CHAPTER 3

Physiology of Decompressive Stress

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> . . . upon the withdrawing of air . . . the little bubbles generated upon the absence of air in the blood juices, and soft parts of the body, may by their vast numbers, and their conspiring distension, variously streighten in some places and stretch in others, the vessels, especially the smaller ones, that convey the blood and nourishment: and so by choaking up some passages, . . . disturb or hinder the circulation of the blouod? Not to mention the pains that such distensions may cause in some nerves and membranous parts..
>
> —*Sir Robert Boyle, 1670, Philosophical transactions*

Since Robert Boyle made his astute observations in the 17th century, humans have ventured into the highest levels of the atmosphere and beyond and have encountered problems that have their basis in the physics that govern this environment, in particular the gas laws. The main problems that humans face when going at altitude are changes in the gas volume within body cavities (Boyle's law) with changes in ambient pressure, as well as clinical phenomena secondary to formation of bubbles in body tissues (Henry's law) secondary to significant decreases in ambient pressure. In the operational aerospace setting, these circumstances are of concern in high-altitude flight (nonpressurized aircraft >5,486 m (18,000 ft), rapid decompression at altitude, flying after diving, and in space operations in the context of extravehicular activities (EVAs). This chapter will focus on pressure changes occurring in the aerospace environment, the associated pathophysiology, pathology, and avenues for risk mitigation and treatment.

Although diving decompression illness and altitude decompression illness are evolved gas disorders, they have very distinct dynamics and clinical pictures as a result of the different gas dynamics and physics; the discussion in this chapter will focus on altitude decompression illness as opposed to diving decompression illness.

For a detailed discussion of acute hypoxia, hyperventilation, and respiratory physiology the reader is referred to Chapter 2, for details on the operational space environment and the potential problems with decompressive stress see Chapter 10, and for diving related problems the reader is encouraged to consult diving and hyperbaric medicine monographs.

THE ATMOSPHERE

Introduction

Variations in Earthbound environmental conditions place limits and requirements on our activities. Even at sea level, atmospheric environmental conditions vary considerably due to latitude, climate, and weather. Throughout the range of aerospace operations, crewmembers and their craft face even larger variations in atmospheric properties that require life support systems and personal equipment for survival and preservation of optimal function. Understanding the physical nature of our atmosphere is crucial to understanding how it can affect human physiology and what protective measures must be employed.

Constituents and Properties of the Atmosphere

The standard atmosphere of Earth at sea level pressure is expressed as 760 millimeters of mercury (mm Hg), which

TABLE 3-1

[a]The Atmosphere of Earth

Gas	*Percentage in Atmosphere*	*Partial Pressure (mm Hg)*
Nitrogen	78.084	593.44
Oxygen	20.948	159.20
Argon	0.934	7.10
Carbon dioxide	0.031	0.24
Other gases	0.003	0.02
Total	100.000	760.00

[a]Clean, dry air at 15°C (59°F), sea level; mean of values every 15° between 15° N and 75° N; Ref: U.S. Standard Atmosphere, 1962.

is equivalent to 1,013.2 millibars [mb or hectoPascals, hPa, hundreds of Pascals (newtons per square meter)], 14.7 psi, and 29.92 in. of Hg. Constituents of the atmosphere we breathe are shown in Table 3-1 and these percentages are consistent throughout the atmosphere of interest to aerospace physiology.

Atmospheric Zones

Temperature and its variation provide much of the basis for subdivisions of Earth's atmosphere into regions defined in Figure 3-1. The lowest zone, the *troposphere*, is the only region of Earth's atmosphere capable of supporting human habitation without artificial support. The troposphere starts at the Earth's surface and extends to the *tropopause*, between 5 and 9 mi [8 to 14.5 kilometer (km); 26,000–48,000 ft]. At its higher levels, above 20,000 ft (3.8 mi; 6 km), at least some degree of artificial support is required in the form of supplemental oxygen. A linear decrease in temperature characterizes the troposphere from sea level (15°C) to the tropopause, typically at approximately 35,000 ft (10.7 km), where the temperature is approximately −55°C. The lapse rate, that is, the rate of decreasing temperature with increase in altitude in the troposphere, is −2°C or approximately −3.5 F per 1,000 ft. Approximately 80% of the atmospheric mass and most of the weather phenomena occur in the troposphere. Variations in temperature, pressure, and humidity in the troposphere account for extreme differences in the environmental conditions we experience as weather.

The tropopause is the division between the troposphere and stratosphere. Aircraft jet engines perform with greater efficiency at lower temperatures, which is one reason cruise is planned near the tropopause where the temperature is lowest. The *stratosphere* starts just above the tropopause and extends up to 50 km (31 mi). Ninety-nine percent of the mass of the air is located in the troposphere and stratosphere. The temperature throughout the lower part of stratosphere is relatively constant. Compared to the troposphere, this part of the atmosphere is dry and less dense. The temperature in this region increases gradually to −3°C due to the absorption of ultraviolet (UV) radiation. This radiation reaching the lower stratosphere from the sun is responsible for creation of ozone, the ozone layer, or ozonosphere. In the process of ozone production and in reactions with ozone, nearly all of the UV radiation is absorbed including the most hazardous form to life, UV-C (wavelengths <280 nm). Much of UV-B (wavelengths between 280 and 320 nm) is also absorbed, although the UV-B reaching the surface is sufficient to be a major cause of melanoma cancers and sunburn. Most of the UV-A (wavelengths between 320 and 400 nm) reaches the Earth's surface, but is needed by humans for production of vitamin D. Although flight in the upper troposphere and lower stratosphere involves exposure to more UV radiation than on the surface, no health risk is currently associated with routine flying operations (see Chapter 8). Flight above the stratosphere and space flight involve risk of exposure to significant levels of radiation.

The higher regions of the atmosphere, 50,000 ft and above, are so thin that pressure suits are required to sustain life. Temperature variations result from variable absorption of the sun's energy in several forms and thermal protection must be incorporated for any exposure in these regions. In the higher regions, flight of air-breathing aircraft becomes impossible and control surfaces are no longer effective. Further description will be left to the references and recommended reading.

The subdivision of the zones described in the preceding text relates to the ability of humans to function based on the partial pressure of oxygen available and need for artificial pressure to sustain life (Table 3-2).

Altitude

Altitude is measured in many different ways using different standards for different purposes. On low-altitude maps provided to pilots, the height of physical features of Earth, like mountains and airfields, is measured in feet above mean sea level (MSL). MSL is the average height of the surface of the sea for all stages of the tide over a 19-year period, usually determined from hourly height readings. With properly set, calibrated, and functioning altimeters, feet above MSL is the altitude viewed by the pilot in an aircraft. This is also known as *pressure altitude* (PA), the altitude in the Earth's atmosphere above the standard datum plane, standard sea level pressure, measured by a pressure altimeter. Pilots are quite interested in the height of their aircraft above the ground. This altitude, above ground level (AGL), is determined by subtracting the elevation in feet above MSL of the ground below the aircraft from the elevation of the aircraft. The routine determination of a safe altitude on a route between navigational aids to avoid terrain and towers is usually viewed on low-level navigational maps as the minimum en route altitude (MEA), which is the altitude between radio fixes that assures acceptable navigational signal coverage and meets obstruction clearance requirements between those fixes. Flying at that altitude with a properly set altimeter ensures adequate separation from obstacles for the entire route segment. PA is the height in the atmosphere at which a given value of standard pressure exists. With 29.92 in. of Hg set in the Kollsman window of the

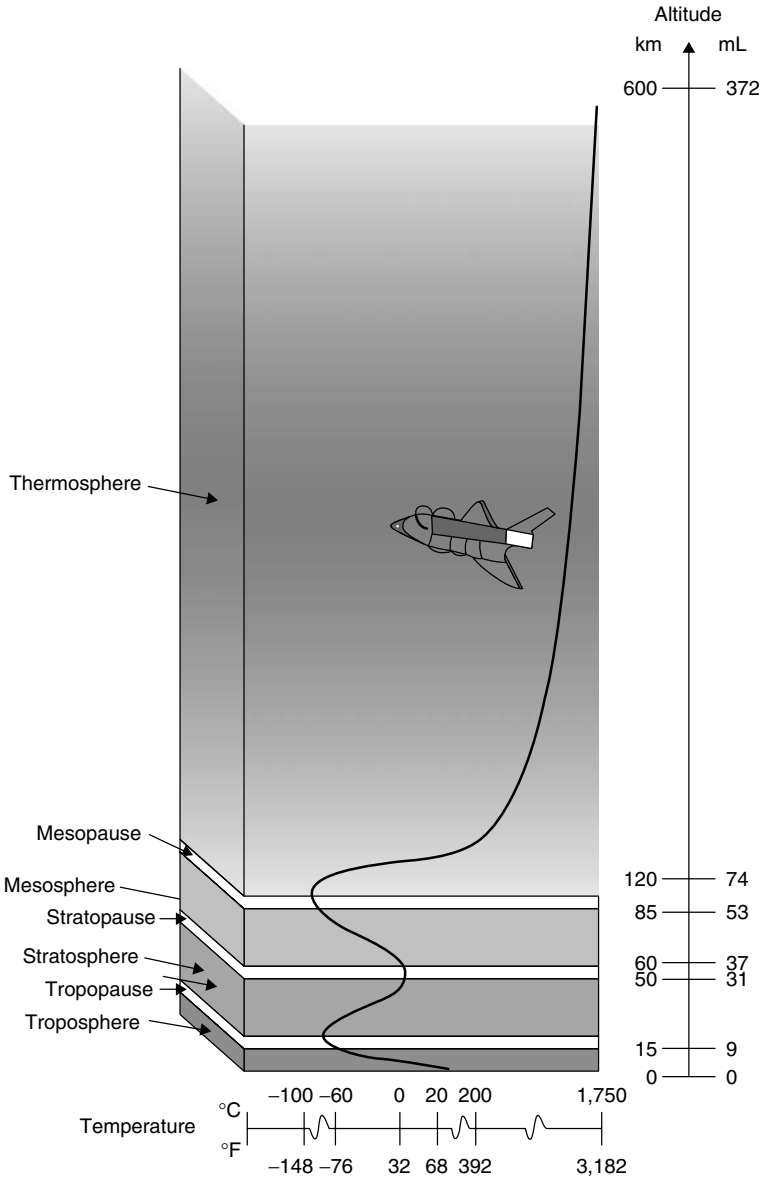

FIGURE 3-1 Zones of Earth's atmosphere.

altimeter, PA is displayed in feet on the altimeters of United States Air Force (USAF) aircraft. Because hectoPascals are a standard in parts of the world, some confusion can arise when pilots "assume" that, for example, 988 means 29.98 in. of Hg when given by an air traffic controller as an altimeter setting because some controllers in the United States leave off the "2."

Air Density, Pressure, and Temperature

The density of air is affected by its pressure, which decreases exponentially with increasing altitude, reaching 50% of sea level density and pressure at approximately 18,000 ft (5.49 km). This relationship is affected in any specific locale by deviations from standard temperature and pressure. Figure 3-2 graphically shows how atmospheric pressure is affected by altitude. The curve depicts how each 10,000-ft increase in altitude results in less change in pressure; 0 to 10,000 ft changing by 237 mm Hg, 10,000 to 20,000 ft changing by 173 mm Hg, and 40,000 to 50,000 ft changing by only 54 mm Hg.

During takeoff, landing, and low-level phases of flight, aircraft altimeters are routinely set to the field altimeter setting to account for variations in local pressure. This procedure avoids significant errors in altitude of the airfield versus what is indicated on the altimeter. Temperature variations from the standard temperature of 15°C also produce errors, which affect terrain clearance. For instance, an aircraft flying at 5,000 ft in −40°C (e.g., Alaska in the winter) would be more than 1,200 ft lower than the indicated altitude *after* correction for local barometric pressure (P_B). Local P_B in the United States is based on inches of Hg. This setting would show the altitude of 0 ft at sea level on such a day. As the local pressure varies, altimeters are set to higher or lower settings to yield the correct field elevation on an aircraft altimeter at a designated point on that field. Above 18,000 ft (flight level 180; altitude in ft/100), altimeters

TABLE 3-2

Physiological Divisions of the Atmosphere

Physiological Division	*Altitude and Pressure Range*	*Problems*	*Solutions*
Physiological zone	0–10,000 ft 0–3,048 m 760–523 mm Hg	Trapped gas expansion/contraction during changes in pressure result in middle ear or sinus blocks; shortness of breath, dizziness, headache, or nausea in unacclimatized individuals or with exercise	Acclimatization or reduced performance
Physiologically deficient zone	10,000–50,000 ft 3,048–15,240 m 523–87 mm Hg	Oxygen deficiency progresses from minor reductions in cognitive and physical capabilities at 10,000 ft to death over approximately 25,000 ft (possibly lower) without supplemental oxygen	Supplemental O_2 and PBA allows good performance to approximately 35,000 ft with progressively less capability
Space equivalent zone	Above 50,000 ft >15,240 m <87 mm Hg	Survival requires assisted PBA[a] or, above approximately 63,000 ft, a full pressure suit and delivery of 100% O_2 to supply at least 140 mm Hg O_2	Pressurized cabin or pressure suit with 100% O_2

[a]PBA = positive pressure breathing for altitude.
(Physiological Training, Air Force Pamphlet 160–5, 1976.)

are routinely set to 29.92 in. of Hg to provide adequate and standardized clearance for aircraft altitude separation. Although the inches of Hg standard for altimeter settings are a pressure indication, it is not normally used in aviation for describing total atmospheric pressure at a given altitude. Elevation is typically measured in ft, meters (m), or km and pressure in psia, mm Hg, or mb.

Light and Sound

Diffusion of light in the lower atmosphere accounts for the blue color of the sky as viewed from Earth's surface, a phenomenon which significantly dissipates as low as approximately 50,000 ft where the blackness of space begins to become apparent. The speed of sound is 761 mph (340 m/s; 1,116 ft/s) at sea level and slower, 660 mph (295 m/s) at 50,000 ft where the temperature is approximately 75°C lower. The speed of sound is a function of the square root of the temperature in °K (°C + 273).

The Gas Laws

A basic understanding of the gas laws is necessary to comprehend the physical nature of the atmosphere and how it interacts with human physiology. The gas laws define physical properties of our atmosphere and provide a basis for understanding how they affect our function during exposure to reduced atmospheric pressure.

Boyle's Law

Robert Boyle (1627–1691) was an Anglo-Irish scientist noted for his work in physics and chemistry. In 1662, Boyle published the finding which states that at a constant temperature, the volume of gas is inversely proportional to its pressure. P_1 and V_1 are the initial pressure and volume, and P_2 and V_2 are the final pressure and volume. Solving this equation for the volume of a contained gas at a different pressure quantitatively describes trapped gas expansion with reduced pressure.

$$P_1 \times V_1 = P_2 \times V_2 \text{ or } P_1/P_2 = V_2/V_1$$

Solving this equation to find the volume of a liter of dry gas taken from sea level to 20,000 ft and 40,000 ft, assuming unrestricted expansion, would result in the following:

1.0 L at sea level

(760 mm Hg × 1 L)/349 mm Hg = 2.2 L at 20,000 ft

(760 mm Hg × 1 L)/141 mm Hg = 5.4 L at 40,000 ft

The problem becomes more complicated by the inclusion of water vapor in the lungs and other spaces in the body as

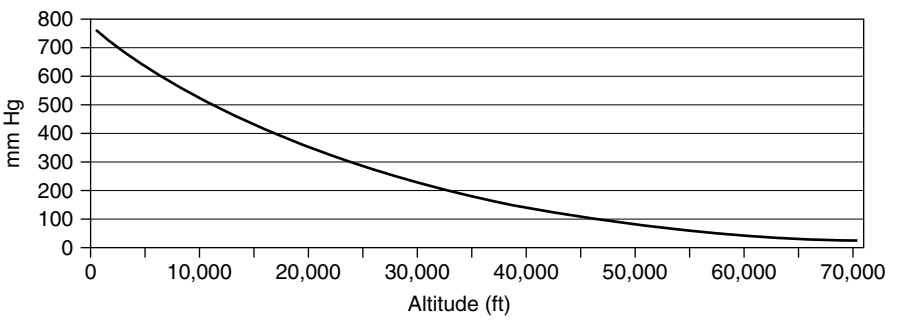

FIGURE 3-2 Atmospheric pressure versus altitude.

described in the section Trapped Gas, Section 3. Figure 3-4 shows the volume and diameter of a wet gas sphere at various pressures and graphically shows how Boyle's law works on trapped gases during decompression and recompression, descent.

Dalton's Law

John Dalton (1766–1844) was an English chemist and physicist. In 1803, he observed that the total pressure of a mixture of gases is equal to the sum of the partial pressures of each gas in the mixture.

$$P_T = P_1 + P_2 + P_3 + \ldots P_n$$

Because the standard atmosphere at sea level is 760 mm Hg, Dalton's law indicates that the sum of partial pressures of the gases that make up the standard atmosphere must equal 760 mm Hg. The pressure of each gas in a mixture of gases is independent of the pressure of the other gases in that mixture. Multiplying the percentage of a gas in the mixture times the total pressure of the mixture yields the partial pressure of that gas.

The standard atmosphere does not include water vapor pressure, primarily due to its variation in the Earth's atmosphere between 0% and 100% relative humidity. This variation amounts to 0% to 6.2% of 760 mm Hg, or 0 to 47 mm Hg at body temperature, 37°C.

Henry's Law

William Henry (1775–1836) was an English chemist who, in 1803, published his findings that the amount of a gas in a solution varies directly with the partial pressure of that gas over the solution. This relationship explains why dissolved nitrogen transitions to a gas phase in blood and tissues during decompressions sufficient to result in supersaturation. The resulting bubbles of nitrogen with minor amounts of oxygen, carbon dioxide, and water vapor can cause decompression sickness (DCS).

Charles and Gay-Lussac's Law

Jacques Alexandre César Charles (1746–1823) was a French inventor, scientist, mathematician, and balloonist. In 1783, he made the first balloon using hydrogen gas; upon release, it ascended to a height of approximately 3 km (2 mi). In 1787, he discovered the relationship between the volume of gas and temperature, known variously as *Gay-Lussac's law* or *Charles's law*.

$$V_1/V_2 = T_1/T_2 \text{ or } V_1/T_1 = V_2/T_2$$

Charles did not publish his findings and Joseph Louis Gay-Lussac first published the finding in 1802, referencing Charles' work. The temperature is in Kelvin degrees, where $^{\circ}K = {}^{\circ}C + 273$. At absolute zero, −273°C, the Kelvin temperature is 0°K. The distinction between Boyle's law and Charles' law is what is held constant, whereas the other two parameters are varied. Boyle's law describes changes in volume with respect to pressure when temperature is held constant. Charles' law describes how volume changes with temperature when pressure is held constant. Although Charles' law is very important from an engineering and chemistry standpoint, the temperature of human body is usually rather constant at body temperature, limiting its effect on physiology. Changes in all three parameters (volume, pressure, and temperature) are better described by the Ideal Gas law, which includes the three parameters in one equation with other factors to improve accuracy.

$$PV = nRT$$

where P = pressure, V = volume, T = temperature, n = number of moles, and R = universal gas constant = 8.3145 J/mol K.

Gaseous Diffusion

Experiments of Thomas Graham (1805–1869), a British chemist, showed that the diffusion of a gas is inversely proportional to the square root of its molecular weight. Therefore, gases of lower molecular weight diffuse more rapidly than gases of higher molecular weight. Diffusion of a gas is also affected by its solubility in the surrounding media and the difference in concentration of the gas between two adjacent volumes. A larger difference in concentration produces greater diffusion. A gas with greater solubility in its solvent, for example tissue or fluids, means more molecules of it will be available to diffuse as limited by the other factors. Gaseous diffusion is fundamental to the physiologic processes of lung and cellular respiration. It further applies to the process of denitrogenation, removal of nitrogen from the body, by breathing 100% oxygen.

Chronic Hypoxia

Terrestrial Environment

The historical distinction between hypoxia in the terrestrial and extraterrestrial/aerospace environment has become increasingly blurred in recent decades. The time at a certain pressure (i.e., altitude) and the time and modality to get to that pressure govern the physiology that will be discussed. The advent of ultra–long-haul flight operations in environments of decreased ambient pressure in civilian air transport operations (1) and potentially in future exploration class spaceflight missions, as well as rapid transport of civilian and military personnel to and prolonged sojourn in high-altitude environments make it very important for the aerospace medicine practitioner to be familiar with the concepts of operational significance that can play a role in those environments. The following paragraphs will review operational considerations and relevant clinical terrestrial syndromes.

Acclimatization

Altitude acclimatization is a process that occurs upon exposure to a hypobaric and hypoxic environment. Different processes occur with the common goal to protect the body tissues against the hypoxic challenge of the environment and

TABLE 3-3

Processes of Acclimatization and Relevant Terminology

Acute Acclimatization (Accommodation)	*Minutes*	*Rise in Heart Rate, Increased Ventilation*
Chronic acclimatization	Days	Increase in hemoglobin (initial decrease in plasma volume followed by increased red cell mass), increased capillary density
Adaptation	Years	Alterations in hypoxic ventilatory response

to allow for continued performance. Many of these processes occur at different speeds and can be summarized in different groupings (Table 3-3).

Owing to the processes discussed in the preceding text, it is difficult to answer the simple question as to how much time is needed to acclimatize to a given altitude, but the key aspects in acclimatization rest in the cardiorespiratory system and the blood that adapt in days to few weeks.

Unfortunately, there is no one single parameter that allows us to physiologically quantify and assess the level and degree of acclimatization. In addition to the lack of a single reliable parameter to assess acclimatization, we are faced with significant interindividual variation in speed and degree of acclimatization. A good clinical rule is to always inquire about past performance at altitude and presence or absence of signs and symptoms of acute mountain sickness (AMS); past performance is a guide to future performance in similar environments and exposures. Special attention needs to be given to any preexisting cardiac or pulmonary disease or conditions that may be exacerbated by exposure to a hypoxic environment.

There are only scarce data addressing acclimatization and the effects of age and gender. There does not appear to be a significant difference in acclimatization between men and women, and older age appears to confer some protection from AMS.

Preacclimatization is a technique used to achieve some degree of acclimatization preceding the exposure in the high-altitude environment. This can be accomplished by using an analog environment such as an altitude chamber or sojourns at altitude; good data to show consistent acclimatization benefit of intermittent hypoxic exposures with nitrogen admixture to the breathing gas (e.g., sleeping in a hypoxic environment) are lacking at this point. The benefits of acclimatization appear to dissipate over a period of 2 to 3 weeks, and it should be noted that pulmonary edema has been described in native highlanders with reexposure to altitude after as little as 12 days at low altitude (2).

Operational Considerations

Reduced Exercise Capability

Aerobic performance is significantly impaired as altitude and maximal oxygen consumption in acclimatized subjects falls from 4 to 5 L/min to approximately 1 L/min at the altitude of Mount Everest. The demands of the hypoxic environment lead to a significant reduction in exercise capacity and many an account of expeditions at extreme altitudes, especially without supplemental oxygen, is filled with vivid descriptions as to the extreme difficulty of exercise (3).

Any attempt to exercise or be physically active at high altitude is accompanied by markedly elevated levels of ventilation. It is noteworthy that ventilation is usually expressed with reference to ambient pressure, body temperature, and with the gas saturated with water vapor [referred to as *body temperature and pressure saturated* (BTPS)]. This measurement reference takes into account more accurately the volume of gas moved by the chest and lungs. Another measurement condition is STPD, which stands for the measurement of ventilation in conditions of **S**tandard **T**emperature, **P**ressure, and **D**ry gas. The latter shows much smaller volume changes at altitude and has no overt relationship to the actual mechanics of breathing (lung/chest wall movements). Oxygen consumption and carbon dioxide production are traditionally reported in STPD reference units, such that the values are altitude independent.

Ventilation measurements at high altitudes can reach near maximum voluntary ventilation levels driven by the powerful hypoxic drive through the peripheral chemoreceptors; during the 1981 Everest expedition at 8,300 m (Pb 271 mm Hg), Pizzo recorded maximum ventilation with a respiratory rate of 86 breaths/min and a tidal volume of 1.26 L/min resulting in a mean ventilation of 107 L/min (4,5).

Reduced Cognitive Ability

The exposure to any hypoxic environment has operational ramifications in that it can sharply reduce the effectiveness of an operator, especially in the first few days following insertion into a high-altitude terrestrial environment. Especially in the first week at altitude, consideration should be given to adequate rest periods (taking into account the temporary degradation of sleep quality at altitude), decreased task intensity, and if possible decreased operational tempo. In addition to the known decrements in cognitive performance associated with varying degrees of hypoxia, the development of severe headaches and neurologic symptoms and signs, as well as pulmonary symptomatology may be harbingers of a clinically relevant high altitude–related illness such as high-altitude cerebral edema (HACE) or high-altitude pulmonary edema (HAPE).

Relevant Clinical Terrestrial Syndromes Related to High Altitude

The emphasis in the discussion of high altitude–related clinical syndromes must be prevention. The hostile environment of extreme high altitudes coupled with the intense desire to accomplish a set goal (e.g., climbing a mountain, executing a

mission) in the context of highly motivated and driven team members may at times be a dangerous combination.

The education of all team members about disease entities and their symptoms that can arise at high altitudes (6,7) is of importance such that everybody may be able to observe their team members and peers. The emergence of any concerning signs or early behavioral alterations such as falling behind, change in attitude, lethargy, and so on should prompt heightened vigilance and early evaluation. Monitoring the dynamics of any signs and symptoms will allow the team to avoid bad outcomes, and to enable any team member with worsening symptoms to descend while they are still able to walk.

Acute Mountain Sickness

AMS is a syndrome encompassing headache, anorexia, lassitude, nausea, and a feeling of malaise. It can be encountered in 15% to 30% of Colorado resort skiers (8) and in up to 67% of climbers on Mount Rainier (9). Many people become symptomatic even at intermediate altitudes of 6,000 to 6,500 ft. Rapid ascent to altitude (flying, driving) may markedly exacerbate the risk. Symptoms usually manifest within hours to first few days at altitude.

The scoring of AMS can be accomplished by using Lake Louise consensus scale or a subset of questions of the environmental symptom questionnaire (ESQ). The ESQ consists of 67 questions in its ESQ III version. Clinically, it is most relevant to insist that headache be present for the diagnosis of AMS. Most practitioners prefer the Lake Louise scoring system due to its simplicity, consisting of a self-assessment (most important), clinical assessment, and afunctional score. Symptomatic therapy with nonsteroidal anti-inflammatory over-the-counter medications relieves the symptoms of headaches. Use of acetazolamide (a carbonic anhydrase inhibitor) is useful in the treatment of symptoms, but more importantly in the prophylaxis of the condition. The latter is advisable if historically a subject has had past episodes of severe mountain sickness or rapid exposure to a significant altitude is expected. Carbonic anhydrase inhibitors will facilitate acclimatization to altitude. Other agents can be used for symptom control, such as dexamethasone or other steroids. The disadvantage of using steroids for the treatment of mountain sickness is their lack of effect on acclimatization and their side effect profile. A rebound effect, that is, reoccurrence of mountain sickness after cessation of steroids at altitude is possible.

If available oxygen will alleviate symptoms of mountain sickness, severe cases may benefit from use of a portable hyperbaric chamber (10), especially in the setting of high-altitude expeditions.

The occurrence of the ataxia in a subject with severe mountain sickness should be taken very seriously as it may be a harbinger of early high-altitude cerebral edema, which if present may preclude safe self-evacuation by going to lower altitude.

High-Altitude Cerebral Edema

HACE usually occurs several days after altitude exposure in the context of mountain sickness. The differentiation between severe mountain sickness and HACE rests in the development of ataxia, impaired cognition, and higher cortical functions (hallucinations, inability to make decisions, severe mental slowing, irrational behavior, errors) as well as neurologic deficits in addition to the symptoms of severe mountain sickness as described earlier (11).

The occurrence of HACE in a hostile high-altitude environment will incapacitate the patient and lead to the need of an evacuation, thereby putting other participants potentially at risk. Avoidance of passive transport to extreme altitude and avoidance of ascending with symptoms of mountain sickness are important factors to avoid unnecessary bad outcomes. HACE may occur together with HAPE. Treatment of HACE consists of descent, the administration of steroids (e.g., dexamethasone), oxygen, and if available, use of a portable hyperbaric chamber with the goal of rendering the patient ambulatory, thereby allowing for further descent from altitude.

High-Altitude Pulmonary Edema

HAPE is a noncardiogenic pulmonary edema, which can occur in up to 1% to 2% of subjects at 12,000 ft (3,650 m), and there appears to be a genetic predisposition in some patients. A careful history will allow identification of this subpopulation. Significant exaggerated elevations of pulmonary arterial pressures in susceptible subjects in response to hypoxia at altitude appear to be causal factors in the pathogenesis of this condition.

Incidence depends on rate of ascent and peak altitude reached; reports from Pheriche (4,243 m) showed an incidence of 2.5% (12); Indian troops flown to an altitude of 3,500 m had an incidence of 0.57% (13).

Symptoms of HAPE are breathlessness, chest pain, headache, fatigue, and dizziness. Signs include mild elevation of temperature, dry cough (especially on exertion), hemoptysis, tachycardia, tachypnea, and cyanosis.

X-rays frequently reveal a pattern of irregular, patchy, later confluent infiltrates in both lower- and mid-lung fields, whereas the apices can be spared at times.

Lowering the pulmonary arterial pressures to provide relief can be accomplished with oxygen and vasodilators such as nifedipine and other agents such as phosphodiesterase inhibitors, which are currently under study for clinical use in this condition.

For individuals that have genetic disposition to this condition, use of prophylactic nifedipine may be a viable option to prevent HAPE.

Alternatively, the ambient pressure can be increased in a portable hyperbaric chamber to achieve improvement and thereby allow for transportability to lower altitude.

Chronic Mountain Sickness (Monge's Disease)

Chronic mountain sickness is a disease entity that can be found in populations remaining at altitude for many years. The key findings include erythrocytosis and related symptoms such as headaches, dizziness, physical fatigue and mental slowing, anorexia, and dyspnea on exertion, cyanosis, and a ruddy complexion. Pulmonary hypertension and right

heart failure may also be present. Obvious contributing causes would be chronic obstructive lung disease, obstructive sleep apnea or sleep-disordered breathing conditions causing hypoxia, and other pulmonary pathology, making the patient more hypoxic and thereby enhancing the erythrocytosis even further. Relocation to low altitude in the absence of pulmonary pathology or other contributing causes is usually curative.

Laboratory investigations reveal an increased red cell count, hemoglobin concentration, and packed red blood cell volume. Pa_{O_2} is decreased and P_{CO_2} is elevated. The increase in alveolar–arterial oxygen tension gradient is likely attributable to increased blood flow to poorly ventilated areas. The electrocardiogram shows right ventricular hypertrophy and increased pulmonary arterial pressures as well as blood viscosity (14–17).

High-Altitude Retinal Hemorrhages

High-altitude retinal hemorrhages (HARH) may be seen in many climbers at very high altitude. The hemorrhages are typically without symptoms and tend to disappear spontaneously over a couple of weeks upon return from altitude. There appears to be a correlation between retinal hemorrhages and HACE (16,17). The subject may develop symptoms if these hemorrhages are close to the macula. The distribution of these hemorrhages and cotton wool spots is of a periarteriolar and perivenous distribution. Typically, no treatment is required and recovery is spontaneous.

High-Altitude Deterioration

Extended stays at altitudes greater than 5,000 m typically result in significant weight loss. Field studies and observations from expeditions certainly introduce a variety of confounding factors, such as cold, limited food supplies or lack of palatable food, or the increased need to burn calories for activities of climbing or walking. It is remarkable that similar observations were made in altitude chamber studies, such as the Operation Everest studies that were 40 days in length, and revealed, despite an unlimited diet and comfortable environmental conditions, that the subjects still lost weight. An increase in basal metabolic rate has been invoked as a causal factor. Furthermore, changes in intestinal absorption of carbohydrates, protein, and fat in the context of hypoxia may also play a role above 5,000 m (15).

Extraterrestrial Environment

Activity outside of the habitat will be required on a regular basis from any Moon- or Mars-based facility to accomplish the objectives of exploration. The pressure suit used during exploration must keep the explorer functional in the absence of an atmosphere on the Moon and near vacuum (4.5 mm Hg) on the surface of Mars. The suit should have as little negative impact on the mission as possible, which means freedom of movement and minimal fatigue. Current National Aeronautics and Space Administration (NASA) EVA suits employ 100% oxygen at 4.3 psia (226 mm Hg) (18,19), which provide more oxygen than available in sea level air. These current suits are too restrictive and heavy for use on Mars or the Moon, and unless dramatic advances in suit technology are achieved, a 4.3 psia EVA suit pressure may not be feasible. Therefore, a much lower suit pressure may need to be considered. Avoiding DCS during the transition from habitat pressure to a suit pressure below approximately 3.7 psia (192 mm Hg) would also require a lower habitat pressure. A hypoxic environment in the habitat and during exploration could be experienced on a daily basis. Some physiologic changes will occur, which are analogous to terrestrial altitude-induced changes.

Adaptive Changes to a Hypobaric Hypoxic Environment

Adaptation to a low level of hypoxia in an artificial habitat environment (acclimation) could be tolerated the same way acclimatization allows thousands of humans to visit or live at high-terrestrial altitudes (3,100 m; 519 mm Hg, 10,200 ft) without supplemental oxygen. Although considerable improvement in function occurs after a few days of exposure to 3,100 m, ventilatory acclimatization would take about a week (20,21). Low gravitational forces on the Moon and Mars may reduce the workload and effect of any hypoxia during routine activity. Although the lower gravity on Mars (38% of Earth) may reduce the impact of pressure suit weight, mass is still a potential problem in terms of momentum and balance during exploration. Many factors will determine the potential atmospheres of Moon and Mars habitats, although some degree of acclimation to hypoxia is likely to be necessary.

Lower Total Pressure

Any reduction in total pressure reduces the effectiveness of electronic cooling fans and complicates atmospheric control and circulation. The engineering challenge must meet the need for close tolerances on levels of humidity, carbon dioxide, and oxygen levels to maintain comfort and physiologic function. Detection and removal of pollutants should be an extrapolation and refinement of the progress made during the International Space Station (ISS) habitation.

Water Balance

Maintenance of a comfortable level of humidity in a low-pressure habitat, for example 40% relative humidity and a temperature at 20°C (68°F), could help to reduce respiratory losses of water. This level of humidity with relatively full coverage clothing would also aid in reducing insensitive water loss.

Operational Considerations

Reduced Cognitive Ability

Acute exposure to 3,048 m (523 mm Hg, 10,000 ft) in Earth's atmosphere produces documented decrements in some cognitive tests (22,23), particularly those involving learning new tasks. In another study, 12-hour exposures to 10,000 ft (3,048 m) with rest or mild exercise produced no significant negative impact on cognitive function, but minor negative effects were observed on night vision

goggle performance under operational lighting (starlight) conditions. Increased reports of headache during the resting exposures at altitude may indicate imminent mild AMS (24). The USAF does not require its aircraft pilots to use supplemental oxygen at or below 10,000 ft during their routine acute exposures.

Reduced Exercise Capability
Even after acclimatization, maximal oxygen uptake is lower at 10,000 ft than at sea level for any individual (25). However, the effect on the submaximal effort during extraterrestrial exploration is unknown.

Communication
A reduced total pressure for a Moon or Mars habitat and pressure suits will affect vocal cord efficiency in sound development, although above a total pressure of 226 mm Hg (4.4 psi; 30,000 ft), verbal communication has not been a problem. Because communication between pressure-suited explorers will require electronic transfer, appropriate amplification and filtration could compensate for lower vocal cord efficiency at suit pressures in the 141 mm Hg (2.7 psia; 40,000 ft) range.

Fire Safety
The National Fire Protection Association (NFPA) has developed an equation that allows calculation of the maximum percentage of oxygen that avoids designation as an atmosphere of increased burning rate. The NFPA 99B: Standard for Hypobaric Facilities (2005;3.3.3.3) defines atmosphere of increased burning rate on the basis of a 12 mm/s burning rate (at 23.5% oxygen at 1 atmospheres absolute (ATA). The equation defining such an atmosphere (NFPA 99B Chapter 3 Definitions; 3.3.3.3) is:

$$23.45/(\text{Total Pressure in Atmospheres})^{(0.5)}$$

The factor 23.45 is the highest percentage of oxygen at sea level, which does not create an atmosphere of increased burning rate.

Even if a pressurized transportation system were used on the surface, continuous wear of a pressure suit would likely be required to provide adequate safety in the event of pressurization failure. The pressure suit must be designed to provide a sufficient level of oxygen and total pressure (minimum of approximately 141 mm Hg O_2; 2.7 psia) to allow normal physiologic function of an acclimated individual and for extensive mobility and maneuverability. If a pressure suit employing as much as 4.3 psi differential cannot be made to meet these requirements, a lower suit pressure may need to be considered.

Decompression illness (DCI) is a term used to encompass DCS and arterial gas embolism (AGE). DCS is a clinical syndrome following a reduction in ambient pressures sufficient to cause formation of bubbles from gases dissolved in body tissues. DCS follows dose–response characteristics at each involved tissue-site, the pathophysiological sequence that may or may not follow, and clinical symptoms that may occur subject to multiple moderating factors (environmental and operational tissue factors as well as marked individual susceptibility).

Historical Aspects

Sir Robert Boyle did pioneering work in the field of high-altitude medicine and was the first to observe bubble formation *in vivo* in one of his experimental animals during decompression in a hypobaric chamber

> "*I shall add on this occasion . . . what may seem somewhat strange, what I once observed in a Viper . . . in our Exhausted Receiver, namely that it had manifestly a conspicuous Bubble moving to and fro in the waterish humour of one of its Eyes.*"

Subsequent clinical evidence of DCS in humans came from air-pressurized mineshaft operations. M. Triger, a French mining engineer, reported in 1841 pain and muscle cramps in coal miners (26). In 1854, two French physicians, B. Pol and T. J. J. Watelle, gave an account of the circumstances in which the disease develops upon exiting the compressed air environment: "One pays only on leaving" and recognized as well that recompression ameliorated the symptoms. They were the first to use the term *caisson disease* named for the compressed air environment the workers were exposed to—analogous to the diving bells (caissons) (27).

In 1869, the French physician L. R. de Mericourt published the first comprehensive medical report on DCS in divers (27). The French physiologist Paul Bert described in his classic treatise *La pression barométrique* (1878) the relationship between bubbles and symptoms of DCS during rapid decompression (28).

The advent of balloons and aircraft with sufficient performance to attain significant altitudes brought the clinical syndrome into the realm of aerospace medicine. In 1906, H. Von Schrötter described in his book *Der Sauerstoff in der Prophylaxe und Therapie der Luftdruckerkrankungen* the symptoms he experienced in a steel chamber after ascending in 15 minutes to 8,994 m (29,500 ft) closely resembling caisson disease (29). Von Schroetter discounted that hypothesis, but Boycott, Damant, and Haldane reviewed his account and wrote in an article in 1908 (30):

> "*Although he concludes that these symptoms could not have been due to caisson disease, we think in view of the data given by Damant and ourselves, that he was probably mistaken, and that the risk of caisson disease at very low pressure ought to be taken into account.*"

This is the first clear reference to altitude DCS in the literature. In 1917, Professor Yandell Henderson provided a detailed theory in which he postulated that it would be possible to get DCS from altitude exposure (31).

J. Jongbloed described in his thesis in 1929 (32,33) the effects of simulated altitude on human subjects and called attention to the similarities of compressed air illness and DCS of altitude. In 1931, Barcroft et al. (34) described pain in the knees experienced in the hypobaric chamber while exercising at altitudes of 9,160 m (30,000 ft), which in hindsight were

most likely manifestations of DCS. In the United States, Dr. H. Armstrong researched the effects of decreased PB on the aviator and described in 1939 bubble formation that he experienced himself while at altitude in the hypobaric chamber (35):

> "*. . . Then I noticed a series of small bubbles in the tendons of my fingers . . . I was certain in my mind they represented aeroembolism..*"

In 1938, Boothby and Lovelace reported a case of transient paraplegia in a fellow physiologist (Dr. J. W. Heim) during an ascent to 10,670 m (35,000 ft) while on oxygen; the paraplegia disappeared upon repressurization to ground level. This case illustrated the potential for serious neurologic DCS at altitude and spurred more research (36).

The recent decades of research have introduced new monitoring capabilities, which have allowed investigation of the bubble manifestation of the disease under controlled laboratory conditions. Ultrasonic echo-imaging Doppler measurements as an index for gas evolution have enhanced our capability to investigate the *in vivo* venous gas phase. The degree of venous bubbles present is graded on a numerical scale referred to as a *venous gas emboli* (VGE) score. The first such scoring system was devised by Spencer in 1976 (37); on this 0 to 4 scale a score of 0 refers to no bubbles and a score of 4 refers to an observation with numerous bubbles obscuring the heart sounds.

The experimental work carried out in the 1970s and 1980s has shown that bubbles can be detected in the circulation of healthy individuals after decompressions without any clinical signs of DCS (38). This confirms the early hypothesis by Behnke (1947), who postulated the existence of "silent bubbles" (39). The paradigm of "bubbles = DCS" appears not to be true in many, if not most cases, and recent research focuses on the pathophysiological cascade that can be started by the *in vivo* gas phase (bubbles) in the different tissue compartments and the dose–response relationships leading to clinically evident DCS manifestations. This explains why the demonstration of VGE in the cardiac chambers correlates poorly with the development of DCS. A significant proportion of subjects do have detectable VGE, but do not develop DCS and some develop DCS without evident VGE (38). As more research data becomes available, there is a trend to recognize certain degree of DCS as a normal physiological response to a defined time-pressure profile environment with the *caveat* of possible individual predisposition and other factors.

Terminology

The clinical syndrome of DCI was first recognized in the diving/compressed air environment and later found recognition in the area of aerospace medicine; this explains the wide variety of terms used to describe the disorder and certain specific clinical manifestations. The term *decompression sickness* is a direct translation from the German term *Druckfallkrankheit*, which was introduced by Benzinger and Hornberger in 1941 (40). Currently, *altitude decompression sickness* or simply *decompression sickness* is the term most widely used and accepted in the aerospace medicine literature.

Older terms include aeroembolism, aeropathy, dysbarism, high-altitude diver's disease, high-altitude caisson disease, mechanicobaropathy, aerobullosis, and aeroarthrosis. *Decompression illness* is a term that was introduced to encompass DCS and arterial gas embolism. There is also the distinct possibility for VGE to become arterialized either by crossing the pulmonary filter or crossing through a shunting mechanism from right to left side of the heart (41). The term *DCI* should not be used synonymously with DCS to avoid confusion in an area with already broad terminology.

The typical clinical manifestations of DCS have received idiomatic descriptions over time, the classical limb and joint pains are referred to as *bends*, a term that was used by fellow workers to describe the particular gait—"doing the Grecian bend"—of workers emerging from caisson work during the construction of the piers of the Brooklyn Bridge in the 1870s (26). Respiratory disturbances are commonly referred to as the *chokes*, skin irritation as *creeps* or *divers itch*, and disturbances of the central nervous system (CNS) with vestibular involvement have been labeled with the term *staggers*.

There are distinct and very important differences between hyperbaric (diving) DCS and hypobaric (altitude) DCS, despite many shared commonalities in history, pathophysiology, and nomenclature (Table 3-4). This is a very important point as there is a tendency to indiscriminately transfer information and inferences from one field of research to another, which at times may be a valid thing to do, more often than not though may be unwise and not justified, thereby leading to potentially erroneous conclusions.

The operational significance of DCS is different in hyperbaric versus hypobaric operations in that a diver will get DCS after mission completion (ascent to the surface from depth), whereas an aviator will experience DCS during his mission at altitude. Furthermore, the aviator will have the potential to endanger others if he or she loses control of his aircraft due to DCS, whereas the diver will likely be putting only himself as an individual at risk.

BUBBLE FORMATION: THEORETIC CONSIDERATIONS

The physical principle responsible for bubble formation with decreases in ambient pressure is the concept of supersaturation, which is based on Henry's gas law that states that the amount of gas dissolved in any liquid or tissue is proportional to the partial pressure of that gas with which it is in contact. A good example that illustrates the physical characteristics of Henry's law as it applies to DCS is the opening of a bottle of carbonated beverage. Before opening, few, if any bubbles are visible in the liquid as the gas pressure above the liquid is in equilibrium with the liquid,

TABLE 3-4

Differences between Hypobaric (altitude) and Hyperbaric (Diving) Decompressive Stress (DCS)

Relevant Differences between Altitude and Diving DCS

Altitude DCS	*Diving DCS*
1. Decompression starts from ground level tissue nitrogen saturated state	1. Upward excursions from saturation diving are rare
2. Breathing gas is usually high in O_2 to prevent hypoxia and promote denitrogenation	2. Breathing gas mixtures are usually high in inert gas due to oxygen toxicity concerns
3. The time of decompressed exposure to altitude is limited	3. The time at surface pressure following decompression is not limited
4. Premission denitrogenation (preoxygenation) reduces DCS risk	4. The concept of preoxygenation is generally not applicable
5. DCS usually occurs during the mission	5. DCS risk is usually greatest after mission completion
6. Symptoms are usually mild and limited to joint pain	6. Neurologic symptoms are common
7. Recompression to ground level is therapeutic and universal	7. Therapeutic chamber recompression is time limited and sometimes hazardous
8. Tissue P_{N_2} decreases with altitude exposure to very low levels	8. Tissue P_{N_2} increases with hyperbaric exposure to very high levels
9. Metabolic gases become progressively more important as altitude	9. Inert gases dominate
10. There are very few documented chronic sequelae	10. Chronic bone necrosis and neurologic damage have been documented

Pilmanis AA, Petropoulos L, Kannan N, et al. Decompression sickness risk model: development and validation by 150 prospective hypobaric exposures. *Aviat Space Environ Med* 2004;75:749–759.

on lowering the pressure above the liquid by opening the bottle, the liquid–gas system re-equilibrates to the lowered ambient pressure by offgassing bubbles.

The mechanisms that are involved in the hyperbaric diving environment as well as the hypobaric altitude environment are thought to be the same in regard to DCS, although the bubble dynamics appear to be different. Decompression to altitude results in a slower release of bubbles compared to the same absolute ratio of pressure change in a hyperbaric environment (42).

The current theories of bubble formation involve two main mechanisms. *De novo* formation of bubbles also referred to as *de novo* nucleation, requires very high degrees of supersaturation and formation of bubbles from preexisting gas nuclei (bubble nuclei), which requires pressure differentials of only fractions of an atmosphere.

The current working hypothesis for the formation of *in vivo* bubbles favors the gas nuclei mechanism. Viscous adhesion, which is the mechanism by which negative pressures are generated in a liquid between moving surfaces (e.g., joints), is of sufficient magnitude to cause *de novo* bubble formation. This mechanism has been invoked to explain vacuum phenomena in joints, the cracking of joints, and the formation of autochthonous (*in situ*) bubbles in the white matter of the spinal cord (43). The following discussion will highlight these mechanisms and factors influencing bubble growth.

The mechanisms and moderating factors in the human body tissues that lead to bubble formation/propagation, clinical symptoms of DCS, and moderating variables are still incompletely understood.

Factors Influencing Bubble Formation

Bubble Nuclei

The conceptual idea of the presence of "bubble nuclei" or "bubble formation centers" in the tissues derives from the physics limiting bubble growth. Very small bubbles should have a propensity to dissolve and disappear due to their very high surface tension. Surface tension is inversely proportional to the bubble radius (law of LaPlace), which would raise the internal pressure of the microbubbles above the external absolute pressure, thereby leading to their dissolution. This would suggest that larger bubbles should not be able to exist if there are no smaller bubbles that precede them, which is an obviously wrong conclusion. If we assume that we would need to create bubbles *de novo,* then experimental evidence shows that forces of approximately 100 to 1,400 ATA are needed. We know that bubble formation occurs at much lower pressure differentials in animals and humans (fractions of 1 ATA). Bubbles can form in fluids at low levels of supersaturation if forces act to pull objects apart which are in close proximity, a process called *tribonucleation*. Furthermore there is experimental evidence showing that compression of animals (shrimp, crabs, and rats) before hypobaric exposure markedly decreases bubble formation and DCS (44). These observations are consistent with the existence of gas nuclei that allow bubble formation at much lower pressure gradients (fractions of 1 ATA). The current understanding of the dynamics of bubble nuclei is that they are generated by motion (and possibly other factors, see section **Mechanical Supersaturation** in subsequent text) and that there is a dynamic equilibrium between generation and destruction of gas nuclei in the tissues (45).

Supersaturation

During decompression from any atmospheric pressure, some quantity of inert gas in the tissues must diffuse into the blood, travel to the lungs, and leave the body in the expired air because the quantity of inert gas that can remain dissolved in tissue is directly proportional to the absolute ambient pressure.

Supersaturation is defined by the following equation:

$$\text{Supersaturation} = \sum P_g + \sum P_v - \sum P_a$$

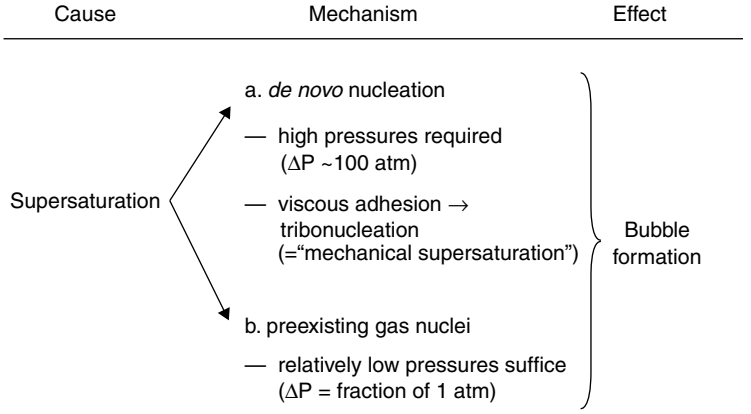

FIGURE 3-3 Synopsis of the different mechanisms involved in bubble formation.

P_g: sum of the tensions of all dissolved gases; P_v: sum of any vapor pressure (e.g., water); P_a: local absolute pressure.

In summary, we can say that supersaturation can occur when either local absolute pressure is low or when the sum of the dissolved gases and vapor pressures is high.

During ascent, the reduction in P_B creates a condition whereby the tissue inert gas tension (P_{N_2} = nitrogen gas partial pressure) is greater than the total P_B. This situation is called *supersaturation*. Therefore, if the decompression exceeds some critical rate for a given tissue, that tissue will not unload the inert gas rapidly enough and will become supersaturated. The probability of bubble formation increases with increasing supersaturation.

Supersaturation due to negative pressure occurs in many mechanical processes resulting in a local reduction of absolute pressure in a liquid system. The flow of a liquid through a local narrowing in a tube, for example, results in a local drop in pressure (Bernoulli principle), which in turn can lead to transient bubble formation (Reynold's cavitation). Sound waves are well known to cause acoustic cavitation in liquid systems. A further mechanism of biological interest is viscous adhesion (Figure 3-3). Viscous adhesion describes the forces generated when two surfaces in a liquid are pulled apart; the negative pressures that can be generated can reach thousands of negative atmospheres. The amount of supersaturation that can be mechanically generated by viscous adhesion is directly proportional to the liquid viscosity and indirectly proportional to the cube of the distances between the two surfaces. Bubbles that are generated by this mechanism are said to be generated by tribonucleation. This mechanism is invoked in the generation of the cracking of joints by pulling apart their articular surfaces, resulting in the generation of a vapor-filled bubble, which collapses upon release of the traction, as well as in the appearance of vacuum phenomena (gaseous cavitation) in joints under traction and in the spinal column within disks, facet joints, and vertebrae (43,45).

Critical Supersaturation

Apparently, a level of supersaturation is reached which the body can tolerate without causing the inert gas to come out of solution to form bubbles. Once the critical supersaturation ratio is reached, however, bubbles develop which can lead to DCS. The English physiologist J. S. Haldane first described the concept of critical supersaturation in 1908 (30). Haldane was commissioned by the British Admiralty to investigate and devise safe decompression procedures for Royal Navy divers, and his work demonstrated that humans could be exposed to hyperbaric pressures and subsequently decompressed without having DCS as long as the total pressure reduction was no greater than 50%. Haldane devised the concept of tissue half-time to define the ability of a particular tissue to saturate/desaturate with nitrogen by 50% (i.e., a tissue would be saturated 50% after the passing of one tissue half-time). He postulated that the body tissues with different perfusion rates can be adequately represented by half-times of 5, 10, 20, 40, and 75 minutes (five-tissue model, constant allowable ratio). Haldane argued that the human body could hypothetically tolerate a 2:1 decrease in ambient pressure without getting DCS symptoms (''2-to-1'' rule). Further operational research showed that the Haldane diving tables consisting of Table 1 for shorter dives up to 30-minute decompression time and, up to a depth of 204 ft sea water (fsw) and Table 2 for longer dives (with bottom times >1 hour and decompression times of >30 minutes) were overly conservative for Table 1 and not safe enough for Table 2. Current theory is based on variable allowed ratio for different tissues; this is influenced by tissue nitrogen half-time, time, and ΔP. This is the reason why no current decompression schedules use Haldane's 2-to-1 rule, but it is discussed here to show a mathematical concept. If Haldane's 2-to−1 relationship of allowable total pressure change is converted to a P_{N_2} to P_B relationship, the critical supersaturation ratio (R) would be:

$$R = \frac{P_{N_2}}{P_B}$$

For example,

$$R = \frac{P_{N_2} \text{ at } 2ATA}{P_B \text{ at } 1ATA} \qquad [1]$$

$$R = \frac{(2)(0.79)}{1} = \frac{1.58}{1} = 1.58$$

In fact, there are apparently a number of critical supersaturation ratios for the various mathematical compartments, representing different tissues.

A person living at sea level and breathing atmospheric air will have a dissolved P_{N_2} of 573 mm Hg in all body tissues and fluids, assuming that P_B equals 760 mm Hg; P_{AO_2} equals 100 mm Hg; P_{ACO_2} equals 40 mm Hg; and P_{AH_2O} equals 47 mm Hg.

$$\begin{aligned} P_B \text{ (sea level)} &= 760 \text{ mm Hg} \\ &= \Sigma \text{ (partial pressures of all alveolar gases)} \\ &= P_{H_2O} (47 \text{ mm Hg}) + P_{CO_2} (40 \text{ mm Hg}) \\ &\quad + P_{O_2} (100 \text{ mm Hg}) + P_{N_2} (573 \text{ mm Hg}) \end{aligned}$$

If that person is rapidly decompressed to altitude, a state of supersaturation will be produced when an altitude is reached where the total P_B is less than 573 mm Hg, a condition that occurs at an altitude of 2,287 m (7,500 ft). Therefore, the altitude threshold above which an individual living at sea level would encounter supersaturation upon rapid decompression is 2,287 m (7,500 ft).

The lowest altitude where a sea-level acclimatized person may encounter symptoms of DCS may be lower than 3,962 m (13,000 ft) (46). However, recent data revealed a 5% threshold at 5,944 m (19,500 ft) (47) using a probit analysis of more than 120 zero-prebreathe, 4-hour exposures with mild exercise to generate an onset curve showing less than 0.001% DCS at 13,000 or below. The degree of supersaturation at 5,489 m (18,000 ft) can be expressed as a ratio, as follows:

$$R = P_{N_2} / P_B \qquad [2]$$

If the tissue P_{N_2} equals 573 mm Hg and P_B equals 372 mm Hg, then R equals 573/372, or 1.54. This value approaches the critical supersaturation ratio expressed by Haldane. The incidence of altitude DCS reaches 50% by 7,010 m (23,000 ft) with zero prebreathe and mild exercise at altitude (47).

Symptoms can occur at much lower altitudes when "flying after diving" or "diving at altitude and driving to higher altitude" (diving in mountain lakes). Many cases of DCS have been documented in divers who fly too soon after surfacing. Altitudes as low as 1,524 to 2,287 m (5,000 to 7,500 ft) may be all that is necessary to induce bubble formation in a diver who has made a safe decompression to the surface. The problem involves the higher tissue P_{N_2} that exists after diving. The Undersea and Hyperbaric Medical Society's recommended surface interval between diving and flying ranges from 12 to 24 hours depending on the type and frequency of diving (48).

Factors Influencing Bubble Growth

Upon decompression to altitude, the factors causing a bubble to grow are as follows:

1. Boyle's law ($P_1V_1 = P_2V_2$) expansion due to reduced pressure
2. Entrance of nitrogen from tissues in the state of supersaturation
3. Entrance of O_2 and CO_2 (negligible effect during decompression from hyperbaric exposures, significant in hypobaric exposures)

Boyle's Law Effects

Once a bubble is formed, its size will increase if the total pressure is decreased (Boyle's law: $P_1V_1 = P_2V_2$). During hyperbaric therapy, bubble size is reduced during compression. The surface tension of a bubble is inversely related to bubble size and opposes bubble growth. Therefore, as total pressure within the bubble is increased, the surface tension opposing bubble growth also is increased. Once a critically small bubble size is achieved, the surface tension is so high that the bubble can no longer exist. The bubble collapses, and its gases are dissolved (44,49).

Gaseous Composition

Nitrogen, or another inert gas, is generally considered to be the primary gas involved in symptomatic bubbles. If nitrogen were the only gas initially present in the newly formed bubble, an immediate gradient would be established for the diffusion of other gases into the bubble. Hence, a bubble will quickly have a gaseous composition identical to the gaseous composition present in the surrounding tissues or fluids. When bubbles are produced upon decompression from hyperbaric conditions, gases other than nitrogen represent only a small percentage of the total gas composition of the bubble. Exposure to a hypobaric environment decreases the partial pressures of all gases including nitrogen. The partial pressures of O_2 and CO_2 at the tissue level are close to independent from hypobaric or hyperbaric conditions because appropriate levels are a prerequisite for life. If we assume that a bubble were to be present at sea level (1 ATA) with O_2 and CO_2 representing 6%, respectively, of its total volume and pressure and we decompress to an altitude of 5,487 m (18,000 ft, 1/2 ATA), then O_2 and CO_2 would each account for 12% (together 24%) of the total volume and pressure of the bubble. If the decompression were instantaneous then O_2 and CO_2 would each account for 6% of the bubble volume, but the partial pressure would be half of the sea level partial pressures, which would cause an immediate influx of O_2 and CO_2 into the bubble accounting for 12% growth in bubble volume in this example. This example (45) illustrates the importance of the metabolic gases O_2 and CO_2 in hypobaric exposures; at this point it is also valuable to remember the important contribution of water vapor to bubble formation and gas behavior in general in a hypobaric environment (Figure 3-9B), especially as we approach water vapor pressure (47 mm Hg) and, therefore Armstrong's line (zone) at 63,000 ft.

Hydrostatic Pressure

The tendency for gases to leave solution and enlarge a seed bubble can be expressed by the following equation introduced by Harvey in 1944 (50):

$$\Delta P = t - P_{ab} \qquad [3]$$

where ΔP is the differential pressure or tendency for the gas to leave the liquid phase, t is the total tension of the gas in the medium, and P_{ab} is the absolute pressure (i.e., the total P_B on the body plus the hydrostatic pressure).

Within an artery at sea level, t equals 760 mm Hg. The absolute pressure, P_{ab}, is 760 mm Hg plus the mean arterial blood pressure (100 mm Hg), or 860 mm Hg. Therefore,

$$\Delta P = 760 \text{ mm Hg} - (760 \text{ mm Hg} + 100 \text{ mm Hg})$$
$$\Delta P = -100 \text{ mm Hg} \quad [4]$$

When the value of ΔP is negative, there is no tendency toward bubble formation or growth. If the value for ΔP becomes zero or positive, bubble formation or growth is likely to occur.

Within a great vein at sea level, P_{O_2} equals 40 mm Hg, P_{CO_2} equals 46 mm Hg, and P_{H_2O} equals 47 mm Hg; therefore, t equals 706 mm Hg and P_{N_2} is 573 mm Hg. Absolute pressure, P_{ab}, is 760 mm Hg plus the mean venous pressure (which in the great veins in the chest may be 0 mm Hg). Therefore,

$$\Delta P = 706 \text{ mm Hg} - (760 \text{ mm Hg} + 0 \text{ mm Hg})$$
$$\Delta P = -54 \text{ mm Hg} \quad [5]$$

By suddenly exposing a person to an altitude of 5,490 m (18,000 ft) without time for equilibration at the new pressure, venous ΔP would have a large positive value:

$$\Delta P = 706 \text{ mm Hg} - (380 \text{ mm Hg} + 0 \text{ mm Hg})$$
$$\Delta P = +326 \text{ mm Hg} \quad [6]$$

The value for t in the earlier equation can also be increased in local areas by high levels of CO_2 production. Hence, in muscular exercise, a high local P_{CO_2} associated with a reduction in P_B causes higher positive values of ΔP than with a reduction in P_B alone. It is important to appreciate that this is a highly localized process, unless the exercise is at anaerobic levels; situations of this nature are not likely to occur for more than a few minutes in the operational aerospace environment due to the ensuing fatigue.

Hydrostatic pressure is, therefore, considered to be a force opposing bubble formation or bubble growth and includes not only blood pressure and cerebrospinal fluid pressure but also local tissue pressure (turgor), which varies directly with blood flow.

Influence of Tissue Perfusion and Diffusion

The rate of inert gas washout from tissues is dependent on perfusion; therefore, factors that alter tissue perfusion influence inert gas washout. Studies in the hypobaric environment have shown that exercise before exposure reduces the risk of DCS while prebreathing oxygen (DCS incidence decreased from 90% to 20%) (51). The putative mechanism for these effects is the increase in cardiac output with increased peripheral circulation as well as vascular volume shifts to the chest during immersion. Negative pressure breathing has similar effects to immersion with increases in cardiac output and increased inert gas washout (52). Changes in body position do have similar influence on inert gas washout; supine position has similar effects to immersion compared to the erect body position. Effects of temperature—in the context of tissue perfusion—are mediated by changes in vascular tone, as warm temperature will result in vasodilatation and enhanced inert gas washout, whereas lowering of the temperature results in vasoconstriction and decreased inert gas washout.

Pathophysiology of Bubbles

The presence of bubbles in tissues has direct and indirect effects. The location of bubbles is important in this context; extravascular bubbles can cause local tissue distortion, dysfunction, and possibly local ischemic changes. The painful sensations of joint pain are thought to be related to compressive effects on periarticular, peripheral nerve fibers. Intravascular bubbles are of lesser importance in the context of hypobaric DCS unlike their role in diving DCS, they may—depending on their location within the vasculature and the tissue—cause symptoms due to local relative hypoperfusion. The indirect effects of bubbles are more complex in nature; the interaction of cells (blood, tissue, endothelium) with the bubble surface leads to the release of mediators, which in turn may influence chemotaxis for leucocytes (polymorphonuclear neutrophils) with subsequent generation of oxygen radicals, complement activation, activation of the intrinsic coagulation pathway, generation of arachidonic acid metabolites, release of endothelium-derived mediators to name just a few. The modulation of these tissue reactions depends furthermore on the target tissues, the bubble load (dose–response), local factors such as degree of ischemia, collateral circulation, reperfusion injury, and environmental factors, for example, hypoxia, exercise, temperature, and rapidity of ambient pressure change (44,49,53).

The putative fate of bubbles formed during decompression is summarized in Figure 3-4. It is important to emphasize that our knowledge is far from complete and that the extravascular bubble dynamics are of more relevance to altitude DCS compared to the intravascular bubbles of diving DCS.

Target Organs of Bubbles Created during Decompressive Stress

Lungs

VGE results in a dose-dependent increase of pulmonary artery pressure and subsequent increase in pulmonary vascular resistance (54). These changes can be attributed to mechanical obstruction of the pulmonary vascular bed and vasoconstriction; hypobaric exposures of greater than 24,000 ft (7,315 m) did not result in appreciable increases in pulmonary arterial pressures (55). In cases with large gas loads that overwhelm the capacity of the pulmonary circulation filter, the embolization of the pulmonary vascular bed results in ventilation–perfusion mismatching leading to decreased peripheral arterial O_2 saturation and decreased end-tidal CO_2 levels (56).

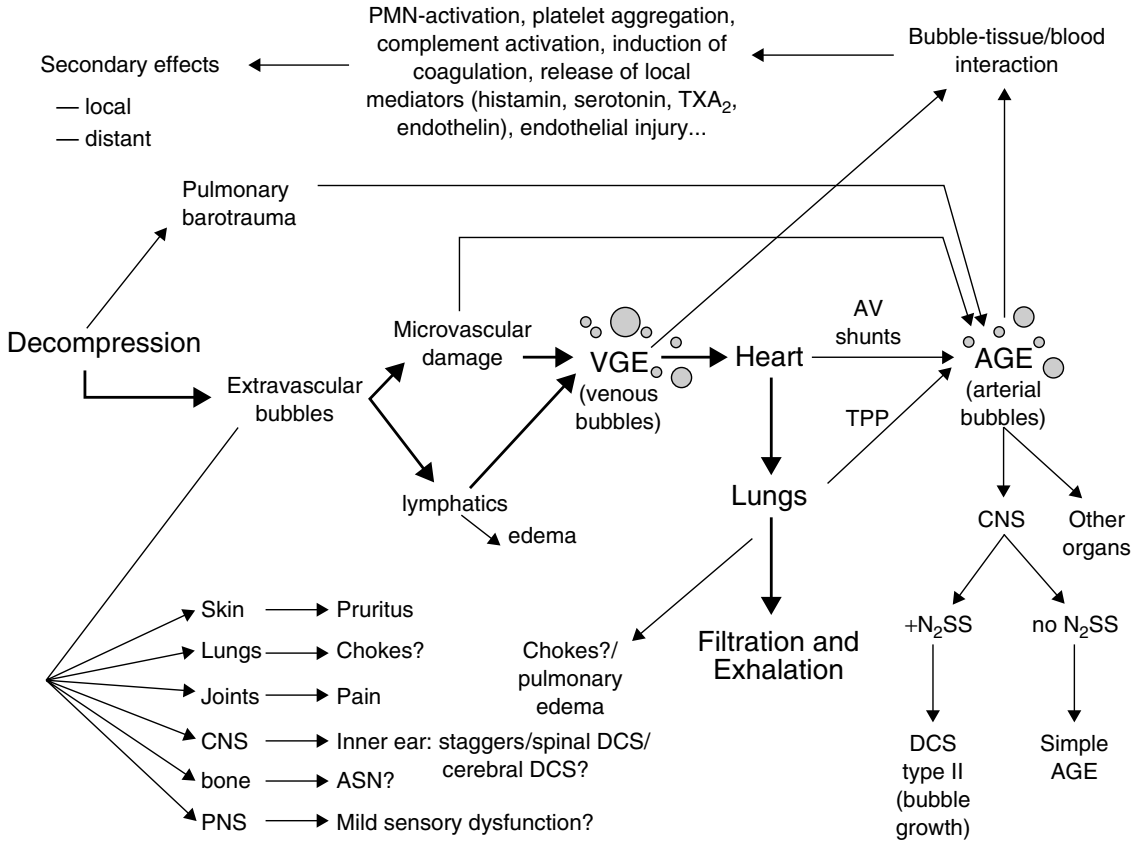

FIGURE 3-4 Synopsis of the putative pathophysiological pathways of bubbles in decompression sickness (DCS), *bold arrows* indicate the major physiological pathway for elimination of inert gas, question marks indicate lack of scientific literature proving the postulated relationship.
PMN, neutrophilic leucocytes TXA_2, thromboxane A_2; VGE, venous gas emboli; AV, arteriovenous; AGE, arterial gas emboli; TPP, transpulmonary passage; CNS, central nervous system; N_2SS, nitrogen supersaturation; DCS type II, serious neurologic (cerebral) decompression sickness; ASN, aseptic bone necrosis; PNS, peripheral nervous system.

In experimental animal studies, large doses of VGE can impair cardiac output and arterial blood pressure (likely due to right ventricular failure and decreased myocardial perfusion). Left ventricular end-diastolic pressure is typically not altered. In addition to the hemodynamic effects of pulmonary VGE, there is evidence of bronchoconstriction and substernal discomfort as well as paroxysmal coughing and permeability changes in the pulmonary vascular bed leading to fluid shifts and pulmonary congestion/edema (57–59).

The lungs are a very efficient filter mechanism that removes VGE from the circulation. This mechanism can be overloaded possibly resulting in spillover of venous bubbles into the arterial circulation (transpulmonary passage of bubbles) (55). Venous bubbles that undergo transpulmonary passage become arterialized and hence can pose the risk of AGE (44,49,55).

Heart

Morphologic abnormalities or variations of the cardiac anatomy resulting in opportunities for shunting between the right and left side of the heart [such as large atrial septal defects (ASDs) or a patent foramen ovale (PFO)] can result in arterialization of venous bubbles and may theoretically represent an increased risk for AGE (44,49,55).

Central Nervous System

When bubbles reach the cerebral vasculature and result in an occlusion to blood flow, the vessels react with a temporary vasoconstriction followed by a marked dilation of the downstream microcirculation and venules. Experimental evidence exists for transport of cerebral gas bubbles through the capillaries into the venous bed. This fact has been offered as an explanation for the fact that approximately 60% of divers with cerebral DCS recover before recompression therapy is initiated; furthermore, this has led to the speculation that neurologic defects following cerebral gas embolism are likely due to secondary changes in the microvasculature (endothelium) as opposed to the transient obstruction to blood flow by the bubbles. Autochthonous bubble formation within the white matter of the spinal cord has been implicated in the pathogenesis of spinal cord DCS as well as epidural vein bubbles and AGE. Experimental studies on cats have shown that severe cardiac arrhythmias and hypertension can be induced by injection of air into the vertebral arteries. This has led to

the conclusion that the cardiac dysfunction in DCS may be closely linked to cerebral embolism (53).

Blood

The interaction of blood components and endothelium with the bubble surface results in a cascade of changes (44,60) Most of the data in this context relate to and emanate from diving-related DCS as opposed to altitude DCS. Thrombocyte aggregation with a low platelet count has been reported. Neutrophils sequester in the pulmonary vascular bed with activation of the intrinsic coagulation pathway, presumably by activation of the contact system activator Hageman factor, and endothelial damage through release of oxygen radicals. Platelets and leucocytes have been shown by electron microscopy to adhere to circulating bubbles. In addition, activation of the complement system takes place; its contribution to the pathophysiologic sequence in DCS however is not clear (49,61).

Human studies in diving DCS have shown increases in hematocrit (hemoconcentration) and decreased platelet count in serious cases of DCS, suggesting microvascular damage with loss of plasma volume (61,62).

Incidence Data

The incidence of altitude DCS in the altitude chamber training environment varies among facilities and countries; European military training facilities (UK) have reported five cases of DCS type I (pain only) over a 5-year period (1983–1987) among 12,000 exposures to 7,622 m (25,000 ft) equal to a rate of 0.41 per 1,000 exposures (62). Data regarding the incidence of DCS in inside observers in the United Kingdom has not been formally reported; anecdotal evidence corroborates its existence (62,63). The United States Navy (USN) reported 41 cases in 20,778 exposures to 7,622 m (25,000 ft) from January 1996 to October 2000 (63). This equals a rate of 2 per 1,000 exposures; inside observers experienced a rate of 0.18% and trainees 0.21%. The experience of U.S. Army for the years 1984 to 1989 was 42 cases of DCS in 21,498 exposures (0.195 per 1,000 exposures; inside observer to student rate ratio was 3.17) (64). The USAF reported for 1985 to 1987 (exposures to 7,622 m (25,000 ft) 34 cases among 80,048 exposures, which translates into an incidence rate of 0.042% (0.4 per 1,000 exposures) (65).

The flight incidence for the USAF during the period 1980 to 1990 was 49 DCS incidents, which translates to a DCS mishap rate of approximately 0.2 to 0.3 per 100,000 flying hours (66).

For a discussion regarding EVA risk in space operations see Chapter 10.

From the operational perspective of the aviator, DCS does not pose a significant risk for any single mission in view of the above numbers; it is a rare event and very serious outcomes (death, disability) are exceptionally rare (one fatality in aviation since 1959) (67). In the past, the threat to the aviator was the reporting process itself because the fact that DCS was experienced did result in grounding of a capable operator. This aspect probably did introduce reporting bias into the reported incidence figures (operational underreporting). To reduce a possible source of reporting bias, negative consequences of reporting should be avoided and detailed education on the possible signs and symptoms of DCS should be given to aircrew (recognition of a symptom is based on the knowledge of a symptom). Reporting of DCS symptoms has become a physiologic incident without punitive ramifications for the flying career of the aviator and as a result data from extreme altitude operation environments (e.g., U2 surveillance aircraft) started to emerge (68). A similar situation in the operational environment was encountered with G-induced loss of consciousness (G-LOC). There was no obvious G-LOC problem apparent among military aviators until a targeted survey, without penalty for reporting incidents, was done and only then the real incidence of G-LOC emerged.

Factors Thought to Affect Decompressive Sickness

Attempts have been made to correlate the incidence of both diving-induced and altitude-induced DCS with various environmental and physiological factors. A review of the existing data documenting the presence or absence of association of these factors with altitude DCS is summarized in the next sections.

Altitude Attained

With increasing altitude, the incidence of DCS increases, as does the ratio of severe to mild cases. The severity of the cases will increase with increasing altitude (47,69).

In a review of 145 cases of altitude-induced DCS necessitating treatment, Davis et al. (70) reported that 13% of these cases occurred with altitude exposures of 7,622 m (25,000 ft) or below and 79% occurred with exposures of 9,146 m (30,000 ft) or greater.

Duration of Exposure

At all altitudes above 5,488 m (18,000 ft), the longer the duration of exposure, the greater the incidence with DCS occurring after 5 hours of exposure to 25,000 and 27,500 ft even after 1 hour of prebreathes. Some subjects, however, will not develop DCS at a given altitude (individual susceptibility), even after extended periods of time (71).

Combination of Environmental Factors to Predict Decompression Sickness Risk

Pilmanis et al. (72) developed an Altitude Decompression Sickness Risk Assessment Computer (ADRAC) model that uses altitude, time at altitude, level of activity, and preoxygenation time for various time, exposure, and preoxygenation scenarios (Figures 3-5A, 3-5B & 3-6).

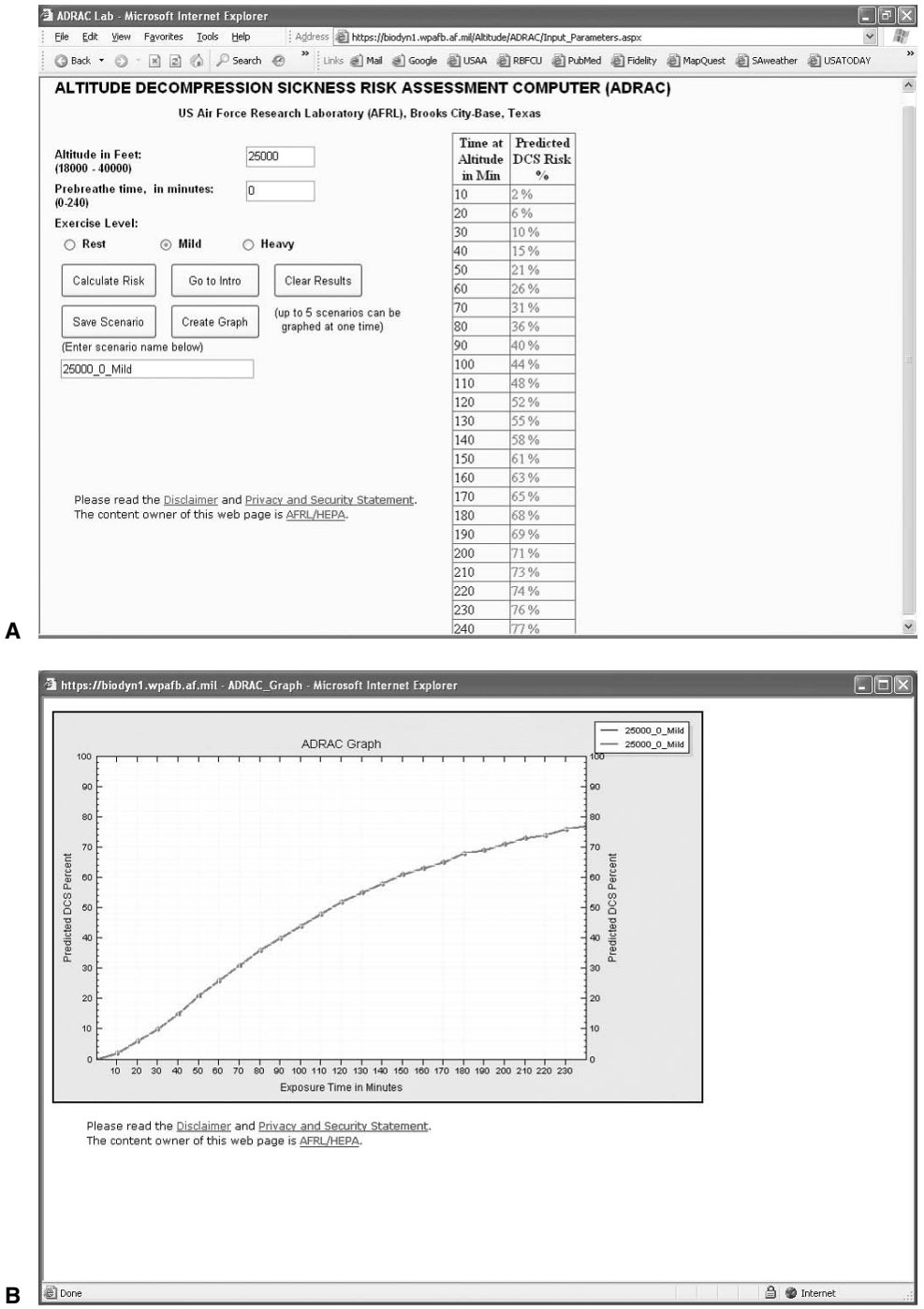

FIGURE 3-5 **A:** Altitude Decompression Sickness Risk Assessment Computer (ADRAC) prediction of DCS risk at 25,000 ft with no pre-breathe and mild exercise. **B:** ADRAC graph of DCS risk at 25,000 ft with no prebreathe and mild exercise.

Previous Exposures to Altitude

Each successive altitude exposure to 25,000 ft does lead to increasing amounts of eliminated inert gas (especially if the breathing gas is 100% oxygen) and therefore results in decreased DCS and VGE incidence compared to a single continuous exposure (73).

The series of cases reported by Davis et al. (70) illustrates the increased incidence of DCS in inside observers (who continuously ambulate in the altitude chamber to monitor their trainees during the exposure). The key DCS risk factor in the aforementioned case series is the physical activity of the inside observer and not the actual repeat exposure itself. Recent experience from the USN suggests that the incidence among students and inside observers may be identical provided that both groups undergo diligent preoxygenation before altitude exposure (74).

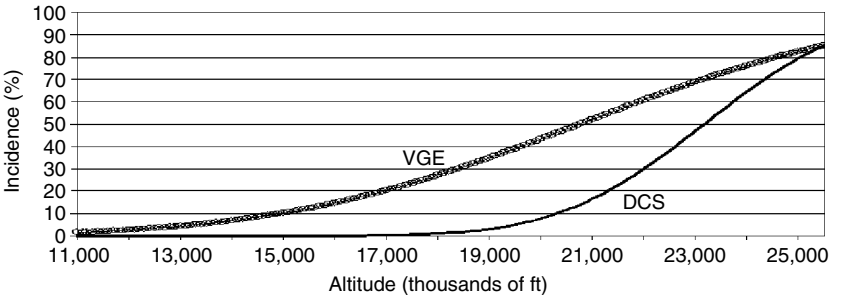

FIGURE 3-6 Zero-preoxygenation altitude threshold curves for decompressive sickness (DCS) and venous gas emboli (VGE).

Flying Following Diving

If an individual breathes a gas at pressures greater than sea level before altitude exposure, his/her susceptibility to DCS will significantly increase. Retrospective case reviews as well as prospective animal and human investigations have resulted in a number of recommendations by various agencies as to the sea level surface interval necessary to safely fly after diving. Recent studies by Pollock et al. showed no apparent increase in DCS risk after dry resting 60 fsw/60 min air dives followed at least 12 hours later by a resting 25,000 ft 3-hour flight while on 100% oxygen (75). The Undersea and Hyperbaric Medical Society reviewed this material and recommended the following (48):

Dive Schedule Minimum Surface Interval

1. No-decompression dives
   a. Less than 2 hours accumulated dive time in the 48 hours preceding surfacing from the last dive wait 12 hours
   b. Multiday, unlimited diving wait 24 hours
2. Dives requiring decompression stops (but not including saturation dives) wait 24 to 48 hours

Saturation diving presents complex problems and is beyond the scope of this chapter. The interested reader is referred to the specialized literature on the subject (see list of **Recommended Reading** in reference section).

Age

Recent work (47) showed increased DCS risk with age in males and decreased DCS risk with age in females, with all subjects showing no difference due to the opposite effects of age based on gender. Height had no effect. Factors that did correlate with increased risk included higher body mass index and lower physical fitness.

Gender

Retrospective studies indicated initially that the incidence of DCS in female subjects is significantly higher than in males (70,76,77). Prospective studies have not revealed any significant differences between male and female for DCS symptoms (47,78). Of note, women using hormonal contraception showed significantly higher DCS susceptibility compared to those not using hormonal contraception during the latter 2 weeks of the menstrual cycle (47).

Exercise

The association between physical exertion at altitude and DCS has been well established. During World War II, altitude chambers were used to select out bends-prone individuals from aircrews. The subjects were taken to an altitude of 12,195 m (40,000 ft) and exercised at altitude until half of them developed bends. The remaining bends-resistant subjects were assigned to high-altitude, unpressurized bomber missions. The effect of exercise on the incidence of DCS is equivalent to increasing the exposure altitude 915 to 1,524 m (3,000 to 5,000 ft). Recent studies on the effect of mild versus strenuous exercise at 10,671 m (35,000 ft) have shown that both significantly increase DCS incidence (79).

Exercise during oxygen prebreathe has been shown to significantly decrease DCS risk by increasing inert gas washout (increased perfusion) (51,80–82). The method has been used successfully to provide additional protection for high-altitude reconnaissance pilots (83) and during preparation for EVA from the ISS (84).

Injury

No convincing evidence exists to associate previous injury with DCS. On the basis of theoretic considerations, however, it is thought that during the acute stages of injury a joint may have increased susceptibility to DCS pain because of perfusion changes associated with the injury and/or healing mechanisms.

Body Build

For a long time, a basic tenet of diving and aerospace medicine has been that obesity increases the susceptibility to DCS; data from work from the United States Air Force School of Aerospace Medicine (USAFSAM) tended to confirm these historic tenets showing an increased DCS risk with increased body mass index (47,85).

Other Factors

Temperature

No good correlation exists between the frequency of DCS and the ambient temperature, with the exception of work done by Balldin in the context of warm water immersion and its effects on increased nitrogen washout (52).

Hypoxia

There is significant overlap between the symptoms of DCS and hypoxia. Hence, careful distinction between the two

entities needs to be made. There is anecdotal evidence suggesting an association of hypoxia and DCS (86). The few published studies suggest no effect of hypoxia (87–89).

Acid–Base Balance

Elevated P_{CO_2} has been associated with the incidence of severe DCS in several studies (39,90,91). Deliberate hyperventilation at altitude has been found to decrease the pain associated with DCS. The question arises as to whether the contribution of elevated P_{CO_2} affects bubble growth or primary modulation of pain perception by altered acid–base balance.

Dehydration

Individuals with an overall high average daily fluid intake were found to be less susceptible to DCS than a comparable group of individuals with a restricted fluid intake over 2 weeks. These findings were corroborated in three separate studies (92–94).

Effects of Microgravity

Under microgravity conditions, fluid shifts (increase in central blood volume) occur, which may have an effect on pulmonary perfusion and modify nitrogen washout dynamics from tissues. Static unloading may produce fewer bubble nuclei. These effects constitute physiological inference without controlled studies under microgravity to corroborate them at this point. To date, there has not been a confirmed DCS event during EVA in the United States and international space programs. Further information will accrue from the medical investigation programs on the ISS. The effect of ambulatory (walking during exposure) versus nonambulatory exposures with the same metabolic cost of activity while decompressed yielded no difference in DCS risk (95), or in total joint pain DCS (96). These papers concluded that walking under 1-G conditions during exposure would not produce DCS levels higher than during supine exposures emulating weightlessness. However, the distribution of joint pain was different with the upper body developing more DCS than the lower body during nonambulatory exposures with the reverse true during ambulatory exposures (96).

Patent Foramen Ovale

This is an area of current investigation and controversy due to its potential impact on selection of personnel for work in environments that may put the individual at risk for DCS. Hypothetically, a PFO could allow arterialization of venous gas bubbles by transforaminal passage of bubbles from the right atrium to the left atrium and make them a possible risk factor for cerebral DCS/AGE (97).

Longitudinal data to define the risks in hyper- or hypobaric environments are not available in the literature. A meta-analysis of the relationship between DCS and PFO in diving showed a risk ratio of 2.52 for PFO, with an incidence of 5.7 cases of type II DCS per 10,000 dives (98). Clinically silent cerebral lesions [magnetic resonance imaging (MRI), T2 weighted images] in divers with hemodynamically significant PFO have been described (99); the clinical significance of this finding is unclear at this point in time.

The data in the altitude DCS setting are sparse at this point; a clear relationship between altitude DCS and PFO has yet to be firmly established. No link between PFO and DCS (41) was found in the six cases of left ventricular gas emboli (LVGE) observed throughout 1,075 subject exposures where echo-imaging of the right and left heart was used. Of the five subjects with LVGE who were evaluated for PFO, three were negative by transthoracic echocardiography (TTE) or transesophageal contrast echocardiography (TEE), one was positive for PFO by TEE, and one displayed a sinus venosus by TEE. It is important to keep in mind that a significant proportion of asymptomatic, healthy adults do have a PFO (prevalence 27.3%) (100). The published literature does not allow the conclusion that subjects should be disqualified from hypobaric duties based on the presence of a PFO alone. The presence of a history of events suggestive of a right to left shunt should trigger further appropriate testing as clinically indicated.

Miscellaneous Factors

Lower physical fitness was shown to be related to increased DCS risk (47,85) in both females and males ($p < 0.05$); the least fit (lowest third of VO_2) 254 versus the most fit (highest third VO_2) 254 subjects whose VO_2 were evaluated. A later analysis with a larger sample size showed a significant relationship between lower physical fitness and increased susceptibility to DCS ($p < 004$).

Preventive Measures

Protection against DCS is based on controlling the tissue nitrogen-to-ambient pressure ratio (P_{N2}/P_B). When an inert gas, such as nitrogen, is breathed, the tension of the gas dissolved in tissue fluids increases until equilibrium with the partial pressure of the gas in the respired medium is reached. With pressure reduction (decompression), supersaturation can occur. Some degree of supersaturation can be tolerated. The critical P_{N2}/P_B ratio differs for each body tissue. When the safe limits of decompression are exceeded, gas separates from solution in the blood and other tissues. This process is the initiating event for DCS, although there is considerable variability between and among individuals as to whether or not DCS results from any event causing bubble formation. For diving, safe decompression limits vary with time and the depth of the dive and are published as decompression tables in a variety of diving manuals, one of which is the USN Diving Manual (101).

The aviator is protected from DCS in two ways, aircraft pressurization and denitrogenation (102). Aircraft pressurization is a method of maintaining the aircraft cabin pressure and, therefore, the physiologic altitude to which the aviator is exposed, at a considerably lower PA than the actual altitude at which the aircraft is flying. With adequate aircraft

pressurization, the individual is not exposed to reduced P_B where bubbles can form.

Denitrogenation is a method by which one breathes 100% O_2 for the purpose of eliminating N_2 from the body before going to altitude. This method is used to protect the individual who must ascend to high altitudes that can produce DCS. With 100% O_2 breathing, O_2 replaces other tissue-dissolved gases, including N_2. Therefore, the amount of N_2 in each body tissue is reduced before ambient pressure reduction occurs. The P_{N2}/P_B ratio is reduced, because the value for P_{N2} is reduced, thereby decreasing the risk.

For example, an aviator rapidly ascends from sea level ($P_B = 760$ mm Hg) to 5,488 m (18,000 ft) ($P_B = 380$ mm Hg). The aircraft pressurization system maintains pressure in the cabin at 2,439 m (8,000 ft) ($P_B = 565$ mm Hg). Assuming that all tissues are saturated at sea level ($P_{N2} = 573$ mm Hg) and that offgassing occurring during the rapid ascent is insignificant, the P_{N2}/P_B ratio would be 1.01:

$$\frac{P_{N_2}}{P_B} = \frac{573 \text{ mm Hg}}{565 \text{ mm Hg}} = 1.01 \quad [7]$$

If the aircraft were not pressurized the P_{N2}/P_B ratio would be 1.51:

$$\frac{P_{N_2}}{P_B} = \frac{573 \text{ mm Hg}}{380 \text{ mm Hg}} = 1.51 \quad [8]$$

If unpressurized flight occurred to 9,140 m (30,000 ft) ($P_B = 226$ mm Hg) the P_{N2}/P_B ratio would be 2.54:

$$\frac{P_{N_2}}{P_B} = \frac{573 \text{ mm Hg}}{226 \text{ mm Hg}} = 2.54 \quad [9]$$

If before unpressurized flight to 9,146 m (30,000 ft) the aviator had denitrogenated at sea level for a long period of time such that one half of the total N_2 was eliminated from his body, the P_{N2}/P_B ratio would be 1.27:

$$\frac{P_{N_2}}{P_B} = \frac{287 \text{ mm Hg}}{226 \text{ mm Hg}} = 1.27 \quad [10]$$

The process of denitrogenation is very effective in eliminating N_2 from the body. When 100% O_2 is breathed using a tightly fitted mask, an alveolar N_2 pressure of nearly zero is established and a marked pressure differential (~573 mm Hg) between the alveoli and body tissues results. N_2 rapidly diffuses from the tissues into the blood, where it is transported to the lung and is exhaled. The amount of N_2 eliminated depends on time and tissue perfusion.

Figure 3-7 shows the total amount of N_2 washed out of the body by denitrogenation. Assuming that the average person contains 1,200 cm^3 of dissolved N_2, slightly more than 350 cm^3 can be eliminated by prebreathing 100% O_2 for 30 minutes. Denitrogenation before initiating ascent to altitude significantly reduces the incidence of altitude DCS as does the operational use of inflight denitrogenation with 100% O_2 at or below 4,878 m (16,000 ft) (103). Once begun, denitrogenation should ideally not be interrupted although recent evidence indicates that breaks in prebreathe, up to 60 minutes in the middle of a 1-hour prebreathe, may not result in increased DCS risk (104).

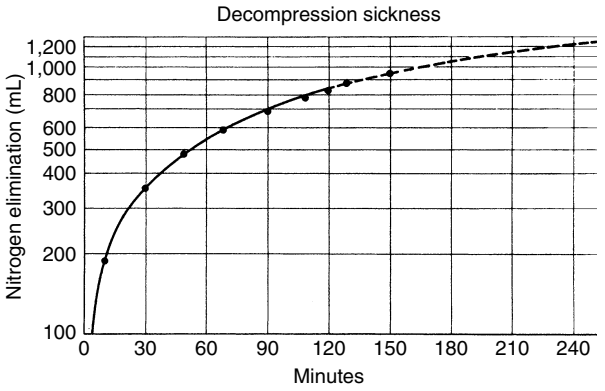

FIGURE 3-7 Denitrogenation curve while breathing 100% oxygen.

Denitrogenation eliminates nitrogen from various tissues at different rates. These rates are dependent on the solubility of nitrogen in specific tissues but, more importantly, also on the circulatory perfusion of the tissues. Therefore, all body tissues come into equilibrium with each other and with respired gas at different times. As a practical matter, then, with altitude exposure (pressure reduction), the P_{N2}/P_B ratio of certain tissues may exceed the critical value for bubble formation, whereas the P_{N2}/P_B ratio of other tissues remains within a safe range. This fact may partially explain why signs and symptoms of DCS occur at characteristic locations in the body.

MANIFESTATIONS OF DECOMPRESSION SICKNESS

In DCS, bubbles can form in all parts of the body. Various target organs, however, seem to be affected most readily, and the effects on these anatomic locations account for the signs and symptoms seen. In this section, the clinical manifestations of bubble formation and the classic syndromes of DCS will be described.

Classification

DCS symptoms have been categorized as type I (pain only) and type II (serious) since introduction of the nomenclature in 1960 by Golding et al. (105). This categorization was created to separate the symptoms into groups based on their response to treatment during or after decompression from caisson work on the Dartford Tunnel in England. This system was somewhat analogous to the four-table treatment scenarios used at that time by the USN as described by Donnell and Norton (106). The four hyperbaric Treatment Tables (I–IV; I-A, and II-A without oxygen available) involved treating increasing symptom severity with more aggressive hyperbaric profiles. The Golding classification in type I and type II DCS has significant clinical shortcomings in the context of hypobaric DCS. Type I and type II DCS do not represent mutually exclusive categories; therefore, it is possible that a subject may have features of both concomitantly. Furthermore the static classification does not take into account that DCS is a

dynamic process, therefore, a patient may transition from a type I DCS class to a type II DCS over time.

The dynamic nature of the condition should be documented by repeat assessments of the clinical examination (especially neurologic examination), response to treatment, progression, relapse of symptoms, time to onset of symptoms (latency), time to start of recompression therapy, as well as results of any investigations. The adherence to DCS examination/assessment checklists may prove valuable to maximize reproducibility of data collection and subsequent analysis.

The USN uses the type I and type II categories of DCS for the Master Diver to determine treatment of diving DCS. The Master Diver provides hyperbaric oxygen (HBO) treatment as needed for USN divers in the absence of a physician on-site (a telephone consultation with the diving physician is part of the process), creating a need for clear guidelines regarding treatment. USAF physicians determine treatment for altitude DCS based on the symptoms and their severity. An accurate description of a case of altitude DCS involves stating the dynamic evolution of each symptom (107) (Table 3-5).

- Spontaneously resolving
- Static
- Relapsing
- Progressive

Each symptom should be stated with the time interval from its onset to the commencement of treatment. Progressive, limb-pain DCS occurring 1 hour before commencement of treatment would provide essential information in determining treatment, unlike "type I DCS." The timeline of any relapsing or progressive symptoms should be further described to include an indication of change and level of intensity. In addition, the response to recompression should be indicated (complete recovery, incomplete recovery, or none) to guide any further treatment options. The careful documentation of pertinent results of any investigations and tests and their respective timing is also of importance to allow for additional parameters for decision making in the context of treatment (Table 3-6).

Decompression Sickness Pain

Altitude DCS pain is seen in 65% to 80% of the cases of altitude-induced DCS (108–110). It tends to be localized in and around the large joints of the body. Sometimes smaller joints, such as interphalangeal areas, may be affected, particularly if these joints underwent significant active motion during altitude exposure.

DCS pain is deep and aching in character and ranges from very mild (joint awareness) to so severe that the patient does not wish to move the affected joint. Active and passive movement of the joint tends to aggravate the discomfort,

TABLE 3-5

Decompressive Stress—Classification and Clinical Consideration

Key Clinical Descriptors	*Affected Organ/Tissue*	*Signs and Symptoms*
Evolution of symptoms: spontaneous resolution/static/relapsing/progressive	Joints, pain only	Mild discomfort at the beginning (ache, "niggles"), progressing to severe, dull, deep, throbbing pain; no single, tender points; relieved by external compression
Response to therapeutic interventions: Pressure/oxygen	Cutaneous and lymphatic manifestations	Transient pruritus (especially trunk, ears, wrists, hands) colloquially known as *creeps*, possibly associated with a scarlatiniform rash; truncal *peau d'orange*,
Meticulous documentation of timeline		Cutis marmorata: marbled/mottled skin lesions [confluent rings of pallor surrounded by cyanosis (blanches to touch)]
Vital signs: heart rate, respiratory rate, degree of pain, measure of oxygenation	Cardiovascular	Circulatory collapse after preceding severe bends, chokes, or other neurologic symptoms Rhythm disturbances (e.g., first degreeAV-block)
	Pulmonary ("chokes")	1. Substernal pain (worse with inspiration) 2. Dyspnea (with or without cyanosis) 3. Dry, nonproductive cough (paroxysms after deep inspiration)
Careful neurologic examination so as to avoid subtle progressive signs	Neurologic: cerebrum and cranial nerves	Altered mental status (impaired memory, judgment, aphasias), frank delirium, fatigue, visual disturbances (sctomas, diplopia, blurred vision), personality changes, loss of consciousness, headache; vertigo, nausea, vomitus, tinnitus
	Cerebellum	Abnormal Romberg test, abnormal gait
	Spinal cord	Sensory/motor deficits, abnormal tendon-reflexes, frank paralysis/paresis
	Vestibular ("staggers")	Vertigo, nausea, vomiting, occasional nystagmus

(Francis J. The classification of decompression illness. Hypobaric Decompression Sickness. San Antonio, Brooks Air Force Base, Texas: Aerospace Medical Association and Undersea & Hyperbaric Medicine Society, 1990. Published June 1992; the table is not part of the old reference, rather a summary table and created by the author (Stepanek).)

TABLE 3-6

Management of Altitude Decompression Sickness

Carefully Assess DCS Symptoms

1. Joint pain or skin symptoms only; A–D; not, 2
   - A. Symptoms present in <2 hr?
     - Surface level oxygen
       - Worsen or fail to improve?
         - Treatment Table 5
           - Worsen or fail to improve?
             - Treatment Table 6
               - Worsen or fail to improve?
                 - Consider extensions and tailing dives until resolution or until symptoms plateau
   - B. Symptoms present in 2 to 6 hr?
     - Treatment Table 5
       - Worsen or fail to improve?
         - Treatment Table 6
           - Worsen or fail to improve?
             - Consider extensions and tailing dives until resolution or until symptoms plateau
   - C. Symptoms present >6 hr?
     - Treatment Table 6
       - Worsen or fail to improve?
         - Consider extensions and tailing dives until resolution or until symptoms plateau
   - D. Symptoms present >36 hr?
     - Reconsider diagnosis of DCS
2. Neurologic, pulmonary, or cardiac symptoms
   - Treatment Table 6
     - Worsen or fail to improve?
       - Consider extensions or Treatment Table 6A and tailing dives until resolve or symptoms plateau

Courtesy of Hyperbaric Medicine Group at Brooks City Base, San Antonio, TX.

whereas local pressure, such as with an inflated blood pressure cuff, tends to relieve the pain temporarily, although other investigators (111) found the technique to be unreliable.

The pain may occur during the altitude exposure, on descent, shortly after descent, or, in rare cases, only become manifest many hours after descent. In nearly all cases, DCS pain occurring at altitude will be relieved by descent because of the increase in P_B. In rare cases, DCS pain relieved by returning to ground level will recur at ground level. In these cases, as well as those cases where pain is not relieved by descent, HBO therapy is the definitive form of treatment. It is important not to treat DCS pain with analgesics as its disappearance may serve as an indicator of the success of hyperbaric therapy.

Thoracoabdominal pain should not be classified as simple DCS pain, but rather as neurologic DCS likely due to spinal chord involvement and treated appropriately (112).

Chokes

The syndrome called *chokes* is rare in both diving and aviation, accounting for less than 4% of DCS cases (108,110) during research exposures. However, this condition may be a life-threatening disorder. The mechanism of chokes is multiple pulmonary gas emboli. The characteristic clinical picture consists of the triad of substernal chest pain, dyspnea, and a dry nonproductive cough, although only three cases of chokes with the full triad were found during a review of 2,525 exposures with 1,030 cases of DCS and 29 cases of chokes (108). Rudge has reviewed the USAF experience from 1966 to 1994 and found that the single most consistently present clinical sign in their series of 15 patients was substernal pain (113). In most cases, the pain is made worse on inhalation. Patients with chokes feel generally and severely ill. Altitude-induced chokes will invariably progress to collapse of the individual if the altitude is maintained. The aviator with chokes may need hyperbaric chamber therapy, although some may resolve during descent before or during ground level oxygen therapy (108).

Neurologic Decompression Sickness

Neurologic DCS presents a clinical picture with signs and symptoms referable to the nervous system. It has become apparent that one should probably limit the term neurologic DCS to those cases in which there is involvement of the CNS. Peripheral nerve involvement with mild paresthesia is commonly associated with altitude DCS and does not appear to increase the gravity of the disorder from a prognostic point of view unless it presents in a dermatomal pattern. CNS involvement, however, can herald significant and permanent neurologic deficits, particularly if aggressive and proper treatment is not instituted promptly.

CNS involvement occurs in 4% of cases of altitude DCS (109). It presents in one of two forms—spinal cord form or brain form. The spinal cord form is seen almost exclusively following diving and is extremely rare following altitude exposure. The brain form of the disorder is more commonly seen following altitude exposure and is uncommon but not rare following diving exposure. The reasons for the variance in the incidence of brain and spinal cord neurologic DCS in diving and altitude exposure have not been elucidated yet. The clinical manifestations of the two forms of this disorder will be discussed separately.

Spinal Cord Decompression Sickness

In many cases, the first symptom of spinal cord DCS is the insidious onset of numbness or paresthesia of the feet. The sensory deficit spreads upward, accompanied by an ascending weakness or paralysis to the level of the spinal lesion. Other cases begin with girdling abdominal or thoracic pain, which precedes the onset of sensory and motor deficits. Within 30 minutes of onset, the entire clinical picture of a partial or complete transverse spinal cord lesion may manifest.

The culprit lesions in spinal cord DCS have been well documented as bubbles formed in or embolized to the paraspinal venous plexus. Poorly collateralized segmental venous drainage of the spinal cord and normally sluggish blood flow through the paraspinal venous plexus can result quickly in mechanical blockage of venous drainage by bubbles and solid elements formed at the blood–bubble

interface. This blockage, in turn, results in a congestive, or ''red,'' infarct of the spinal cord (50). This is extremely rare in altitude DCS and may be found more frequently in diving DCS cases.

Brain Form of Decompression Sickness

In most cases, the clinical picture of a patient having the brain form of DCS is one of spotty sensory and motor signs and symptoms not attributable to a single brain locus. Headache, at times of a migrainous nature, is commonly present. Visual disturbances, consisting of scotomas, tunnel vision, diplopia, or blurring, are common. At times, extreme fatigue or personality changes that range from emotional lability to a significantly flattened affect are the presenting symptoms.

For the physician not acquainted with the clinical picture of multiple brain lesions, the diagnosis can be very difficult. A number of these patients have been misdiagnosed as hysterical and have progressed to vasomotor collapse because proper and immediate definitive treatment was not rendered.

Circulatory Manifestations

Generally, circulatory impairment is manifested as shock following the development of chokes or severe neurologic impairment (secondary collapse). Circulatory collapse without other symptoms preceding the development of shock (primary collapse) occurs rarely. The so-called post-decompression collapse following altitude exposure, with the shock state occurring after descent to the ground level, has been described as a separate type of circulatory impairment. It probably is not separate but rather represents delay in onset as sometimes seen with other types of altitude DCS.

Possible mechanisms of circulatory collapse include direct involvement of the vasomotor regulatory center or massive blood vessel endothelial damage by bubbles, with a subsequent loss of intravascular volume. Extreme hemoconcentration has been documented in many cases, with hematocrits up to 70% (61).

Circulatory collapse is marked by its lack of response to fluid replacement, which is similar to the lack of response commonly seen in cases of severe head injury that results in a central sympathectomy.

Cutaneous Signs and Symptoms

Skin symptoms may present as pruritus or formication only (''creeps''). It is important to keep in mind that some of these skin DCS manifestations may also be mediated by involvement of peripheral nervous system elements. The sensation generally passes within 20 to 30 minutes, and no treatment is necessary. A transient scarlatiniform skin rash may occur. Skin symptoms, however, may present with the appearance of mottled or marbled skin lesions; this condition is also referred to as *cutis marmorata*. This condition does not appear to carry excess risk for neurocirculatory compromise in hypobaric DCS (114)—in contrast to diving DCS, where it is a clear warning sign of more serious DCS—as was previously hypothesized (71). Therapy depends on the circumstances, in case of cutis marmorata in the setting of diving a full USN-Treatment Table 6 would be warranted, in the setting of hypobaric exposure an immediate USN-Treatment Table 5 may be appropriate depending on how rapidly the condition resolves following repressurization to ground level. Cutis marmorata associated with diving must alert the treating physician to the potential imminent development of more serious DCS manifestations and should be treated analogous to type II DCS (102).

Pitting edema, if seen alone, is considered a minor manifestation of DCS in that it will resolve spontaneously without sequelae. Pitting edema is thought to arise from lymphatic blockage by bubbles. It rarely results from altitude exposure. Localized pain in lymph nodes may occur as well and recompression typically provides prompt pain relief.

Constitutional Signs and Symptoms

Following decompressions to altitude, mild, transient fatigue is frequently encountered in the operational as well as research setting in subjects and chamber attendants. This symptom is usually ignored, although it may be accompanied by distinct malaise and lack of appetite. The significance and etiology of this fatigue has not been thoroughly investigated, but it may represent mild impairment of mental and nervous function. Severe exhaustion should alert the clinician; this may be an indicator of concomitant or impending more severe DCS and should prompt a detailed physical examination to avoid missing other subtle signs and symptoms (112).

Chronic Effects

Aseptic bone necrosis is a debilitating condition, common among divers and caisson workers. It has been described in merely one well-documented case following altitude exposure (115,116). The evidence to link aseptic bone necrosis with altitude DCS is anecdotal at best. From the diving literature we know that areas of bone infarction, if located in juxta-articular locations, rapidly lead to erosion of overlying cartilage and severe osteoarthritis. The shoulders, knees, and hips are the only joints affected. Early lesions are asymptomatic and are only found on radiographic surveys. The exact relationship between aseptic bone necrosis and episodes of DCS is unknown. The disease is seen when compressed air exposure occurs on a regular and frequent basis and is seldom seen in less than 1 year after beginning such exposures.

DIAGNOSIS AND MANAGEMENT OF DECOMPRESSION SICKNESS

DCS rarely occurs unless one of the following conditions exists:

1. Exposure to altitudes greater than 5,488 m (18,000 ft)
2. Exposure to altitude shortly following exposure to compressed gas breathing [e.g., self-contained underwater

breathing apparatus (scuba) diving or hyperbaric chamber exposure]. DCS has occurred while flying in pressurized aircraft at a cabin altitude as low as 1,372 m (4,500 ft) following scuba diving in the preceding 3 hours

The following procedures are highly recommended in all cases of DCS (including DCS pain only) persisting after a dive or after a flight:

1. Administer 100% O_2 using a well-fitted aviator's mask or anesthesia mask.
2. If a hyperbaric chamber is on-site, the patient should be immediately treated according to the proper Treatment Table.
3. If there is no on-site hyperbaric chamber, arrangements should be made to immediately transport the patient to the nearest hyperbaric facility capable of administering proper treatment. The patient should be kept on 100% O_2 by mask while awaiting and during transportation to the chamber. If the patient has DCS pain only, the symptoms of which clear completely without recurrence within 2 hours postexposure while awaiting transport, the transport to the hyperbaric chamber can be cancelled. If the symptoms occur outside of the 2-hour time window postexposure, then a hyperbaric therapy (Treatment Table 6) is advisable.
4. If DCS pain is relieved while awaiting transport but recurs, the patient should be transported to the hyperbaric chamber and treated even if symptoms are relieved again after recurrence.
5. Any patient with signs or symptoms of persisting neurologic DCS, chokes, or circulatory collapse should be immediately transported to the nearest hyperbaric chamber for treatment, regardless of whether the symptoms persist.
6. Transportation must be at or near the ground level P_B of the site at which the patient embarks. Aircraft used for the movement of these patients must possess this pressurization capability. In no case should the cabin PA be more than 305 m (1,000 ft) higher than the PA at the point of embarkation. If at all possible, it is best to avoid moving patients to a hyperbaric chamber located at a PA greater than 1,067 m (3,500 ft) higher than the point of embarkation.
7. Personnel tending to the patient during transport and during recompression therapy should be able to provide advanced cardiac life support (ACLS). It is crucial for the inside attendants to rigorously comply with recommended decompression stops and oxygen breathing at depth to avoid excess nitrogen onloading during hyperbaric therapy with the attendant risk of DCS upon decompression from the respective Treatment Table.
8. Return to flying no earlier than 72 hours after resolution of pain-only DCS or complete resolution of any neurologic signs/symptoms.

HYPERBARIC THERAPY FOR DECOMPRESSION SICKNESS

Physiologic Basis of Hyperbaric Therapy

Hyperbaric therapy is achieved by applying physical factors related to the pressure environment. The elevation of the partial pressure of inspired gases (O_2 with hyperbaric O_2 therapy) and the subsequent increase in the amount of the various gases that enter into physical solution in body fluids (washout dynamics) are of key importance. The use of hyperbaric O_2 therapy for treating DCS results hypothetically in some bubble size reduction, a positive nitrogen gradient to reduce the size of bubbles and resolve them, perfusion of ischemic tissues, and correction of local tissue hypoxia.

When an individual is exposed to a change in P_B, a bubble deep within the body tissues responds to the pressure change. During compression, the surrounding P_B is increased, producing a reduction in bubble volume in accordance with Boyle's law. Clinically, it is important to weigh the potential risk of use of high pressures (risk of oxygen toxicity and nitrogen onloading during air breaks) for a prolonged period of time versus the modest decrease in the physical size of any bubble (Figure 3-7). During compression, the bubble becomes smaller and the surface tension increases.

Applying hyperbaric pressure in treating DCS will, therefore, either eliminate the bubbles entirely or reduce their size to a significant extent. The amount of size reduction will depend on the absolute bubble size at the onset of therapy. Although some bubbles may not be eliminated completely by the initial application of pressure, their reduction in size aids in partially restoring circulation in the case of intravascular bubbles and reducing the mechanical effects of extravascular bubbles.

Bubbles that are too big to resolve upon the initial application of pressure will continue to decrease in size with the time spent at increased pressure while breathing 100% oxygen to continue denitrogenation. This gradual decrease in size is due to the diffusion of gases from the bubble to the surrounding tissues and fluids. Diffusion of gases from the bubble occurs because the partial pressure of gases within the bubble increases when the volume is reduced during compression. The elevated partial pressure of gases inside the bubble creates a gradient favorable for inert gas elimination from the bubble as tissue denitrogenation continues, as presented in Figure 3-8. This principle is the foundation of the efficacy of hyperbaric O_2 therapy. The oxygen window is equal to the partial pressure difference between the partial pressure of N_2 in the bubble and alveolar N_2 partial pressure. We can therefore understand that breathing high partial pressures of O_2 will increase the oxygen window by maximizing the above-mentioned partial pressure difference between the alveoli (zero nitrogen while breathing 100% oxygen) and the bubbles and body tissues. Figure 3-8 also shows that if the individual breathes air, the favorable gradient will lessen with time as the surrounding tissues and

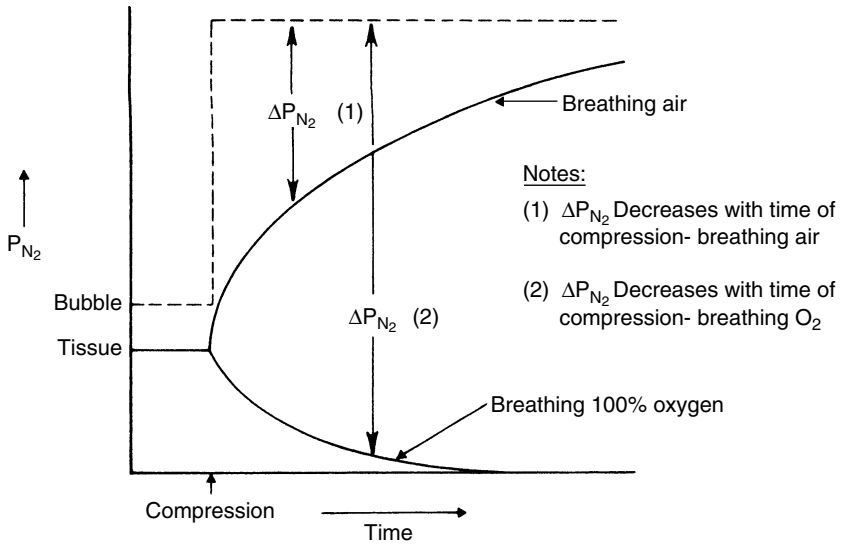

FIGURE 3-8 Bubble nitrogen gradients when breathing pure oxygen.

fluids approach equilibrium at the new N_2 partial pressure. Therefore, the bubble will be resolved more rapidly if the individual breathes 100% O_2 because a favorable gradient for nitrogen elimination from a bubble will improve with time, and the bubble will more rapidly diminish in size. During hyperbaric therapy, the patient intermittently breathes 100% O_2 at increased pressure. Breathing 100% O_2 provides an increased gradient for eliminating N_2 from evolved bubbles and aids in their resorption. The increased gradient also speeds the elimination of N_2 from supersaturated tissues, and thereby helps prevent further bubble formation. Therefore, if a sufficient time is spent at depth, all bubbles will resolve.

Hyperbaric oxygenation results in increased O_2 tension in the capillaries surrounding ischemic tissue. The increased O_2 tension extends the O_2 diffusion distance from functioning capillaries and corrects the local tissue hypoxia. Overcoming the tissue hypoxia tends to disrupt the vicious cycle of hypoxia-induced tissue damage that causes tissue edema and interferes with circulation and oxygenation.

Treatment of Altitude Decompression Sickness

Although the vast majority of DCS cases occurring at altitude will be completely relieved by descent to ground level, approximately 6.9% of cases may persist and require treatment (117). In addition, less than 1% of patients will experience the initial onset of symptoms of DCS after descent, so-called *delayed cases*. Deaths from altitude DCS are exceptionally rare in contrast to diving induced DCS.

Before 1959, more than 17,000 cases of altitude-induced DCS were documented. Of these cases, 743 were reported as serious, including 17 fatalities. Davis et al. (71), commenting on a review of these 17 fatalities, made the following observations. All died in irreversible shock that was unresponsive to fluid replacement and drug therapy. Almost all cases began as simple DCS pain, neurologic manifestations, or chokes, which only after several hours progressed to circulatory collapse and death. It should be noted that none of the 17 fatalities were treated by hyperbaric therapy. In their review of 145 cases of altitude DCS treated in hyperbaric chambers, these same authors emphasized that shock was the initial clinical picture in only one case, whereas seven other cases began with other manifestations and progressed to shock. In this series of patients, no fatalities occurred among those who were treated in hyperbaric chambers (71). In 1988, another fatality (68) occurred due to exposure to 8,537 m (28,000 ft) for more than 30 minutes secondary to a faulty canopy seal in a F-100 flight. The aviator had symptoms at altitude, delayed landing and complained of persistent dyspnea after landing, and finally reported to the emergency room with a 1-hour delay after landing; hyperbaric therapy was initiated 3 hours after presentation (transport to hyperbaric facility). The patient, who was overweight and 51 years, died 5.5 hours after presentation during hyperbaric therapy (USN Treatment Table 6A) with pulmonary symptoms (''chokes'') terminating in ventricular fibrillation.

As early as 1945, Behnke (40) advocated the use of compression therapy to treat cases of altitude DCS that did not resolve upon descent to ground level. It was not until 1959 that a USAF aviator was successfully treated by compression (106). In 1963, Downey et al. (118) using a human serum *in vitro* model, demonstrated the persistence, at ground level, of bubbles formed at altitude. Upon compression to pressures greater than sea level, the bubbles cleared. *In vivo* confirmation of Downey's work was reported by Leverett et al. in 1963 (119).

Because many physicians have no training in recognition or treatment of altitude DCS, it is important for aircrew to be aware of the symptoms of DCS and the need to seek medical attention from informed personnel. Altitude DCS is typically resolved during descent to a lower altitude while breathing 100% oxygen in accordance with current USAF directives. Continued breathing of 100% oxygen on the ground for 2 hours is sometimes effective treatment for select mild cases of DCS that do not resolve completely during descent (120). The reason for resolution of symptoms

with this procedure is twofold: (i) The gas emboli (bubbles) are subjected to increased pressure during descent which will reduce their size and effect (117); (ii) breathing 100% oxygen partially denitrogenates blood and tissues. This reduces the potential for bubble growth and results in shrinkage of existing bubbles in tissues adjacent to capillaries, where the diffusion gradient will favor nitrogen leaving the tissue and entering the denitrogenated blood.

DCS Treatment Synopsis

- 100% oxygen
- Descend as soon as practical
- Declare Inflight emergency
- Land at the nearest airfield with qualified medical assistance (military flight surgeon or civil aeromedical physician) available

HBO therapy is the standard of care, and it is successful in treating DCS symptoms which do not resolve before landing or which involve neurologic or pulmonary (respiratory) symptoms. The additional pressure of the hyperbaric treatment further reduces the size of existing bubbles. Breathing 100% oxygen during the HBO treatment ensures no further nitrogen is delivered to the tissues and helps to oxygenate tissues where bubbles may have blocked delivery of oxygenated blood. HBO treatment of DCS, whether from altitude or hyperbaric exposures, has been documented to be more successful if begun as soon as practical after symptoms appear. When symptoms are reported later, treatment is not as effective. The nature and severity of the symptoms dictate the specific hyperbaric profile for treatment and may require multiple treatments for complete resolution. The USAFSAM's Hyperbaric Medicine Division (FEH) serves as the primary source of information and consultation on treatment of DCS for the USAF.

Treatment of USAF altitude chamber reactors is guided by USAFSAM/FEH (Hyperbaric Medicine Division) directives based on time since treatment and the symptoms at time of treatment. Some treatment scenarios involve ground level oxygen and the rest utilize HBO therapy. HBO treatment scenarios include modified USN Treatment Table 5 and 6 profiles to 60 fsw (121) breathing 100% oxygen with air breaks to avoid oxygen toxicity. The profiles last from 135 to 285 minutes not including descent time. Treatment Table 6A to 165 fsw for 319 minutes is employed for treating air embolism and only rarely for DCS cases, which do not resolve with Treatment Tables 5 or 6. At 165 fsw, air or a nitrox mix is used to prevent oxygen toxicity. Owing to the renitrogenation that takes place at 165 fsw and the relatively small reduction in bubble size with the extra pressure (Figures 3-9A and 3-9B), Table 6A is generally not considered a good choice for treatment of DCS. The algorithm to assist in treatment shown in the subsequent text was developed at the USAFSAM Hyperbaric Medicine Division.

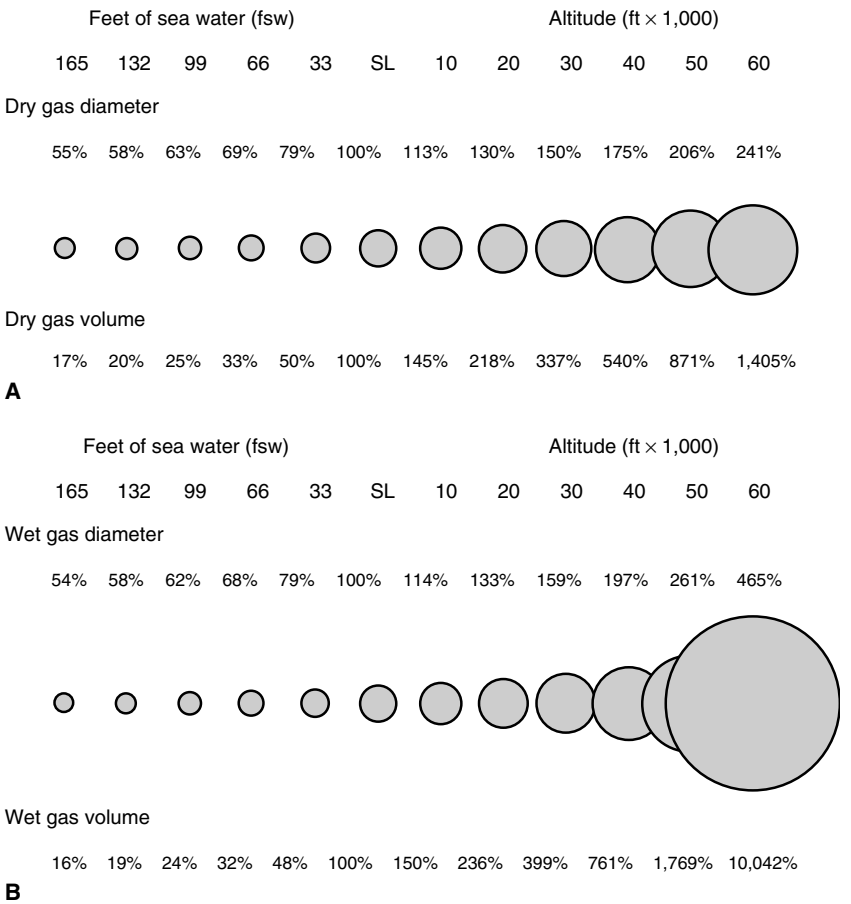

FIGURE 3-9 **A and B**: Bubble volume changes with altitude.

Of the approximately 1,000 cases of DCS observed in subjects during 20 years of altitude DCS research chamber activity at Brooks City Base, 89 subjects were treated with HBO by the Hyperbaric Medicine Division, all with complete resolution of symptoms. The remaining cases were successfully treated with 2 hours of ground level oxygen (GLO) (120) or with no treatment.

Treatment Procedures

If the aviator had only symptoms of joint pain that resolved upon recompression to one ATA from altitude, then the individual may be treated with 2 hours of 100% GLO, followed by 24 hours of observation. Should symptoms persist after recompression to ground level from altitude or recur, then transfer to a hyperbaric treatment facility should be arranged. The use of surface level 100% oxygen as a therapeutic modality applies only under select circumstances:

1. Altitude (NOT diving)-induced DCS only, bends pain only
2. Pain during the exposure or within 2 hours of exiting the altitude exposure
3. NOT for paresthesiae, neurologic symptoms or respiratory (chokes) symptoms
4. Successful therapy is disappearance of all symptoms after 2 hours of surface level 100% oxygen
5. Oxygen therapy should be continued for 1 hour after all symptoms have resolved
6. Minimum of 2 hours of oxygen is advisable even if symptoms resolve immediately
7. Maximum time on surface level 100% oxygen is 3 hours
8. If symptoms worsen or recur go to Treatment Table 5 or 6
9. If symptoms do not improve in 30 to 60 minutes go to Treatment Table 5 or 6
10. If symptoms do not resolve completely within 2 hours go to Treatment Table 5 or 6

The importance of a thorough but expeditious patient examination cannot be overemphasized; some patients may not report/be aware of subtle neurologic symptoms that actually might alter therapy. In case of a clear therapeutic emergency, that is, cardiovascular collapse, severe chokes, marked neurologic deficit, the neurologic examination is clearly not essential as a first priority. The patient presenting with stable symptoms, after a hyperbaric recompression, with a recurrence of symptoms or before initiating patient transport represents the situation where a thorough, repeat neurologic examination is most valuable. The examination may allow reclassification into a different treatment algorithm possibly modifying your choice of treatment tables as discussed in the subsequent text. The examination should allow a clearer definition of the anatomic area affected (supratentorial/infratentorial, spinal cord, peripheral nerves, muscle/musculoskeletal). Ideally, in the interest of reproducibility and consistency, such an examination should follow a standard protocol, possibly in the form of a DCS examination checklist (122).

Although a number of treatment tables are used successfully throughout the world, the USN Treatment Tables are considered authoritative for treating DCS in this country. Before 1964, air Treatment Tables were used in the therapy of DCS. The therapeutic success was not satisfactory and therefore Goodman and Workman (123) developed the oxygen Treatment Tables now labeled as Tables 5 and 6. The oxygen Treatment Tables were adopted by the USN in 1967 and have proved to be highly effective in treating DCS. Lack of response or worsening symptoms for pain-only DCS after ground level oxygen therapy warrants use of Treatment Table 5. If the symptoms do not disappear or worsen on a Treatment Table 5, then the patient is committed to Treatment Table 6.

Treatment Table 6 is reserved as a first step for cases involving the CNS or cardiopulmonary systems and for recurrences of previously treated DCS. The USN Treatment Table 7 is used only in life-threatening situations when other treatment tables have failed to resolve symptoms of serious type II DCS or cerebral gas embolism. Because patients treated on Table 7 will be in the hyperbaric chamber for at least 48 hours, this treatment should only be undertaken when all medical and nonmedical care of the patient can be provided in the chamber for this period of time. When long delays between onset and treatment occur, the manifestations of DCS become more serious. They seem to be aggravated by the development of secondary edema and vascular obstruction or impairment from thrombosis. Hyperbaric oxygenation in such circumstances probably provides more benefit than does the mechanical compression of bubbles.

Patients should stay in the vicinity of the treatment facility for at least 24 hours after hyperbaric therapy. Furthermore, exercise, alcohol, flying, diving, or altitude exposure should be avoided for 72 hours after the hyperbaric treatment. Patients should be told to stay well hydrated and expect some degree of fatigue after the hyperbaric chamber treatment. Delayed ear pain may occur, which may be prevented by performing a Toynbee or Valsalva maneuver before going to bed and again the next morning.

Adjuvants to Hyperbaric Therapy

Oxygen and hyperbaric therapy are the only definitive treatments for DCS. In serious cases of DCS, a marked loss of intravascular volume can occur by transudation of plasma across damaged capillary walls. Hemoconcentration producing hypoperfusion of tissue and sludging of red blood cells should be avoided or corrected by prompt and adequate administration of rehydration. Patients with CNS or respiratory DCS or arterial gas embolism should receive intravenous (IV) Ringer's lactate or normal saline solution (121). Solutions containing only Dextrose (e.g., D5W) should be avoided as they may contribute to edema as the dextrose is metabolized. Patients who are fully conscious may receive oral rehydration, typically 1 to 2 L of water, juice, or noncarbonated drinks are adequate. Frequent checks of urinary output are the best guide to the adequacy of the fluid therapy. Urinary output should be maintained at 1 to 2 mL/kg/hr.

Dexamethasone, 20 mg IV followed by 4 mg intramuscularly every 6 hours, may be useful in the prevention or treatment of CNS edema (124). IV methylprednisolone with an initial dose of 30 mg/kg followed by constant IV infusion at a rate of 5.4 mg/kg/hr may be used as well. Aside from the possible benefits in the treatment of cerebral edema, there is currently no conclusive evidence for a beneficial therapeutic impact of corticosteroid therapy on DCS outcome.

In cases of neurologic DCS affecting the spinal cord resulting in immobility, the prophylactic use of heparin, preferably low molecular weight heparin (LMWH), is recommended to prevent deep venous thrombosis (DVT) (125,126). Heparin *per se* does not appear to have a beneficial effect in the treatment of DCS aside from the prevention of DVT (127,128) and may hypothetically increase the risk of bleeding (spinal chord, brain, and inner ear may show evidence of hemorrhage in severe DCS). In spinal chord DCS, an indwelling urinary catheter should be placed because these patients commonly develop a neurogenic bladder.

The use of Lidocaine in antiarrhythmic doses (loading dose 1.5 mg/kg, followed by a maintenance drip rate of 1 mg/min) as a neuroprotective agent in DCS is currently under investigation; several studies have shown favorable results (129).

The use of IV perfluorocarbon emulsions combined with 100% O_2 in the prevention as well as therapy of DCS has shown promising results in animal studies and may become available for clinical use (130–133). Perfluorocarbon emulsions function as very efficient oxygen and nitrogen carriers, thereby improving tissue oxygenation and denitrogenation.

Cases of DCS following diving do not result in near drowning as frequently as do cases of cerebral air embolism; nevertheless, the possibility of near drowning must be considered and treatment begun when warranted. In such cases, intensive pulmonary care is mandatory. Endotracheal intubation, assisted ventilation with monitoring of end-tidal CO_2 (57), and appropriate correction of acidosis may be necessary.

None of the earlier procedures should delay movement of the patient to a hyperbaric chamber except when necessary as immediate life-sustaining measures. It is just as important, however, to institute or continue such procedures after hyperbaric therapy is begun as part of the overall intensive care management of serious cases.

Return to Flying Duty

Aeromedical disposition of aircrew who have DCS varies among the different branches of the US Department of Defense. The USAF has policies in place that allow return to flying duty 72 hours after a simple, fully resolved case of DCS not involving CNS symptoms. The aviator needs to be seen by his local flight surgeon who documents a normal neurologic examination before returning the aviator to flying status. DCS with neurologic involvement usually requires 72 hours of grounding. DCS with neurologic involvement that resolves without residual deficits requires a clearing evaluation by a neurologist, concurrence with the decision to return to flying status by the hyperbaric medicine physician at the Davis Hyperbaric Laboratory in San Antonio and the Major Command flight surgeon before return to flying status. Aviators with residual deficits after a DCS incident are disqualified from flying duties. The aviator may apply for a waiver and the decision will be made on a case-by-case basis after review and examination by the Aeromedical Consultation Service at Brooks City Base and their emanating recommendation will be the basis for the final waiver decision at Major Command level.

The USN follows the following policies: a simple, single episode of type I (pain only) DCS event results in grounding of the aviator for a period of 3 to 7 days. The aviator may return to flying duty thereafter, provided there are no residual deficits on physical examination. Type II DCS requires grounding for 14 to 30 days; return to flying status is possible provided there are no residual deficits on physical examination by the flight surgeon. Aviators with residual neurologic deficits may apply for a waiver and a review by the Hyperbaric Medicine Committee at the Naval Aerospace Medical Institute will consider each application on a case-by-case basis.

DIRECT EFFECTS OF PRESSURE CHANGES

Gas contained within body cavities is saturated with water vapor, the partial pressure of which is related to body temperature. Because body temperature is relatively constant (37°C), the partial pressure of the water vapor is also constant at 47 mm Hg. Therefore, the following relationship can be expressed as Boyle's law with reference to wet gas:

$$V_i\,(P_i - P_{H_2O}) = V_f\,(P_f - P_{H_2O}) \qquad [11]$$

where V_i is the initial volume of the gas; V_f is the final volume of the gas; P_i is the initial pressure of the gas in the cavity in mm Hg; P_f is the final pressure of the gas in the cavity in mm Hg; and P_{H_2O} is the partial pressure of water vapor (47 mm Hg at 37°C). Over a given pressure reduction, wet gas will expand to a greater degree than dry gas (Figures 3-9A and 3-9B). The relative gas expansion is a ratio of the final volume of the gas (V_f) to the initial volume (V_i) of the gas and is expressed in the following equation:

$$\text{Relative gas expansion} = \frac{V_f}{V_i} = \frac{P_i - P_{H_2O}}{P_f - P_{H_2O}} = \frac{(P_i - 47)}{(P_f - 47)} \qquad [12]$$

Figure 3-10 illustrates the increased volume of wet gases at a given pressure over that of a dry gas.

When one experiences a change in ambient pressure, a pressure differential is established between gas-containing body cavities and the external environment. To the extent that gas can move between body cavities and the external environment, this pressure differential will be relieved. It can also be relieved by a change in the volume of the body cavity

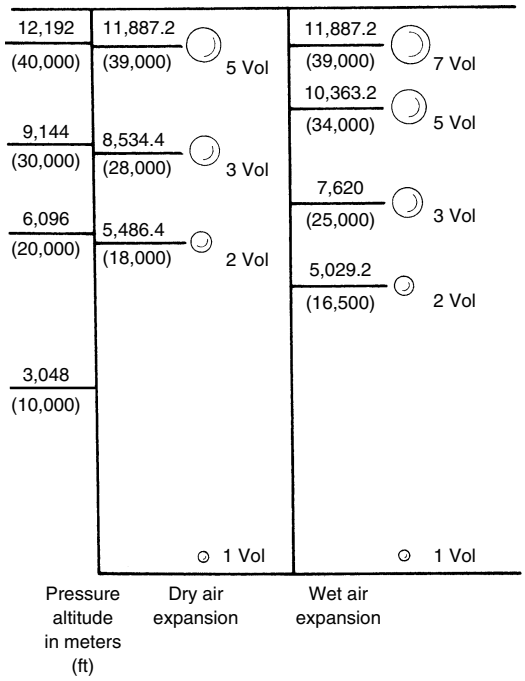

FIGURE 3-10 Volumes of wet and dry gases.

(compliance). When the pressure differential is not relieved, pathologic effects on involved tissues are likely to occur. The magnitude of the pathologic effects is related to the ratio of the pressure of the gas within the affected body cavity to the ambient pressure and not to the absolute value of the pressure differential. This is predictable from examining the pressure–volume relationships of Boyle's law. Therefore, divers, for example, experience more difficulties with the mechanical effects of pressure change when descending from sea level to 33 fsw [10 meter seawater (msw)] (Equations 13 and 14), than they do when descending from 99 to 132 fsw (30 to 40 msw) (Equations 15 and 16). Note that the pressure differential is identical for both circumstances, but the pressure ratio is considerably different.

Pressure differential:

$$P_f - P_i = 1520 \text{ mm Hg} - 760 \text{ mm Hg} = 760 \text{ mm Hg} \quad [13]$$

Pressure ratio,

$$\frac{P_f}{P_i} = \frac{1520 \text{ mm Hg}}{760 \text{ mm Hg}} = 2 \quad [14]$$

Pressure differential:

$$P_f - P_i = 3800 \text{ mm Hg} - 3040 \text{ mm Hg} = 760 \text{ mm Hg} \quad [15]$$

Pressure ratio,

$$\frac{P_f}{P_i} = \frac{3800 \text{ mm Hg}}{3040 \text{ mm Hg}} = 1.25 \quad [16]$$

Medically significant pressure changes occur in both flying and diving. There is a marked difference, however, between these two operations with respect to the magnitude and rate of the pressure changes. An aviator descending to sea level from 7,620 m at 1,520 m/min (25,000 ft at 5,000 ft/min) will experience a total pressure change of 478 mm Hg at a rate of 2.3 mm Hg/s. A diver descending from sea level to 165 fsw (50 msw) at a rate of 60 ft/min (18 m/min) will experience a total pressure change of 3,800 mm Hg at a rate of 23 mm Hg/s.

In general, it is possible to successfully cope with the changes in P_B that occur within the flying or diving envelopes. As long as the pressure in the various body cavities can equalize with the ambient pressure, large pressure changes can be tolerated. For example, meaningful work has been performed by aviators at pressures equivalent to 0.1 (ATA) atm abs (17,982 m or 59,000 ft) and by divers at pressures equivalent to 69 atm abs (686 m or 2,250 ft).

If equalization of pressure is not attained, difficulties ranging from mild discomfort to severe pain, tissue damage, and complete incapacitation will be experienced. The areas of primary concern are the lungs, middle and inner ear, paranasal sinuses, teeth, and the gastrointestinal tract.

The Lungs: Pulmonary Barotrauma and Arterial Gas Embolization

Unless air is continually exchanged between the lungs and the outside environment during changes in ambient pressure, severe pathologic disorders can result from the effects of Boyle's law. Airflow during pressure change will not occur with voluntary breathholding or the apneic phase of tonoclonic seizure.

Consider the potential problem of a breathholding descent during diving. The average total lung capacity is 5,800 cm^3. The residual volume (i.e., the volume to which the lungs can be reduced with forceful expiration) is 1,200 cm^3. If the air volume within the lungs is reduced below 1,200 cm^3, the actual lung volume will decrease no further due to the elastic and fibrous skeletal structure of the lung tissue. The volume deficit is made up by the leakage of plasma and whole blood into the lungs. This is the classic description of the pathologic condition called *lung squeeze* and is more common in breathholding diving than in descent from altitude. To achieve lung squeeze, the air volume within the lungs must be reduced to approximately 20% of the original volume. To achieve this on descent from altitude, an aviator would have to make a breathholding descent from 11,890 m (39,000 ft) to sea level. A breathholding dive to 132 fsw (40 msw), however, will result in such a fivefold decrease in the original lung volume. Such a dive is well within the capabilities of many expert divers.

In compressed gas diving, respirable gas is supplied to the diver from the surface, from a diving bell or hyperbaric chamber, or from a scuba. The gas may be supplied through regulators designed to match intrapulmonary gas pressure to the surrounding ambient pressure. The compressed gas–supplied diver avoids lung squeeze on descent but runs an added risk on ascent. During ascent to the surface, the diver must continually equilibrate the intrapulmonary pressure to the surrounding pressure. This equilibration is usually

accomplished by releasing gas from the lungs by normal breathing or, in the event of the loss of gas supply at depth, by slow continual exhalation on ascent. Failure to do so results in intrapulmonary gas expansion according to Boyle's law and, after the elastic limit of the thorax is reached, a relative rise of intra-alveolar pressure. A rise in intra-alveolar pressure of 50 to 100 mm Hg above ambient pressure is sufficient to force gas into extra-alveolar compartments, resulting in one or more of the clinical conditions grouped under the term *pulmonary overpressure accidents/pulmonary barotrauma*.

Pressure differentials sufficient to cause a pulmonary overpressure accident in the compressed gas–supplied diver can occur on ascents as shallow as from 2 m (6.6 ft) to the surface. In the aviator, concern regarding pulmonary barotraumas is justified as well. Sufficient pressure differentials can be attained due to rapid decompression at high altitude, possibly coupled with exacerbating factors such as concomitant performance of an anti-G straining maneuver against a closed glottis and concomitant positive pressure breathing.

Autopsies of fatalities following pulmonary overpressure accidents have demonstrated extra-alveolar gas in essentially every tissue examined. Following such an accident, however, the clinical picture seen will be that of arterial gas embolism, mediastinal and subcutaneous emphysema, and/or pneumothorax. The latter two manifestations are recognized by physical and radiographic examination and are managed by conventional measures. The manifestations of arterial gas embolism have an immediate onset following the rapid pressure reduction and may include loss of consciousness, local or generalized seizures, visual field loss or blindness, weakness, paralysis, hypoesthesia, or confusion. A patient presenting with any of these signs or symptoms within 15 minutes of exposure to a rapid pressure reduction must be assumed to have suffered an arterial gas embolism and be treated emergently for such.

Predisposing Factors

In addition to breathholding during ascent, pulmonary overpressure accidents can also occur as a consequence of preexisting disease that limits the egress of gas from the lungs. Therefore, the risk is increased by asthma, chronic bronchitis, air-containing pulmonary cysts, and other obstructive airway disease. Some pulmonary overpressure accidents have occurred without demonstrable cause in patients who exhaled during ascent and had no subsequent lung disorders. In these cases, local pulmonary air trapping is thought to have occurred by redundant tissue, mucous plugs, or similar mechanisms establishing a one-way valve in a small air passage, which allowed gas to pass during compression but not during decompression.

In the context of aeromedical evacuations of casualties, it is important to remember that an increasing number of cases of gas embolism are caused by the introduction of air or other gas into the arterial or venous system during surgical procedures or following the establishment of indwelling arterial catheters. With the increasing use of indwelling catheters and surgical procedures involving invasive instrumentation of the cardiovascular system, the number of gas embolism cases has also increased. Stoney et al. (134) have estimated that the accidental introduction of air through arterial lines occurs in more than 1 in 1,000 cases.

Diagnosis

The most difficult differential diagnosis is between gas embolism and neurologic DCS when decompression is involved. This diagnosis is important because of the need to select a proper Treatment Table. The key factor in reaching a proper diagnosis is the time before the onset of symptoms and history. The onset is immediate with gas embolism, with symptoms usually occurring swiftly after rapid pressure reduction.

The diagnosis of a surgical gas embolism should be considered in any patient with indwelling arterial or venous lines (particularly a central line). The sudden onset of seizure or coma is frequently the presenting sign. Venous gas embolism is more common and much less of a problem due to the microfiltration capability of the lungs. Nonetheless, it may present as a systemic embolism in the presence of a PFO with right to left shunting, ASD/PFO, pulmonary microcirculation, or through arteriovenous (AV) shunts (42).

In surgical cases, general anesthesia may mask the unusual symptoms; however, failure of the patient to awaken normally or the presentation of an unexplained neurologic deficit should alert one to the diagnosis of possible intraoperative gas embolism. A neurologic examination may reveal a myriad of CNS findings depending on the location of the gas. Funduscopic examination may reveal arteriolar bubbles in some instances. Computed tomographic (CT) scanning or MRI of the head may be used diagnostically when it is immediately available, but therapy should not be delayed while waiting for an imaging procedure.

In the diagnosis and treatment of gas embolism, time and appropriate life support measures (ACLS) are of the essence. Although some patients survive a delay of up to 24 hours, the experience of treatment facilities, with a mortality range of 20% to 25%, indicates that time from embolization to treatment is a most important factor.

Treatment

To provide effective therapy for gas embolism, it is important to remember the basic difference between DCS (air or gas bubbles evolving from solution) and gas embolism (gas bubbles that enter the arterial or venous circulation directly). Although the manifestations of DCS are diverse, they are rarely fatal when treated by proper hyperbaric therapy within hours to days of occurrence. Conversely, the onset of gas embolism is a sudden, dramatic, and immediately life-threatening event. Bubbles obstruct the systemic or pulmonary arterial circulation. As decompression continues, they expand to produce local endothelial cell damage and herniation into the vessel walls. In addition, plasma proteins react to the invading bubbles by denaturization and attachment to the bubble wall. Activation and agglutination of platelets to the bubbles occur (61), with release of very

potent vasoactive amines and prostaglandins, which produce immediate hypoxia symptoms that may appear as neurologic deficits.

The rationale for hyperbaric therapy for DCS also applies to the management of gas embolism: mechanical compression of bubbles and hyperbaric oxygenation of tissues. Because of the massive amounts of air that are often introduced into the cerebral circulation of gas embolism victims, it is usually necessary to mechanically compress the entrapped air maximally.

The Trendelenburg (30° head-low) position has been considered the ideal position to further decrease the likelihood of further introducing air volume into the CNS. This position increases cerebral hydrostatic pressure and, in some cases, forces small bubbles from the arterial circulation across the cerebral capillary bed into the venous circulation, where they produce less potential harm to the victim. At the same time, this position may enhance cerebral edema formation. It is currently not a routine recommendation, unless the patient benefits from the augmented cardiac output. Supine positioning of the patient is preferred. It must be emphasized that 100% O_2 breathing cannot be administered at 6 ATA abs (Treatment Table 6A) due to the extremely short time to CNS O_2 toxicity. Convulsive seizures would occur in less than 5 minutes. Elevated oxygen percentages, however, can be administered in the form of 50/50 Nitrox (a mixture of 50% O_2 and 50% N_2). This mixture will assist in correcting tissue hypoxia and ischemia because of the improved oxygen diffusion distance.

When it has been determined that maximum benefit has been attained from the mechanical compression of the entrapped air, the patient must be brought to shallower depths so that 100% O_2 can be administered. Because of the advantages of treating with 100% O_2, the USN Diving Manual suggests initial compression to 2.8 atm abs (18 msw or 60 fsw) for one 20-minute oxygen breathing period before making the decision on whether to pressurize to 6 ATA (50 msw or 165 fsw) (102).

Hyperbaric therapy is the only definitive treatment for AGE. All other methods are adjunctive in nature. As soon as the diagnosis is made, the patient should be placed in the chamber and rapidly compressed with air to 60 fsw (18 msw, 2.8 ATA). The patient is placed on 100% O_2 for a 20-minute breathing period. If symptoms improve, treatment continues on Table 6. If symptoms do not change or worsen, the patient is compressed to 6 ATA (165 fsw, 50 msw) and treatment continues on Table 6A.

Variation from the standard Table 6A is potentially harmful to both the patient and inside observers and should not be done without prior consultation with experts in diving medicine.

Adjunctive measures that should be used in the treatment of AGE are IV fluids and possibly steroids in pharmacologic doses (see also discussion "adjunctive measures to hyperbaric therapy" in the preceding text). Hemoconcentration is frequently seen in AGE and may be related to tissue hypoxia and edema. Divers are also commonly dehydrated secondary to pressure diuresis and lack of normal oral fluid intake. Vigorous hydration is important to minimize sludging and obstruction of microvascular blood flow caused by the elevated hematocrit, while avoiding fluid overload. Balanced saline solution (Ringer's lactate) or isotonic saline without dextrose should be administered intravenously at the rate of 1 L/hr until the patient voids or is catheterized for at least 500 mL. Sugar (glucose) is specifically not given to prevent further dehydration secondary to glycosuria and a resultant osmotic diuresis as well as the potential for edema formation. Once adequate hydration is achieved, the rate is slowed to 150 to 200 mL/hr for the remainder of the treatment.

Dexamethasone may be administered intravenously in a dose of 20 mg followed by 4 mg intramuscularly every 6 hours for 24 to 48 hours (124); this may prove to be beneficial in cases with evidence of cerebral edema. Till now, there is no conclusive evidence showing a clear therapeutic benefit of corticosteroids in this context; therefore, the question of their use remains open in this setting. There is furthermore no supportive evidence for the idea that steroids may increase an individual's susceptibility to oxygen toxicity. Anticoagulant or antiplatelet medications are not recommended as routine therapy of AGE, unless neurologic symptoms cause an inability to walk, in that case adjunctive DVT prophylaxis with LMWH should be initiated (125–128).

Transport of Patients

One-hundred percent O_2 should be started as soon as possible, using a tightly fitted aviator's or anesthesia-type mask. The patient should be placed in a recumbent position while awaiting and during transport to the hyperbaric chamber. If transport is required, it is of utmost importance to maintain near sea-level pressure. The use of "low-flying" helicopters is contraindicated if ground transportation is available. Even slight decreases in pressure cause bubble enlargement and may significantly alter the clinical course of the patient.

During transport, IV fluids should be administered using balanced saline solutions or normal saline. Patients having CNS or respiratory DCS or AGE should be accompanied during transport by personnel capable of providing intensive respiratory and ACLS care.

Immediate hyperbaric therapy is essential. Good response, however, has been seen in some cases after long delays before reaching the chamber. This makes it mandatory to give the patient the benefit of a trial of compression and hyperbaric O_2 even in the late case. Of course, every minute that elapses before the start of compression makes the prognosis more guarded.

Return to Flying Duties after Arterial Gas Embolization

A decision as to when and if to return a person to flying duties following AGE is complex. Consideration must be given to the circumstances under which the gas embolism occurred and the presence or absence of underlying pulmonary pathology (as predictors of recurrence) as well as evidence for residual neurologic pathology. A rational approach is

to consider a cerebral gas embolism ahead injury. The patient evaluation strategies following head injuries used by the appropriate regulating agencies (Federal Aviation Administration or military authorities) provide a basis for decisions on return to flying duties. In no case, however, should a patient return to such duties earlier than 3 weeks following such an incident to assure complete pulmonary healing has occurred.

Other Gas-Containing Cavities

Direct effects of pressure change on the ear, paranasal sinuses, and teeth are described in Chapter 15 and Chapter 20. This section addresses effects on the body and the important distinction between wet and dry gas and the implications of pressure changes on medical equipment.

Water Vapor and Gas Expansion

The mechanical effects of expansion and contraction of a trapped physiologic gas follow Boyle's law closely due to the relatively constant temperature of human tissue where gases are located. During decompression (ascent), trapped gases would expand because a differential pressure develops as the external pressure decreases. Many trapped gases remain essentially constant in volume due to their structure, for example, sinuses and the middle ear. Instead of responding by increasing volume, these trapped gases exert a differential pressure on surrounding tissues, which can cause severe, potentially disabling pain and potential physical damage to tissues.

The constant pressure (47 mm Hg) of water vapor at body temperature plays an increasing role in gas expansion during ascent as the partial pressures of the other expanded gases decrease. For example, water vapor makes up only 1% of the volume of a trapped gas bubble at 6 atmospheres (165 fsw) and 6% at sea level, but 33% of a trapped gas bubble at 40,000 ft. Due, in part, to the water vapor occupying more of the available pressure in alveoli, P_{AO_2} becomes extremely low above 45,000 ft. Even with 30 mm Hg of additional pressure applied to the lungs through pressure breathing for altitude (PBA) at 50,000 ft and 60 mm Hg of PBA at 60,000 ft, the P_{AO_2} is the same as breathing air above 18,000 ft.

At this writing, no pulse oximetry results have been obtained from humans using current oxygen equipment during exposure to 60,000 ft in an altitude chamber while breathing 100% oxygen with 70 mm Hg of PBA.

Above 63,000 ft, Armstrong's line, an unprotected human would experience vaporization of tissue water because the ambient pressure is 47 mm Hg, the same as the partial pressure of water at body temperature. The vaporization of body water above Armstrong's line is referred to as *ebullism*. Ebullism is different from embolism, which results from respiratory air being forced into the circulation by an overpressure in the lungs. The altitude or pressure at which ebullism occurs varies with the temperature and pressure in specific tissues. As an example, peripheral tissues are at a lower temperature than internal tissues and could ebullize at a lower pressure (higher altitude). Similarly, blood pressure in the arterial system would result in ebullism at lower pressure, higher altitude, than 63,000 ft. Any artificial increase in pressure around the body would also lower the potential for ebullism. One mechanism is a pressure suit and another is pressure PBA, which keeps the lung at a higher pressure. Although not protecting the rest of the body, PBA can at least provide a temporary increase in oxygen available to the tissues. Current equipment is inadequate to provide sufficient partial pressure of oxygen to tissues above 60,000 ft, even with assisted pressure breathing for altitude (APBA). This involves the use of a counterpressure jerkin worn to allow 60 mm Hg of pressure to be tolerated for more than a couple minutes.

Effects of Trapped Gases during Pressure Change

Because the volume of a sphere is a function of the cube of its radius and the diameter only twice the radius, a large volume change represents a relatively small change in diameter. However, it is the pressure differential, not volume change, which results in most of the effects listed in the subsequent text.

- Expansion of trapped gastrointestinal gas.
- Barotitis media (ear block) may be defined as an acute or chronic traumatic inflammation of the middle ear produced by a pressure differential (either positive or negative) between the air in the tympanic cavity and contiguous air spaces and that of the surrounding atmosphere. To alleviate the pressure differential, several maneuvers can be performed (Toynbee, Valsalve, Frenzel, etc.). The Toynbee maneuver entails pinching your nose, closing your mouth, and swallowing, thereby resulting in decreasing nasopharyngeal pressure against middle ear and Eustachian tube pressure. The Valsalva maneuver involves increasing the nasopharyngeal pressure against a closed Eustachian orifice; pinching your nose and blowing while your mouth is also closed. The Frenzel maneuver may also be performed by thrusting the jaw forward to open the Eustachian tube, thereby providing a path for equalization of pressure.
- Barosinusitis (sinus block) is an acute or chronic inflammation of one or more of the nasal accessory sinuses produced by a pressure difference (usually negative) between the air in the sinus cavity and the surrounding atmosphere. The condition is characterized by pain in the affected region typically during descent; this pain can develop suddenly and be so severe that the individual will be severely distracted and incapacitated.
- Barodontalgia (tooth pain) is also a case of a trapped gas exerting positive or negative pressure on surrounding tissue as a result of the difference between the pressure inside the tooth or the apical root of the tooth in the maxillary sinus and the pressure outside the tooth.
- Lung overinflation due to breath-hold or inadequate equalization of pressure during decompression can result in serious problems.
  - Pulmonary overexpansion
    - Pulmonary embolism (air in arterial circulation)

- Pneumothorax (air in lung pleural cavity)
- Pneumomediastinum (air in the mediastinum)

The Gastrointestinal Tract

Gas is normally contained in the stomach and the large bowel. As previously discussed, wet gases expand to a greater extent than do dry gases. Expansion within the closed confines of the gastrointestinal tract during ascent can cause stretching of the enclosing organ and produce abdominal pain. In addition to pain, respiration can also be compromised by gas expansion, forcing the diaphragm upward. If pain is allowed to proceed and relief is not obtained by belching or the passing of flatus, flight operations will be jeopardized. Severe pain may cause a vasovagal reaction with hypotension, tachycardia, and fainting. The best treatment of gastrointestinal tract discomfort due to gas expansion is the avoidance of gas-producing foods. Chewing gum may promote air swallowing and should be avoided at least during ascent. The crewmember should be instructed to pass gas when discomfort occurs. Abdominal massage and physical activity may promote the passage of gas. If this is unsuccessful, a descent should be initiated to an altitude at which comfort is achieved.

Other Gas-Containing Cavities

Direct effects of pressure change on the ear, paranasal sinuses, and teeth are described in Chapter 18. This section addresses these effects on the gastrointestinal system and on medical equipment.

Effects of Pressure Change on Medical Equipment

Varying volumes of gas may be trapped in medical equipment being used in the aerospace or hyperbaric environment. Examples of such equipment include drip chambers for IV fluids, endotracheal cuffs, water traps used with chest tubes, and sphygmomanometer cuffs.

During ascent, an unvented sphygmomanometer cuff will inflate and tighten around a patient's arm. If air is used to inflate an endotracheal cuff, significant ambient pressure reductions, particularly as seen with ascents from hyperbaric environments, can cause tracheal mucosal sloughing if allowed to persist. A wise precaution is to inflate endotracheal cuffs with normal saline rather than air in such environments. Water levels in water traps should be checked often or opened to ambient pressure when significant changes in pressure occur. The air space in IV line drip chambers will decrease in volume with increased pressure in hyperbaric chambers. Additional air will have to be added to the drip chamber to monitor the drip rate. On ascent, the volume of air will increase, and if added air is not replaced with fluid, IV air will inadvertently be administered.

The possible effects of changes in pressure on all medical equipment should be considered before such equipment is used either in a hyperbaric chamber or in flight. When possible, the equipment should be functionally tested in the pressure environment in which it is to be used before it is used with patients.

Ebullism

With the planned expansion of the operational ceiling for new, modern fighter aircraft (e.g., F-22 Raptor, Eurofighter 2000) to 18,287 m (60,000 ft), we are approaching the atmospheric zone which may result in human exposures to ambient pressures below 47 mm Hg. This is the equivalent of the saturated water vapor pressure at body temperature (37°C). Upon exposure to such an environmental pressure, spontaneous boiling and degassing of body tissues and fluids will occur. This process is referred to as *ebullism* and the pressure-equivalent altitude at which it is expected to occur is referred to as the *Armstrong line* [19,201 m (63,000 ft)]. Owing to variations in pressure and temperature in the body, ebullism may occur in exposed human tissues as low as 16,763 m (55,000 ft), or higher in the case of tissue below body temperature and partly pressurized by an anti-G suit or a counterpressure jerkin. Therefore, referring to the "Armstrong line" as "Armstrong zone" would probably be more appropriate. The data that are available on the physiological changes occurring in this extreme pressure environment are derived from animal studies and a few accidental human exposures (135).

Animal studies (unprotected exposures) have shown rapid loss of consciousness (within 9–12 seconds), immediate tissue hypoxia, rapid increase in venous pressures, circulatory arrest (in seconds), apnea, and spastic rigidity within 30 seconds followed by flaccid paralysis. Provided that the structural integrity of lungs, heart, and cerebrum is maintained, recovery after exposures to 90 to 210 seconds of a hard vacuum is possible.

In one case of accidental exposure to 36,574 m (120,000 ft) during a test of a space suit, pressurization of the suit was lost and the subject remembered the sensation of his saliva boiling on his tongue. Rapid recompression resulted in regaining of consciousness at 4,267 m (14,000 ft) and the subject was not hospitalized after the incident and did not have any apparent complications. In a second incident, an individual was exposed to 22,554 m (74,000 ft) for 3 to 5 minutes in an industrial setting without any protective equipment. The individual was comatose with decerebrate posturing and had frank pulmonary hemorrhage after the exposure. Aggressive HBO and intensive care therapy resulted in full recovery without any evidence of neurologic deficits after the incident (1 year after the exposure neurologic testing was above baseline) (134).

There are currently no medical treatment protocols available for ebullism, as it was thought that such an exposure would likely not be survivable. The cases given in the preceding text illustrate the need for aggressive therapy aimed at reestablishing pulmonary gas exchange and support circulation. Hyperbaric O_2 therapy or at least 100% ground level O_2 needs to be considered together with aggressive intensive care therapy.

The quest to fly higher and dive deeper has expanded man's pressure environmental envelope well beyond that to which he is physiologically adapted. Pathologic changes

resulting from exposure to these environments have defined new sets of clinical syndromes specifically related to pressure changes. Studies of the pathophysiology underlying these syndromes have unmasked two separate categories of disorders: indirect effects of pressure change resulting from the evolution of gas from solution and direct effects of pressure change on gas-containing body cavities. In addition, it is now recognized that the pressure environment represents a physiologic continuum from the increased pressures encountered by divers to the decreased pressures encountered by aviators and astronauts. This continuum is dramatically exemplified by the diver who surfaces safely only to experience DCS a few hours later while flying at low altitude.

As we have learned more about the physiologic changes that occur with changes in pressure, we have been able to develop rational treatment methods to cope with the medical disorders they bring about. Therefore, hyperbaric therapy, with specific treatment profiles for mild and severe DCS and for gas embolism, has lessened mortality and the incidence of permanent residual deficits. Adjuvants to hyperbaric therapy are increasing our ability to deal with these disorders.

CONCLUDING REMARKS

Advances in technology have allowed the development of systems capable of transporting air and space crewmembers into increasingly more severe pressure environments. The increased altitudes in the operational ceilings of the next generation fighter aircraft as well as the extensive EVA necessary to construct the ISS have drawn renewed attention to the disease processes associated with the changes in ambient pressure in the operational aerospace environment. Technologic advances have made possible the development of the life-support equipment necessary to prevent the pathophysiologic consequences of exposure to these environments. Unfortunately, the development of practical, effective life-support systems tends to lag behind the development of transport systems. Historically, this lag resulted from a lack of knowledge about the physiologic consequences of exposure to hostile environments. The effective and safe use of advanced flying and diving systems depends on our ability to educate the operators about the risk and symptomatology of DCS, efficient reporting mechanisms of DCS incidents, continuous reassessment of our clinical classification, documentation and evaluation of DCS, and the creation of effective risk-mitigation, risk-quantification, and risk-prediction strategies for the environment the operators face.

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