partial pressure must rise until the sum of all partial pressures equals 2.82 ata. The oxygen window is the concentration gradient between nitrogen in the bubble and in the tissue down which nitrogen diffuses. The size of the oxygen window increases as the tissue nitrogen tension is reduced by perfusion.

The oxygen gradient is steepest because it is metabolically consumed. Helium and nitrogen extend further into tissue than oxygen because they are not consumed and are eliminated only by perfusion. The nitrogen gradient is steeper than the helium gradient because nitrogen is less diffusible than helium. This makes helium more available for removal by the circulation. Since an inert gas in a bubble must diffuse back into tissue before removal, its elimination after decompression is slower than its uptake at depth.[25–27]

BUBBLE FORMATION

Gas Nuclei

Studies by Hills[27] and Powell[28] suggest that only 5 or 10 per cent of the inert gas absorbed during normal diving is released as bubbles after decompression. While this may seem a small fraction, it agrees with both in vitro and in vivo observations that bubble formation is not widespread and is limited to discrete nucleation sites, whose number fluctuates with changing environmental and physiological conditions.

These phenomena are illustrated in observations of bubble formation under the transparent shells of shrimp. Table 4–2 shows the results of experiments by Daniels, who decompressed shrimp from sea level to altitude.[29] Bubble formation rose with increasing altitude as additional nucleation sites were recruited to about 3.5 bubbles per shrimp (Table 4–2, Lines 1 to 4). When the shrimp were hydrostatically compressed for 2 min to 201 ata prior to altitude exposure (Table 4–2, Line 5), bubble formation fell to 0.5 bubbles per shrimp. Nucleation sites that can be deactivated in this manner are known as *gas nuclei* and are believed to contain free gas that is dissolved by hydrostatic pressure.[30–32] With a 24-hour sea level recovery period between pressure treatment and altitude exposure, bubble formation returned to its initial level, indicating that gas nuclei were reactivated or created (Table 4–2, Line 6). Evans and Walder found that bubble formation increased when shrimp were exercised after pressure treatment but before altitude exposure.[33] McDonough and Hemmingsen observed decreased bubble formation in various immobilized marine animals and suggested that exercise caused bubble formation through a mechanism known as *tribonucleation*.[34–37]

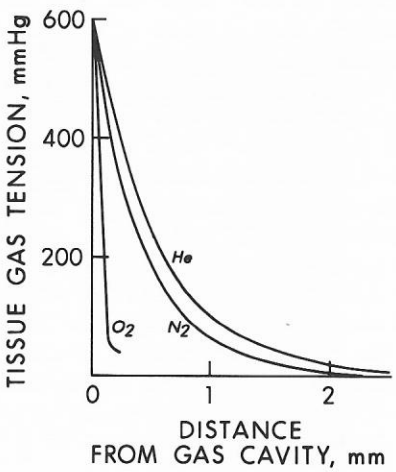

FIGURE 4–10. Dissolved gas concentration gradients around a bubble filled with oxygen, nitrogen, or helium. The oxygen concentration gradient is steepest because oxygen is metabolized in tissue as it diffuses out of the bubble. Nitrogen and helium are metabolically inert and are removed from tissue only by perfusion. Helium extends further into tissue than nitrogen because it diffuses more quickly. (Redrawn from Van Liew HD: Coupling of diffusion and perfusion in gas exit from subcutaneous pockets in rats. Am J Physiol 214:1176–1185, 1968.)

TABLE 4–2. Bubble Formation in Shrimp Decompressed to Altitude After Hydrostatic Pressure Treatment

	RECOVERY PERIOD	HYDROSTATIC PRESSURE TREATMENT	15 MIN ALTITUDE EXPOSURE	BUBBLES PER SHRIMP
1.	—	—	27,500 ft (0.33 ata)	0.0
2.	—	—	33,500 ft (0.25 ata)	0.5
3.	—	—	42,000 ft (0.17 ata)	3.2
4.	—	—	53,000 ft (0.10 ata)	3.5
5.	—	200 ata for 2 min	53,000 ft (0.10 ata)	0.5
6.	24 hrs	200 ata for 2 min	53,000 ft (0.10 ata)	3.2

Data from Daniels S, Eastaugh KC, Paton WDM, Smith EB: Micronuclei and bubble formation: A quantitative study using the common shrimp, crangon. *In* Bachrach AJ, Matzen MM (eds): Underwater Physiology. 8th ed. Bethesda, Undersea Medical Society, 1984.

Tribonucleation

Tribonucleation causes bubble formation as a result of large negative pressures generated by viscous adhesion between surfaces separating in liquid.[38–40] These negative pressures, which can be hundreds of atmospheres or more, place the liquid in tension and may cause either spontaneous (de novo) bubble formation or bubble formation from gas nuclei.

Bubbles created by tribonucleation can persist[41] and act as gas nuclei for later bubble formation. The lifetime of such a nucleus is determined by the rate at which it dissolves. Mechanisms that stabilize a nucleus against surface tension can prolong its lifetime. Proposed stabilization mechanisms include gas in hydrophobic crevices[30] and surface active shells around bubbles.[42, 43] Such shells have been observed surrounding bubbles in sea water.[44]

While it is unclear whether stabilization mechanisms play a significant role in decompression sickness, the evidence strongly suggests that the creation and destruction of gas nuclei are in dynamic equilibrium. If exercise shifts this equilibrium toward creation, more bubbles form and the risk of decompression sickness increases. The risk decreases, on the other hand, if pressure treatment shifts the balance toward destruction.

The marine animal experiments[29, 33–37] provided evidence for gas nuclei but did not demonstrate their role in decompression sickness. This link was suggested in experiments that pretreated rats at pressure before decompression from a 2-hour exposure at 240 fsw on air (Fig. 4–11).[45] Without pressure treatment, the incidence of decompression sickness was 83 per cent. With a brief pressure treatment at 600 fsw, the decompression sickness incidence was 74 per cent, and with a 1000 fsw pressure treatment, the incidence decreased to 64 per cent. Thus, pressure treatment reduced decompression sickness in rats as well as eliminated gas nuclei in marine animals.

MECHANISMS OF DECOMPRESSION SICKNESS

Joint Pain

The sites of bubble formation in divers are less mysterious than might be expected. Cracking sounds in joints are caused by collapsing bubbles formed by tribonucleation during the

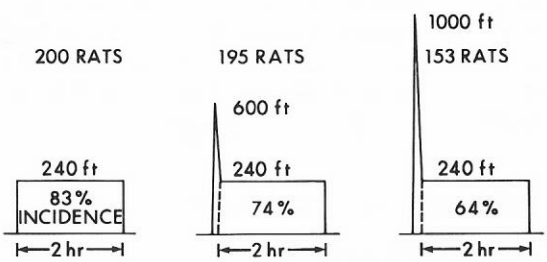

FIGURE 4–11. Decompression sickness in rats subjected to pressure treatment before a 2-hr exposure at 240 fsw on air. The incidence of decompression sickness decreased from 83 per cent with no pressure treatment, to 74 per cent after a 600 fsw treatment, and to 64 per cent after a 1000 fsw treatment, suggesting that preexisting gas nuclei are responsible for the bubbles that cause decompression sickness in rats. (From Vann RD: Decompression theory and application. *In* Bennett PB, Elliott DH (eds): The Physiology and Medicine of Diving. London, Bailliere Tindall, 1982.)

separation of joint surfaces.[41, 46] Tribonucleation occurs in marine animals despite the lack of mammalian joint structure and may occur during the relative motion of tendons, ligaments, and bones. The collapse of a bubble with an associated sound is known as *vaporous cavitation.*[47] As the dissolved gas content increases or the hydrostatic pressure decreases, a transition occurs from vaporous to *gaseous cavitation,* which is soundless and leaves a stable bubble.

Gas-filled joints have been detected after diving or during altitude exposure by radiographs and by the presence of crepitus.[48–51] Ferris and Engle reported that gas in joint capsules was asymptomatic, while gas in perivascular and periarticular tissues was frequently accompanied by pain.[48] This gas appeared radiographically as discrete, round bubbles in the popliteal fat pad behind or lateral to the neck of the femur or as a fine longitudinal streaking along tendon or muscle bundles in the popliteal fossa. In stereoscopic studies, these regions appeared as ribbon-like shadows apparently in the fascial planes and along tendons. With recompression, both crepitus and shadows disappeared but reappeared upon immediate decompression.

Thomas and Williams found gas in the knee joints of all subjects exposed to an altitude of 20,000 feet.[52] Gas accumulations as large as 50 to 75 ml were sometimes present at higher altitudes but were not always accompanied by pain (Fig. 4–12A). Joint aspiration showed this gas to be in approximate equilibrium with gases in the blood. Knee radiographs of 27 subjects having moderate to severe pain at 35,000 feet revealed irregular collections of gas in periarticular tissues as well as small discrete bubbles and streaking along fascial planes and tendons (Fig. 4–12B). Bubbles and pain were associated in 46 of 74 observations (62 per cent), while streaking and pain were associated in 47 of 62 observations (76 per cent).

Besides joint pain, acute altitude exposure often produced recurrent, transient, sharp pains of moderate intensity in the hands and feet.[48] These pains were accompanied by crepitus in the tendon sheaths. Palpation of the tendon sheaths revealed bubbles that, when milked away, often relieved the pain. Ferris and Engle cite such observations to argue that decompression pain is of extravascular rather than of intravascular origin.

Spinal Decompression Sickness and the Vacuum Phenomenon

After the limbs, the most common site of decompression sickness is the spinal cord. Spinal symptoms are generally manifested as disturbances of the sensory and motor systems ranging from " pins and needles" and marginal

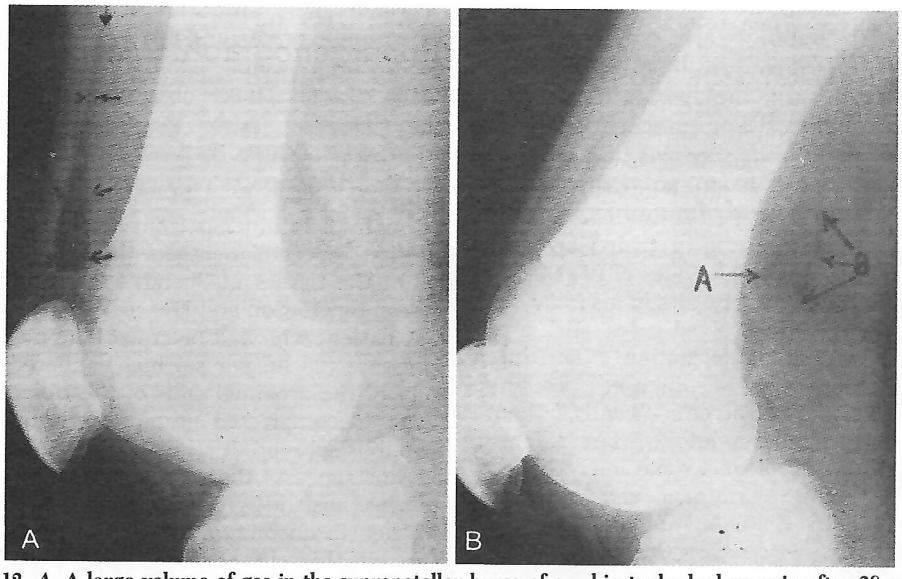

FIGURE 4–12. *A,* **A large volume of gas in the suprapatellar bursa of a subject who had no pain after 28 min at 38,000 feet of altitude.** *B,* **Discrete and irregular bubbles (A) posterior to the distal end of the shaft of the femur. The wavy streak of gas (B) appears to lie in a facial plane or along a tendon. The subject had moderately severe pain after three sets of deep-knee bends during 10 min at 35,000 feet. (From Thomas SF, Williams OL: High altitude joint pains (bends): Their roentgenographic aspects. Radiology 44:259–261, 1945.)**

weakness to total loss of sensation and paralysis.[53] The legs are most frequently affected.

The spinal lesions responsible for these symptoms are presumably caused by bubbles whose origin may be in the normal occurrence of free gas in the spine at sea level (Fig. 4–13).[54] This was first observed by Fick in 1910 and is now known as the *vacuum phenomenon.*[55, 56] Fick ascribed the vacuum phenomenon to reduced pressure in the joints as a result of movement, a mechanism currently recognized as tribonucleation.[38, 39, 41] The vacuum phenomenon is associated with aging joints, injury, or structural pathology and is frequently seen in intervertebral discs[57–59] but also has been observed in the epidural space surrounding the spinal cord.[60] Ford found the gas in a lumbar disc to be 90 to 92 per cent nitrogen.[16]

Unlike joint pain, spinal decompression sickness appears to be an intravascular rather than an extravascular phenomenon owing to the peculiar nature of the spinal circulation.[6] The venous plexus of the spinal cord is like a lake into which tributaries flow. It is valveless, under low pressure, and subject to the intrathoracic pressure changes accompanying respiration. These factors result in low blood flow of variable direction. Bubbles and bubble-induced thrombi are particularly likely to obstruct the venous plexus leading to ischemic spinal damage.

Intravascular Bubbles and Doppler Bubble Detection

Intravascular bubbles are commonly observed after decompression, but their origin is obscure, since blood is highly resistant to bubble formation.[30, 40, 62, 63] The prevalence of bubbles in and around joints suggests that intravascular bubbles may have an extravascular beginning. The cavitation damage that accompanies tribonucleation in mechanical systems is severe enough to erode steel[64] and might cause capillary damage in vivo. A blood-gas interface introduced into a damaged capillary could initiate a continuous stream of intravascular bubbles, much like bubbles in beer grow and escape from a seed bubble on a glass. Observations that bubbles are usually present in blood draining from limbs affected by altitude decompression sickness support this hypothesis.[65]

TABLE 4–3. Precordial Doppler Bubble Grading Scale

Grade 0	No bubbles
Grade I	Occasional bubbles
Grade II	Bubbles in less than half cardiac periods
Grade III	Bubles in all cardiac periods
Grade IV	Continuous bubbles

Data from Spencer MP: Decompression limits for compressed air determined by ultrasonically detected blood bubbles. J Appl Physiol 40:227–235, 1976.

In contrast to the lazy circulation of the spinal cord, most of the venous circulation carries bubbles directly to the right heart where a Doppler ultrasonic bubble detector can be used to convert the bubble signals into sounds.[28] These sounds are graded according to a scale such as that shown in Table 4–3.[66]

The relationship between decompression sickness and the Doppler bubble grade is shown in Figure 4–14 for subsaturation diving, altitude exposure, and saturation diving.[67] The x-axis is the bubble grade, and the y-axis is the incidence of decompression sickness which occurred at each grade. These observations suggest that high Doppler bubble grades, with decompression risks of 30 to 50 per cent, are poor predictors of decompression sickness, while low bub-

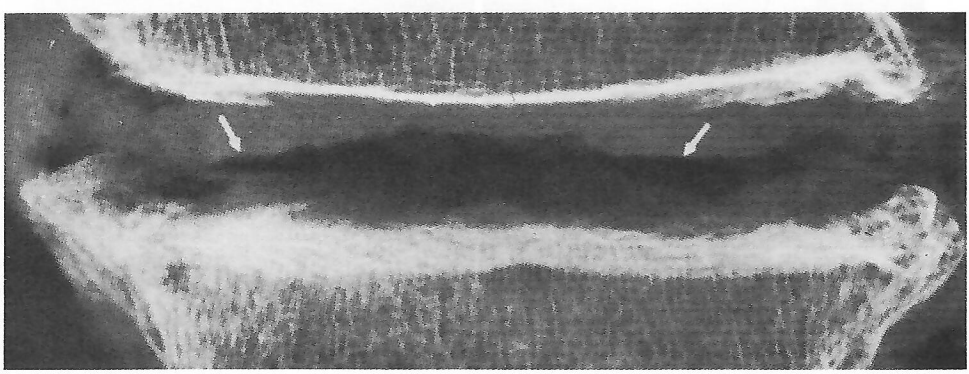

FIGURE 4–13. The vacuum phenomenon in an intervertebral disc. A collection of gas in the discal cleft appears as a radiolucent area *(arrows).* (From Resnick D, Niwayama I: Diagnosis of Bone and Joint Disorders. Philadelphia, WB Saunders Company, 1981, p 1373.)

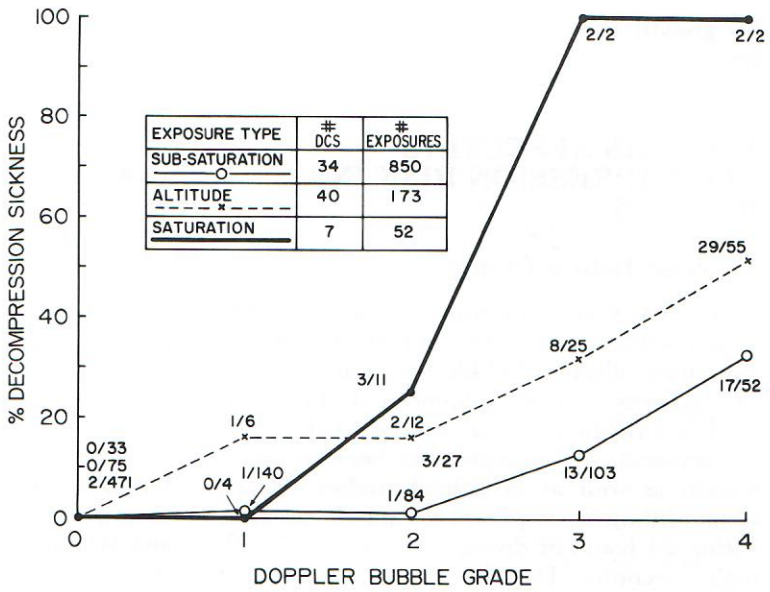

FIGURE 4–14. The relationship between Doppler bubble grade and the incidence of decompression sickness for subsaturation air diving, altitude exposure, and nitrogen-oxygen saturation diving. The risk of decompression sickness is small at low bubble grades and increases at higher grades. Low bubble grades are good predictors of decompression safety, but high grades are poor predictors of decompression sickness.

ble grades are good predictors of decompression safety. A breakdown of 84 decompression incidents (Table 4–4) shows that 87 per cent of all decompression sickness was associated with Grades 2, 3, or 4, and 100 per cent of Type II decompression sickness was associated with Grades 3 or 4.[68] Thus, while Doppler may be unsatisfactory for the early diagnosis of decompression sickness as was once hoped,[69] it can be useful to develop low-risk decompression procedures for which high bubble grades are not permitted.

Pulmonary and Arterial Bubbles

Excessive numbers of venous bubbles cause pulmonary irritation leading to bronchoconstriction and pulmonary decompression sickness (the chokes). At low gas loads, the lungs filter intravascular bubbles well and generally prevent their entry into the arterial circulation. When the filtering capacity of the lungs is exceeded, however, bubbles cross from the pulmonary to the arterial circulation. Sheep with high precordial bubble grades frequently had bubbles in the carotid artery.[28]

The brain and many other tissues appear to be resistant to local bubble formation despite high levels of nitrogen supersaturation,[70] and true cerebral decompression sickness is a rare event.[6] Bubbles can enter the cerebrovascular circulation, however, after arterial gas embolism or when venous bubbles are inadequately filtered or pass through pulmonary shunts or cardiac defects. (Fryer reports that about one quarter of the population have patent foramina ovalae.[71]) Arterial bubbles also can seed other organs and expand as they enter regions supersaturated with inert gas. The brain is particularly vulnerable to such bubbles due to its location and bubble buoyancy.

TABLE 4–4. Precordial Doppler Bubble Grades for 84 Decompression Incidents

	Bubble Grade				
	0	I	II	III	IV
Type I DCS	2	9	11	29	19
Type II DCS	—	—	—	7	7

From Vann RD, Dick AP, Barry PD: Doppler bubble measurements and decompression sickness. Undersea Biomed Res 9(Suppl 1):24, 1982.

Micro-Air Embolism

Serious decompression sickness occasionally occurs inexplicably after dives that are well within the no-decompression exposure limits and that should be too brief to cause trouble. Walder proposed that these unusual events are the results of *micro-air embolism* in which minor damage to lung tissue releases a small number of bubbles into the arterial circulation.[72] This damage might be caused by pulmonary blebs that rupture or by mucus from a recent cold which blocks a terminal bronchiole. The resulting arterial bubbles could cause bub-

ble growth and decompression sickness in tissues that would otherwise be bubble-free.

FACTORS AFFECTING DECOMPRESSION RISK IN HUMANS

Exercise Before Diving

The risk of decompression sickness is determined primarily by depth and bottom time, but any factor affecting bubble formation or inert gas exchange also will influence risk. Increased bubble formation due to exercise before decompression, for example, has been noted in human as well as in animal studies. Heavy weight-lifting accompanied by muscle soreness within 24 hours of diving was associated with high precordial Doppler bubble grades and Type II decompression sickness.[73, 74] Weight-lifting would be expected to increase the frequency of tribonucleation and the vacuum phenomenon. Other forms of pre-exposure exercise have been implicated in unexpected decompression sickness after diving and during altitude exposure.[75, 76]

Adaptation

Conversely, the risk of decompression sickness is reduced by frequent exposure to pressure.[77] Haldane recognized this effect, now known as *adaptation*, and recommended part-time duties for new compressed-air workers.[78] Walder observed that during their first 10 exposures, the incidence of decompression sickness in compressed-air workers fell from 12 to 3 per cent.[79] After 10 days without pressure exposure, the incidence returned to its initial level. Adaptation was specific for each pressure and reoccurred when the working pressure increased.[77]

Some of the unexpected cases of decompression sickness which occur after innocuous dive profiles may be due to the absence of adaptation. First-time divers or infrequent vacation divers who have accumulated free gas in and around their joints as a result of tribonucleation and the vacuum phenomenon may have an elevated susceptibility to decompression sickness. If the free gas were eliminated by hyperbaric oxygen exposure before diving began, this susceptibility might be reduced.

The effects of pre-dive exercise and adaptation are consistent with the proposed dynamic equilibrium between the creation and destruction of gas nuclei. The creation of additional nuclei (vacuum phenomena) by tribonucleation during pre-dive exercise would result in the release of more than the expected 5 to 10 per cent free gas volume upon decompression. Adaptation during repeated compression-decompression cycles, on the other hand, could eliminate some of the nuclei and reduce the gas volume that formed upon decompression. The elimination of nuclei by hyperbaric oxygen exposure might be the most effective way of producing adaptation.

Exercise at Depth

Exercise affects inert gas exchange as well as bubble formation. Exercise at depth accelerates inert gas uptake by elevating perfusion. Behnke and Willmon demonstrated that exercise at sea level increased the whole body gas exchange rates of both nitrogen and helium.[80] Recent studies investigated nitrogen elimination at sea level after short air dives with rest or exercise at depth.[81] Figure 4–15 shows resting nitrogen elimination curves measured at sea level after dives to 130 feet for 10 min. Mean nitrogen elimination 60 min post-dive was 64 per cent greater after the exercising dives than after the resting dives, indicating that exercising divers absorb more nitrogen than resting divers.

By raising the volume of gas absorbed during a dive, exercise at depth increases decompression risk and time needed for safe decompression. Van Der Aue found that resting divers had a decompression risk of 11 per cent, while working divers had a risk of 21 per cent on the same schedules.[82] He also observed that decompression sickness occurred most frequently in parts of the body which were exercised vigorously at depth. (Vigorous exercise may have caused tribonucleation.) In other tests, Van Der Aue reported that air decompression schedules that were safe for resting divers produced 20 to 30 per cent decompression sickness in working divers.[83] Buhlmann found that divers doing light work during helium-oxygen dives required 20 to 40 per cent more decompression time than resting divers.[84]

Recent studies have shown how decompression is affected by 60 min of exercise at 100 fsw with a nitrogen-oxygen breathing mix having an oxygen partial pressure of 0.7 atm.[85] These results are shown in Figure 4–16 in which the x-axis defines the dive conditions, and the y-axis is the decompression time. The number of decompression incidents over the number of trials appears at the top of each bar. Dry, resting

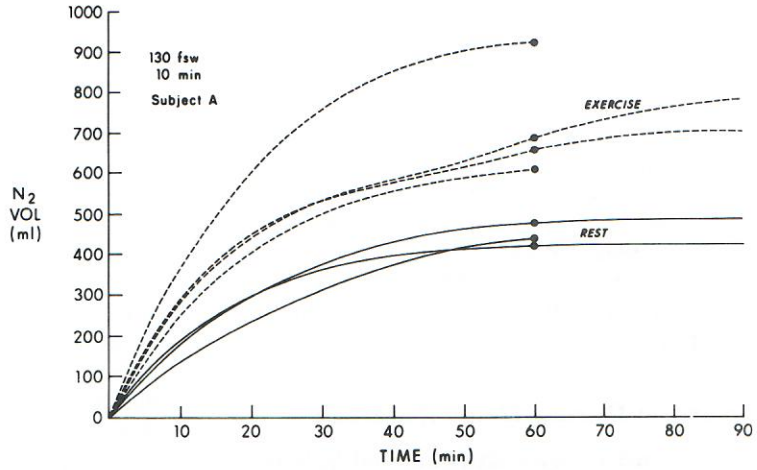

FIGURE 4–15. Respiratory nitrogen elimination curves taken at sea level from a resting subject after 10 min dives to 130 fsw. The subject exercised at depth during dives with elimination curves marked "exercise" *(dashed lines)*. During dives with elimination curves marked "rest" *(solid lines)*, the subject rested at depth. (From Dick AP, Vann RD, Mebane GY, and Feezor MD: Decompression induced nitrogen elimination. Undersea Biomed Res 11(4):369–380, 1984.)

exposures required only 40 min of decompression. In wet trials during which the divers exercised at depth and rested during decompression, both decompression sickness incidence and decompression time increased. After light exercise, 90 min of decompression were required, while 115 min were needed after moderate exercise. The 115-min schedule was insufficient to prevent decompression sickness after heavy exercise. Thus, a wet dive with heavy exercise at depth and resting decompression can require more than three times the decompression time of a dry, resting dive.

The safety of a decompression schedule is determined not only by the total stop time but also by the distribution of this time over depth. Stops too deep or too long are ineffective in eliminating excess inert gas and may cause additional gas uptake. Stops too shallow or too short can promote extensive bubble growth, which must be reduced by extra decompression time before the surface can be safely approached.

Exercise After Decompression

In the early days of decompression diving, U.S. Navy and Royal Navy divers routinely exercised during decompression as it was believed that exercise would accelerate inert gas elimination and increase decompression safety.[8, 86] When subsequent altitude and diving experiments showed that exercise increased the severity and incidence and reduced the onset time of decompression sickness, Van Der Aue recommended that exercise during or after decompression be avoided.[87, 88]

Van Der Aue applied his prohibition to both kinds of exercise, despite the fact that the early studies only investigated exercise after decompression, because the two forms of exercise were thought to have the same effects. Exercise

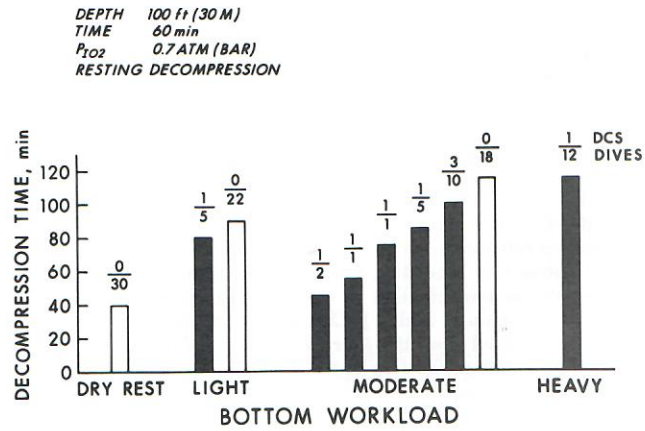

FIGURE 4–16. The effect of exercise at depth on decompression time and the incidence of decompression sickness. For a given workload at depth, the incidence of decompression sickness decreased as the decompression time was extended. Higher workloads required longer decompression times. (From Vann RD: Decompression theory and application. *In* Bennett PB, Elliott DH: The Physiology of Diving and Compressed Air Work. 3rd ed. London, Bailliere Tindall, 1982, pp 352–382.)

after decompression, however, causes increased bubble formation when the body is supersaturated with inert gas as a result of tribonucleation. These bubbles are eliminated slowly since gas in the bubbles is isolated from the circulation.

This effect is illustrated in Figure 4–17 in which the rate of krypton elimination from a subject's hand increased upon recompression from an altitude of 38,000 feet to sea level.[89] Thus, exercise after decompression should be avoided.

Exercise During Decompression

If extensive supersaturation and bubble formation do not occur during decompression, it is reasonable to suppose that exercise would accelerate inert gas elimination. Balke provided evidence to this effect in showing that exercise during oxygen breathing prior to altitude exposure delayed the onset of altitude decompression sickness.[90]

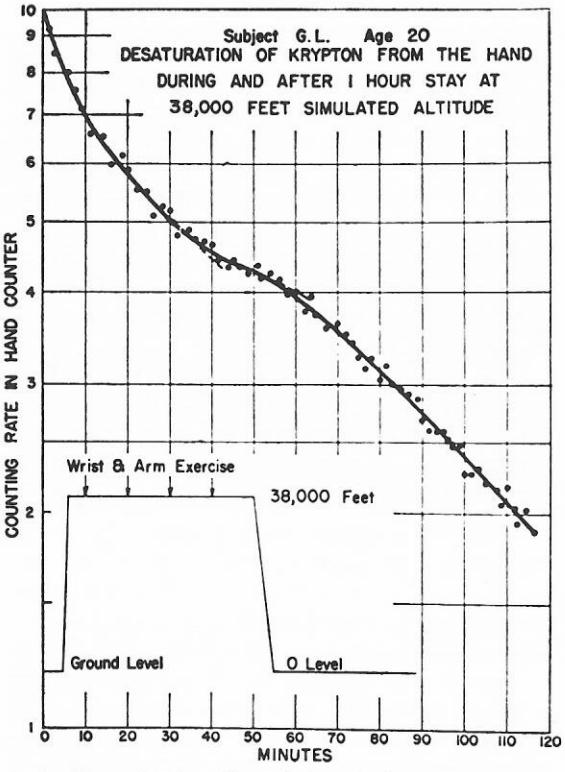

FIGURE 4–17. The effect of altitude decompression on the rate of krypton elimination from a subject's hand. The elimination rate increased upon recompression to sea level. (From Tobias CA, Jones HB, Lawrence JH, Hamilton JG: The uptake and elimination of krypton and other inert gases by the human body. J Clin Invest 28:1375–1385, 1949. Reproduced from the *Journal of Clinical Investigation* by copyright permission of the American Society for Clinical Investigation.)

The hypothesis that exercise during decompression could improve decompression safety and reduce decompression time was tested during dives to 100 and 150 fsw in which divers breathed 0.7 atm oxygen in nitrogen and performed light exercise for 60 min at depth and either rested or continued exercise during decompression.[85] Exercise during decompression reduced the incidence of decompression sickness and allowed shorter decompression stops. After the 100-fsw dive, one-third less stop time was needed with light exercise instead of rest during decompression. After the 150-fsw dive, stops were unreasonably long with resting decompression but were practical with exercise.

Thermal Effects

Exercise during decompression may exert part of its effect by warming a diver and preventing the decreased perfusion that accompanies hypothermia.[91] This would reduce decompression risk and stop time because warm divers eliminate nitrogen more rapidly than cold divers.[92]

As with exercise, however, the phase of the dive determines the effect that the thermal state will have upon decompression. A diver who is cold during decompression will *eliminate* less nitrogen while a diver who is cold at depth will *absorb* less nitrogen. Divers who were cold at depth during no-decompression diving were shown to have fewer intravascular bubbles than warm divers.[93] A diver who absorbs additional nitrogen at depth because he is warm will have an increased risk of decompression sickness. Divers in hot water suits are more likely to develop decompression sickness than colder divers in wet suits.[94] In trials of surface decompression with the divers in the water at depth and in a dry chamber during decompression, the incidence of decompression sickness was greater in warm water than in cold water.[83] Divers who are cold during or after decompression have a greater incidence of decompression sickness than warm divers because they eliminate nitrogen less effectively.[95, 96]

Individual Susceptibility

Much of the variability of decompression sickness is a result of differences in individual susceptibility. Fryer, for example, found that of 2199 subjects exposed twice at an altitude of

28,000 feet, 95.2 per cent had no problems, while 4.3 per cent developed decompression sickness once and 0.5 per cent twice.[71] Paton and Walder followed 376 compressed-air workers during 40,000 exposures in which the mean incidence of decompression sickness was 0.87 per cent.[97] Fifty-five per cent of this population had an incidence of below the mean, 11 per cent had an incidence equal to the mean, 6 per cent had twice the mean incidence, and 10 per cent had five times the mean incidence. The remaining 18 per cent had an incidence 28 times the mean, but as these workers quit after only a few exposures, their incidence is not reliable.

Susceptibility to decompression sickness is known to increase with age and obesity. Gray estimated that a 28-year-old man was twice as susceptible to altitude decompression as an 18-year-old, and a 70-inch-tall, 196-lb man was twice as susceptible as a 126-lb man of the same height.[98] Gray found that the best correlation with susceptibility occurred when both age and body type were considered together. Dembert observed that Navy divers who had the greatest skinfold thickness developed decompression sickness nine times more often than thinner divers.[99]

The effect of obesity on decompression risk is readily explained by the high nitrogen solubility in fat which causes increased nitrogen absorption and bubble growth. This was pointed out by Haldane[8] and has been demonstrated frequently in later years. The increased decompression risk with age is probably related to a more frequent occurrence of the vacuum phenomenon which accompanies the degeneration of aging joints.[57–60] Indeed, the vacuum phenomenon is more likely whenever joint surfaces are of eccentric fit,[41] and an eccentric joint configuration might predispose an individual to decompression sickness regardless of age.

RISK AND SAFETY IN DECOMPRESSION

No-Decompression Diving

Decompression risk has become easier to assess since introduction of the method of maximum likelihood.[100] This statistical technique can be applied to binary data, such as the presence or absence of decompression sickness, and has, for the first time, allowed objective analysis of decompression experience.

Maximum likelibood was applied to 1998 air and nitrogen-oxygen no-decompression dives in which there were 136 cases of decompression sickness for an overall incidence of 6.8 per cent.[101] These dives are shown in Figure 4–18 in which the x-axis is bottom time in min, and the y-axis is depth in fsw. The crosses represent at least one decompression incident, and the

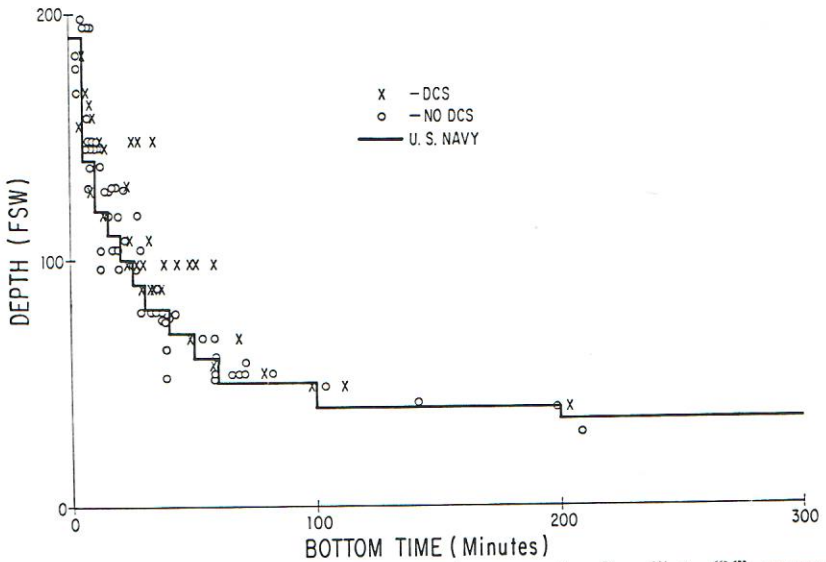

FIGURE 4–18. The results of 1998 air or nitrogen-oxygen no-decompression dives.[101] An "X" represents at least one incident of decompression sickness and an "O" at least one safe dive. The solid line is the U.S. Navy no-decompression exposure limit.[102]

circles represent at least one safe dive. The solid line defines the U.S. Navy no-decompression exposure limits.[102] All dives were included in the analysis whether wet, dry, warm, cold, working, or resting, and no consideration was given to whether the divers had exercised before, during, or after diving or were adapted to decompression by frequent diving.

Analysis of these data by maximum likelihood allows the decompression risk to be estimated for any no-decompression dive. Dives with estimated risks of 1 and 5 per cent are shown as curves in Figure 4–19. Each point on these curves represents the depth and bottom time of a no-decompression dive, which has a predicted risk of 1 or 5 per cent. A 100-min dive to 50 fsw, for example, has a predicted risk of 1 per cent. The Navy no-decompression exposure limits and shorter limits proposed by Huggins are also shown.[103] For dives from 190 to 130 feet, the Navy limits had risks of between 0.5 and 2 per cent. For dives from 120 to 50 feet, the risks fell between 2 and 3 per cent, and for shallower dives, the risks were between 5 and 7 per cent. Huggins' shorter limits reduced the risks to between 0.2 and 2 per cent.

Table 4–5 shows the estimated bottom times for no-decompression dives at 50 and 100 fsw at risks of 1, 2, and 3 per cent. At 50 feet, increasing the risk from 1 to 2 per cent adds 21 min to the allowable bottom time. A 3 per cent risk allows an additional 15 min. At 100 feet, increasing the risk from 1 to 2 per cent adds 5 min, and to 3 per cent, another 4 min. These and other risk estimates[104] apply to the mean behavior of a relatively large diver population and assume that all divers are equally likely to develop decompression sickness. In reality, the risk to a given diver on a specific day depends upon his individual susceptibility and cannot be predicted with certainty.

TABLE 4–5. The Effect of Bottom Time on Decompression Risk for No-Decompression Dives

Depth	Bottom Times at Indicated Decompression Risk (%)		
	1%	2%	3%
50 fsw	69 min	90 min	105 min
100 fsw	16 min	21 min	25 min

From Vann RD: DCS risk and no-stop air diving. Undersea Biomed Res 12(Suppl 1):30, 1985.

Closely related to no-decompression diving, particularly in sport diving, are repetitive and multilevel dives. Several sets of tables exist for these forms of diving, and more are under development, but little information is available on their effectiveness. Limited studies conducted by Thalmann at the Navy Experimental Diving Unit indicate that the Navy repetitive dive tables are overly conservative for some no-decompression dives but not conservative enough for some decompression dives.[105]

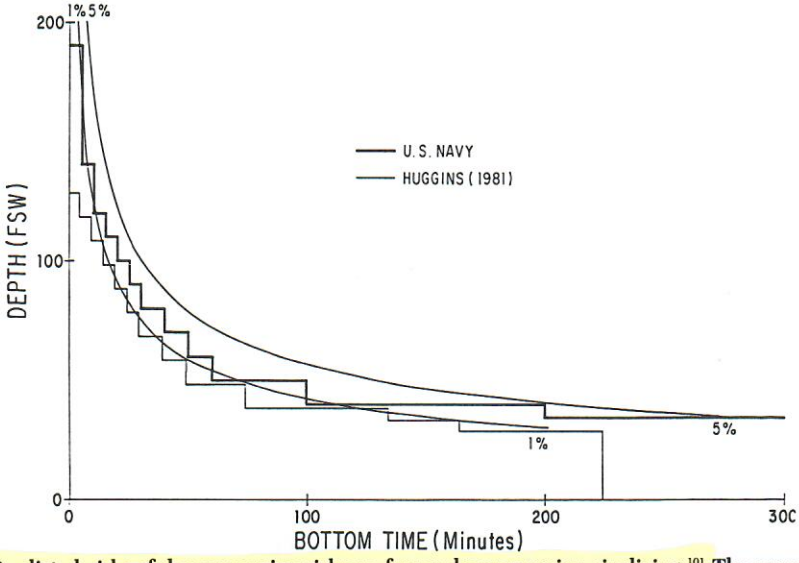

FIGURE 4–19. Predicted risks of decompression sickness for no-decompression air diving.[101] The curves represent 1 per cent and 5 per cent decompression risks. The U.S. Navy no-decompression exposure limits[102] and Huggins shorter exposure limits[103] are also shown.

Decompression Computers

The ultimate solution for multilevel, repetitive diving is the diver-worn decompression computer. This concept is nearly 40 years old, and a number of working models have been manufactured or evaluated,[106–113] but not until recently has the hardware been available to build reasonably reliable instruments.[114–117] These instruments incorporate a mathematical model of the decompression process which must be safe over a wide range of dive profiles. Such a model has not been easy to develop. A decompression computer should be tested under controlled conditions over its expected range of use before it is sold, but just as tests of a new drug cannot cover all possibilities, even decompression trials cannot ensure infallibility.

Because there are no published records documenting the use of decompression computers, it is difficult to draw firm conclusions concerning their safety. Some divers use them extensively and report significant safe increases in repetitive dive bottom times. There have been a few decompression incidents involving computers, however, as would be expected in the wide employment of any decompression procedure. Eight of these cases reported to the Divers Alert Network[118] are presented in Table 4–6. All divers were male, and the computers used appeared to function properly and to have been employed correctly. Table 4–6 shows that six cases involved decompression dives (the 40-year-old diver made cautionary stops), seven involved repetitive dives, seven involved divers older than 30, and eight involved dives to 100 fsw or deeper. If Table 4–6 has a message, it is that divers over the age of 30 who make repetitive decompression dives deeper than 100 fsw are the most likely to develop decompression sickness when decompression computers are used.

Decompression Diving

Even when the number of decompression incidents is known, the decompression risk cannot be estimated without knowledge of how many dives were made. Indeed, risk estimates are difficult to obtain for any decompression

TABLE 4–6. Decompression Incidents Reported to the Divers Alert Network (DAN) After Dives with Decompression Computers

	DIVE PROFILE				SYMPTOMS			
Age	Depth (fsw)	Bot. Time (min)	Dec. Time (min)	Surf. Int. (min)	Onset	Description	TREATMENT	COMMENT
34	136 133	29 19	30 9	180 —	In water	Arm and shoulder pain	None	Decomp. dives previous 2 days
23	120 96	25 22	21 11	180 —	15 min post dive	Arm and shoulder pain	Table 6A: Minor residual stiffness	—
33	174 174	27 18	60 77	240 —	In water	Headache, limb pain, and fatigue	Table 5: Full relief	Untreated symptoms 2 days ago
59	96 90–50	23 22	ND ND	145 —	45 min post dive	Neck and shoulder—pain and numbness	None: Resolved after 1 hr	—
36	108 70	48 30	17 ND	95 —	5 min post dive	Arm pain and tingling; lost dexterity	Table 5: Mild residual stiffness	Hard work on 2nd dive
40	105 40 30	18 55 60	5 3 3	53 161 —	22 hrs post dive in plane	Foot, hand, and cheek—cold and numb	None: Resolved after 24 hrs	1 to 2 ND dives/day previous 6 days
39	140 140 120 100 120	5 5 30 5 5	ND ND 28 ND ND	30 30 60 25 —	5 min post dive	Shoulder pain	Table 6	—
37	224	Unknown		—	In water	Apnea, paralysis, and severe pain	Multiple HBO: Residual paralysis	No problems on similar dives

TABLE 4–7. Estimated Decompression Risks and Safe Decompression Times for U.S. Navy Standard Air Decompression Schedules

	Depth (fsw)	Bottom Time (min)	USN Dec. Time[102] (min)	Est. Risk[104] (%)	Est. Safe Decomp. Time[105] (min)
1.	60	100	15	2–4	—
2.	80	70	24	3	—
3.	100	40	17	0.5	—
4.	60	180	57	11–16	171
5.	80	120	74	10–14	222
6.	150	40	60	5	120
7.	190	30	63	5	60
8.	150	60	113	12–15	>339
9.	190	40	103	9–11	>309

procedure. The U.S. Navy standard air decompression tables[102] are widely quoted, for example, but little information has been available on their safety until the recent tests by Thalmann[105] and the maximum likelihood analysis by Weathersby.[104] Navy schedules with decompression times ranging from 10 to 30 min have estimated decompression risks of 1 to 3 per cent as shown in Table 4–7. Long dives, such as 180 min at 60 fsw or 120 min at 80 fsw, have estimated risks of 10 to 16 per cent and require triple the decompression time specified by the Standard Air Tables. Deeper and shorter dives, such as 40 min at 150 fsw or 30 min at 190 fsw, have estimated risks of 5 per cent and require double the standard decompression time. Longer dives, such as 60 min at 150 fsw or 40 min at 190 fsw, have estimated risks of 9 to 15 per cent and are not safe even with triple the standard decompression time.

Tables requiring longer decompressions than the U.S. Navy Standard air decompression tables have been published in recent years. The Royal Navy Physiological Laboratory (RNPL) air diving tables,[119, 120] developed from the conservative Blackpool compressed air tables,[121] are very long and have a good reputation for safety,[122] although the results of their use are not readily available. The new Canadian Armed Forces tables[123] are shorter than the RNPL tables and were developed in a careful series of laboratory trials[124–127] but have not yet been field tested.

Increasing the decompression time reduces, but does not eliminate, the risk of decompression sickness. Figure 4–20 shows decompression schedules from seven sources for a 20-min air dive to 200 fsw.[8, 102, 119, 128–130] The longest of these schedules, from the RNPL table, was used after a dry chamber dive to 190 fsw.[85] Decompression sickness occurred, despite the schedule's length, when a diver restricted the

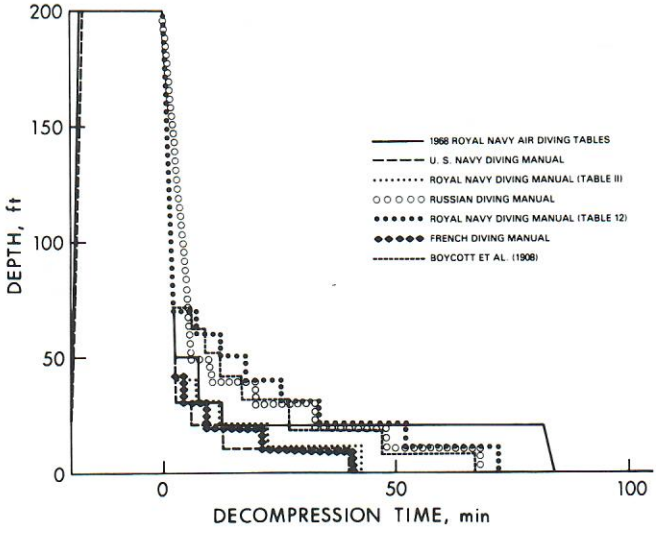

FIGURE 4–20. Seven decompression schedules for a 20-min air dive at 200 fsw. An incident of decompression sickness occurred on the longest of these schedules after a 190 fsw dive during which a diver restricted the circulation to his arm during a nap at the 20 fsw stop. (From Vann RD: Decompression theory and application. *In* Bennett PB, Elliott DH: The Physiology of Diving and Compressed Air Work. 3rd ed. London, Bailliere Tindall, 1982, pp 352–382.)

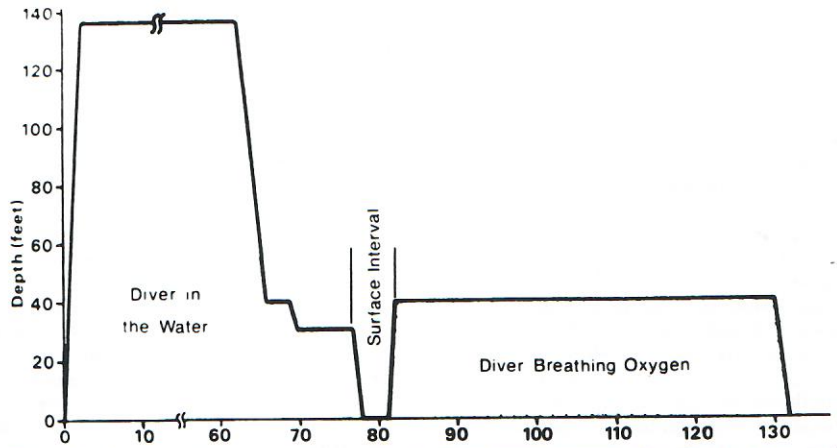

FIGURE 4–21. The U.S. Navy method for surface decompression using oxygen. The diver is removed from the water after his 30 fsw stop and is recompressed within 5 min to 40 fsw in a surface chamber where he breathes 100 per cent oxygen. (From U.S. Navy Diving Manual, NAVSEA 0994-LP-001-9010, January 1979.)

circulation to one arm during a nap at the 20-fsw stop. Once again, physiological factors, particularly when normal function is impaired, significantly affect decompression risk.

Oxygen

Extended bottom times are sometimes necessary in military, commercial, or scientific diving or in compressed-air work[131] but not in recreational diving. This problem is best solved by the careful use of oxygen. An elevated oxygen partial pressure reduces nitrogen absorption at depth and accelerates bubble elimination during decompression (see Oxygen Window section). Both factors decrease the decompression time. Raising the oxygen partial pressure from 0.7 to 1.4 atm reduces decompression time from 90 to 20 min after a 60-min nitrogen-oxygen dive to 100 fsw and from over 195 min to 100 min after a 60-min dive to 150 fsw.[85]

Oxygen is also effective in surface decompression (Fig. 4–21) during which the diver is removed from the water after his 30-fsw stop and is recompressed to 40 fsw in a surface chamber while breathing 100 per cent oxygen.[102] Bubbles that form during the brief surface interval are eliminated by the large oxygen window at 40 fsw in a manner similar to the 60-fsw oxygen treatment tables (see Fig. 4–9). Surface decompression and oxygen breathing, however, introduced hazards not present in air diving and should not be used without proper training and equipment.

SUMMARY

Because of the many environmental and biological factors affecting bubble formation and inert gas exchange, it should not be surprising that decompression sickness is unpredictable and that the safety of a dive is determined by more than just depth and time. Unfortunately, depth and time are the only parameters that can be measured conveniently and must be used to best advantage to estimate the limits of diving safety.

Decompression and other diving hazards make an occasional accident inevitable. While such accidents may be statistically rare, they must be anticipated because their consequences can be both physically and financially devastating.[132] Communications should be available for notifying an accident response system such as the Divers Alert Network,[118] adequate ground or water transportation should be pre-arranged, oxygen should be on-hand for surface use, and recompression facilities should be available within a reasonable distance. Equally important, initial diver training should teach that there are no depth-time limits that confer immunity from decompression sickness or from diving accidents in general. Only with these precautions can the greatest diving safety be assured.

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Chapter 5

Mixed Gas Diving

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Although air has been the standard gas for divers for many years, extensions of depth and time for diving have generated a need for gas mixtures other than air.[1] These may be various mixtures of nitrogen and oxygen[2]; mixtures of helium and oxygen; trimixes of oxygen, nitrogen, and helium[3]; or experimental gas mixtures such as hydrogen-oxygen and neon-oxygen. All of these mixtures provide advantages over air under specific conditions and have been used in either operational or experimental diving.

The term "mixed gas" refers to breathing media other than air or oxygen. The most commonly used gas mixtures are nitrogen-oxygen (nitrox), helium-oxygen (heliox), and helium-nitrogen-oxygen (trimix). Appropriate inspired oxygen partial pressure (pO_2) is a key factor in mixed gas diving. The inspired pO_2 must be maintained lower than 1.6 bar to avoid central nervous system oxygen toxicity and above 0.16 bar to prevent hypoxia. During long saturation dives the inspired pO_2 must be maintained below 0.5 bar to avoid pulmonary oxygen toxicity. Air can be used during saturation excursions from an undersea habitat or saturation chamber, provided pulmonary and central nervous system oxygen tolerance limits are not exceeded and depths are not in the range to produce nitrogen narcosis.

NITROGEN-OXYGEN (NITROX)

Air has been used as a breathing gas since the beginning of diving. Diving bells using compressed air were described in the sixteenth century.[4] Its principal advantage is that it is readily available and inexpensive to compress into cylinders or to use directly from compressors with surface-supplied equipment.[4] It is not the "ideal" breathing mixture because of the decompression obligation accrued by breathing nitrogen at increased partial pressure, and because of the narcotic effects of nitrogen at increased pressure.

Mixtures of oxygen and nitrogen that contain less oxygen than the usual proportions of air (21 per cent oxygen, 79 per cent nitrogen) provide protection from oxygen toxicity with moderately deep diving (>130 feet) and are useful in saturation exposures during which divers are subjected to increased ambient pressure for days.[5] With such exposures, oxygen partial pressure may be high enough to cause pulmonary toxicity after prolonged exposure (see Chapter 8). To prevent oxygen toxicity, the pO_2 must be reduced to levels between 0.2 and 0.35 bar. To achieve this pO_2, nitrox mixtures with reduced oxygen percentage are used. Nitrox mixtures are designed to provide a pO_2 of 0.3 to 0.35 bar at saturation depth. Table 5–1 shows typical nitrox mixtures for shallow habitat saturation exposures. Numerous shallow habitat saturation exposures have been carried out during the past two decades. These ranged in depth from 30 fsw to 140 fsw[6] and employed normoxic nitrox mixes or air.[5] In these studies no evidence of pulmonary oxygen toxicity was found in exposures up to 30 days.[7]

When exposing saturation divers to normoxic nitrox mixtures, care must be taken to prevent exposure to mixtures that contain dangerously low levels of oxygen. Such exposures can occur in nitrox mixtures of less than 15 per cent oxygen at 1 ata. Nitrox saturation dives begin with air if the dive is shallow (e.g., 40 fsw, where pO_2 = 0.44 bar); one technique used to establish a safe pO_2 is to allow the oxygen to be consumed in the habitat to the percentage

TABLE 5–1. Characteristics of Nitrox Mixtures Used for Habitat Saturation Diving

SAT. DEPTH *fws*	SAT. PRESS *bar abs*	O_2-AIR %	pO_2-AIR *bar abs*	O_2-NITROX %	pO_2-NITROX *bar abs*
40	2.21	21	0.46	13.6	0.3
60	2.82	21	0.59*	10.6	0.3
80	3.42	21	0.72*	8.8	0.3
100	4.03	21	0.85*	7.4	0.3
120	4.64	21	0.97*	6.5	0.3
140	5.24	21	1.10*	5.7	0.3

*Air cannot be used at these depths because of pulmonary oxygen toxicity.

required by replacing atmospheric gas with small amounts of 100 per cent nitrogen.[8] Once a normoxic concentration is established in the habitat, oxygen is replenished to match consumption and maintain pO_2 at the decided concentration. More commonly, the chamber is compressed to about 16 fsw with air to achieve a pO_2 of 0.35 bar, then the remainder of the compression is done with nitrogen. Carbon dioxide must also be removed in this closed environment. This is usually done with a carbon dioxide absorbent such as lithium hydroxide.

Two nitrox mixing patterns are shown in Figure 5–1. In the left panel is depicted a typical nitrox mixing pattern for a small habitat with two divers saturated at 66 feet for several days. In this example pO_2 will fall from the initial 0.6 bar to 0.3 bar over 41 hours as the two aquanauts consume oxygen. During this period consumed oxygen is replaced by nitrogen to achieve the desired mixture. Once a 10 per cent oxygen mixture is established, oxygen is replenished as consumed and carbon dioxide is scrubbed from the atmosphere. The right panel of Figure 5–1 shows a more typical procedure. Air is used for compression to 16 fsw (0.30 bar O_2). The remainder of the compression is with 100 per cent nitrogen. Consumed oxygen is replaced by adding air or oxygen. Normoxic nitrox mixtures create problems with narcosis at depths greater than 120 fsw, and helium is commonly used below that depth.

Decompression

Although a benefit is achieved with normoxic nitrox (pO_2 between 0.21 and 0.35 bar) with regard to pulmonary oxygen toxicity in saturation dives, a greater decompression debt is incurred owing to the increased partial pressure of nitrogen. The increased nitrogen partial pressure results in greater tissue content of nitrogen than is achieved when breathing air. Using normoxic mixtures for short duration (subsaturation) dives would result in significant increases in decompression time with little advantage in lung protection from oxygen. In saturation diving, however, the longer decompression time is tolerable as an alternative to pulmonary oxygen toxicity. Extension of decompression time for saturation diving can be accounted for in operational planning.

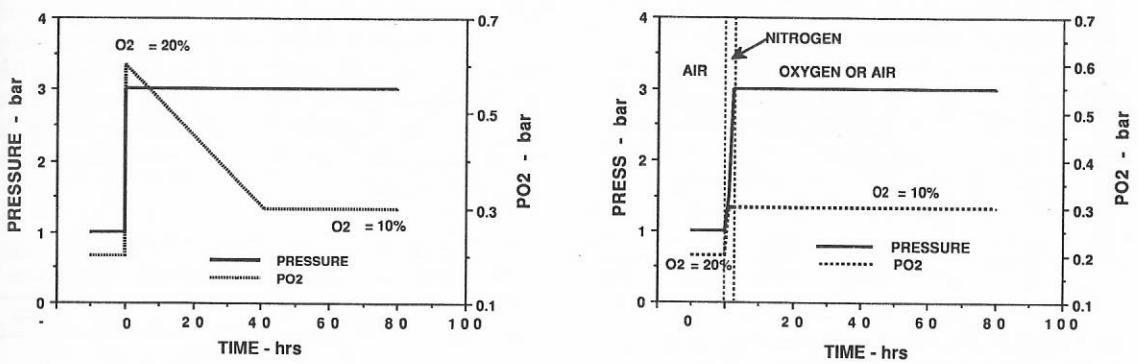

FIGURE 5–1. Two methods for changing nitrogen and oxygen concentrations in a saturation diving habitat. In the left panel, divers descend to 3 bar pressure (66 fsw) in the chamber, and breathe down the oxygen concentration until it reaches 0.3 bar and 10 per cent concentration. Nitrogen is added to replace consumed oxygen until the desired percentage of oxygen is achieved. In the right panel, the diving habitat is compressed to 0.3 bar pO_2 (16.5 fsw) with air, then compression is continued with 100 per cent nitrogen to achieve 66 fsw (3 bar) depth. Air or oxygen is added to maintain the 10 per cent O_2 environment.

Oxygen-Enriched Nitrox

Recently, interest has been expressed in nitrox mixtures that have increased oxygen partial pressure. Mixtures of 30 per cent oxygen, for example, contain a reduced partial pressure of nitrogen and, compared with air dives at the same depth, result in less nitrogen content of tissues. The mixture thus confers a decompression safety factor if standard air decompression procedures are followed, or longer dive times can be achieved at the same depth because the nitrogen partial pressure is equivalent to partial pressures of nitrogen at shallower depths with air. Figure 5–2 illustrates equivalent nitrogen partial pressures for actual depth with several oxygen-enriched nitrox mixtures.

The decompression procedure that must be followed when nitrox is used is based on the concept of equivalent air depth (EAD). This procedure equates the inspired nitrogen pressure of a nitrox mixture at one depth to that of air at another depth—the EAD. This procedure has been used for over 20 years with semiclosed and closed-circuit mixed gas underwater breathing apparatus. Such equipment is both very expensive and complicated. In recent years, nitrox use in open-circuit diving equipment has increased significantly. The following equation is used to calculate the EAD:

$$EAD = [\frac{(1 - fiO_2)}{0.79} \times (D + 33)] - 33$$

where fiO_2 = decimal fraction of oxygen in the mixture and D = depth in feet. For example, using 32 per cent oxygen, 68 per cent nitrogen, and a depth of 130 feet,

$$[\frac{(1 - .32)}{0.79} \times (130 + 33)] - 33$$

EAD = 107.3 fsw.

Using the next deeper standard air decompression table (110 fsw), the diver would be able to descend to a depth of 130 feet and follow no-decompression limits or decompress as if the dive were made to 110 feet. The no-decompression time for an air dive to 130 feet (U.S. Navy standard decompression tables) is 10 minutes, while 20 minutes would be available using a 32 per cent oxygen nitrox mixture. A standard nitrox mixture containing 32 per cent oxygen has been adopted by the National Oceanic and Atmospheric Administration (NOAA) to avoid the computation errors and oxygen limitation problems often encountered during EAD calculations. This standard mixture is known as NOAA nitrox I (NNI); 130 feet is the maximum depth to which this mixture can be used without exceeding oxygen limits. No-decompression limits for several gas mixtures are shown in Table 5–2.

Although longer bottom times can be achieved with oxygen-enriched nitrox, two serious problems can arise when using these mixtures. There is a real risk of acute central nervous system oxygen toxicity when those mixtures are used improperly in operational diving. The acceptable maximum oxygen partial pressure to prevent acute oxygen toxicity during diving (U.S. Navy standards) is 1.6 bar (20 fsw with 100 per cent oxygen). With a 40 per cent oxygen mixture, this level is achieved at 4.4 bar (113 fsw). Divers using enriched-oxygen nitrox must be aware of the potential for acute oxygen toxicity, which is usually manifest by a seizure with deeper dives (Fig. 5–2). An underwater seizure is a catastrophic event that is likely to cause death of the diver and risks others who attempt rescue.

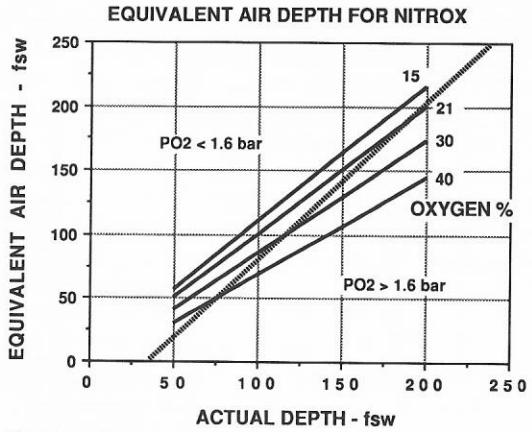

FIGURE 5–2. Equivalent air depths when using oxygen-enriched nitrox at several concentrations of oxygen. Equivalent depth is less than actual depth for mixes with greater than 21 per cent oxygen. The diagonal dotted line identifies the boundary for safe oxygen partial pressure (<1.6 bar). When diving with enriched nitrox mixtures, depth should not exceed the intersection of the dotted line and the mixture line.

TABLE 5–2. No-Stop Times for Dives from 40 to 120 fsw, Using Several Gas Mixtures

FSW →	40	60	80	100	120
Air	200	60	40	25	15
He (0.7)	390	133	51	29	18
N_2 (0.7)	367	74	39	27	19
NN1 (32%)	310	100	59	40	25

Helium and nitrogen are mixed to constitute 70 per cent, with oxygen the remaining 30 per cent. NN1 is NOAA nitrox 1, a 32 per cent oxygen mixture. Time is given in minutes.

A second problem with oxygen-enriched nitrox is the need for precise mixing of the gases to establish known concentrations of oxygen and nitrogen. Increased pO_2 nitrox mixtures are readily made by adding air to oxygen under pressure. Gas proportions in these mixtures are often determined by calculating partial pressures. Although this technique is theoretically capable of determining exact gas partial pressures, inaccuracy of gauges and manifolds often results in mixtures that deviate from calculated values. These mixtures should be analyzed for gas content by independent gas analysis to be certain of oxygen safety limits and to determine an equivalent depth for calculation of decompression schedules. Errors in gas composition that produce errors of 5 to 10 fsw in equivalent depth will result in improper decompression and can increase risk for decompression sickness. Divers using oxygen-enriched breathing gas must be familiar with the complexities of partial pressure tables and calculate new decompression schedules based on the nitrogen partial pressure of the breathing gas. It should be obvious that dive computers, often used for air decompression, cannot be used with oxygen-enriched nitrox because their gas kinetic models are based on the usual nitrogen concentrations found in air. Meters should become available for use with nitrox.

HELIUM-OXYGEN (HELIOX)

Helium-oxygen gas mixtures were studied in the 1930's by Behnke and Willmon,[9] and End described a deep heliox dive in 1938. These investigators were searching for an inert gas that could eliminate the problem of narcosis found with air breathing below 150 fsw. Operational diving was limited to depths shallower than 150 feet in the early twentieth century due to severe narcosis produced by air breathing.[10] The laboratory studies of Behnke and Willmon were tested operationally when the submarine *Squalus* sank in 240 fsw.[11] Recovery of the submarine and rescue of the crew were accomplished using surface-supplied helium-oxygen diving. At the completion of this operation, heliox diving was established as the method for deep diving (below 150 fsw). The clarity of thought and the manual dexterity retained on helium at depths below 200 fsw were praised by divers at the time as a major advance.

Since this early experience with helium, diving to depths greater than 2000 fsw has been accomplished with this gas mixture, and extensive research on its effect has been conducted (see Chapters 4, 7, and 23). The ability of helium to prevent narcosis is most likely based on lipid-water partition coefficients and lipid solubility.[12] The low solubility of helium in lipid appears to contribute to its non-narcotic properties.[13–15] The lack of narcotic effects of this gas unmasked a new diving disorder—the high pressure nervous syndrome (HPNS)—which appears to result from direct pressure effects on excitable cells and a complete lack of narcotic effect of helium (see Chapter 7 for further discussion).

Surface-Supplied Heliox Diving

Surface-supplied heliox diving remains useful for single survey and rescue dives or for short duration working dives for which surface decompression can be used to shorten in-water decompression time. Current practice is to use saturation diving with heliox for diving projects below 150 fsw when a large amount of dive time is needed (e.g., 40 or more man-hours). Surface-supplied helium diving is an extension of surface-supplied air diving and as such follows many of the operational procedures developed for air diving. Important differences, however, do exist between air and heliox surface-supplied diving.

Because heliox mixtures vary in oxygen content as a function of diving depth to avoid oxygen toxicity, tables for decompression from surface-supplied dives are based on helium partial pressure and not on actual depth. The U.S. Navy helium-oxygen decompression tables illustrate the fundamental principles of mixed gas diving and oxygen decompression. The arrangement of the tables is such that the partial pressure of helium (pHe) in the breathing medium (not depth) and time are the factors that determine decompression obligation. To select an appropriate decompression schedule, the pressure (expressed in feet of seawater absolute, fswa) of the dive is multiplied by the fraction of helium (fiHe) in the breathing medium to determine the partial pressure of helium. For example,

$$\text{Depth} = 200 \text{ fsw}, \; fiO_2 = 0.2, \; \text{fiHe} = 0.8$$
$$(200 + 33) \times .80 = 187 \text{ pHe (fswa)}$$

A helium partial pressure table of 190 fswa would then be the appropriate decompression schedule for this dive, and the actual time of the dive would be used to determine decompression obligation.

Standard heliox partial pressure tables are available in the U.S. Navy Diving Manual.[16] Many commercial diving corporations use alternate helium partial pressure tables that often are proprietary. Tables for helium-air decompression are also available. Decompression schedules for heliox are determined for the depth of dive and for the partial pressure of helium achieved in the dive, which depends on the percentage of helium and the depth. Most heliox decompression schedules require a switch to 100 per cent oxygen at 50 fsw and usually incorporate surface decompression with oxygen to reduce total in-water time. During ascent and decompression stops, the helium-oxygen mixture is breathed until 50 fsw is reached, at which point the breathing medium is changed to oxygen. Oxygen breathing continues throughout the 50 and 40 fsw decompression stops. At the end of the 40 fsw stop the diver is brought directly to the surface. Provisions within the tables also allow for surface decompression (in a chamber) for the latter part of decompression. The surface decompression has several advantages: the diver is in a controlled chamber environment where loss of body heat is prevented, communications are improved, and oxygen toxicity can be detected and treated early. Another advantage is that the diving support vessel can break its moor and get under way rather than remain on station for the total decompression time. Table 5–3 is calculated from the U.S. Navy surface-supplied helium-oxygen decompression tables[16] and shows a typical decompression profile for heliox diving. During the "bottom time" of a dive, the oxygen content of the breathing medium is maintained as high as is allowed by the oxygen partial pressure limits, thereby keeping the partial pressure of helium as low as possible and reducing the rate of helium uptake.

TABLE 5–3. Decompression Profile for a Helium-Oxygen Dive

DEPTH *fsw*	TIME *min*	GAS
110	7	$He\text{-}O_2$
90	2	$He\text{-}O_2$
80	6	$He\text{-}O_2$
70	7	$He\text{-}O_2$
60	10	$He\text{-}O_2$
50	10	O_2
40	87	O_2

Table is calculated for a 250 fsw dive or 30 mins using 16% oxygen in helium and a U.S. Navy MK-12 surface-supplied diving system. Helium partial pressure table for this time-depth and oxygen percentage give a partial pressure table of 244 fsw, which is rounded off to the next highest depth of 250 fsw absolute.

Some commercial diving tables expand even further on the above principles by adding air and nitrox mixtures at various points in the dive profile. If the breathing medium during deep decompression stops of a helium-oxygen dive is changed from helium-oxygen to air at a depth where nitrogen narcosis and oxygen toxicity are not limiting, helium elimination will occur at the maximum possible rate since there will be no helium in the inspired gas. Some nitrogen uptake will occur during this time, and therefore the total tissue insert gas partial pressure will not drop as fast as if oxygen were breathed. However, a more rapid reduction in the total inert gas pressure will occur owing to the physical properties of the gases. On ascent from shallower depths, a nitrox mixture containing more oxygen than air (but with an acceptable pO_2) can be used to reduce the nitrogen in the breathing medium. When the breathing medium at shallow depths (< 50 fsw) is switched to oxygen, both helium and nitrogen will be eliminated at the maximum possible rates. This type of procedure can reduce total ascent time for a particular dive when compared with the U.S. Navy tables and can reduce the quantity of expensive helium required for the dive. Numerous variations of this generic type of dive profile exist in the commercial diving industry. Most decompression schedules for heliox require longer decompression time than that for air. In some no-decompression dives, use of heliox may provide slightly longer bottom times.[16] Table 5–2 illustrates this point with several gas mixtures.

Saturation Diving with Heliox

An important advance in diving technology resulted from the work of Bond,[17] who conducted saturation experiments with heliox.[18] This work demonstrated that divers could spend prolonged periods (weeks) under pressure without serious physiological changes. Working dives using this technique have been conducted at depths over 1000 feet in open sea for periods of up to 3 to 4 weeks. Breathing gases for these saturation dives are mixed with extreme care, since dives of 1000 feet where normoxic mixtures (0.3 to 0.5 bar oxygen) require that oxygen concentrations be held to tolerances of 0.10 per cent to avoid hypoxia and oxygen toxicity. Figure 5–3 shows typical percentage of oxygen in heliox for various depths. Changes of less than 1 per cent at deeper depths can shift the oxygen level to an unsafe proportion.

Typical deep saturation diving operations at

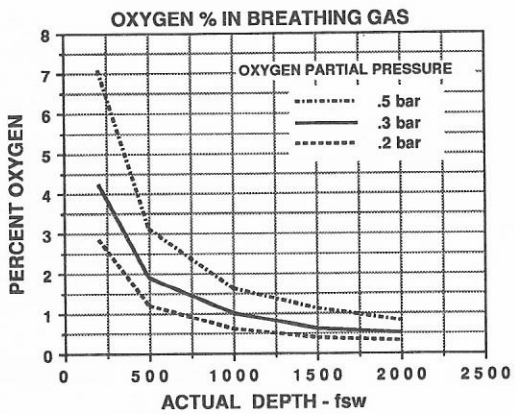

FIGURE 5–3. Oxygen percentage of heliox for deep diving. Three oxygen concentrations are shown, which span the safe pO_2 range for avoiding oxygen toxicity.

present avoid sea floor habitats as originally conceived by Bond and co-workers.[17, 18] Although habitat operations are useful for scientific or exploratory projects, underwater construction, particularly in undersea oil recovery operations in deep water, cannot be supported by underwater habitats. Most working saturation dives are currently conducted using a shipboard chamber (deck decompression chamber [DDC]) and a pressurized transfer chamber (PTC) that delivers divers to the worksite (Fig. 5–4). With this method, divers can be easily supported by a ship's crew through transfer locks on the shipboard chamber for the duration of the dive, then decompress once over several days. The DDC can be supported easily compared with a sea floor habitat. The transfer chamber is mated to the DDC and is pressurized to equalize with the pressure inside the DDC, which is held at the pressure of the worksite. Divers transfer from the habitat chamber to the transfer chamber under pressure. When all hatches are secured, the transfer chamber is detached and lowered to the worksite, where one or more divers can leave the transfer chamber to perform whatever work is needed. Continuous shifts of divers can conduct operations on a 24-hour schedule in prolonged projects.

The Helium Environment

With the frequent use of helium saturation diving, several unique problems were discovered which result from the helium gas. Because of its small molecular size, helium is highly diffusible and can penetrate many pressure seals not affected by nitrogen. Electronic parts, cables, vacuum tubes, and pressure-proof watches are examples of equipment that has been damaged by unexpected penetration of helium. However, design modifications of equipment to be used in heliox environments have eliminated most of the helium diffusion problems.

An amusing but troublesome problem with helium atmospheres is the change in voice which has become characteristic of this environment.[19] The high-pitched "Donald Duck" quality of the voice at first imports humor, which soon reverts to concern for communication with the divers. The voice change induced by helium renders communication difficult and in many cases impossible. Initial efforts to communicate under these conditions depended on memorized responses so that dive supervisors could translate the poorly understood communication.

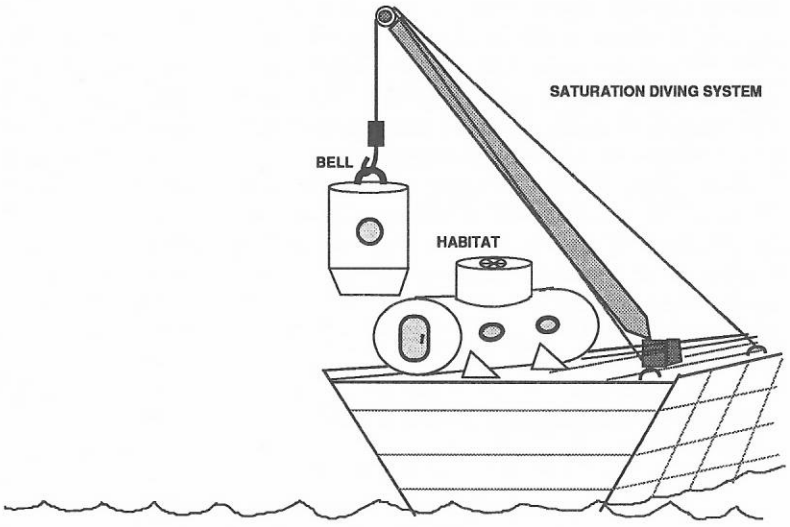

FIGURE 5–4. Schematic diagram of a saturation diving system. A deck chamber (habitat) provides long-term shelter for divers under pressure. A transfer chamber is used to lower the divers under pressure to the worksite. Between work tasks, divers reside in the habitat chamber until the work is complete. Decompression is done over several days in the habitat chamber.

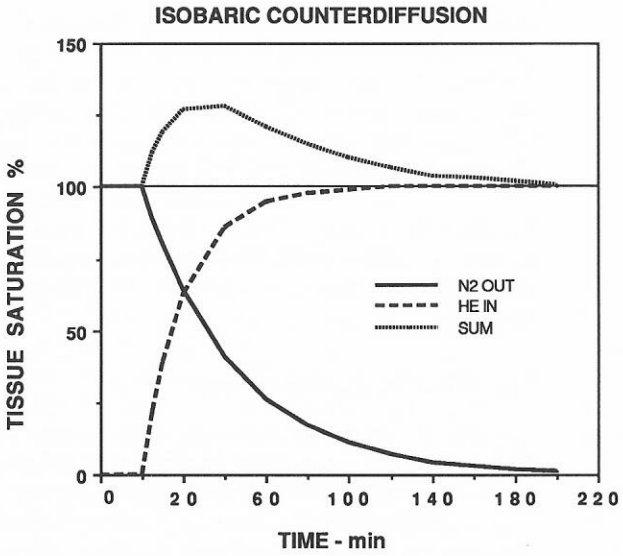

FIGURE 5–5. Tissue gas concentration curves during switching of two breathing gases of differing diffusion rates. The incoming gas diffuses more rapidly than the outgoing gas; a net increase in inert gas concentration curves can cause decompression sickness. Curves shown are typical of a switch from air to heliox at constant pressure.

Electronic voice encoding has significantly improved communications. This technique reconstructs normal voice characteristics by frequency filtering and spectral shifting. The resultant voice, although not ideal, significantly improves communicability of divers conversing in a heliox environment.

Physiological effects of heliox were studied in a series of dives conducted by a joint American-Japanese research team (operation Sea Dragon). Recounting of this work is provided in several papers by Hong and co-workers.[20–22] They noted an increase in basal metabolism in divers living at a depth of 985 fsw. All divers lost weight in spite of increased food consumption[21] and felt cold when ambient temperature fell below 80°F. This latter perception is predictable from the high thermal conductivity of compressed helium. Most divers in a helium environment need several blankets to keep warm when sleeping, even when ambient temperature is near 80°F.[22] Cardiac conduction and contractile force may also be affected by helium. Ask and Tyssebotn[23] recently demonstrated altered cardiac performance in rabbits exposed to 960 fsw helium. Their data show small effects that are likely to be insignificant in humans; however, the finding of an inert gas effect in cardiac tissues is of interest. Helium effects on the central nervous system are discussed in detail in Chapter 7 and will not be repeated here.

HELIUM-NITROGEN-OXYGEN (TRIMIX)

Bennett's discussion of trimix and of the Atlantic series of dives in Chapter 7 provides adequate review of this topic. This gas mix is used at deep depths (over 2000 fsw) to alleviate HPNS.[1, 24, 25] The theoretical basis for this mixture is discussed in Chapter 7. The successful use of this mixture by Bennett and colleagues[26] is an excellent example of basic research applied to operational diving. Reduction of HPNS with trimix was accomplished by the addition of 5 to 10 per cent nitrogen to heliox. The small amount of nitrogen opposes the hyperexcitable state that results from a high pressure helium environment.[26]

Trimix is also used in shallower working dives to reduce the cost of helium and to reduce narcotic effects of nitrogen. In this case, helium is added to air in varying proportions.

HYDROGEN-OXYGEN

Hydrogen offers the potential for minimal narcotic effects based on its solubility.[12, 13, 15] An important operational limitation of hydrogen use, however, is its extreme flammability. Mixtures of hydrogen and oxygen are explosive except in situations where the percentage of oxygen is less than 2 per cent.[27] Mixtures of this type are applicable at depths below 600 fsw (see Fig. 5–3). Gardette, Rostain, and coworkers[27, 28] recently described several successful hydrogen-oxygen dives to 1480 fsw. On such a dive, divers begin with heliox, and at 650 fsw (200 msw) switch to a nonexplosive mixture of hydrogen-helium-oxygen. On return to the surface, the breathing gas is switched back to heliox when a higher percentage of oxygen is required. Gas switching of this kind under pressure can result in decompression sickness from counter-

diffusion of gases (see below). Deep hydrogen-oxygen diving eliminates the need for large stores of helium. The use of helium in deep diving and other demands for helium have increased the cost and have reduced the availability of this gas. Hydrogen gas can be obtained from electrolysis of water and is potentially more abundant than helium. Although most current hydrogen diving is experimental, the diminishing supply of helium may make hydrogen-oxygen gas mixes an attractive alternative to helium in the future.

OTHER INERT GASES

Although mixtures containing neon, argon, and xenon[14, 29] have been used experimentally in deep diving exposures, none of these gases are useful because of their narcotic properties and in some cases their increased density, which limits ventilation. These gases are obtained by fractional distillation of liquefied air and are expensive to produce.

ISOBARIC COUNTERDIFFUSION

During the PSIV series of deep dives conducted by Lambertsen and co-workers,[30] gas-containing skin lesions were found in some divers exposed to 1000 fsw pressure breathing a helium-neon-oxygen mixture while in a helium-oxygen environment. These skin lesions were eliminated when the diver was placed in a sealed suit and surrounded by the same gas as the breathing medium.[30] Graves and colleagues[31] reported further observations on this phenomenon and described the diffusion kinetics responsible for the effect. Figure 5–5 shows the mechanism that causes gas phase to form in tissues during switching of gases at fixed ambient pressure. The effect requires that two gases have different diffusion and solubility coefficients, and the gas with the higher coefficient replaces the lower coefficient gas. Under these conditions the high coefficient gas diffuses rapidly into tissue, while the low coefficient gas diffuses out more slowly. Total inert gas concentration will rise and supersaturate tissues. The supersaturation can reach levels that cause gas phase formation and clinical decompression sickness. Counterdiffusion effects can be separated into superficial effects involving the skin and deep effects involving other organs and tissues not affected by the surface interface with the inert gas. Superficial counterdiffusion depends on gas diffusion through the skin and causes bubbles in superficial tissues, including skin and subcutaneous tissue. Deep counterdiffusion occurs in tissues without exposed surfaces and depends on perfusion to supply and remove inert gas. Typical gas switches that cause gas phase formation are air to helium, hydrogen to helium, neon to helium,[32] and, in experimental animals, nitrous oxide to nitrogen.[33] In operational diving, gas switches suspected of causing a counterdiffusion problem are accompanied by a small pressure increase to avoid supersaturation.

Other operational aspects of mixed gas diving, such as excursion from saturation, mixed gas scuba, mixing of gases, and undersea habitats, can be found in references 34, 35, 36, and 37.

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Chapter 8

The Toxicity of Oxygen, Carbon Monoxide, and Carbon Dioxide

STEPHEN R. THOM *and* JAMES M. CLARK

OXYGEN

Paradoxically, the same gas that is required to sustain life by preventing loss of consciousness and death from hypoxemia has toxic properties that affect all living cells at sufficiently high pressure and duration of exposure.[1–4] The rate of development of toxic effects is determined by the oxygen partial pressure (pO_2) rather than the oxygen percentage of the inspired gas. The specific manifestations of oxygen poisoning that occur in humans or animals are determined by interactions between oxygen dose, with respect to both pO_2 and duration of exposure, and relative susceptibilities of the exposed tissues. Although continued exposure to a toxic pO_2 will ultimately cause functional disruption and cellular damage in any organ system of the body, effects on the lung, brain, and eye are most prominent under practical conditions of exposure. These effects are described below.

Biochemistry of Oxygen Toxicity

Gerschman[5, 6] and Gilbert[7, 8] first proposed that oxygen toxicity is caused by the production of free radical intermediates in excessive concentrations during exposure to increased oxygen pressures. The initial involvement of these agents is now well established, and several excellent reviews summarizing what is known about the biochemistry of oxygen free radicals are available.[9–13] Although exact mechanisms are not yet known, free radical intermediates including superoxide anions, hydrogen peroxide, hydroperoxy and hydroxyl radicals, and singlet oxygen are potentially toxic to cell membranes, enzymes, nucleic acids, and other constituents. Along with better understanding of oxygen free radicals has come a greater awareness of the universal dependence of vital biological processes on cellular antioxidant defenses such as superoxide dismutase, catalase, and the glutathione system. It is now thought that the same oxygen pressures required to sustain life would cause lethal oxygen poisoning in the absence of these defenses.

Pulmonary Oxygen Toxicity

Studies in the monkey[14–17] have shown that the pathological response of the lung to oxygen toxicity can be differentiated into two overlapping phases of progressive deterioration. The first is an acute exudative phase consisting of interstitial and alveolar edema, intra-alveolar hemorrhage, fibrinous exudate, hyaline membranes, swelling and destruction of capillary endothelial cells, and destruction of type I alveolar epithelial cells. The exudative phase merges into a subacute proliferative phase that is characterized by interstitial fibrosis, fibroblastic proliferation, hyperplasia of type II alveolar epithelial cells, and partial resolution of earlier acute changes. The relative prominence

of individual components in each phase is influenced by interactions of external variables, such as level of inspired pO_2 and exposure duration, with internal factors such as species differences in pulmonary tissue reactivity and susceptibility to hyperoxic exposure.

Pathological changes that are similar or identical to those caused by pulmonary oxygen toxicity in experimental animals are also found in the lungs of human patients who die after prolonged oxygen therapy.[18–21] Although such alterations are not specific for pulmonary oxygen poisoning, the clinical course of these patients in conjunction with the known susceptibility of humans to oxygen toxicity leave no reason to doubt that the observed pathological changes are in fact caused by pulmonary oxygen toxicity. In experimental animals and presumably also in humans, recovery from pulmonary oxygen intoxication is accompanied by complete resolution of changes typical of the acute exudative phase of pathology. When exposure to hyperoxia is sufficiently prolonged for the development of prominent proliferative changes, however, recovery from these pathological effects is greatly delayed and incomplete resolution may leave permanent residual scarring of the lung.

Symptoms of pulmonary oxygen poisoning begin insidiously as a mild substernal irritation that becomes progressively more intense and widespread in parallel with increasing frequency of cough. When extreme in degree, symptoms that appear to originate in the trachea and major bronchi are characterized by a constant burning sensation, which is exacerbated by inspiration and is associated with uncontrollable coughing. The most severe symptoms are associated with dyspnea on exertion or even at rest. Onset of symptoms is variable among different individuals but usually occurs after about 12 to 16 hours of exposure at 1.0 ata,[22] 8 to 14 hours at 1.5 ata,[23, 24] and 3 to 6 hours at 2.0 ata.[25, 26]

Changes in pulmonary function which have been measured in humans during and after prolonged exposures to oxygen pressures of 1.0 ata or higher include decrements in inspiratory and expiratory lung volumes and flow rates, carbon monoxide diffusing capacity, and lung compliance.[2, 4, 22–30] Arterial oxygenation was maintained at rest during early reversible stages of pulmonary intoxication[26, 29, 30] but was detectably impaired during exercise after exposure for 48 to 60 hours at 1.0 ata[29] or for 16 to 19 hours at 1.5 ata.[23, 30] In normal humans exposed continuously to oxygen pressures ranging from 1.0 to 3.0 ata, pulmonary mechanical function is impaired earlier and more severely than gas exchange function.[24, 30]

Although it is not possible to identify with certainty a level of hyperoxia which can be tolerated indefinitely with no pulmonary effects, normal humans have been exposed for periods ranging from 7 days at 0.55 ata[31] to 30 days at 0.3 ata[32, 33] with no detectable manifestations of pulmonary intoxication. However, exposure for 24 hours at 0.75 ata causes pulmonary symptoms in association with a significant decrease in vital capacity,[22] and the rate of pulmonary intoxication increases progressively at higher oxygen pressures.[24–26, 30] Nevertheless, the great majority of current applications of hyperoxia in therapy and diving do not cause pulmonary symptoms or functional deficits.[34]

Administration of hyperbaric oxygenation causes pulmonary symptoms in patients only when used very aggressively for serious conditions, such as severe decompression sickness or arterial gas embolism. Some degree of substernal discomfort is also frequently experienced by commercial divers who use intermittent hyperoxia to hasten inert gas elimination after unusually long or deep dives. When hyperbaric oxygenation is combined with saturation exposure in the treatment of refractory decompression sickness, it is not uncommon for the attendants and the patient to experience pulmonary symptoms. In all of these situations, irreversible pulmonary intoxication can be avoided by careful monitoring of symptoms and appropriate alternation of hyperoxic and normoxic exposure periods.

Central Nervous System Oxygen Toxicity

Overt manifestations of CNS oxygen poisoning include the diverse symptoms and signs listed in Table 8–1. These observations were made in divers who breathed oxygen at pressures of 3.0 ata or higher until they experienced neurological effects. The studies were designed to develop reliable methods for detecting the onset of CNS oxygen poisoning prior to the occurrence of convulsions.

Extensive investigation in hundreds of divers failed to identify a consistent preconvulsive index of CNS oxygen poisoning. Minor symptoms did not always precede the onset of convulsions, and even when a preconvulsive aura did occur, it was often followed so quickly by seizures that it had little practical value. Electroencephalography also proved to be a poor

TABLE 8–1. Signs and Symptoms of CNS Oxygen Poisoning in Normal Men

Facial pallor	Respiratory changes
Sweating	Hiccoughs
Bradycardia	Air hunger
Palpitations	Inspiratory predominance
Depression	Diaphragmatic spasms
Apprehension	Nausea
Visual symptoms	Spasmodic vomiting
Dazzle	Fibrillation of lips
Constriction of visual field	Lip twitching
Tinnitus and auditory hallucinations	Twitching of cheek, nose, eyelids
Vertigo	Syncope
	Convulsions

Adapted from Donald KW: Oxygen poisoning in man. Br Med J 1:667–672, 712–717, 1947.

index of incipient CNS intoxication, because brain electrical activity was not altered consistently prior to seizure onset. More recent studies have confirmed that EEG alterations in humans occur only upon initiation of the actual seizure.[35]

Although mechanisms are not known, it is well established that exercise and underwater immersion, independently or together, accelerate the onset of oxygen convulsions and can precipitate their occurrence at oxygen pressures as low as 1.6 ata.[36–39] Oxygen convulsions are also accelerated by the presence of acute hypercapnia, whether it be induced by elevation of inspired pCO_2, increased breathing resistance, or narcotic depression of ventilation.[3] The adverse effects of acute hypercapnia are mediated by cerebral vasodilation and delivery of a higher oxygen dose to the brain.[40]

Extensive investigation in animals and in humans[1, 3, 4, 35, 37] has established that oxygen convulsions are not inherently harmful. However, the condition under which they occur may make them extremely hazardous. For example, the occurrence of convulsions in an unattended diver can lead to death by drowning. Similarly, convulsions are especially hazardous in patients with fractures, osseous nonunion, head injury, cardiac abnormality, or recent surgery.

CNS oxygen toxicity in association with hyperbaric oxygen therapy is rare. The reported incidence of convulsions is approximately 0.01 per cent when care is taken to screen against factors that are known to increase risk of intoxication.[34, 41]

Visual Effects of Oxygen Toxicity

Visual manifestations of oxygen poisoning are influenced by many variables in addition to oxygen dose.[3, 42] These additional influences include the age of the exposed individual, the method of oxygen administration, and the presence of underlying conditions that may modify susceptibility to oxygen poisoning.

Retrolental Fibroplasia

Retrolental fibroplasia is a unique condition that may be induced by exposure of the premature infant to any elevation of arterial pO_2 above the normal range.[3, 42] Risk factors include gestational age less than 30 weeks, birthweight less than 1500 grams, and concurrent problems such as sepsis and intraventricular hemorrhage.[43, 44] Initial constriction of the developing retinal vessels is followed by endothelial cell destruction and arrest of the retinal circulation at an incomplete stage of development.[3, 42, 43] The remaining endothelial cells later undergo a disorganized and profuse proliferation to produce a fibrous mass of vascular tissue that ultimately causes irreversible retinal detachment and permanent blindness. Vitamin E therapy is apparently effective in reducing the severity of retrolental fibroplasia.[44]

Irreversible Effects on Visual Function

Animal studies involving extremely prolonged oxygen exposures have demonstrated severe pathological effects, such as visual cell death, retinal detachment, and cytoid body formation.[42] In guinea pigs exposed to oxygen at 3.0 ata, histopathological changes found in the corneal endothelium and lens epithelium, as well as in the retinal plexiform and inner nuclear layers, indicate that pathological effects may be more severe when the entire eye is exposed to oxygen than when hyperoxygenation occurs only by the arterial circulation.[45]

Histological studies of oxygen-induced ocular pathology have not been performed in humans. However, one patient who was exposed to 80 per cent oxygen at 1.0 ata for five months as therapy for myasthenia gravis developed nearly total blindness in association with marked constriction and "silver-wire" formation of the retinal arterioles.[46]

Reversible Loss of Peripheral Vision in Humans

Behnke and co-workers[47] first reported nearly complete, bilateral loss of peripheral vision, leaving only small islands of central vision, in a man who breathed oxygen at 3.0 ata for 3.5

hours. Recovery was essentially complete within 50 minutes postexposure. Other investigators[35, 48] also observed reversible losses of peripheral vision in subjects exposed to similar conditions.

This phenomenon was recently studied more intensively with repeated measurements of visual fields and acuity in 18 subjects exposed to oxygen at 3.0 ata for up to 3.5 hours.[35] Loss of peripheral vision started at 2.5 to 3.0 hours of exposure and progressed to involve about 50 per cent of the visual field area on average, with individual losses as great as 90 per cent at 3.5 hours of exposure. Central visual acuity was not significantly altered. Recovery of peripheral vision was essentially complete within 30 to 45 minutes after exposure termination. Mechanisms for the progressive loss of peripheral vision and its rapid recovery are not known at present.

Individual Predisposition to Oxygen Effects

An apparently increased susceptibility to visual loss during hyperoxic exposure was found in an individual who had recovered many years previously from retrobulbar neuritis in one eye.[49] While serving as a volunteer for an oxygen exposure at 2.0 ata, this subject experienced a progressive loss of vision in the previously affected eye over the last 2 hours of a 6-hour exposure. The visual field gradually expanded over the first 4 hours of recovery, but two paracentral scotomas remained and gradually cleared over a period of about 3 weeks. The observed visual disturbances appeared to involve two separate processes. One consisted of visual field constriction followed by relatively rapid reversal, while the other appeared to represent recurrence of unilateral retrobulbar neuritis with a much slower recovery.

Progressive Myopia

Approximately one third of the patients who receive daily hyperbaric oxygen treatment for a variety of chronic disease states develop some degree of myopia which usually starts after 2 to 4 weeks of therapy and is progressive thereafter.[50, 51] If the individual is initially hyperopic, the refractive error is normalized. After the series of hyperbaric oxygen therapies has ended, reversal of the myopia is nearly always complete over a period of 3 to 6 weeks. Occasionally, complete reversal of myopia can require as long as 6 to 12 months.[51] Although the basis for the myopia has not been determined, elimination of other possible causes implicates a reversible change in lens shape or metabolism.[52]

In a series of 25 patients who received a total of 150 to 850 one-hour exposures at 2.0 to 2.5 ata over a period of 2 to 19 months for refractory leg ulcers, 7 of 15 patients who had clear lens nuclei at the start of therapy developed cataracts. These persisted in five individuals and were only partially reversible in two others after termination of the therapy series.[53] The lens changes were associated with myopia that also was only partially reversible. Fortunately, most clinical conditions that respond favorably to hyperbaric oxygenation do not require such long cumulative periods of oxygen exposure.

Modification of Oxygen Tolerance

The rate of development of oxygen poisoning in intact animals and humans can be influenced by a variety of conditions, procedures, and drugs (Table 8–2). Factors that hasten the onset or increase the severity of toxic effects are listed on the left side of Table 8–2. Although none of these factors should be considered to be an absolute contraindication to the application of hyperbaric oxygenation, the presence of one or more of the listed influences as part of a disease process or its therapy should be regarded as an indication for caution.

Factors listed on the right side of Table 8–2 have been found to delay the onset or decrease the severity of overt manifestations of oxygen poisoning. Some are potentially useful as protective agents under appropriate conditions of O_2 exposure. Unfortunately, most have side

TABLE 8–2. Factors that Modify Rate of Development of Oxygen Poisoning

HASTEN ONSET OR INCREASE SEVERITY	DELAY ONSET OR DECREASE SEVERITY
Adrenocortical hormones	Acclimatization to hypoxia
CO_2 inhalation	Adrenergic blocking drugs
Dextroamphetamine	Antioxidants
Epinephrine	Chlorpromazine
Hyperthermia	Gamma-aminobutyric acid
Insulin	Ganglionic blocking drugs
Norepinephrine	Glutathione
Paraquat	Hypothyroidism
Hyperthyroidism	Reserpine
Vitamin E deficiency	Starvation
	Succinate
	Trisaminomethane
	Intermittent exposure*
	Disulfiram*
	Hypothermia*
	Vitamin E*

*Potentially useful as protective agents.

Adapted from Clark JM, Lambertsen CJ: Pulmonary oxygen toxicity: A review. Pharmacol Rev 23:37–133, 1971.

effects or other limitations that preclude their practical use in humans. Furthermore, effective protection against the multiple and diverse effects of O_2 toxicity requires wide distribution of the protective agent throughout all body tissues, as well as effective opposition to toxic effects of O_2 on a variety of enzymatic targets. The same agent may delay some effects of O_2 toxicity while hastening the onset of others. For example, administration of disulfiram delays the onset of convulsions in animals exposed to O_2 at 4.0 ata,[54, 55] but it enhances the progression of pulmonary intoxication at 1.0[56] or 2.0 ata.[57]

At the present time, the most effective and practical means for extension of oxygen tolerance in humans is the systematic alternation of oxygen exposure intervals with relatively brief normoxic intervals.[3, 4] Initially observed by Soulie,[58] the practical applications of this procedure were first elaborated by Lambertsen,[59] and its efficacy has been demonstrated in animals[60, 61] and in humans.[62] Intermittent O_2 exposure delays the onset of toxic effects in all organs and tissues, and it has none of the limitations that are associated with pharmacological protective agents. The basis for the inherent superiority of this procedure as a means for extension of O_2 tolerance resides in its dependence upon the periodic, sequential elevation and reduction of O_2 tension rather than the passage of a chemical agent across cellular membrane barriers.

CARBON MONOXIDE

Carbon monoxide (CO) is produced by the incomplete combustion of carbonaceous material. The sources of CO are plentiful and with the exception of carbon dioxide (CO_2), CO is the most abundant pollutant present in the lower atmosphere.[63] With a diver, the typical source of poisoning is contaminated air from improperly directed compressor engine exhaust, so that CO can be taken up in the air intake system. In addition to environmental sources, CO is also produced endogenously. It is a byproduct of heme catabolism and may account for perhaps 0.5 per cent saturation of hemoglobin in venous blood.[64–66] This section will focus on exogenous sources of CO and on the clinical impact of this exposure.

The toxic effects of CO result from its binding to hemoglobin and, possibly, other cellular proteins. Clinical consequences seem to be determined by a complex interaction that involves both the extent of CO binding and the physiological alterations associated with exposure. That is to say, the pathophysiology of CO is mediated by both the hypoxia associated with hemoglobin binding, as well as cardiovascular dysfunction giving rise to an ischemic insult.

Uptake

Inhaled CO rapidly diffuses across the alveoli and binds to hemoglobin. The relative affinity of CO for hemoglobin is some 200-fold greater than that of O_2, with some variation within the population.[67, 68] CO uptake follows an exponential function.[69] The rate of uptake is dependent on the percentage of inspired CO and O_2, on the ventilatory rate, and on the duration of exposure to CO.[68, 70]

Elimination

CO elimination also follows an exponential relationship.[70–73] The kinetics in any particular instance, however, is complex and appears to depend on the rate of ventilation, inspired O_2 partial pressure, and possibly the pattern of CO exposure (e.g., brief or prolonged, continuous or discontinuous).[69–76] Thus, in a clinical setting, attempts to estimate a maximum carboxyhemoglobin (COHgb) level by extrapolation using an approximate COHgb half-life (see Table 8–1) is fraught with uncertainty. Recent experience would also suggest that this is unnecessary, as the mortality and morbidity risks have not been found to correlate with the COHgb level.[76, 77]

Mechanism of CO Toxicity

There is a competition between CO and O_2 for binding to hemoproteins. The relative affinity of CO to hemoglobin ranges from 220- to 290-fold greater than that of O_2.[67, 68, 78] Hence, despite a relatively high O_2 partial pressure in the vasculature, CO binds to hemoglobin, which will reduce O_2 carrying capacity.[79, 80] Carboxyhemoglobin increases the affinity of unbound hemoglobin for O_2, thus causing a leftward shift and a more hyperbolic shape in the oxyhemoglobin dissociation curve.[81] These later effects cause a lower tissue and intracellular pO_2 than would otherwise be expected for any given blood O_2 content.

Coburn[82] has estimated that at any given time perhaps 10 to 15 per cent of the total body burden of CO is bound to extravascular proteins. There are a rather large number of proteins that bind CO, but only myoglobin, cytochrome *c* oxidase, and cytochrome P_{450}-linked

enzymes have been studied with consideration to probable in vivo effects.[83–88] Even at ambient arterial O_2 tensions, CO can bind to myoglobin, which would interfere with O_2 utilization by muscle cells.[89, 80] There is no strong evidence that CO may alter in a significant fashion in vivo cytochrome P_{450}-linked enzyme activity.[91–94] Chance and co-workers[95] demonstrated that CO can bind to cytochrome *c* oxidase and emphasized that this effect was particularly enhanced during a change from anoxia to normoxia. Hence, CO binding might be expected at a time when there is a transiently high pCO to pO_2 ratio. There is uncertainty regarding the pO_2 in the vicinity of cellular mitochondria; however, even conservative estimates suggest that the tissue pCO in severe CO poisonings is only one tenth that necessary to cause 50 per cent enzyme inhibition.[96, 97] Recent data does suggest that there may be a mild compromise in mitochondrial respiratory function.[98]

As the carboxyhemoglobin level increases during CO poisoning, there is an increasing hypoxia. As pCO/pO_2 ratios increase, CO binding to proteins would be expected to increase. This has been shown with myoglobin when arterial oxygenation is reduced to below 40 mm Hg.[89, 90] A similar phenomenon may occur with cytochrome oxidase. Thus, the pathophysiology of CO may be altered, and binding at extravascular sites may take on increased importance as the carboxyhemoglobin level rises.

Animal studies involving carbohydrate metabolism and respiration have failed to identify any difference between hypoxic hypoxia and CO-mediated hypoxia, thus arguing against a cellular component to CO poisoning.[99–101] When cellular functions and not metabolism are assayed, however, animal studies have suggested that CO-mediated impairment of hemoglobin function cannot solely explain the degree of impairment observed.[102–104] Observations on the effects of very low carboxyhemoglobin levels (~4 to 5 per cent), which should have only negligible effects on tissue pO_2, also suggest that a separate, cellular-level lesion may be present.[105–107]

Pathophysiology

As carboxyhemoglobin levels rise, cerebral vessels dilate,[108] and both coronary blood flow and capillary density increase.[109–111] These are acute, compensatory reactions to CO poisoning. As CO exposure continues, central respiratory depression arises, possibly due to cerebral hypoxia.[112] Animal and human reports have described cardiac effects including a myriad of dysrhythmias, as well as pathological changes that include myocardial hemorrhages, degeneration of muscle fibers, leukocyte infiltration, mural thrombi, and multifocal myocardial necrosis.[113–116]

Acute mortality from CO may be mediated through cerebral hypoxia, either from respiratory depression or from direct, progressive pulmonary shunting and ventilation perfusion imbalance, causing a lowering of arterial O_2 tension.[80, 110, 117] Animal studies suggest that acute mortality may be principally caused by cardiac dysrhythmias, and thus death is from an ischemic insult.[118] There are indications that myocardial impairment may begin at the relatively low carboxyhemoglobin level of approximately 20 per cent. Animals that do not die acutely, but instead show neurological deterioration over the days subsequent to poisoning, appear to have a combined hypoxic and ischemic insult during acute exposure. That is, they have acutely high carboxyhemoglobin levels, and during this hypoxic stress, the normal vascular compensatory reactions are thwarted by a period of hypotension perhaps mediated through CO cardiac toxicity.[82, 118, 120, 121]

Clinical Findings

Among the earliest complaints associated with the rising carboxyhemoglobin level are frontal headache and nausea.[122] Of limited clinical value, but perhaps of value experimentally to suggest a tissue-level CO insult, are findings of diminished visual evoked responses,[122–124] visual brightness discrimination,[125] and subtle auditory dysfunction[126] with carboxyhemoglobin levels less than 10 per cent. It is extremely important to emphasize that while carboxyhemoglobin levels can perhaps be loosely associated with symptomatology, there is no direct correlation between a carboxyhemoglobin level and the severity of symptoms. This has been borne out in the authors' experience treating over 200 cases of acute CO poisoning, as well as in experience reported by others.[76, 77, 127, 128] Grossly speaking, at carboxyhemoglobin levels greater than 20 per cent, patients may experience severe headache, palpitation, confusion, weakness, syncope, and seizures. Objectively, in addition to alterations in neurological status, tachycardia and tachypnea may be noted. Notable in its absence, it is extraordinarily rare to observe "cherry red" coloration of skin except among those who have died.[129–131]

Morbidity and mortality risks appear to be

TABLE 8–3. Delayed Neurological Sequelae of CO Poisoning

Choreoathetosis	Hemiplegia
Cortical blindness	Hysteria
Dementia	Mutism
Depression	Parkinsonism
Disorientation	Peripheral neuropathy
Epilepsy	Personality changes
Gait disturbances	Speech disturbances
Hearing impairment	Urinary/fecal incontinence

greater among patients with prior cardiovascular disease and with age greater than 60 years and among those who have suffered an interval of unconsciousness during CO exposure.[127] The duration of coma portends greater risk, but it appears that any history of loss of consciousness places the patient at greater risk of CO-mediated morbidity. Approximately 30 to 40 per cent of CO victims die prior to hospitalization.[76, 131] Of those hospitalized, approximately 2 per cent die, 10 per cent make a partial recovery, and 10 per cent or more suffer what are described as delayed neurological deteriorations.[116, 131, 132]

Delayed neurological deterioration subsequent to CO poisoning was first reported by Grinker.[133] Since then several reports have described the clinical features of this disorder (Table 8–3).[127, 134–138] As might be expected, there are not uniform pathological correlations with these varied signs and symptoms. The lesions are often associated with patchy white matter damage and commonly are referred to as myelinopathy or leukoencephalopathy[132, 134–141] Among the reports of gray matter damage, the frequency of involvement of the basal ganglia is striking.[140, 141] Pathological changes similar to these may arise subsequent to any form of ischemic-hypoxic brain insult.[137, 142] There appears, however, to be a markedly greater risk among CO victims. In a large retrospective survey, Shillito and colleagues reported an incidence of delayed neurological sequelae of 0.8 per cent.[143] Meigs and Hughes observed this phenomenon in 9 of 105 cases.[116] More recent studies involving rigorous and quantitative estimations of neurological function have indicated that the incidence may be 10 to 40 per cent among patients admitted to a hospital for CO poisoning.[77, 131] Some recent opinions that reflect a small experience downplay the patient's risk.[144] Others, however, have emphasized the alarming onset of these changes in patients who seem to have recovered.[145, 146]

Treatment

In addition to general supportive care, supplemental O_2 inhalation is a cornerstone in the treatment of CO poisoning. Carboxyhemoglobin dissociation is hastened by an elevation in the O_2 partial pressure of inspired gas. Hyperbaric O_2 hastens dissociation beyond a rate achievable by breathing pure O_2 at sea-level pressure.[71, 75, 147] Due to this fact, hyperbaric O_2 has been used to treat severe CO poisoning for more than 25 years. Numerous reports attest to the efficacy of hyperbaric O_2 in reversing severe neurological and cardiovascular depression in CO poisoning.[148–153] Experience has demonstrated that hyperbaric O_2 may reverse CO-mediated neurological depression even after the carboxyhemoglobin level has fallen.[152, 154, 155] In a large retrospective study, Goulon and coworkers demonstrated that prompt administration of hyperbaric O_2 may dramatically reduce mortality.[151]

A recent separate issue regarding therapy has involved interest in treating patients with an increased risk for developing delayed neurological sequelae, even if they do not necessarily manifest evidence of serious poisoning. Several reports have indicated that prompt administration of hyperbaric O_2 may reduce the incidence of delayed neurological sequelae.[156–158] Assessment of the mechanism for hyperbaric O_2-mediated reduction in neurological sequelae is obviously hampered by a poor understanding of the mechanism behind the clinical disorder itself. Among the hypothesized mechanisms, lipid peroxidation within the central nervous system secondary to the hypoxic-ischemic insult has been suggested.[159] Brain lipid peroxidation was recently identified in an animal model, and hyperbaric O_2 was shown to block this process.[160] The underlying biochemistry responsible for this effect is not as yet fully elucidated.

Based on the body of information currently available, it is generally recommended that patients who manifest signs of serious intoxication should be referred for hyperbaric treatment. Clinical data support the administration of hyperbaric O_2 to any patient who has suffered an interval of unconsciousness, as they are at greater risk of suffering delayed neurological sequelae.[76, 77] The determination of subtle central nervous system involvement can be difficult. Utilization of a modified psychometric screening battery has been found to be useful in identifying compromised patients.[161] The body of clinical data available suggests that functional testing, rather than a carboxyhemoglobin level, may be a more sensitive method for determining the appropriate treatment among less severely symptomatic patients.

CARBON DIOXIDE

Carbon dioxide is a product of oxidative metabolism and hence is not a toxin in the most traditional sense. Intoxication results either from exposure to respiratory gases containing high concentrations of CO_2 or from retention of autogenous CO_2 due to inadequate ventilatory equipment or pathological states (e.g., emphysema). In diving medicine, acute CO_2 intoxication can be caused by inadequate CO_2 elimination from closed spaces (e.g., diving bells, submersibles, underwater habitats, recompression chambers) or from closed or semi-closed underwater breathing equipment.[162, 163]

Any physiological or toxic action of CO_2 must be referable to an increased partial pressure of molecular CO_2 and/or to an increased hydrogen ion concentration.[163] Since molecular CO_2 freely crosses cell membranes to penetrate intracellular as well as extracellular fluid compartments, these two potential agents are inseparable. In a similar manner, any toxic effects of CO_2 are superimposed upon and, to some extent, inseparable from fundamental physiological influences that include the following: (1) stimulant actions of CO_2 on central and peripheral chemoreceptors provide an important link in the regulation of internal, acid-base homeostasis; (2) relaxant effects of CO_2 on vascular smooth muscle are involved in the regulation of brain circulation; (3) excessive CO_2 partial pressures can depress the same neural structures that are stimulated by lower levels of pCO_2; and (4) CO_2-induced acidosis has nearly simultaneous influences on a wide range of biochemical reactions on both sides of membrane and vascular barriers.[162, 163]

Acute Exposure to Hypercapnia

Acute exposure to CO_2 at concentrations ranging from 0 to more than 20 per cent at normal atmospheric pressure produces effects that range from barely detectable stimulation of ventilation to loss of consciousness and convulsions, depending on the level inspired[162, 163] (Table 8–4). The ventilatory response to CO_2 administration is nearly linear over minute volumes of about 12 to 65 liters/minute for inspired levels of 4 to 10 per cent and gradually levels off to approach 90 liters/minute for 30 per cent inspired CO_2.[162] The curve for cerebral blood flow has a similar configuration in the monkey and presumably also in humans, with a nearly linear increase over the arterial pCO_2 range of about 30 to 80 mm Hg.[164]

TABLE 8–4. Signs and Symptoms of Acute Hypercapnia in Normal Men

Percent CO_2* (sea-level equivalent)	Effect
0–4	No CNS derangement
4–6	Dyspnea, anxiety
6–10	Impaired mental capabilities
10–15	Severely impaired mental function
15–20	Loss of consciousness
> 20	Uncoordinated muscular twitching, convulsions

*Biological activity of a gas is determined by its partial pressure rather than its concentration. Hence, at depth the effect of an inspired gas becomes greater.

Exposure of humans to inspired CO_2 concentrations of 15 to 20 per cent causes an abrupt and violent onset of respiratory distress that is accompanied by rapid loss of consciousness and spasms of neuromuscular twitching.[162, 163] Therapeutic exposures to inspired CO_2 levels of 20 to 30 per cent in oxygen cause convulsions within 1 to 3 minutes.[162, 163] Any accidental exposure to such a high CO_2 concentration would be extremely dangerous, because even one breath causes the onset of mental incapacitation.[162] Electrocardiographic responses to similar levels of hypercapnia include tachycardia, nodal and ventricular premature contractions, inverted P-waves, and increased amplitude of T-waves.[165, 166] In monkeys and dogs exposed to CO_2 concentrations of 30 to 40 per cent, cardiac activity was sustained for many hours and remained stable when inspired pCO_2 was gradually reduced to zero.[167, 168] However, when the dogs were moved abruptly to room air, most of the animals experienced ventricular fibrillation and death.[168] Presumably, the terminal arrhythmias were caused by failure to allow sufficient time for restoration of normal cardiac excitability by reversal of ionic shifts induced by prolonged and extreme hypercapnia.[163]

Elevation of inspired pCO_2 during exercise interferes with the elimination of metabolically produced CO_2.[163] Under these conditions, a balance between the rates of CO_2 elimination and its production is restored by concurrent increments in arterial pCO_2 and the rate of pulmonary ventilation.[169–172] Physically fit young men are able to achieve maximum levels of oxygen uptake ($\dot{V}O_2$) during exposure to inspired pCO_2 levels up to 21 mm Hg[169, 171] and can tolerate working at 80 per cent of maximum $\dot{V}O_2$ at an inspired pCO_2 of 40 mm Hg.[172]

Chronic Exposure to Hypercapnia

Chronic pCO_2 elevations in all body fluids can occur in patients with pulmonary insufficiency[173] or in normal individuals who are exposed to increased inspired pCO_2 levels for experimental purposes[170, 174] or as a potential consequence of inadequate CO_2 removal from a closed-system aerospace or undersea habitat.[163] Compensatory responses to sustained hypercapnia include renal,[175] acid-base,[176–178] respiratory,[173, 174] and circulatory[179] adaptations. The kidney responds initially by increasing the tubular reabsorption of bicarbonate and later complements this with increased ammonia production to enhance excretion of hydrogen ions.[175] Together, these processes augment both extracellular and intracellular concentrations of bicarbonate and other bases to return hydrogen ion concentrations toward normal levels.[176–178] The acid-base alterations are associated with respiratory adjustments that are manifested in normal humans by a shift of the pulmonary ventilation-arterial pCO_2 response curve to higher pCO_2 levels with no change in the slope of the curve.[174] Studies in monkeys show that cerebral blood flow responses to arterial pCO_2 elevation are also attenuated during exposure to chronic hypercapnia as manifested, in this case, by reduction in the slope of the curve with no apparent change in the initial response threshold.[180]

Normal humans have been exposed to inspired pCO_2 levels of 30 mm Hg for up to 11 days and 21 mm Hg for 30 days with no pathological or residual effects.[170, 174] Ventilatory and acid-base adjustments that occurred during the first day of chronic hypercapnia were promptly reversed upon resumption of air breathing. The ability to perform heavy exercise while breathing an inspired pCO_2 level of 21 mm Hg is not impaired by 30 days of chronic exposure.[170]

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