14 DECOMPRESSION PHYSIOLOGY AND PRACTICE

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Decompression illness is a disease of the industrial revolution, a consequence of the invention of the air pump which made diving, caisson work and altitude exposure possible. The paralysis and death suffered by nineteenth-century divers and caisson workers (Jaminet 1871; Smith 1873; Heller *et al.* 1900) were practical stimuli to Haldane in the early twentieth century and lead to the method of staged decompression (Chapter 13), which all but eliminated death and permanent injury and made productive work in compressed air a reality.

There is overwhelming evidence that bubbles form on decompression and are responsible for cardiopulmonary failure, but the aetiologies of the less severe manifestations are poorly understood. Relevant environmental factors and the physics, physiology and pathophysiology of the bubble theory, reviewed in other chapters, are summarized below as they apply to avoiding the disease.

Even perfect mechanistic knowledge, however, would not eliminate the need for procedures to reduce pressure safely. Statistical methodology for developing decompression procedures from empirical observation is discussed, and a summary of current modes of diving is presented.

Decompression is a pragmatic activity, and many decompression studies were neither scientifically designed nor reported. While the conclusions of these studies are sometimes uncertain, they contain observations that are otherwise unavailable and are discussed below with their limitations noted. Future studies are expected to support firmer conclusions as the recently introduced statistical methodology has reinforced the importance of experimental and epidemiological design.

PATHOPHYSIOLOGICAL BASIS OF THE BUBBLE THEORY

The observer relies on clinical judgement to classify post-dive signs and symptoms, but classification can be uncertain because decompression illness and air embolism may have similar presentations and common elements in their aetiology (Francis & Smith 1991). In recognition of this ambiguity, subsequent reference generally will be to *decompression illness* (DCI) rather than decompression sickness, even though pulmonary barotrauma may rarely be involved (Francis & Smith 1991).

Decompression illness is classified by the affected organ system. Some decompression illness symptoms are attributed to extravascular or stationary bubbles and other symptoms to intravascular bubbles, which may originate at remote sites. The effects of bubbles may be mechanical or biochemical. The most severe form, which involves the cardiopulmonary system, is rare today. The lungs are occasionally affected but not as frequently as the central nervous system, where symptoms are usually referrable to the spinal cord rather than the brain. The most familiar forms are pain and itching or rash.

Cardiopulmonary Decompression Illness

In a review of the early literature, Hoff (1948) found that a massive influx of bubbles into the heart and lungs displaced the blood, causing death from cardiovascular collapse and asphyxia. Animal studies by Bert (1878) and Heller *et al.* (1900) found bubbles in the venous circulation shortly

after decompression from elevated pressure. These bubbles could cause unconsciousness, shock and death. Similar effects were not uncommon in humans after severe decompression (Jaminet 1871; Admiralty Report 1907). Modern experiments have confirmed these findings while demonstrating that the responses to bubbles are dose-dependent, ranging from negligible to fatal according to the volume of gas released (Gersh & Catchpole 1951; Powell 1972a,b).

Pulmonary Decompression Illness

Pulmonary decompression illness may have two forms. The first is caused by barotrauma in which direct damage to the lungs releases alveolar gas into local tissues and blood. The effects of barotrauma can follow any dive independent of dissolved gas content and may be quite different from the effects of venous gas emboli. Pulmonary barotrauma can result in arterial gas embolism and possibly neurological decompression illness, and this possibility may act, in part, as 'background noise' in the attempted quantification of decompression incidents initiated by gaseous supersaturation (see 'Neurological Decompression Illness').

The second form of pulmonary decompression illness includes, to use the old terminology, pulmonary decompression sickness or 'chokes', which is indicated in animals by rapid shallow respiration (Behnke 1951; Lehner & Lanphier 1989). In humans, mild chokes presents as sore throat and cough upon deep inspiration. Coughing can become paroxysmal and be accompanied by severe chest pain, dyspnoea and unconsciousness (Behnke 1951; Ferris & Engle 1951). In the early days of decompression, an attack of severe chokes often forecast a grave clinical outcome (Hoff 1948). While chokes is usually rapidly reversed by prompt recompression, untreated chokes can lead to oedema, pulmonary hypertension and respiratory insufficiency. Pulmonary decompression illness has contributed to a number of deaths as a result of severe altitude exposure (Dixon 1992) but is infrequent today, probably because exposures are less severe than in the past.

The tracheobronchial tree often becomes inflamed during chokes (Ferris & Engle 1951). Pulmonary or venous gas emboli are an unlikely cause of this finding as they can be present in great quantity without inducing symptoms (see Chapter 15). Arterial embolization of the bronchial circulation also is thought improbable as arterial emboli would most likely affect the brain and chokes usually occurs without cerebral symptoms (see 'Pressure Profile'). Ferris and Engle (1951) propose that chokes is a vascular reaction to bubbles in the mucus membranes of the tracheobronchial system not unlike skin mottling (see 'Skin Bends and Counterdiffusion').

Neurological Decompression Illness

Three mechanisms have been proposed for the initiation of neurological decompression illness by bubbles: arterial gas emboli, extravascular bubbles and vascular obstruction by venous bubbles.

The pathological consequences of arterial gas embolism arising from lung overexpansion are well recognized (Chapter 17), but further problems may occur should arterial emboli reach areas of the systemic circulation which are supersaturated with inert gas from previous diving. Expansion of these bubbles might lead to effects beyond those associated with an otherwise uncomplicated air embolism. This mechanism may be relevant in the severe cerebral and spinal decompression illness reported after relatively innocuous dives which terminate with pulmonary barotrauma (Neuman & Bove 1990).

The cardiovascular collapse observed in the nineteenth century from venous gas embolism (see 'Cardiopulmonary Decompression Illness') is avoided today by restricting dive depth and bottom time and by decompression stops which allow inert gas to be eliminated before bubble growth becomes excessive. Nonetheless, bubbles are routinely detected by ultrasound in the venous blood and right heart even after dives not considered severe (Chapter 15). In animals, these bubbles have been demonstrated to enter the arterial circulation through defects in the wall separating the chambers of the heart (patent foramen ovale or PFO; Jenssen *et al.* 1991). In humans, retrospective studies have indicated a greater incidence of PFO in divers who have had cerebral or spinal decompression illness than in a control population or in divers who have had pain-only symptoms (Moon *et al.* 1989, 1991; Wilmshurst *et al.* 1986, 1990). Definitive evidence for PFO as an active mechanism in decompression illness awaits a prospective study.

In the absence of PFO or pulmonary barotrauma, arterial bubbles are rare because the lungs are a reasonably good filter for gaseous emboli

(Butler *et al.* 1980; Powell *et al.* 1982). Arterial emboli can occur, however, if the bubble volume exceeds the filtering capacity of the lungs (Spencer & Oyama 1971), if pulmonary pathology is present (Butler & Hills 1985), or if the pulmonary arterial pressure increases as a result of gaseous obstruction (Butler & Katz 1988). The passage of venous bubbles through the lungs was also promoted by repetitive diving in mice and guinea-pigs (Gait *et al.* 1975), and repetitive diving was found to be a reliable means of producing spinal decompression illness in goats (Hills 1971) and dogs (Sykes & Yaffe 1985).

The arterial embolus theory cannot account for all observations concerning neurological decompression illness. Both solid and gaseous emboli seek the brain as their principal target organ (Hallenbeck & Andersen 1982), but cerebral injury after decompression is much less common than spinal injury. Gas bubbles injected directly into the arterial circulation of the spinal cord in dogs at sea level produced anoxic lesions in grey matter (Francis *et al.* 1989; Pearson *et al.* 1990), but when spinal decompression illness was induced by a provocative dive, traumatic extravascular lesions were found almost exclusively in the white matter (Palmer 1986). White matter lesions also predominate in humans with spinal decompression injury (Haymaker & Johnson 1955; Kitano & Hayashi 1981).

Bubble formation was observed in the white matter of dogs even when the spinal circulation was arrested at pressure to preclude the possibility of arterial embolization after decompression (Francis 1990). Bubble formation occurred only at depths greater than 26 m (85 ft), however, suggesting the presence of *autochthonous* or *in situ* extravascular bubbles which expanded when a threshold supersaturation was exceeded.

The obstruction by bubbles of the venous drainage of the spinal cord has been observed and also proposed as a mechanism for injury (Hallenbeck & Anderson 1982). This mechanism depends, in particular, upon bubble-induced biochemical damage which can trigger thrombosis, hypoxic injury, and activation of the complement, histamine, bradykinin and prostaglandin systems (Hallenbeck & Anderson 1982; Chryssanthou 1989; Ward 1989). Bubbles have also been observed to increase the permeability of the blood–brain barrier (Hills & James 1991). There appears to be no reason why arterial, autochthonous and venous bubbles could not contribute separately or together to decompression-induced cerebral and spinal cord injury by both mechanical and biochemical mechanisms. The resolution of this issue awaits further study.

Joint Pain

The most common symptom of decompression illness, joint pain, has at least three possible origins: neurogenic, medullary and articular (Nashimoto & Lanphier 1991). While phantom elbow pain has been reported in a one-armed diver (Elliott 1991), neurogenic pain originating at a remote site appears rare, and no apparent brain or spinal cord lesions were found in goats affected only by limb pain (Palmer *et al.* 1978).

Bubbles in the periosteal envelope or medullary cavity have been proposed as a cause of medullary pain (Lanphier 1991a), and bubbles which distend the venous sinusoids have been suggested as the cause of dull, aching pain (Walder 1991). A 'bone compartment syndrome' from intramedullary bubbles may be responsible for both pain and dysbaric osteonecrosis (Lanphier 1991a). Osteonecrosis, the death and possible failure of bone, is considered a long-term consequence of diving. It is associated statistically with decompression illness after diving and caisson work (Davidson 1976; Ohta & Matsunaga 1974; Cross 1987; Zhang *et al.* 1991), is less common with more conservative military decompression procedures (Harvey & Sphar 1976) and occurs only rarely at altitude (Allen *et al.* 1974).

Radiographs of painful knees at altitude during the Second World War implicated an articular mechanism for joint pain. Figure 14.1 shows an aspherical bubble, approximately 10 cm long and 1 cm at its highest point, which appears to disect adjacent muscle layers posterior to the knee and parallel to the femur (Pilmanis, pers. comm. 1990). The bubble was associated with severe pain at the site most distal to the knee. In subjects exposed to both hypobaric and hyperbaric decompression, similar occurrences of pain were reported, suggesting that decompression illness pain has the same mechanisms and sites both at altitude and after diving (Behnke 1971).

The relationship between bubbles and pain was addressed in two studies of altitude exposure at 10 668 m (35 000 ft) in which both knees were radiographed when one became painful (Thomas &

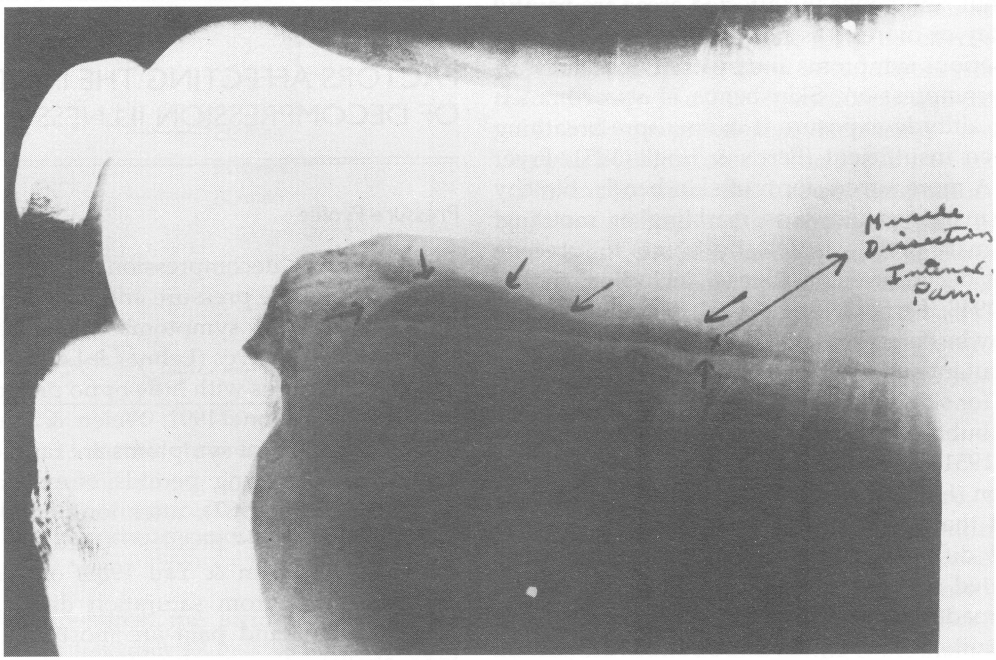

FIG. 14.1. Radiograph of a bubble behind the knee of a subject at an unknown altitude *c.* 1945. US Army Air Force School of Aerospace Medicine, Randolph Field, Texas. (Courtesy of Dr A. A. Pilmanis)

Williams 1944, 1945; Webb *et al.* 1944; Ferris & Engle 1951). Free gas was found in the knee joints of all subjects, with or without pain. Bubbles posterior to the femur in the upper posterior fossa and popliteal fat were statistically associated with pain, as were streaks of gas which appeared to be along fascial planes or tendons as in Fig. 14.1. The severity of pain and size of the gas lesion was associated with bubbles in the popliteal fat.

Acute altitude exposure also produced transient pains in the hands and feet, which were accompanied by crepitus in the tendon sheaths (Ferris & Engle 1951). Palpation of the tendon sheaths revealed bubbles that, when milked away, often relieved the pain. Ferris and Engle (1951) argued that decompression pain is probably extravascular rather than intravascular as: (1) there is no local cyanosis; (2) anoxic pain is usually maximal during the reactive hyperaemia of recovery; (3) local recompression sufficient to occlude blood flow relieves rather than intensifies pain; (4) bubbles associated with pain on X-ray have an articular not vascular distribution; (5) pain relieved by recompression recurs at the same site upon decompression 4–6 h later.

Nims (1951) proposed that expanding extravascular bubbles might cause pain by mechanically distorting sensory nerve endings. Thus, delayed symptom onset after diving would be due to gradual bubble growth, and bubble shrinkage upon recompression would give immediate relief. This mechanism may explain many incidents of decompression illness but not the occurrence of symptoms hours after descent from altitude (Rush & Wirjosemito 1990; Weien & Baumgartner 1990; Bason & Yacavone 1991) or cases refractory to recompression therapy.

These observations are inconsistent with a simple mechanical mechanism and may reflect biochemical phenomena (Hallenbeck & Andersen 1982). Biochemical damage might accumulate as long as bubbles are present and could explain the less than satisfactory recovery with long delays to recompression therapy (Lam & Yau 1988; Rudge & Shafer 1991).

Skin Bends and Counterdiffusion

Rapid ascent to sea level or to a decompression stop after a short, deep dive is often followed by itching (pruritis) and rash (urticaria), commonly known as 'skin bends' (Hamilton 1991). Less frequently, skin bends is manifested as a sense of heat. Skin bends usually disappears within an

hour, but sometimes the affected areas are painful for a day or more. It is not generally followed by more serious symptoms and by itself does not warrant recompression. Skin bends is also common during altitude exposure if oxygen pre-breathing has been insufficient (Ferris & Engle 1951; Fryer 1969). A more severe form of skin bends, blotchy purple markings known as 'marbling' or 'mottling' (cutis marmorata), is felt by some to precede serious decompression illness, including chokes (Hoff 1948; Ferris & Engle 1951; Hamilton 1991), but may be coincidental.

Subcutaneous bubbles are the common explanation for skin bends, and there are rare reports of visible bubbles under the skin at altitude (Ferris & Engle 1951) and in tunnel workers after decompression (Hempleman 1991). Rashbass (1957) postulated that skin bends is a consequence of the inward diffusion of nitrogen, since itching was prevented by warm water immersion. Bennett (1991) made a similar observation. Hard-hat divers in dry suits, however, noted that a cold arm itched while an arm covered with a warm sweater did not itch (Lanphier 1991b). As warm skin is well perfused and cold skin is poorly perfused (see 'Blood Flow Regulation'), this indicates that nitrogen eliminated by blood flow is more important in skin bends than nitrogen absorbed by diffusion.

The nature of bubble formation in the skin has been clarified by the study of cutaneous counterdiffusion which occurs when a subject breathes a slowly permeating gas (see 'Bubble–Tissue Diffusion') such as nitrogen while surrounded by a rapidly permeating gas such as helium. These studies were reviewed by Lambertsen (1989). The permeation of tissue by a gas is governed by its diffusivity–solubility product. A net inward flux of gas causes subcutaneous supersaturation and extravascular bubble formation, which can occur without pressure change. In human exposures at elevated pressure, intense itching was accompanied by hard, raised, bloodless lesions and severe vestibular dysfunction. In animals immersed in helium at sea level while breathing nitrous oxide, bubbles dissected subcutaneous tissue causing capillary damage manifested as severe bruising. Continued counterdiffusion resulted in fatal venous gas embolization.

FACTORS AFFECTING THE INCIDENCE OF DECOMPRESSION ILLNESS

Pressure Profile

The nature of decompression illness is strongly influenced by the pressure and breathing gas profile. Neurological symptoms are most common after short deep dives (Lehner & Lanphier 1989) or altitude exposures with little or no preoxygenation (Bason & Yacavone 1991; Weien & Baumgartner 1990). Neurological symptoms are rare for altitude exposures with long periods of preoxygenation (Waligora *et al.* 1987), after long, shallow, low-pressure caisson profiles (Medical Research Council 1971; Lam & Yau 1988) or during slow decompression from saturation dives (Berghage 1976). Chokes and pain are most common after long, shallow dives or altitude exposure (Lehner & Lanphier 1989).

The association of spinal decompression illness with short, deep dives suggests that tissues responsible for spinal symptoms may exchange inert gas more rapidly than tissues responsible for pain. If this is true, then slower initial decompression may reduce inert gas tension and autochthonous bubble formation in spinal tissue (Francis 1990) and may decrease venous gas emboli (Neuman *et al.* 1976; Smith & Stayton 1978; Pilmanis 1990) and arterialized venous bubbles. Reduced ascent rates or short decompression stops, therefore, might decrease the incidence of spinal decompression illness if either the autochthonous or arterial bubble mechanisms were active (see 'Neurological Decompression Illness').

Adaptation to Decompression

For caisson work and helium–oxygen diving, decompression risk appears to be reduced by frequent exposure to pressure, an effect which has been called *adaptation, accommodation, acclimatization* and *acclimation*. Haldane recognized this effect, and recommended part-time duties for new caisson workers (Rubenstein 1968). Figure 14.2 shows the incidence of decompression illness as a function of the number of exposures during construction of the Tyne tunnel (Walder 1968). During

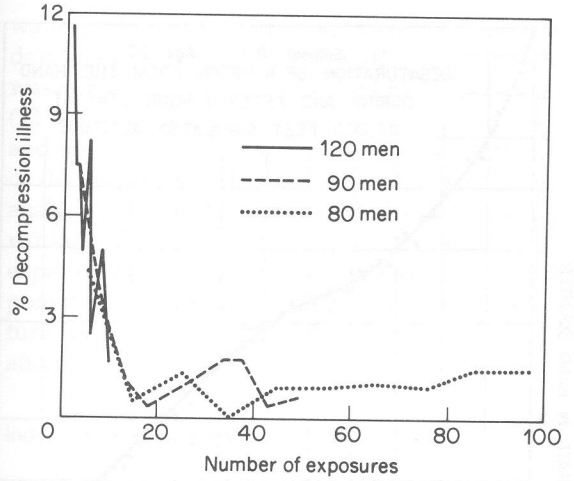

FIG. 14.2. Adaptation during compressed air work. The incidence of decompression illness decreased with repeated hyperbaric exposure. (After Walder 1968)

the first 10 exposures, the incidence of decompression illness fell from 12 to 3%. After 10 days without pressure exposure, the incidence returned to its initial level. Adaptation was specific for each pressure and re-occurred when the working pressure increased (Walder 1975). Evidence for adaptation was also found in a recent Hong Kong tunnel project where the incidence of decompression illness was 3.7 times greater for the first five exposures than for subsequent exposures (Lam & Yau 1988).

Adaptation during air diving has been difficult to demonstrate objectively. Using Doppler-detected precordial bubbles as an index of adaptation, Eckenhoff and Hughes (1984) could find no evidence in 14 subjects during 12 daily air dives for 30 min at 45 m (150 ft). Data from recreational diving accidents, moreover, suggest that decompression illness increases rather than decreases with repetitive multi-day diving (Vann *et al.* 1989b).

The evidence for adaptation in diving is strongest for helium–oxygen exposures. Divers making progressively deeper no-stop exposures had a greater tolerance than divers making the deeper exposures first (Hempleman 1967). In dives to 82–91 m (270–300 ft) for 15–20 min, one incident of decompression illness occurred in 12 trials of 'worked-up' divers and six incidents in 6 trials without work-up ($P < 0.001$; Elliott 1969). In dives to 36 m (120 ft) for 40 min, no incidents occurred in 40 trials of worked-up divers and six incidents in 17 trials of fresh divers ($P < 0.005$; Thalmann *et al.* 1984; Thalmann 1986). The work-up effect seemed to persist for up to 4 days. Seven divers who made three dives to 36 m (120 ft) for 20 min at 5-day intervals had progressively decreasing precordial Doppler bubble scores (Vann 1989b).

An explanation for helium adaptation might be faster saturation for helium than for nitrogen (see 'Inert Gas Exchange'). Short helium dives would more closely approach caisson exposure saturations than short nitrogen dives. Helium adaptation has important implications for helium decompression (see 'Helium–Oxygen Diving').

Exercise During and After Decompression

In the first half of the twentieth century, US and Royal Navy divers routinely exercised during decompression as it was believed that exercise would accelerate inert gas elimination and reduce decompression risk (Boycott *et al.* 1908; Ellsberg 1929). Subsequent altitude and diving experiments, however, showed that exercise increased the incidence and severity of decompression illness and reduced the onset time. After decompression to 11 582 m (38 000 ft) of altitude, for example, Gray observed a 32% increase in incidence in subjects who did five push-ups and five deep-knee bends every 15 min (Cook 1951). The increased incidence was equivalent to an additional 1524 m (5000 ft) of decompression.

In diving experiments, Van Der Aue *et al.* (1949) found a 34% increase in the incidence of decompression illness in divers who lifted 25 lb weights for 2 h after no-stop dives at 12, 30 and 46 m (40, 100 and 150 ft). Van Der Aue titled his report, 'The effect of exercise during decompression . . .', even though he had tested exercise only *after* decompression. Van Der Aue recommended that both forms of exercise be avoided, and this prohibition endured for 30 years.

If exercise at depth increases the risk of decompression illness, presumably by accelerating nitrogen uptake (see 'Blood Flow Regulation'), might it not also accelerate nitrogen elimination and decrease risk? Balke (1954) provided evidence to this effect in showing that exercise during oxygen breathing before altitude exposure delayed symptom onset. In similar studies where subjects either rested or exercised during oxygen breathing before decompression to 9144 m (30 000 ft), there were 10 incidents of decompression illness in 16 resting

trials and no incidents in 10 exercising trials ($P < 0.01$; Vann *et al.* 1989a).

This concept was also tested in dives at 30 and 45 m (100 and 150 ft). Divers performed light exercise for 60 min at depth and either rested or exercised during decompression (Vann 1982a). Exercise during decompression appeared to reduce decompression time by about 30%.

Why should exercise during decompression reduce risk and exercise after decompression increase risk if both accelerate inert gas exchange? The objective of decompression is to minimize or avoid bubble formation so that inert gas can be eliminated as it was absorbed at depth, in the dissolved state. If decompression progresses too far, inert gas becomes isolated from the circulation in bubbles. This decreases the difference between the tissue and arterial inert gas tensions, which reduces the elimination rate (see 'Oxygen Window').

This effect was illustrated during krypton elimination at 11 582 m (38 000 ft; Tobias *et al.* 1949). Elimination decreased during exercise at altitude where bubbles form but increased upon recompression to sea level where bubbles resolve (Fig. 14.3).

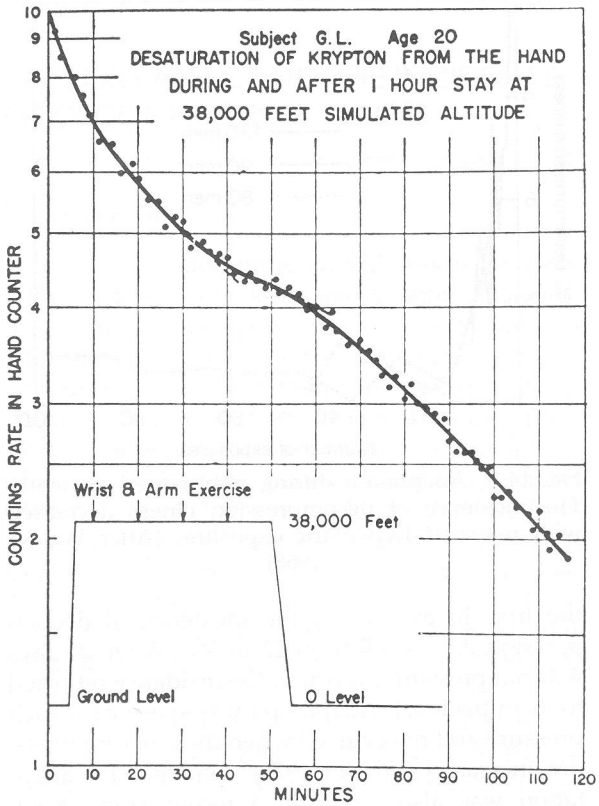

FIG. 14.3. The effect of altitude decompression on the rate of krypton elimination from a subject's hand. The elimination rate increased upon recompression to sea level. (Reproduced with permission from Tobias *et al.* 1949)

Exercise at Depth

Exercise at depth can increase the risk of decompression illness and the time needed for safe decompression. Van Der Aue *et al.* (1945) found that resting divers had an 11% risk, whereas working divers had a 21% risk on the same schedules. Decompression illness occurred most frequently in limbs exercised vigorously at depth. In other tests, Van Der Aue *et al.* (1951) reported that air decompression schedules which were safe for resting divers produced 20–30% decompression illness in working divers. Buehlmann (1975) found that divers doing light work during helium–oxygen dives required 20–40% more decompression time than resting divers. Vann (1982a) found that immersed divers exercising at 2 litres/min oxygen consumption at depth and resting during decompression could require up to three times the decompression time of dry, resting divers.

Exercise before Diving

Increased bubble formation due to exercise before decompression has been demonstrated in animal studies (Harvey *et al.* 1944b; Whitaker *et al.* 1945; Evans & Walder 1969; McDonough & Hemmingsen 1984a,b, 1985a,b) and suggested by anecdotal reports linking weightlifting and long-distance bicycle racing with an increased risk of decompression illness in humans (Vann 1982b; Nishi *et al.* 1982). Other forms of pre-exposure exercise have been associated with unusual decompression illness after diving (Hughes & Eckenhoff 1986) and during altitude exposure (Piwinski *et al.* 1986).

Temperature and Immersion

Exercise during decompression may exert part of its effect by warming a diver and preventing the decreased perfusion which accompanies hypothermia (see 'Blood Flow Regulation'). Balldin (1973a), for example, found that 2 of 10 subjects developed decompression illness symptoms at altitude after breathing oxygen while immersed in

water at 37 °C, but 9 of 10 subjects who were dry developed symptoms ($P < 0.01$). No difference was noted, however, for decompression in warm (22 °C) or cold (7–13 °C) water (Thalmann 1985), and immersion was estimated to increase the risk of decompression illness by less than 30% in an analysis of 797 dry, resting dives and 727 wet, working dives (Weathersby *et al.* 1990). Specific experimental trials are needed to sort out the potentially complex interactions between temperature, immersion and inert gas uptake or elimination.

Individual Susceptibility

Some of the variability of decompression illness appears to result from differences in individual susceptibility. This is best seen in caisson workers who are followed over many exposures. Lam and Yau (1989) found that a previous history of decompression illness was associated with future bouts of the illness. Paton and Walder (1954) studied 376 compressed air workers during 40 000 exposures with a mean incidence of decompression illness of 0.87%. Fifty-five percent had an incidence of below the mean, 11% had an incidence equal to the mean, 6% had twice the mean incidence, and 10% had five times the mean incidence. The remaining 18% had an incidence 28 times the mean but left work after only a few exposures.

Age and body fat are among the possible causes of individual variability. Age has been considered a contributing factor since the first study of decompression illness by Pol and Watelle (1854; see Gray 1951). Age was implicated as a risk factor in 11 reports on diving, caisson and altitude exposure (Gray 1951; Bradley 1987). Three reports found no association with age (Wise 1963; Dembert *et al.* 1984; Lam & Yau 1989). Gray (1951) estimated a 28-year-old man to be twice as susceptible to decompression illness as an 18-year-old based upon a relationship between age and altitude decompression illness which was developed from data on 52 000 subjects. The factors associated with age which may affect susceptibility include body fat, degenerative joint disease, changes in pulmonary function and cardiovascular disease (Dembert 1989).

As with age, body fat has been implicated as a risk factor for decompression illness since the earliest observations (Gray 1951). The effect of body fat is usually explained by high nitrogen solubility, which increases nitrogen absorption and bubble growth. Three animal studies and 12 human studies report an association between decompression illness and body fat in diving, altitude and caisson work (Dembert 1989; Lam & Yau 1989), whereas two diving studies found no association (Wise 1963; Curley *et al.* 1989). Based upon a relationship between altitude decompression illness and weight to height ratios for 49 000 subjects, Gray (1951) estimated that a 178 cm (70 inch) tall man weighing 89 kg (196 lb) was twice as susceptible as a 57.3 kg (126 lb) man of the same height.

The reports of Wise (1963) and Curley *et al.* (1989) stand out in finding no association between decompression illness and body fat. Wise (1963) studied 1131 US Navy divers, 63% of whom experienced decompression illness, while Curley *et al.* (1989) studied 376 Navy divers, 30% of whom experienced the illness. The reason for the lack of association is unknown, and several factors are possible. Navy divers may be younger and healthier than other subjects. Body fat may have a different effect for short dives than for caisson or altitude exposures. High body fat may protect against decompression illness in cold water.

Multiple Risk Factors

Multiple factors appear to be important in determining individual susceptibility. Gray (1951) found susceptibility best described when age and body type were considered together. Susceptibility differences of 2:1 and 5:1 could be distinguished with age and body type separately, but differences of 8:1 could be distinguished with age and body type together. Lam and Yau (1989) controlled for the effects of multiple variables by logistic regression and found increased individual susceptibility associated with Body Mass Index, previous incidents of decompression illness and job (engineer or miner).

Data interpretation and hypothesis testing with traditional statistical methods are difficult, if not impossible, when multiple variables are present, i.e. adaptation, exercise, immersion, temperature, dive phase, age, body fat, etc. The univariate analysis used in most of the studies cited above can lead to invalid conclusions (Lam & Yau 1989), and important variables were often uncontrolled or unmeasured. The best that can be accomplished with these methods and much of the available data

is a qualitative indication of factors which may be important under restricted circumstances.

Alternatively, statistical modelling by maximum likelihood can assess the effects of confounding variables as easily as variables of interest, if sufficient data are at hand, and can provide both risk estimates and significance tests. Logistic regression, for example, may be used to test multiple risk factors (Lam & Yau 1989; Kumar *et al.* 1990; Lehner & Lanphier 1989; Daniels 1989), while survival analysis may be used to address both risk factors and dive profile effects (see 'Probabilistic Modelling'). Unfortunately, much of the existing data is unsuitable due to inaccuracy or insufficient information. Future studies must emphasize data quality if quantitative answers are to be obtained.

BUBBLE FORMATION

If bubbles are to be avoided, their origin must be understood. This should begin with a study of non-living systems.

Why Bubbles Form

Bubbles form as a result of gas and vapour supersaturation which is defined as the dissolved gas tension (P_g) and vapour pressure (P_v) in excess of the absolute pressure (P_{abs}):

$$\text{supersaturation} = P_g + P_v - P_{abs} \qquad (1)$$

The probability that bubbles will form increases with the supersaturation, but large supersaturations may sometimes be sustained without bubble formation.

Equation (1) shows that supersaturations can occur when the absolute pressure is reduced as well as from increased dissolved gas tension or vapour pressure. A water column is a familiar example. In a standing water column, the pressure at the base is increased by hydrostatic compression. In a hanging water column, the pressure at the top is reduced by hydrostatic tension. If the column is sufficiently long, the pressure at the top becomes *negative* and causes bubbles to form. These bubbles limit the height to which a pump can raise water (Derry & Williams 1960). Equation (1) shows that increases in gas tension and reductions in absolute pressure both contribute to supersaturation (Vann & Clark 1975).

Supersaturation caused by negative pressure occurs during many mechanical processes which reduce the local absolute pressure in a liquid system. Water flowing through a constriction in a tube undergoes a pressure reduction described by the Bernoulli principle. This reduction can cause Reynolds' cavitation (Harvey 1947). A sound wave has a negative pressure phase which can cause acoustic cavitation (Strasberg 1959). When closely opposed surfaces in liquid are pulled apart, the flow of liquid into the widening gap is resisted by viscosity, and the local absolute pressure decreases due to *viscous adhesion* (Cottrell 1964). This can cause supersaturation, and Hayward (1967) applied the term *tribonucleation* to the cavitation which may result.

A lubricant in viscous tension due to shear between a bearing and a shaft is subject to supersaturation and cavitation (Floberg 1964). Supersaturation and bubble formation occur when a ball rolls down a surface (Ikels 1970) and in the viscous adhesive on tape when the tape is pulled from a surface (Cottrell 1964). The supersaturation generated when surfaces are pulled apart is directly proportional to the liquid viscosity and indirectly proportional to the cube of the distances between the surfaces. Theoretically, its magnitude can reach thousands of negative atmospheres (Campbell 1968; Dowson *et al.* 1971).

Bubbles may form by *vapourous* or *gaseous cavitation*, as was clearly demonstrated in acoustic studies (Strasberg 1959). During the negative pressure phase of a sound wave, water undersaturated with gas forms a transient, vapour-filled bubble. During the positive pressure phase, the bubble collapses with an audible crack, as it only contains water vapour, and its pressure is much less than ambient. This is vapourous cavitation. As the tension of gas dissolved in the water is raised, the negative pressure for cavitation is reduced. When the water approaches saturation with gas, dissolved gas diffusing into the bubble prevents its immediate collapse, and a stable bubble forms without a sound. This is gaseous cavitation.

How Bubbles Form

The most common mode of bubble formation is from a pre-existing gas phase known as a *gas nucleus*. A spherical bubble can act as a gas nucleus

but is dissolved by surface tension and has a limited lifespan. Surface tension raises the internal pressure of a bubble (P_{int}) above the external absolute pressure (P_{abs}) as defined by LaPlace's Law:

$$P_{int} - P_{abs} = \frac{2\gamma}{R}$$

where γ is surface tension and R is the bubble radius. If the dissolved gas tension, P_g, surrounding the bubble is less than the bubble pressure, P_{int}, gas diffuses out of the bubble and it dissolves. ($P_{int} - P_{abs}$) is about 1 ata (101 kPa) for a 1 micron bubble in water and increases as the bubble shrinks, which accelerates the collapse rate.

If gas nuclei are the source of bubble formation, they must be stabilized against surface tension or continuously replaced as they dissolve. A gas nucleus may be stabilized by a shell of material at the gas–liquid interface which provides mechanical strength or impedes outward diffusion (Yount 1979; Johnson & Cooke 1981). Gas nuclei are also stabilized in hydrophobic crevices which do not readily fill with water (Harvey *et al.* 1944a; Strasberg 1959; Apfel 1970; Tikuisis 1986). Depending on their stability, gas nuclei grow into bubbles at supersaturations of several tenths of an atmosphere up to about 20 ata (2.03 MPa; Yount & Strauss (1976).

In vitro gas nuclei can be eliminated by compression, which raises the gas pressure causing it to diffuse into adjacent liquid and dissolve (Harvey *et al.* 1944a; Yount & Strauss 1976). Compression before altitude exposure markedly reduced visible bubble formation in transparent shrimp at altitude (Evans & Walder 1969; Daniels *et al.* 1984), and compression before diving reduced decompression illness in rats after decompression (Vann *et al.* 1980). These observations are consistent with the presence of pre-existing gas nuclei in animals.

In the absence of gas nuclei, bubbles must form *de novo* or from nothing. With no dissolved gas, theory and measurment indicate a *de novo* nucleation threshold of about 1400 ata (141 MPa; Zheng *et al.* 1991). The highest experimentally generated negative pressure was −281 ata (28.5 MPa) at the centre of a spinning Z-shaped tube (Briggs 1950). The highest gas supersaturation thresholds were 122–365 ata (12.4–37.0 MPa) depending on the gas solubility (Gerth & Hemmingsen 1976; Finkelstein & Tamir 1985).

Because of the low supersaturations required to form bubbles in animals, they would appear to originate from gas nuclei rather than from *de novo* nucleation. Bubble formation in shrimp and guinea-pigs occurred at decompressions of 0.7 ata (71 kPa; Daniels 1989). In humans, precordial bubbles were detected by ultrasound at an altitude of 3658 m (12 000 ft; Dixon 1985) and after 3.6 m (12 ft) air saturation dives (Eckenhoff 1992). These represent decompressions of 0.4 ata (40.5 kPa) and gaseous supersaturations of 0.3 ata (30.4 kPa).

Bubbles also form during the decay of ambient radiation which Walder and Evans (1974) proposed as the source of gas nuclei in tissue. These nuclei would be spherical and have limited lifespans, but radiation would form new nuclei as the old ones dissolved.

Where Bubbles Form

There is evidence for gas nuclei in humans at normal atmospheric pressure. Bubbles form in human joints from supersaturation caused by viscous adhesion during movement. Joint cracking is the collapse of bubbles during vaporous cavitation (Roston & Haines 1947; Unsworth *et al.* 1971), whereas gaseous cavitation leaves behind stable bubbles known as *vacuum phenomena*. These are detected by radiograph and CT-scan in the fingers, wrists, elbows, shoulders, spine, sacroiliac joint, ilium, symphis pubis, hips and knees (Vann 1989a). Vacuum phenomena are observed when joints placed in traction fill with gas and water vapour. Figure 14.4 shows a vacuum phenomenon in the hip of a 1-year-old girl (Fuiks & Grayson 1950).

Vacuum phenomena of the spine are found within discs, facet joints, vertebrae and the spinal canal itself. Spinal vacuum phenomena are more common with advancing age (Marr 1953; Gershon-Cohen *et al.* 1954; Ford & Goodman 1966; Gulati & Weinstein 1980) and are diagnostic of degeneration (Knutsson 1942). Vacuum phenomena in the discs, facet joints and vertebrae can migrate into the epidural space of the spinal canal (Gulati & Weinstein 1980; Austin *et al.* 1981). Figure 14.5 is a CT-scan of a 52-year-old man with chronic back pain and gas in the lumbar spinal canal (Austin *et al.* 1981). Persistent gas also has been observed in the cervical canal (Elster & Jensen 1984).

Vacuum phenomena are evidence for gas nuclei in the joints of the limbs and spine, which are principal sites of decompression illness. The re-

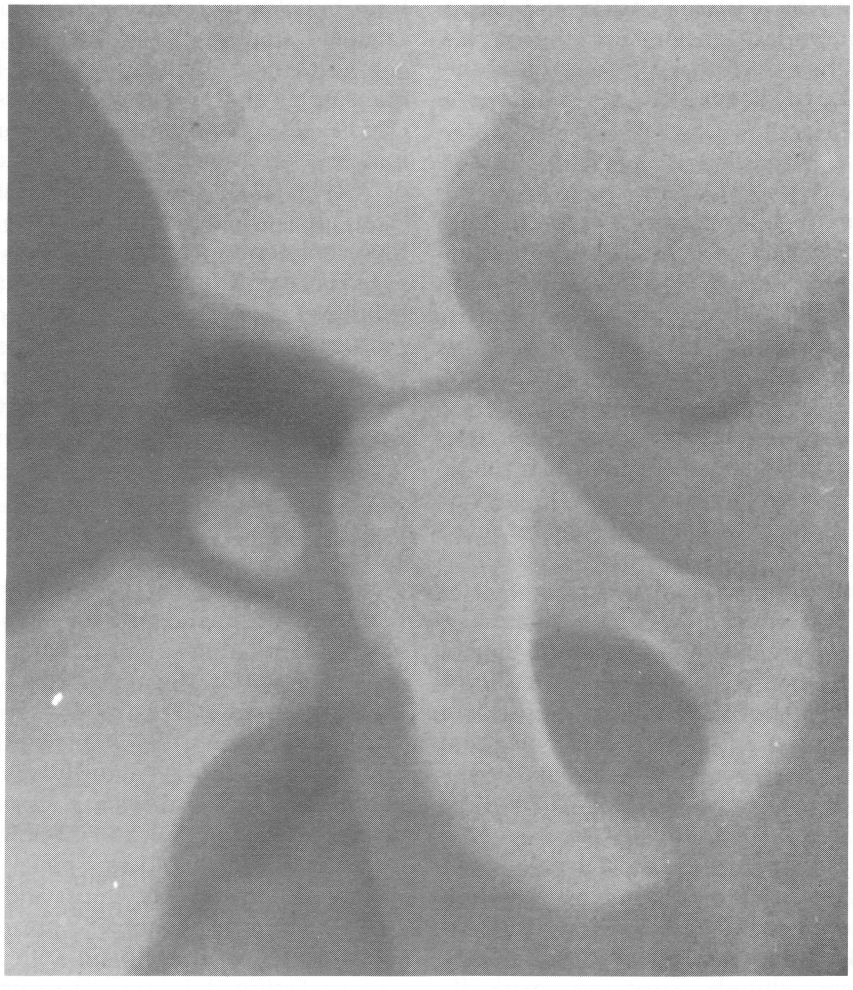

FIG. 14.4. A vacuum phenomenon in the hip joint of a 1-year-old girl. The void expands when the leg is placed in traction. (Reproduced with permission from Fuiks & Grayson 1950)

sponse of vacuum phenomena to decompression is suggested in Fig. 14.6. In Fig. 14.6a, vacuum phenomena were produced by traction of the wrist (Yousefzadeh 1979), while, in Fig. 14.6b, similar voids were found at altitude (Thomas & Williams (1945). The formation and existence of vacuum phenomena demonstrate that gas nuclei are routinely and asymptomatically present in humans at sea level without need for stabilization against surface tension. With decompression, gas nuclei in distensible joint spaces might expand asymptomatically, whereas those in fascial planes (Fig. 14.1) might dissect along the paths of least resistance producing pain and, as noted in cutaneous counterdiffusion (see 'Skin Bends and Counterdiffusion'), perhaps capillary disruption.

Joint movement may increase the formation of gas nuclei by gaseous cavitation due to viscous adhesion. The effects of movement on bubble formation are indicated in animal experiments. Violent activity just before altitude decompression caused increased bubble formation in cats (Harvey *et al.* 1944b; Whitaker *et al.* 1945). Exercise after hydrostatic compression but before altitude decompression increased bubble formation in shrimp (Evans & Walder 1969). Immobilized marine animals could tolerate gaseous supersaturations of up to 51 ata (5.2 MPa) without bubble formation, but 2 ata (202 kPa) could not be tolerated when the animals moved voluntarily or were mechanically stimulated (McDonough & Hemmingsen 1984a,b, 1985a,b).

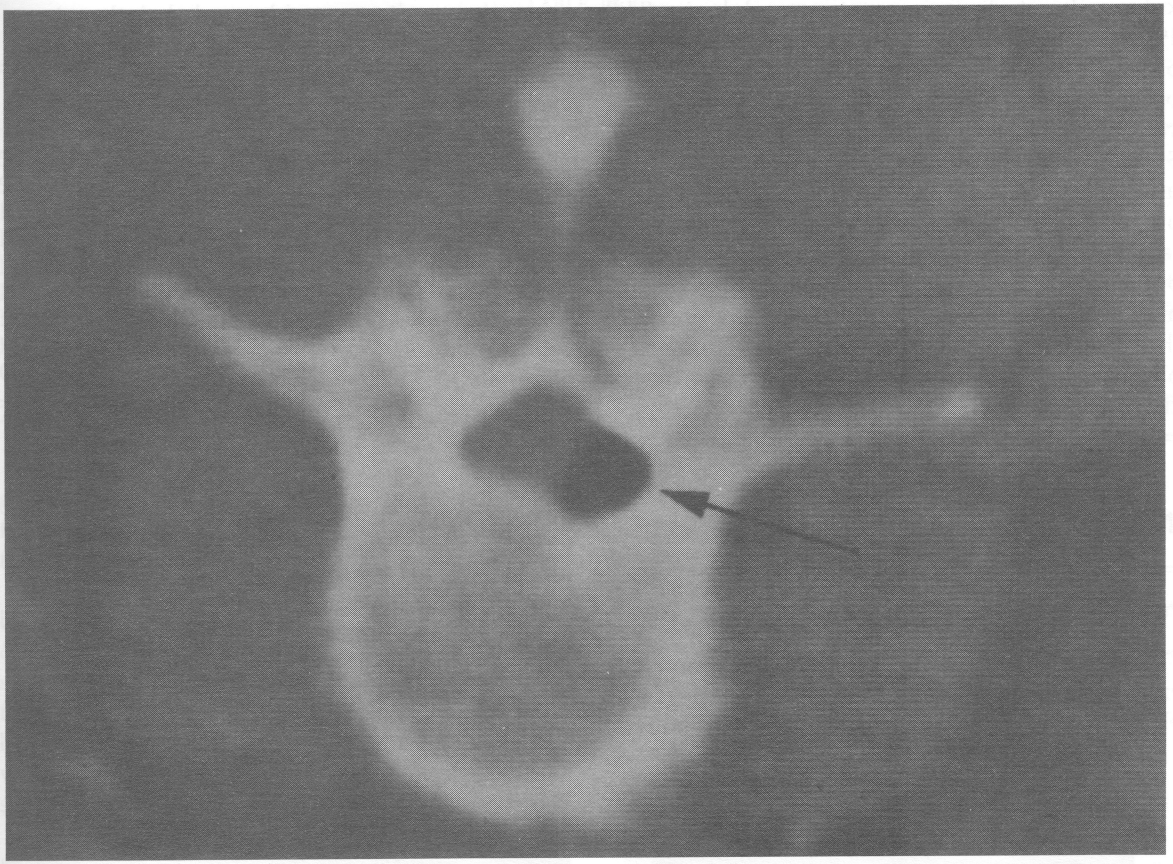

FIG. 14.5. Gas within the spinal canal of the L3 level. (Reproduced with permission from Austin *et al.* 1981)

Equilibrium between the creation and elimination of gas nuclei might be modulated by repeated caisson exposure (adaptation) or by pre-dive exercise. Susceptibility to decompression illness and the extent of symptoms would be determined by the number of available nuclei and their locations. Autochthonous bubbles in the spinal cord (Francis 1990) might form from nuclei created by viscous adhesion during movement.

Bubbles are common in blood after decompression, but do they form there? This question was first addressed by Erasmus Darwin (1774). To avoid contaminating blood with air during handling, Darwin isolated blood-filled sections of vessel between sutures before exposure to vacuum. No bubbles formed in isolated vessels. Other blood samples which were freely exposed in air, however, bubbled vigorously. Similar results were observed for gall and urinary bladders. Darwin's studies have been confirmed with isolated inferior vena cavae and urinary bladders from rats, rabbits and dogs at altitudes of 18 000–22 860 m (60 000–75 000 ft; Okang & Vann 1989). Other studies of bubble formation in blood reached the same conclusion: blood is resistant to bubble formation (Harvey *et al.* 1944a; Ikels 1970).

While bubbles do not form in isolated blood, they might form in living animals due to turbulence or Reynolds' cavitation (Hennessy 1989). However, rats killed before exposure to pressure had vascular bubbles, as did rats exposed alive (Hempleman 1968; Smith-Sivertsen 1976). This indicated a source of bubbles other than turbulence. Vascular bubbles in dead animals were avoided by removing the lungs and immersing the animals in water to prevent the inward diffusion of gas. Thus, the skin and lungs appeared to be the sites of bubble formation in the dead rats. The skin as a source of bubbles is consistent with a cutaneous origin for venous bubbles in counterdiffusion (see 'Skin Bends and Counterdiffusion').

Rapid decompression results in lesions of the

kidney, heart, liver, mesentery and brain (Hill 1912), but bubbles do not appear to form in these organs at normal ascent rates. Using Doppler probes implanted around the arterial and venous vessels of kidney and brain in sheep, Powell and Spencer (1981) did not detect venous bubbles unless arterial bubbles were noted first. Thus, organs not involved in motion or not in direct contact with air did not appear to be primary sites for bubble formation. The principal sites of bubble formation supported by experimental evidence are the skin, the joints and the spinal cord. Bubbles at other sites appear to be transported there by the circulation.

INERT GAS EXCHANGE

Pulmonary Exchange

The effect of pulmonary ventilation on inert gas exchange depends upon the solubility of gas in blood (Eger 1974). Highly soluble anaesthetic gases (e.g. nitrous oxide and halothane) are exchanged slowly at low ventilation rates. Insoluble diving gases (e.g. nitrogen and helium) are exchanged rapidly in normal lungs at all ventilation rates, and equilibration of alveolar–arterial gases is virtually complete. In small quantities, venous gas emboli do not significantly affect pulmonary inert gas exchange, but an excessive quantity of bubbles can block pulmonary capillaries causing regional ventilation–perfusion inequalities (Hlastala *et al.* 1979; Butler *et al.* 1989). This would return inert gas to the tissues and might delay its elimination.

Perfusion

The exchange of dissolved inert gas between arterial blood and tissue begins with the delivery or removal of gas by blood flow. In an *ideal* tissue, inert gas exchange is determined by the blood flow per unit tissue volume (*perfusion*) multiplied by the ratio of the solubilities of gas in blood and tissue (*partition coefficient*). Ideal tissues are described as *perfusion-limited* and are 'well-stirred' with no inert

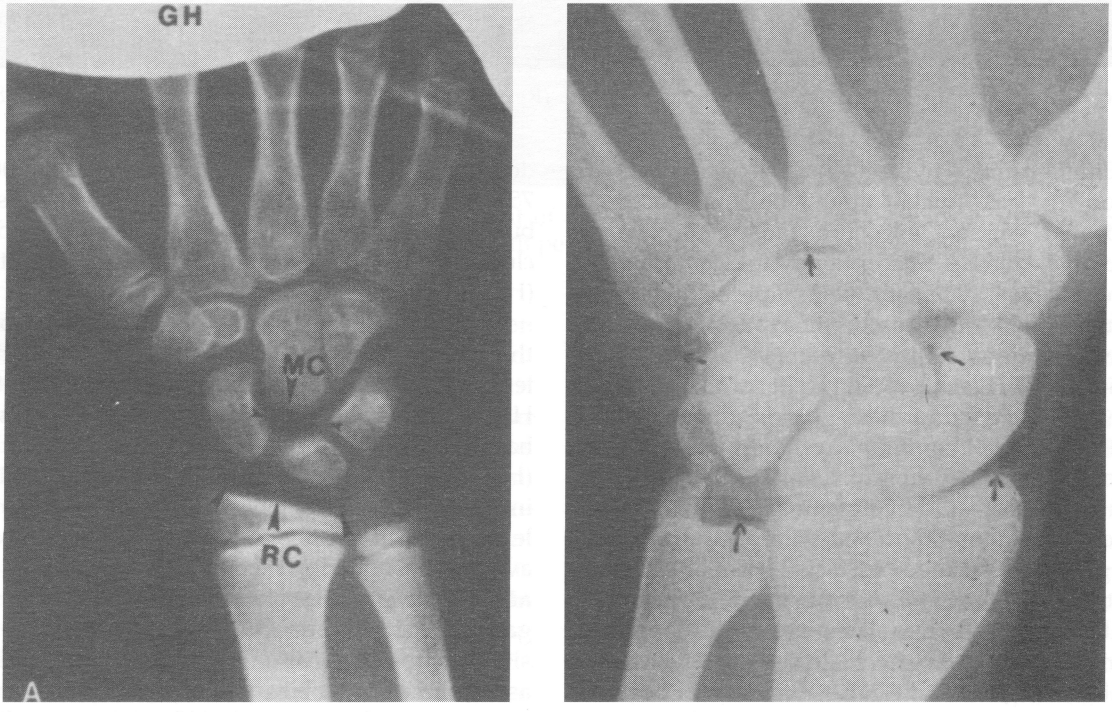

FIG. 14.6. (A) Vacuum phenomena of the wrist produced by traction (reproduced with permission from Yousefzadeh 1979). (B) Gas voids in the wrist produced by altitude decompression. (Reproduced with permission from Thomas and Williams 1945)

TABLE 14.1
Representative inert gas exchange parameters

	Nitrogen	*Helium*
Solubility in water at 37 °C (ml gas/ml water/ata)[a]	0.0145	0.0099
Solubility in oil at 37 °C (ml gas/ml water/ata)[a]	0.076	0.0168
Partition coefficient (sol. water/sol. water)	1.0	1.0
Partition coefficient (sol. water/sol. oil)	0.19	0.59
Diffusivity at 37 °C (cm^2/min)[b]	1.81×10^{-5}	3.78×10^{-3}
Permeability in water (diffusivity × sol. water) (cm^2/ata/min)	2.62×10^{-5}	3.74×10^{-4}
Permeability in oil (diffusivity × sol. oil) (cm^2/ata/min)	1.38×10^{-4}	6.35×10^{-5}
Intercapillary distance[c]	7–200 μm	
Capillary length[c]	180–1000 μm	

[a] Behnke & Yarbrough (1939); [b] Gertz & Loeschcke (1954); [c] Altman & Ditmer (1971) and Renkin *et al.* (1981).

gas concentration gradients. Inert gas elimination from a well-stirred tissue is a mono-exponential function of time.

Experimental measurements of inert gas solubility in blood and tissue are limited (Weathersby & Homer 1980). Available data indicate that gas solubilities in blood and aqueous tissue differ little from those in water over a wide range of solubilities. Thus, all gases in ideal aqueous tissue would be expected to equilibrate at nearly the same rate for a given perfusion.

There are no measured solubilities for lipid tissues (Weathersby & Homer 1980), and common practice has been to assume solubilities measured for oil (Buehlmann 1975). The solubilities of nitrogen and helium in oil and water reported by Behnke and Yarbrough (1939) are listed in Table 14.1 to illustrate the principle, but should not be taken as the actual solubilities in blood and tissue. The blood-to-lipid (water-to-oil) partition coefficient for nitrogen is 0.19, while that for helium is 0.59. Thus, in ideal perfusion-limited lipid tissue (oil), helium would be expected to exchange three times faster than nitrogen. Figure 14.7 shows that the whole-body elimination of helium is faster than of nitrogen, an observation traditionally attributed to a difference in solubility (Behnke & Willmon 1941; Behnke 1942).

Real tissue and whole-body elimination curves are multi-exponential, indicating non-ideal behaviour (Shaw *et al.* 1935; Paradise *et al.* 1971; Sparks & Mohrman 1977; Homer *et al.* 1989). Recognizing that tissues are perfused heterogeneously, Boycott *et al.* (1908) proposed that the body was made up of five ideal parallel tissues ranging from well perfused (5 min half-time) to poorly perfused (75 min

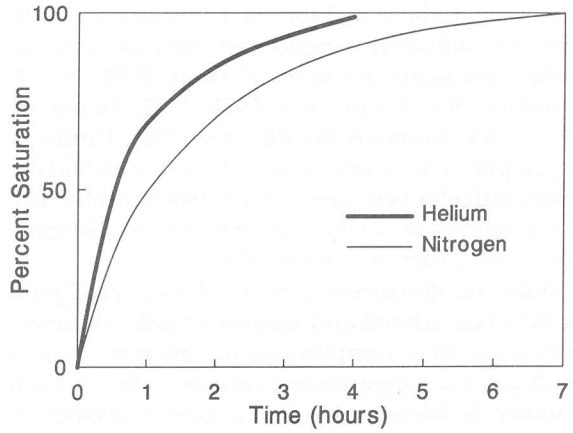

FIG. 14.7. The elimination of helium and nitrogen from resting subjects (Behnke & Willmon 1941; after Behnke 1942)

half-time). This hypothesis of heterogeneous, perfusion-limited tissue was used for many years to analyse and interpret inert gas exchange data (Behnke 1937; Jones 1951), but it is now recognized that diffusion could have effects which might be difficult to distinguish from the effects of perfusion heterogeneity.

Blood–Tissue Diffusion

Diffusion effects could include diffusion between heterogeneous regions of tissue, within capillary domains, or between adjacent arterial and venous vessels. Inert gas tension gradients and diffusion between adjacent regions of tissue may occur in tissues of heterogeneous solubility or perfusion (Perl *et al.* 1960, 1965). Simulations indicate that gradients can develop between 1 cm thick tissue

regions when regional flow differences exceed 3:1 (Homer *et al.* 1989). Diffusion between heterogeneous tissue regions was a possible explanation for the continued absorption of a nitrogen isotope by the human knee after the isotope source had been removed from the inspired gas (Weathersby *et al.* 1986a).

Gas diffuses between blood and tissue within capillary domains. Blood flow in adjacent capillaries may be concurrent (in the same direction) or countercurrent (in opposite directions). Diffusion distances are small in most tissues (Altman & Dittmer 1971; Renkin *et al.* 1981), and diffusivities are reasonably large (Gertz & Loeschcke 1954; Kawashiro *et al.* 1975). For concurrent capillary flow with diffusivities and diffusion distances on the order of those in Table 14.1, calculations indicate that diffusion is rapid and inert gas concentration gradients are minimal (Kety 1951; Perl & Chinard 1968; Levitt 1970, 1971, 1972; Hennessy 1971, 1974; Homer & Weathersby 1986). Diffusion might play a more important role in tissues such as bone, articular cartilage (Anson 1966) and the eye (Kronheim *et al.* 1976), where diffusion distances are on the order of millimetres.

With countercurrent flow in adjacent capillaries or between arterial and venous vessels, diffusion effects are more complex and the interpretation of inert gas exchange measurements is less certain (Homer & Weathersby 1983). Gas molecules in venous vessels can diffuse into adjacent arterial vessels and be retained in tissue (Aukland *et al.* 1967; Sejrsen & Tonnesen 1968; Duling & Berne 1970; Gronlund *et al.* 1989), an effect which is more pronounced for rapidly diffusing gases (Piiper & Meyer 1984; Piiper *et al.* 1984). When inert gas exchange and blood flow distribution to muscle were measured simultaneously, Novotny *et al.* (1990) found that gas exchange was slower than predicted on the basis of the measured flow distribution. The retention of gas in tissue by countercurrent diffusion was a possible explanation for this observation and might be one reason that tissue half-times in decompression models are longer than would be expected on the basis of physiologically reasonable blood flow.

Blood Flow Regulation

Body position, temperature, immersion, oxygen and exercise influence whole-body respiratory nitrogen exchange and can affect the risk of decompression illness. These effects are modulated by blood flow regulation which was reviewed by Pendergast and Olszowka (1989) as applied to decompression. Flow distribution is determined by local peripheral vascular resistance and can change frequently. Vascular resistance is regulated *extrinsically* by the sympathetic nervous system, which maintains *basal* constriction of arterioles, and precapillary sphincters and *intrinsically* by local effects of temperature, systemic hormones and metabolites (e.g. lactate and carbon dioxide). Metabolically active tissues which exert strong intrinsic control can have high and low blood flows in adjacent regions. Increased flow in one organ may be accompanied by decreased flow in another. During exercise, for example, the flows to kidney and liver decrease.

Immersion in cold water and a horizontal body position translocate blood to the chest, which increases central blood volume, cardiac output and peripheral blood flow (Pendergast & Olszowka 1989). Cold water immersion reduces peripheral blood flow, which improves thermal insulation. Exercise and shivering elevate muscle temperature and blood flow. Muscle flow is regulated intrinsically, while flow to skin and subcutaneous fat is regulated both extrinsically and intrinsically. Oxygen is a vasoconstrictor (Plewes & Farhi 1983), and elevated oxygen partial pressures decrease nitrogen elimination (Anderson *et al.* 1991).

Respiratory nitrogen elimination during oxygen breathing was increased by changing the body position from vertical to horizontal (Balldin 1973a), by immersion in warm water (Balldin & Lundgren 1972) and by light exercise (Vann *et al.* 1992). Warm water immersion (Balldin 1973b) and exercise (Vann *et al.* 1992) also provided significant protection from decompression illness during subsequent altitude exposures.

Exercise at depth during diving appeared to increase nitrogen uptake. Nitrogen elimination measured at sea level after exercising no-stop air dives was greater than after resting dives (Dick *et al.* 1984). Figure 14.8 shows that divers exercising during 25 min exposures at 30 m (100 ft) eliminated 20–60% more nitrogen after 1 h at sea level than did resting divers.

Greater nitrogen uptake due to immersion was suggested by a higher incidence of decompression illness after no-stop air dives for subjects exercising in cold water than for subjects exercising in a dry chamber (Fig. 14.20; Thalmann *et al.* 1989).

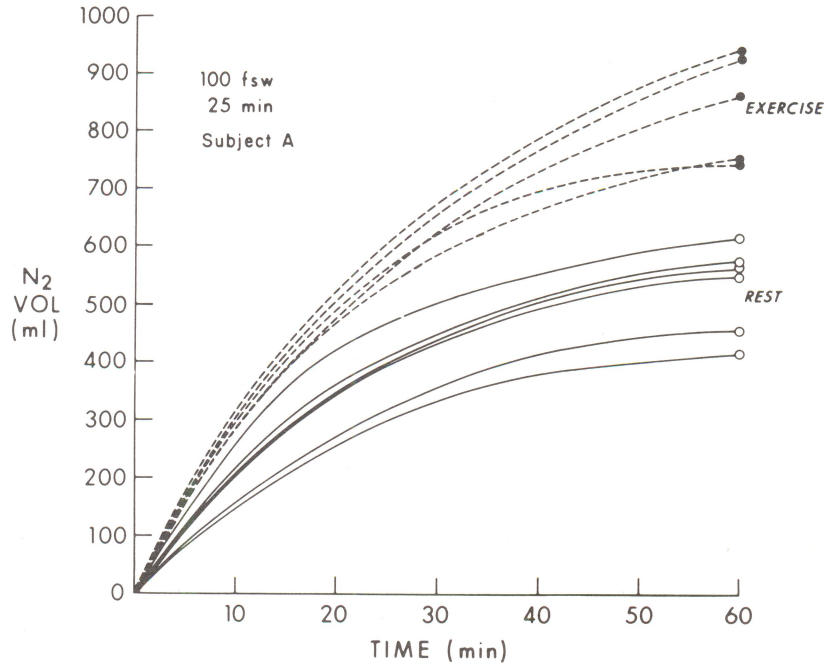

FIG. 14.8. Respiratory nitrogen elimination measured during rest at sea level after resting and exercising dives to 30 m (100 ft) for 25 min. (Reproduced with permission from Dick *et al.* 1984)

No difference in incidence was noted, however, between dry and wet exposures during decompression dives (Thalmann 1985; Weathersby *et al.* 1990). For decompression diving, increased gas elimination during decompression may cancel increased uptake at depth with no net effect on the risk of decompression illness.

The total volume of nitrogen eliminated through the lungs does not appear to be correlated with pain-only decompression illness, as indicated in Fig. 14.9 (Vann & Gerth, in press). Nitrogen elimination was measured during 180 min of oxygen breathing before altitude exposure. The *x*-axis represents nitrogen elimination over the entire 180 min period and during 30 min intervals. The *y* axis is the ratio of nitrogen eliminated by subjects who did not develop decompression illness to those who did. Over the entire period (labelled 0–180), the subjects without decompression illness eliminated only slightly more nitrogen than subjects with decompression illness. When the nitrogen elimination ratio was examined, in 30 min intervals, this was also true for the first 2 h, but subjects free from decompression illness were found to eliminate 70% more nitrogen in the third hour.

The absolute volume of nitrogen eliminated in the third hour was small. Thus, the tissues responsible for mild decompression symptoms at altitude would appear to exchange nitrogen slowly and to have a low nitrogen storage capacity. The large increase in nitrogen uptake produced by exercise at depth (Fig. 14.8) probably reflected rapid uptake by muscle with which mild decompression symptoms are not normally associated. Large capacity tissues may contribute their nitrogen to venous gas emboli.

Oxygen Window

Haldane (1922) pointed out that a bubble in the body is absorbed because its nitrogen partial pressure is greater than the nitrogen tension in the arterial blood. This difference is the driving force for the elimination of bubbles and has been called the *partial pressure vacancy* (Momsen 1942), the *inherent unsaturation* (Hills 1966) and the *oxygen window* (Behnke 1967, 1975). The oxygen window is a direct consequence of the metabolic conversion of oxygen into carbon dioxide.

Metabolism converts a relatively insoluble gas, oxygen, into carbon dioxide, which is some 21 times more soluble. Figure 14.10 shows the effect on dissolved gas tension of exchanging oxygen for