

**DIVING MALADIES, DRUGS, BUBBLE TROUBLE, AND OXYGEN DOSE**  
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**INTRODUCTION**

**Overview**

Diving has its own brand of medical complications, linked to ambient pressure changes. For brief consideration, a few of the common medical problems associated with compression-decompression and diving follow. The bubble problem has been long discussed, but we can start off by summarizing a few consensus opinions concerning decompression sickness. A cursory discussion of some drugs follows, and a discussion of bubble trouble and oxygen dose.

**Clinical Observations**

But to start off, a few clinical observations are listed, not to scare the reader, but rather to point out that diving, like all other environmentally changing activities, has its own set of risk factors. Risk, obviously here, relates to pressure changes and exposure times:

1. in 1976, Palmer and Blakemore reported that 81% of goats with CNS bends and 33% with limb bends exhibited permanent spinal cord damage on autopsy;
2. in 1978, the same investigators reported that clinically bent, but cured, goats, also exhibited brain damage on autopsy;
3. in 1979, a Workshop in Luxemborg reported that even asymptomatic dives may cause permanent brain and spinal impairment;
4. in 1982, Idicula reported CT scans of the brains of veteran divers showed characteristics similar to punch drunk divers;
5. in 1984, Edmonds conducted psycholological and psychometric studies on abalone divers in Australia and reported strong evidence for dementia;
6. in 1985, Hoiberg reported the USN divers who once suffered the bends had a higher rate of headaches, vascular diseases, and hospitalizations than a matched sample who had never been bent;
7. in 1986, Morris reported that English divers with more than 8 years experience has significantly poorer short term memory;
8. in the 1980s and 1990s, Workshops repeatedly voiced concern about the long term effects of transient hematological changes in divers, such as sedimentation, red cell configuration, alteration of lipoprotein, platelet reduction, and vascular stress;
9. in 1984, Brubakk noted ultrasonically detected bubbles (VGE) in animals for as long as a month after hyperbaric exposure;
10. now, Calder examines the spinal cord of every diver in the United Kingdom who dies of any cause;
11. in 1985, Dick reported that mild (self) neurological complaints are common after diving and go untreated, and that many serious cases never violated the USN Tables.

Of course, it comes as no surprise that the medical community continues to push for shorter and shallower exposures, ultra conservatism in tables and meters, and all other risk ameliorating avenues. Enough said here, the above list points out some concerns for all of us. Conservative approaches, coupled to the most modern and correct biophysical models, are the best means to staging diver ascents in any circumstance. Period.

## Bends

Clinical manifestations of decompression sickness, or decompression illness (DCI), can be categorized as pulmonary, neurological, joint, and skin DCI, as summarized by Vann. All are linked to bubbles upon pressure reduction, with embolism also included in the categorization. Pulmonary DCI manifests itself as a sore throat with paroxysmal cough upon deep inspiration, followed by severe chest pain, and difficult respiration, a condition collectively called the *chokes*. Chokes is seen often in severe high altitude exposures. Neurological DCI affects the heart, brain, and spinal cord, through arterial gas emboli, venous gas emboli, shunted venous gas emboli (VGE that pass through the pulmonary circulation and enter the arterial circulation), and stationary, extravascular (*autochthonous*) bubbles. Joint DCI is a common form of mild bends, affecting the nervous (*neurogenic*), bone marrow (*medullar*), and joint (*articular*) assemblies. Neurogenic pain is localized at remote limb sites, usually without apparent cerebral or spinal involvement. Bubbles in the bone have been proposed as the cause of both dull aching pain and bone death. Expanding extravascular bubbles have been implicated in the mechanical distortion of sensory nerve endings. Skin DCI manifests itself as itching, rash, and a sense of localized heat. Skin DCI is not considered serious enough for hyperbaric treatment, but local pain can persist for a few days. Blotchy purple patching of the skin has been noted to precede serious DCI, especially the chokes.

Most believe that bends symptoms follow formation of bubbles, or the gas phase, after decompression. Yet, the biophysical evolution of the gas phase is incompletely understood. Doppler bubble and other detection technologies suggest that:

1. moving and stationary bubbles do occur following decompression;
2. the risk of decompression sickness increases with the magnitude of detected bubbles and emboli;
3. symptomless, or *silent*, bubbles are also common following decompression;
4. the variability in gas phase formation is likely less than the variability in symptom generation.

Gas phase formation is the single most important element in understanding decompression sickness, and is also a crucial element in preventative analysis.

Treatment of decompression sickness is an involved process, requiring a recompression chamber and various hyperbaric treatment schedules depending on the severity of the symptoms, location, and initiating circumstance. Recompression is usually performed in a double lock hyperbaric chamber, with the patient taken to a series of levels to mitigate pain, first, and then possibly as deep as 165 *fsw* for treatment. Depending on the depth of the treatment schedule, oxygen may, or may not, be administered to washout inert gas and facilitate breathing. Treatment of air embolism follows similar schedules.

## High Pressure Nervous Syndrome

Hydrostatic pressure changes, particularly in the several hundred *atm* range, are capable of affecting, though usually reversibly, central nervous system activity. Rapidly compressed divers, say 120 *fsw/min* to 600 *fsw*, breathing helium, experience coarse tremors and other neurological disorders termed *high pressure nervous syndrome* (HPNS). At greater depths, near 800 *fsw*, cramps, dizziness, nausea, and vomiting often accompany the tremor. Although HPNS can be avoided by slowing the compression rate, the rate needs to be substantially reduced for compressions below 1,100 *fsw*.

While the underlying mechanisms of HPNS are not well understood, like so many other pressure related afflictions, the use of pharmacological agents, some nitrogen in the breathing mixture, staged compressions, alcohol, and warming have been useful in ameliorating HPNS in operational deep diving.

Gas induced osmosis has been implicated as partially causative in high pressure nervous syndrome. Water, the major constituent of the body, shifting between different tissue compartments, can cause a number of disorders. Mechanical disruption, plasma loss, hemoconcentration, and bubbles are some. Under rapid pressure changes, gas concentrations across blood and tissue interfaces may not have sufficient time to equilibrate, inducing balancing, but counter, fluid pressure gradients (osmotic gradients). The strength of the osmotic gradient is proportional to the absolute pressure change, temperature, and gas solubility.

## Inert Gas Narcosis

It is well known that men and animals exposed to hyperbaric environments exhibit symptoms of intoxication, simply called *narcosis*. The narcosis was first noticed in subjects breathing compressed air as early as 1835. The effect,

however, is not isolated to air mixtures (nitrogen and oxygen). Both helium and hydrogen, as well as the noble (rare) gases such as xenon, krypton, argon, and neon, cause the same signs and symptoms, though varying in their potency and threshold hyperbaric pressures. The signs and symptoms of inert gas narcosis have manifest similarity with alcohol, hypoxia (low oxygen tension), and anesthesia. Exposure to depths greater than 300 *fsw* may result in loss of consciousness, and at sufficiently great pressure, air has been used as an anesthetic. Individual susceptibility to narcosis varies widely from individual to individual. Other factors besides pressure potentiate symptoms, such as alcohol, work level, apprehension, and carbon dioxide levels. Frequent exposure to depth with a breathing mixture, as with DCS, affords some level of adaptation.

Many factors are thought contributory to narcosis. Combinations of elevated pressure, high oxygen tensions, high inert gas tensions, carbon dioxide retention, anesthetically blocked ion exchange at the cellular interface, reduced alveolar function, and reduced hemoglobin capacity have all been indicted as culprits. But, still today, the actual mechanism and underlying sequence is unknown.

The anesthetic aspects of narcosis are unquestioned in most medical circles. Anesthesia can be induced by a wide variety of chemically passive substances, ranging from inert gases to chloroform and ether. These substances depress central nervous system activity in a manner altogether different from centrally active drugs. Anesthetics have no real chemical structure associated with their potency, and act on all neural pathways, like a bulk phase. Physicochemical theories of anesthetics divide in two. One hypothesis envisions anesthetics interacting with hydrophobic surfaces and interfaces of lipid tissue. The other postulates anesthetic action in the aqueous phases of the central nervous system. The potency and latency of both relate to the stability of gas hydrates composing most anesthetics. The biochemistry of anesthetics and narcosis in divers has not, obviously, been unraveled.

### **Hyperoxia And Hypoxia**

Elevated oxygen tensions (*hyperoxia*), similar to elevated inert gas tensions, can have a deleterious effect on divers, aviators, and those undergoing hyperbaric oxygen treatment. The condition is known as oxygen toxicity, and was first observed, in two forms, in the final quarter of the 1800s. Low pressure oxygen toxicity (Lorraine Smith effect) occurs when roughly a 50% oxygen mixture is breathed for many hours near 1 *atm*, producing lung irritation and inflammation. At higher partial pressures, convulsions develop in high pressure oxygen toxicity (Bert effect), with latency time inversely proportional to pressure above 1 *atm*. Factors contributing to the onset of symptoms are degree of exertion, amount of carbon dioxide retained and inspired, and individual susceptibility. Early symptoms of oxygen poisoning include muscular twitching (face and lips), nausea, tunnel vision, difficulty hearing and ringing, difficulty breathing and taking deep breaths, confusion, fatigue, and coordination problems. Convulsions are the most serious manifestation of oxygen poisoning, followed ultimately by unconsciousness. Oxygen toxicity is not a problem whenever the oxygen partial pressures drop below .5 *atm*.

Oxygen toxicity portends another very complex biochemical condition. Elevated oxygen levels interfere with the enzyme chemistry linked to cell metabolism, especially in the central nervous system. Reduced metabolic and electrolytic transport across neuronal membranes has been implicated as a causative mechanism. The role of carbon dioxide, while contributory to the chain of reactions according to measurements, is not understood, just as with inert gas narcosis. On the other hand, it has been noted that only small increases in brain carbon dioxide correlate with severe symptoms of oxygen toxicity. Carbon dioxide seems to play an important, though subtle, part in almost all compression-decompression afflictions.

Breathing air at atmospheric pressure after the onset of oxygen toxicity symptoms can restore balance, depending on severity of symptoms. Deep breathing and hyperventilation can also forestall convulsions if initiated at the earliest sign of symptoms.

When the tissues fail to receive enough oxygen, a tissue debt (*hypoxia*) develops, with varying impact and latency time on body tissue types. Hypoxia can result with any interruption of oxygen transport to the tissues. Although the nervous system itself represents less than 3% of body weight, it consumes some 20% of the oxygen inspired. When oxygen supply is cut, consciousness can be lost in 30 *seconds* or less, respiratory failure follows in about a *minute*, and irreparable damage to the brain and higher centers usually occurs in about 4 *minutes*. Obviously, the brain is impacted the most. The victim of hypoxia may be unaware of the problem, while euphoria, drowsiness, weakness, and unconsciousness progress. Blueness of the lips and skin results, as blood is unable to absorb enough oxygen to maintain its red color. When oxygen partial pressures drop below 0.10 *atm*, unconsciousness is extremely rapid.

Hypoxia is a severe, life threatening condition. However, if fresh air is breathed, recovery is equally as rapid, providing breathing has not stopped. If breathing has stopped, but cardiac function continues, artificial respiration can

stimulate the breathing control centers to functionality. Cardiopulmonary resuscitation can be equally successful when both breathing and heart action have ceased.

### **Hypercapnia And Hypocapnia**

Tissue carbon dioxide excess (*hypercapnia*) can result from inadequate ventilation, excess in the breathing mixtures, or altered diver metabolic function. All tissues are affected by high levels of carbon dioxide, but the brain, again, is the most susceptible. The air we breathed contains only some 0.03% carbon dioxide. As partial pressures of carbon dioxide approach 0.10 *atm*, symptoms of hypercapnia become severe, starting with confusion and drowsiness, followed by muscle spasms, rigidity, and unconsciousness. Carbon dioxide at 0.02 *atm* pressure will increase breathing rate, and carbon dioxide at 0.05 *atm* pressure induces an uncomfortable sensation of shortness of breath. Factors which increase the likelihood and severity of hypercapnia include corresponding high partial pressure of oxygen, high gas densities, breathing dead spaces, and high breathing resistance.

Any process which lowers carbon dioxide levels in the body below normal (*hypocapnia*), can produce weakness, faintness, headache, blurring of vision, and, in the extreme case, unconsciousness. Hypocapnia often results from hyperventilation. The respiratory system monitors both carbon dioxide and oxygen levels to stimulate breathing. Rising carbon dioxide tensions and falling oxygen tensions trigger the breathing response mechanism. Hyperventilation (rapid and deep breathing) lowers the carbon dioxide levels, leading to hypocapnia.

Extended breathholding after hyperventilation can lead to a condition known as shallow water blackout. Following hyperventilation and during a longer breathholding dive, oxygen tensions can fall to a very low level before a diver returns to the surface and resumes breathing. Oxygen levels are lowered because exertion causes oxygen to be used up faster, but also the sensitivity to carbon dioxide drops as oxygen tension drops, permitting oxygen levels to drop even further. Upon ascension, the drop in the partial pressure of oxygen in the lungs may be sufficient to stop the uptake of oxygen completely, and, with the commensurate drop in carbon dioxide tension, the urge to breathe may also be suppressed.

While the short term effects of both hypercapnia and hypocapnia can be disastrous in the water, drowning if consciousness is lost, the long term effects following revival are inconsequential. Treatment in both cases is breathing standard air normally. Residual effects are minor, such as headache, dizziness, nausea, and sore chest muscles.

Carbon dioxide seems to be a factor in nearly every other compression-decompression malady, including decompression sickness, narcosis, hyperoxia, and hypoxia. It is a direct product of metabolic processes, with about 1 l of carbon dioxide produced for every 1 l of oxygen consumed. Carbon dioxide affects the metabolic rate, and many other associated biochemical reactions. The physical chemistry of carbon dioxide uptake and elimination is much more complex than that of inert gases, such as nitrogen and helium. Transfer of inert gases follows simple laws of solubility (Henry's law) in relation to partial pressures. Carbon dioxide transport depends on three factors, namely, gas solubility, chemical combination with alkaline buffers, and diffusion between the cellular and plasma systems. Only relatively small changes in partial pressures of carbon dioxide can induce chain reactions in the three mechanisms, and larger scale biological impact on gas exchange and related chemistry.

### **Barotrauma**

With pressure decrease, air contained in body cavities expands. Usually, this expanding air vents freely and naturally, and there are no problems. If obstructions to air passage exist, or the expanding air is retained, overexpansion problems, collectively called barotrauma, can occur. One very serious overexpansion problem occurs in the lungs. The lungs can accommodate overexpansion to just a certain point, after which continued overpressurization produces progressive distention and then rupture of the alveoli (air exchange sacs). Problems with lung overexpansion can occur with pressure differentials as small as 5 *fsw*. This distention can be exacerbated by breathholding on ascent or inadequate ventilation, and partial obstruction of the bronchial passageways.

The most serious affliction of pulmonary overpressure is the dispersion of air from the alveoli into the pulmonary venous circulation (arterial embolism), thence, into the heart, systemic circulation, and possibly lodging in the coronary and cerebral arterioles. Continuing to expand with further decrease in pressure, these emboli (bubbles) can block blood flow to vital areas. Clinical features of arterial gas embolism develop rapidly, including dizziness, headache, and anxiety first, followed by unconsciousness, cyanosis, shock, and convulsions. Death can result from coronary or cerebral occlusion, inducing cardiac arrhythmia, shock, and circulatory and respiratory failure. The only treatment for air embolism is recompression in a hyperbaric chamber, with the intent of shrinking emboli in size, and driving the air out of the emboli into solution.

Gas from ruptured alveoli may pass into the membrane lining the chest, the parietal pleura, and also rupture the

lining (*pneumothorax*). Trapped in the intrapleural lining, the gas may further expand on ascent, and push against the heart, lungs, and other organs. Often the lungs collapse under the pressure. Symptoms of pneumothorax include sudden chest pain, breathing difficulty, and coughing of frothy blood. Recompression is the indicated treatment for a concomitant condition, along with thoracentesis.

Gas trapped in the tissues about the heart and blood vessels, and the trachea (*mediastinal emphysema*), can adversely impact the circulation, particularly, the venous flow. Symptoms include pain in the sternum, shortness of breath, and sometimes fainting. The condition is exacerbated on ascent as gas trapped in tissues expands. In severe cases, hyperbaric treatment is utilized.

If the bubbles migrate to the tissues beneath the skin (*subcutaneous emphysema*), often a case accompanying mediastinal emphysema, their presence causes a swelling of neck tissue and enhanced local pressure. Feeling of fullness, and change of voice are associated with subcutaneous emphysema. Treatment consists of oxygen breathing, which accelerates tissue absorption of the air trapped in the neck region.

Pressure increases and decreases can be tolerated by the body when they are distributed uniformly, that is, no local pressure differentials exist. When pressure differentials exist, outside pressure greater than inside pressure locally, and vice versa, distortion of the shape of the local site supporting the pressure difference is the outcome. Burst alveoli are one serious manifestation of the problem. Other areas may suffer similar damage, for instance, the ears, sinuses, teeth, confined skin under a wetsuit, and the intestines. Though such complications can be very painful, they are usually not life threatening. When local pressure differentials develop because of inside and outside pressure imbalances, blood vessels will rupture in attempt to equalize pressure. The amount of rupture and degree of bleeding is directly proportional to the pressure imbalance.

Pressures in ear spaces in the sinuses, middle ear, and teeth fillings are often imbalanced during compression-decompression. To accommodate equalization when diving, air must have free access into and out of these spaces during descent and ascent. Failure to accommodate equalization on descent is termed a squeeze, with outside pressure greater than inside (air space) pressure, while failure to accommodate equalization on ascent is called a reverse block, with inside pressure (air space) greater than ambient pressure. In the case of the ear, it is the eustachian tube which does not permit air passage from the throat to the middle ear. The sinuses have very small openings which close under congestive circumstance, inhibiting air exchange. Similarly, small openings in and around teeth fillings complicate equalization of the air space under the filling (usually a bad filling). In all cases, slow descents and ascents are beneficial in ameliorating squeeze and reverse block problems.

### **Altitude Sickness**

At altitudes greater than some 7,000 *ft*, decreased partial pressures of oxygen can cause arterial hypoxemia. Under hypoxic stimulation (low oxygen tension), hyperventilation occurs with secondary lowering of arterial carbon dioxide and production of alkalosis. Newcomers to high altitude typically experience dyspnea (shortness of breath), rapid heart rate, headache, insomnia, and malaise. Symptoms disappear within a week, and general graded exercise may hasten acclimatization.

Acclimatization is usually lost within a week at lower altitudes. Although increased oxygen at depth may be beneficial, the surface malaise often precludes diving until acclimatization. In itself, altitude sickness is not life threatening.

### **Pulmonary Edema**

Pulmonary edema (fluid buildup in the lungs) can affect nonacclimatized individuals who travel within a day or two to elevations near, or above, 10,000 *ft*. Symptoms usually appear within 18 *hrs* after arrival, consisting of rasping cough, dyspnea, and possible pain in the chest. Treatment requires immediate removal to lower altitude, hospitalization with rest, oxygen, and diuretic therapy. Prevention includes adequate acclimatization and reduced levels of exertion. A month of graded exercise may be requisite. Again, increased oxygen partial pressures at depth are helpful, but diving rigors can precipitate pulmonary edema. Symptoms might resemble the chokes (decompression sickness).

Pulmonary edema can be a serious, even fatal, affliction, as noted by its yearly toll on mountain climbers. At altitude, evidence of cough, shortness of breath, or tightness serves as a warning. Rapid treatment, including lower altitude, hospitalization, and appropriate therapy, is recommended.

### **Hypothermia And Hyperthermia**

Exposure to cold results in heat loss, called *hypothermia*, with the rate dependent upon body area, temperature difference, body fat, insulation properties of wet or dry suit, and physical activity. Exercise always increases heat loss. As core temperatures drop, symptoms progress from shivering, to weakness, to muscle rigidity, to coma, and then death.

Rewarming at the earliest signs of hypothermia is prudent. While more of a cold water problem, hypothermia can also occur in relatively warm and even tropical waters. Severe hypothermia is a life threatening condition.

Shivering and a feeling of being very cold are first symptoms of hypothermia, and the situation gets worse fast. Rewarming in dry clothing is standard and obvious treatment, as well as ingestion of balanced electrolytes. Exercise, caffeine, and alcohol are to be avoided. Care in the choice of protective suit to conserve body heat, attention to feelings of cold, and good physical condition help to minimize hypothermia.

Inadequate ventilation and body heat loss, called *hyperthermia*, usually in the presence of high environmental temperatures and low body fluid levels, lead to a progressive raising of temperatures in vital organs. As temperatures rise, symptoms progress from profuse sweating, to cramps, to heat exhaustion, to heat stroke, to coma, and then death. Dehydration is a contributing factor. Replacement of body fluids and reduction of body temperature are necessary in effective treatment of hyperthermia. Cool water immersion is employed in severe cases, but the usual treatment consists of fluids, salt, and full body ventilation. Like hypothermia, severe hyperthermia is life threatening.

Hyperthermia can be avoided by proper attention to water intake and protection from environmental heat. Environmental temperatures above body temperature are potentially hazardous, especially with increasing levels of physical exertion.

### **Dysbaric Osteonecrosis**

Bone rot (*dysbaric osteonecrosis*) is an insidious disease of the long bones associated with repeated high pressure and saturation exposures. Deep and saturation diving portend problems with temperature control in environmental suits, habitats, respiration and surface monitoring, compression and decompression, inert gas reactivity, communication, oxygen levels, and many others, all falling into an operational control category, that is, problems which can be ameliorated through suitable application of sets of established diving protocols. But aseptic bone necrosis is a chronic complication about which we know little.

Affecting the long bones as secondary arthritis or collapsed surface joints, lesions, detected as altered bone density upon radiography, are the suspected cause. Statistics compiled in the early 1980s by the US Navy, Royal Navy, Medical Research Council, and commercial diving industry suggest that some 8% of all divers exposed to pressures in the 300 *fsw* range exhibited bone damage, some 357 out of 4,463 examined divers. No lesions were seen in divers whose exposures were limited to 100 *fsw*. Some feel that very high partial pressures of oxygen for prolonged periods is the ultimate culprit for bone lesions, leading to fat cell enlargement in more closed regions of the bone core, a condition that reduces blood flow rate and probably increases local vulnerability to bubble growth. The facts, however, are still not clear. And commercial divers continue to be at higher risk of osteonecrosis.

## **DRUGS**

### **Pharmaceuticals**

Very few studies have systematized the overall effects of drugs underwater. Drug utilization by divers is connected with medication used to ameliorate diving problems, medication used to treat illness, and recreational drugs. Recent studies suggest that drug effects are compounded at increasing depth, having been described as potentiating, antagonizing, and unpredictable as far as altered behavior with increasing pressure. Side effects can be subtle and also variable, possibly exacerbated by other risk factors such as cold water, oxygen, or nitrogen concentrations. Many different types of drugs are utilized.

1. Among the more common drugs used by divers are decongestants, taken for ear and sinus relief. These drug products are typically antihistamines, providing relief by constricting blood vessels, reducing tissue swelling, and opening passages between sinuses and middle ear for air exchange. Antihistamines often produce drowsiness and decreased mental acuity. Another decongestant, with trade name terfenadine, has no sedative effects. Drugs addressing motion sickness may lead to functional motor impairment. Antihistamines, particularly *meclizine* and *dimenhydratate* are often employed for motion sickness, additionally causing sedation. The skin patch drug, *scopolamine*, also possesses sedative properties, with some additional side effects of blurred vision and dry mouth. Individual reactions vary widely.
2. Sedative and pain agents also alter mental function. Anti-anxiety drugs, such as *valium*, *halcion*, and *dalmane*, are strong agents, producing significant changes in mental outlook. Muscle relaxants, such as *flexiril* and *robaxin*, induce drowsiness. Analgesics containing *propoxyphene*, *codein*, *oxycodone*, or *hydrocodone* reduce mental

and physical exercise capacity. Agents used in the treatment of depression or psychosis cause sedation, and have been noted to induce cardiac dysfunction. Tradename drugs in this category, *elavil*, *haldol*, and *sinequan*, impair cognitive abilities.

3. Hypertension drugs can limit diving performance. Diuretics, like *lasix* and *hydrochlorothiazide*, cause fluid loss, possibly compounding dehydration and electrolytic imbalance. Agents affecting heart rate and peripheral vasculature may cause drowsiness and reduce blood flow capacity. These drugs include *metoprolol*, *hytrin*, *tenex*, and others. Bronchodilators, used in the treatment of asthma, include *theophylline* and *steroids*. In the former category, tradename drugs, such as *theodur*, *uniphyl*, *metaprel*, and *ventolin* can cause cardiac dysrhythmias and CNS impairment. Gastrointestinal drugs containing histamines can also affect the central nervous system, causing drowsiness and headache. Antacids seem to have no noted adverse effects on divers.

According to the diving medical community at large, the bottom line on drugs underwater is caution, since little is known about many, particularly newer ones. Narcotics and hallucinogens, alcohol, and heavy doses of caffeine have been linked to reduced mental and physical acuity, sedation, vasodilatation, diuresis, and dehydration on the mild side, and extreme neurological, respiratory, and cardiovascular stress on the more severe side.

## BUBBLE TROUBLE

### Empirical Practices

Utilitarian procedures, entirely consistent with phase mechanics and bubble dissolution time scales, have been developed under duress, and with trauma, by Australian pearl divers and Hawaiian diving fishermen, for both deep and repetitive diving with possible in-water recompression for hits. While the science behind such procedures was not initially clear, the operational effectiveness was always noteworthy and could not be discounted easily. Later, the rationale, essentially recounted in the foregoing, became clearer.

Pearling fleets, operating in the deep tidal waters off northern Australia, employed Okinawan divers who regularly journeyed to depths of 300 *fsw* for as long as one hour, two times a day, six days per week, and ten months out of the year. Driven by economics, and not science, these divers developed optimized decompression schedules empirically. As reported by Le Messurier and Hills, deeper decompression stops, but shorter decompression times than required by Haldane theory, were characteristics of their profiles. Such protocols are entirely consistent with minimizing bubble growth and the excitation of nuclei through the application of increased pressure, as are shallow safety stops and slow ascent rates. With higher incidence of surface decompression sickness, as might be expected, the Australians devised a simple, but very effective, in-water recompression procedure. The stricken diver is taken back down to 30 *fsw* on oxygen for roughly 30 *minutes* in mild cases, or 60 *minutes* in severe cases. Increased pressures help to constrict bubbles, while breathing pure oxygen maximizes inert gas washout (elimination). Recompression time scales are consistent with bubble dissolution experiments.

Similar schedules and procedures have evolved in Hawaii, among diving fishermen, according to Farm and Hayashi. Harvesting the oceans for food and profit, Hawaiian divers make between 8 and 12 dives a day to depths beyond 350 *fsw*. Profit incentives induce divers to take risks relative to bottom time in conventional tables. Three repetitive dives are usually necessary to net a school of fish. Consistent with bubble and nucleation theory, these divers make their deep dive first, followed by shallower excursions. A typical series might start with a dive to 220 *fsw*, followed by 2 dives to 120 *fsw*, and culminate in 3 or 4 more excursions to less than 60 *fsw*. Often, little or no surface intervals are clocked between dives. Such types of profiles literally clobber conventional tables, but, with proper reckoning of bubble and phase mechanics, acquire some credibility. With ascending profiles and suitable application of pressure, gas seed excitation and any bubble growth are constrained within the body's capacity to eliminate free and dissolved gas phases. In a broad sense, the final shallow dives have been tagged as prolonged safety stops, and the effectiveness of these procedures has been substantiated *in vivo* (dogs) by Kunkle and Beckman. In-water recompression procedures, similar to the Australian regimens, complement Hawaiian diving practices for all the same reasons.

While the above practices developed by trial-and-error, albeit with seeming principle, venous gas emboli measurements, performed off Catalina by Pilmanis on divers making shallow safety stops, fall into the more *scientific* category perhaps. Contrasting bubble counts following bounce exposures near 100 *fsw*, with and without zonal stops in the 10-20 *fsw* range, marked reductions (factors of 4 to 5) in venous gas emboli were noted when stops were made. If, as some suggest, venous gas emboli in bounce diving correlate with bubbles in sites such as tendons and ligaments, then

safety stops probably minimize bubble growth in such extravascular locations. In these tests, the sample population was small, so additional validation and testing is warranted.

### **Bubble Issues**

Recent years have witnessed many changes and modifications to diving protocols and table procedures, such as shorter nonstop time limits, slower ascent rates, discretionary safety stops, ascending repetitive profiles, multilevel techniques, both faster and slower controlling repetitive tissues, smaller critical tensions ( $M - values$ ), longer flying-after-diving surface intervals, and others. Stimulated by observation, Doppler technology, decompression meter development, theory, statistics, or safer diving consensus, these modifications affect a gamut of activity, spanning bounce to multiday diving. Of these changes, conservative nonstop time limits, no decompression safety stops, and slower ascent rates (around  $30 f_{sw}/min$ ) are in vogue, and have been incorporated into many tables and meters. As you might expect, recent developments support them on operational, experimental, and theoretical grounds.

But there is certainly more to the story as far as table and meter implementations. To encompass such far reaching (and often diverse) changes in a unified framework requires more than the simple Haldane models we presently rely upon in 99% of our tables and dive computers. To model gas transfer dynamics, modelers and table designers need address both free and dissolved gas phases, their interplay, and their impact on diving protocols. Biophysical models of inert gas transport and bubble formation all try to prevent decompression sickness. Developed over years of diving application, they differ on a number of basic issues, still mostly unresolved today:

1. the rate limiting process for inert gas exchange, blood flow rate (perfusion) or gas transfer rate across tissue (diffusion);
2. composition and location of critical tissues (bends sites);
3. the mechanistics of phase inception and separation (bubble formation and growth);
4. the critical trigger point best delimiting the onset of symptoms (dissolved gas buildup in tissues, volume of separated gas, number of bubbles per unit tissue volume, bubble growth rate to name a few);
5. the nature of the critical insult causing bends (nerve deformation, arterial blockage or occlusion, blood chemistry or density changes).

Such issues confront every modeler and table designer, perplexing and ambiguous in their correlations with experiment and nagging in their persistence. And here comments are confined just to Type I (limb) and II (central nervous system) bends, to say nothing of other types and factors. These concerns translate into a number of what decompression modelers call dilemmas that limit or qualify their best efforts to describe decompression phenomena. Ultimately, such concerns work their way into table and meter algorithms, with the same caveats. Phase models treat these issues in a natural way, gory details of which are found in the References.

The establishment and evolution of gas phases, and possible bubble trouble, involves a number of distinct, yet overlapping, steps:

1. nucleation and stabilization (free phase inception);
2. supersaturation (dissolved gas buildup);
3. excitation and growth (free-dissolved phase interaction);
4. coalescence (bubble aggregation);
5. deformation and occlusion (tissue damage and ischemia).

Over the years, much attention has focused on supersaturation. Recent studies have shed much light on nucleation, excitation and bubble growth, even though *in vitro*. Bubble aggregation, tissue damage, ischemia, and the whole question of decompression sickness trigger points are difficult to quantify in any model, and remain obscure. Complete elucidation of the interplay is presently asking too much. Yet, the development and implementation of better computational models is necessary to address problems raised in workshops, reports and publications as a means to safer diving.

## Computational Issues

The computational issues of bubble dynamics (formation, growth, and elimination) are mostly outside the traditional framework, but get folded into halftime specifications in a nontractable mode. The very slow tissue compartments (halftimes large, or diffusivities small) might be tracking both free and dissolved gas exchange in poorly perfused regions. Free and dissolved phases, however, do not behave the same way under decompression. Care must be exercised in applying model equations to each component. In the presence of increasing proportions of free phases, dissolved gas equations cannot track either species accurately. Computational algorithms tracking both dissolved and free phases offer broader perspectives and expeditious alternatives, but with some changes from classical schemes. Free and dissolved gas dynamics differ. The driving force (gradient) for free phase elimination increases with depth, directly opposite to the dissolved phase elimination gradient which decreases with depth. Then, changes in operational procedures become necessary for optimality. Considerations of excitation and growth invariably require deeper staging procedures than supersaturation methods. Though not as dramatic, similar constraints remain operative in multiexposures, that is, multilevel, repetitive, and multiday diving.

Other issues concerning time sequencing of symptoms impact computational algorithms. That bubble formation is a predisposing condition for decompression sickness is universally accepted. However, formation mechanisms and their ultimate physiological effect are two related, yet distinct, issues. On this point, most hypotheses makes little distinction between bubble formation and the onset of bends symptoms. Yet we know that silent bubbles have been detected in subjects not suffering from decompression sickness. So it would thus appear that bubble formation, per se, and bends symptoms do not map onto each other in a one-to-one manner. Other factors are truly operative, such as the amount of gas dumped from solution, the size of nucleation sites receiving the gas, permissible bubble growth rates, deformation of surrounding tissue medium, and coalescence mechanisms for small bubbles into large aggregates, to name a few. These issues are the pervue of bubble theories, but the complexity of mechanisms addressed does not lend itself easily to table, nor even meter, implementation. But implement and improve we must.

### 1. Perfusion And Diffusion

Perfusion and diffusion are two mechanisms by which inert and metabolic gases exchange between tissue and blood. Perfusion denotes the blood flow rate in simplest terms, while diffusion refers to the gas penetration rate in tissue, or across tissue-blood boundaries. Each mechanism has a characteristic rate constant for the process. The smallest rate constant limits the gas exchange process. When diffusion rate constants are smaller than perfusion rate constants, diffusion dominates the tissue-blood gas exchange process, and vice-versa. In the body, both processes play a role in real exchange process, especially considering the diversity of tissues and their geometries. The usual Haldane tissue halftimes are the inverses of perfusion rates, while the diffusivity of water, thought to make up the bulk of tissue, is a measure of the diffusion rate.

Clearly in the past, model distinctions were made on the basis of perfusion or diffusion limited gas exchange. The distinction is somewhat artificial, especially in light of recent analyses of coupled perfusion-diffusion gas transport, recovering limiting features of the exchange process in appropriate limits. The distinction is still of interest today, however, since perfusion and diffusion limited algorithms are used in mutually exclusive fashion in diving. The obvious mathematical rigors of a full blown perfusion-diffusion treatment of gas exchange mitigate table and meter implementation, where model simplicity is a necessity. So one or another limiting models is adopted, with inertia and track record sustaining use. Certainly Haldane models fall into that categorization.

Inert gas transfer and coupled bubble growth are subtly influenced by metabolic oxygen consumption. Consumption of oxygen and production of carbon dioxide drops the tissue oxygen tension below its level in the lungs (alveoli), while carbon dioxide tension rises only slightly because carbon dioxide is 25 times more soluble than oxygen.

Arterial and venous blood, and tissue, are clearly unsaturated with respect to dry air at 1 *atm*. Water vapor content is constant, and carbon dioxide variations are slight, though sufficient to establish an outgradient between tissue and blood. Oxygen tensions in tissue and blood are considerably below lung oxygen partial pressure, establishing the necessary ingradient for oxygenation and metabolism. Experiments also suggest that the degree of unsaturation increases linearly with pressure for constant composition breathing mixture, and decreases linearly with mole fraction of inert gas in the inspired mix.

Since the tissues are unsaturated with respect to ambient pressure at equilibrium, one might exploit this window in bringing divers to the surface. By scheduling the ascent strategically, so that nitrogen (or any other inert breathing

gas) supersaturation just takes up this unsaturation, the total tissue tension can be kept equal to ambient pressure. This approach to staging is called the zero supersaturation ascent.

## 2. Bubbles

We do not really know where bubbles form nor lodge, their migration patterns, their birth and dissolution mechanisms, nor the exact chain of physico-chemical insults resulting in decompression sickness. Many possibilities exist, differing in the nature of the insult, the location, and the manifestation of symptoms. Bubbles might form directly (*de novo*) in supersaturated sites upon decompression, or possibly grow from preformed, existing seed nuclei excited by compression-decompression. Leaving their birth sites, bubbles may move to critical sites elsewhere. Or stuck at their birth sites, bubbles may grow locally to pain-provoking size. They might dissolve locally by gaseous diffusion to surrounding tissue or blood, or passing through screening filters, such as the lung complex, they might be broken down into smaller aggregates, or eliminated completely. Whatever the bubble history, it presently escapes complete elucidation. But whatever the process, the end result is very simple, both separated and dissolved gas must be treated in the transfer process.

Bubbles may hypothetically form in the blood (intravascular) or outside the blood (extravascular). Once formed, intravascularly or extravascularly, a number of critical insults are possible. Intravascular bubbles may stop in closed circulatory vessels and induce ischemia, blood sludging, chemistry degradations, or mechanical nerve deformation. Circulating gas emboli may occlude the arterial flow, clog the pulmonary filters, or leave the circulation to lodge in tissue sites as extravascular bubbles. Extravascular bubbles may remain locally in tissue sites, assimilating gas by diffusion from adjacent supersaturated tissue and growing until a nerve ending is deformed beyond its pain threshold. Or, extravascular bubbles might enter the arterial or venous flows, at which point they become intravascular bubbles.

Spontaneous bubble formation in fluids usually requires large decompressions, like hundreds of atmospheres, somewhere near fluid tensile limits. Many feel that such circumstance precludes direct bubble formation in blood following decompression. Explosive, or very rapid decompression, of course is a different case. But, while many doubt that bubbles form in the blood directly, intravascular bubbles have been seen in both the arterial and venous circulation, with vastly greater numbers detected in venous flows (venous gas emboli). Ischemia resulting from bubbles caught in the arterial network has long been implied as a cause of decompression sickness. Since the lungs are effective filters of venous bubbles, arterial bubbles would then most likely originate in the arteries or adjacent tissue beds. The more numerous venous bubbles, however, are suspected to first form in lipid tissues draining the veins. Lipid tissue sites also possess very few nerve endings, possibly masking critical insults. Veins, thinner than arteries, appear more susceptible to extravascular gas penetration.

Extravascular bubbles may form in aqueous (watery) or lipid (fatty) tissues in principle. For all but extreme or explosive decompression, bubbles are seldom observed in heart, liver, and skeletal muscle. Most gas is seen in fatty tissue, not unusual considering the five-fold higher solubility of nitrogen in lipid tissue versus aqueous tissue. Since fatty tissue has few nerve endings, tissue deformation by bubbles is unlikely to cause pain locally. On the other hand, formations or large volumes of extravascular gas could induce vascular hemorrhage, depositing both fat and bubbles into the circulation as noted in animal experiments. If mechanical pressure on nerves is a prime candidate for critical insult, then tissues with high concentrations of nerve endings are candidate structures, whether tendon or spinal cord. While such tissues are usually aqueous, they are invested with lipid cells whose propensity reflects total body fat. High nerve density and some lipid content supporting bubble formation and growth would appear a conducive environment for a mechanical insult.

To satisfy thermodynamic laws, bubbles assume spherical shapes in the absence of external or mechanical (distortion) pressures. Bubbles entrain free gases because of a thin film, exerting surface tension pressure on the gas. Hydrostatic pressure balance requires that the pressure inside the bubble exceed ambient pressure by the amount of surface tension,  $\gamma$ . At small radii, surface tension pressure is greatest, and at large radii, surface tension pressure is least.

Gases will also diffuse into or out of a bubble according to differences in gas partial pressures inside and outside the bubble, whether in free or dissolved phases outside the bubble. In the former case, the gradient is termed free-free, while in the latter case, the gradient is termed free-dissolved. Unless the surface tension is identically zero, there is always a gradient tending to force gas out of the bubble, thus making the bubble collapse on itself because

of surface tension pressure. If surrounding external pressures on bubbles change in time, however, bubbles may grow or contract.

Bubbles grow or contract according to the strength of the free-free or free-dissolved gradient, and it is the latter case which concerns divers under decompression. The radial rate at which bubbles grow or contract depends directly on the diffusivity and solubility, and inversely on the bubble radius. A critical radius,  $r_c$ , separates growing from contracting bubbles. Bubbles with radius  $r > r_c$  will grow, while bubbles with radius  $r < r_c$  will contract. Limiting bubble growth and adverse impact upon nerves and circulation are issues when decompressing divers and aviators.

### 3. Bubble Seeds

Bubbles, which are unstable, are thought to grow from micron size, gas nuclei which resist collapse due to elastic skins of surface activated molecules (surfactants), or possibly reduction in surface tension at tissue interfaces or crevices. If families of these micronuclei persist, they vary in size and surfactant content. Large pressures (somewhere near 10 *atm*) are necessary to crush them. Micronuclei are small enough to pass through the pulmonary filters, yet dense enough not to float to the surfaces of their environments, with which they are in both hydrostatic (pressure) and diffusion (gas flow) equilibrium. When nuclei are stabilized, and not activated to growth or contraction by external pressure changes, the skin (surfactant) tension offsets both the Laplacian (film) tension and any mechanical help from surrounding tissue. Then all pressures and gas tensions are equal. However, on decompression, the seed pockets are surrounded by dissolved gases at high tension and can subsequently grow (bubbles) as surrounding gas diffuses into them. The rate at which bubbles grow, or contract, depends directly on the difference between tissue tension and local ambient pressure, effectively the bubble pressure gradient. At some point in time, a critical volume of bubbles, or separated gas, is established and bends symptoms become statistically more probable. On compression, the micronuclei are crunched down to smaller sizes across families, apparently stabilizing at new reduced size. Bubbles are also crunched by increasing pressure because of Boyle's law, and then additionally shrink if gas diffuses out of them. As bubbles get smaller and smaller, they probably restabilize as micronuclei.

### 4. Slow Tissue Compartments

Based on concerns in multiday and heavy repetitive diving, with the hope of controlling staircasing gas buildup in exposures through critical tensions, slow tissue compartments (halftimes greater than 80 minutes) have been incorporated into some algorithms. Calculations, however, show that virtually impossible exposures are required of the diver before critical tensions are even approached, literally tens of hours of near continuous activity. As noted in many calculations, slow compartment cannot really control multiday diving through critical tensions, unless critical tensions are reduced to absurd levels, inconsistent with nonstop time limits for shallow exposures. That is a model limitation, not necessarily a physical reality. The physical reality is that bubbles in slow tissues are eliminated over time scales of days, and the model limitation is that the arbitrary parameter space does not accommodate such phenomena.

And that is no surprise either, when one considers that dissolved gas models are not suppose to track bubbles and free phases. Repetitive exposures do provide fresh dissolved gas for excited nuclei and growing free phases, but it is not the dissolved gas which is the problem just by itself. When bubble growth is considered, the slow compartments appear very important, because, therein, growing free phases are mostly left undisturbed insofar as surrounding tissue tensions are concerned. Bubbles grow more gradually in slow compartments because the gradient there is typically small, yet grow over longer time scales. When coupled to free phase dynamics, slow compartments are necessary in multiday diving calculations.

### 5. Venous Gas Emboli

While the numbers of venous gas emboli detected with ultrasound Doppler techniques can be correlated with nonstop limits, and the limits then used to fine tune the critical tension matrix for select exposure ranges, fundamental issues are not necessarily resolved by venous gas emboli measurements. First of all, venous gas emboli are probably not the direct cause of bends per se, unless they block the pulmonary circulation, or pass through the pulmonary traps and enter the arterial system to lodge in critical sites. Intravascular bubbles might first form at extravascular sites. According to studies, electron micrographs have highlighted bubbles breaking into capillary

walls from adjacent lipid tissue beds in mice. Fatty tissue, draining the veins and possessing few nerve endings, is thought to be an extravascular site of venous gas emboli. Similarly, since blood constitutes no more than 8% of the total body capacity for dissolved gas, the bulk of circulating blood does not account for the amount of gas detected as venous gas emboli. Secondly, what has not been established is the link between venous gas emboli, possible micronuclei, and bubbles in critical tissues. Any such correlations of venous gas emboli with tissue micronuclei would unquestionably require considerable first-hand knowledge of nuclei size distributions, sites, and tissue thermodynamic properties. While some believe that venous gas emboli correlate with bubbles in extravascular sites, such as tendons and ligaments, and that venous gas emboli measurements can be reliably applied to bounce diving, the correlations with repetitive and saturation diving have not been made to work, nor important correlations with more severe forms of decompression sickness, such as chokes and central nervous system (CNS) hits.

Still, whatever the origin of venous gas emboli, procedures and protocols which reduce gas phases in the venous circulation deserve attention, for that matter, anywhere else in the body. The moving Doppler bubble may not be the bends bubble, but perhaps the difference may only be the present site. The propensity of venous gas emboli may reflect the state of critical tissues where decompression sickness does occur. Studies and tests based on Doppler detection of venous gas emboli are still the only viable means of monitoring free phases in the body.

## 6. Multidiving

Concerns with multidiving can be addressed through variable critical gradients, then tissue tensions in Haldane models. While variable gradients or tensions are difficult to codify in table frameworks, they are easy to implement in digital meters. Reductions in critical parameters also result from the phase volume constraint, a constraint employing the separated volume of gas in tissue as trigger point for the bends, not dissolved gas buildup alone in tissue compartments. The phase volume is proportional to the product of the dissolved-free gas gradient times a bubble number representing the number of gas nuclei excited into growth by the compression-decompression, replacing just slow tissue compartments in controlling multidiving.

In considering bubbles and free-dissolved gradients within critical phase hypotheses, repetitive criteria develop which require reductions in Haldane critical tensions or dissolved-free gas gradients. This reduction simply arises from lessened degree of bubble elimination over repetitive intervals, compared to long bounce intervals, and need to reduce bubble inflation rate through smaller driving gradients. Deep repetitive and spike exposures feel the greatest effects of gradient reduction, but shallower multiday activities are impacted. Bounce diving enjoys long surface intervals to eliminate bubbles while repetitive diving must contend with shorter intervals, and hypothetically reduced time for bubble elimination. Theoretically, a reduction in the bubble inflation driving term, namely, the tissue gradient or tension, holds the inflation rate down. Overall, concern is bubble excess driven by dissolved gas. And then both bubbles and dissolved gas are important. In such an approach, multidiving exposures experience reduced permissible tensions through lessened free phase elimination over time spans of two days. Parameters are consistent with bubble experiments, and both slow and fast tissue compartments must be considered.

## 7. Adaptation

Divers and caisson workers have long contended that tolerance to decompression sickness increases with daily diving, and decreases after a few weeks layoff, that in large groups of compressed air workers, new workers were at higher risk than those who were exposed to high pressure regularly. This acclimatization might result from either increased body tolerance to bubbles (physiological adaptation), or decreased number and volume of bubbles (physical adaptation). Test results are totally consistent with physical adaptation.

Yet, there is slight inconsistency here. Statistics point to slightly higher bends incidence in repetitive and multiday diving. Some hyperbaric specialists confirm the same, based on experience. The situation is not clear, but the resolution plausibly links to the kinds of first dives made and repetitive frequency in the sequence. If the first in a series of repetitive dives are kept short, deep, and conservative with respect to nonstop time limits, initial excitation and growth are minimized. Subsequent dives would witness minimal levels of initial phases. If surface intervals are also long enough to optimize both free and dissolved gas elimination, any nuclei excited into growth could be efficiently eliminated outside repetitive exposures, with adaptation occurring over day intervals as noted in experiments. But higher frequency, repetitive and multiday loading may not afford sufficient surface

intervals to eliminate free phases excited by earlier exposures, with additional nuclei then possibly excited on top of existing phases. Physical adaptation seems less likely, and decompression sickness more likely, in the latter case. Daily regimens of a single bounce dive with slightly increasing exposure times are consistent with physical adaptation, and conservative practices. The regimens also require deepest dives first. In short, acclimatization is as much a question of eliminating any free phases formed as it is a question of crushing or reducing nuclei as potential bubbles in repetitive exposures. And then time scales on the order of a day might limit the adaptation process.

## Hyperbaric Chambers

Hyperbaric chambers are used to treat a number of maladies with different high pressure gases, maladies such as wounds, gangrene, DCI, Lyme disease, and multiple sclerosis (MS). Often the treatment mixture is oxygen (or mostly oxygen), and the treatment process is called hyperbaric oxygen therapy (HBOT). This is particularly true for wounds, gangrene, and MS. With DCI, treatment includes mixtures of nitrogen, helium, and oxygen blended in proportions to avoid oxygen toxicity and inert gas narcosis. The combination of increased ambient pressure and elevated levels of oxygen help to dissolve bubbles and also wash out inert gases.

Oxygen, when breathed under increased atmospheric pressure, is a potent drug. Hyperbaric oxygen, if administered indiscriminantly, can produce noticeable toxic effects. Safe time-dose limits have been established for hyperbaric oxygen, and these profiles form the basis of treatment protocols. The past 10 to 15 years have seen the introduction of disease specific hyperoxic dosing. Emergency cases, such as carbon monoxide poisoning or cerebral arterial gas embolism (AGE) may only require one or two treatment schedules. In cases where angiogenesis is the primary goal, as many as 20 to 40 visits to the hyperbaric chamber may be requisite. The precise number of treatments often depends upon the clinical response of the patient. Transcutaneous oximetry can often provide more exacting dose schedules, improving treatment and cost effectiveness. With the exception of DCI and AGE, periods of exposure last approximately 2 hours. Treatments may be given once, twice, or occasionally three times daily, and provided in both inpatient and outpatient settings.

Several beneficial mechanisms are associated with intermittent exposure to hyperbaric doses of oxygen. Either alone, or more commonly in combination with other medical and surgical procedures, these mechanisms serve to enhance the healing process in treatable circumstances.

1. *Hyperoxygenation* provides immediate support to poorly perfused tissues in sections of compromised blood flow. The elevated pressure within the hyperbaric chamber results in a 10 to 15 fold increase in plasma oxygen concentrations. Translated to arterial oxygen tensions, values near 1,500 to 2,000 *mmHg* are observed, thereby producing a 4 fold increase in the diffusion length of oxygen from functioning capillaries. While this form of hyperoxygenation is only temporary, it does buy time and maintain tissue viability until corrective measures or new blood supply are established.
2. *Neovascularization* represents an indirect and delayed response to hyperbaric oxygen therapy. Therapeutic effects include enhanced fibroblast division, neof ormation of collagen, and capillary angiogenesis in areas of sluggish vascularization, such as radiation damaged tissue, refractory osteomyelitis, and chronic ulceration in soft tissue.
3. *Antimicrobial inhibition* has been demonstrated at a number of levels. Hyperbaric oxygen induces toxin inhibition and toxin inactivation in clostridial perfringens (gas gangrene). Hyperoxia enhances phagocytosis and white cell oxidative killing, and has been shown to support aminoglycoside activity. Recent studies suggest that prolonged antibiotic screening follows application of high pressure oxygen.
4. *Phase reduction*, application of Laplace's and Boyle's law to separated gases in tissue and blood, forms the basis of hyperbaric treatment of decompression sickness and arterial gas embolism, as known for more than a century. Commonly associated with divers and diving, AGE is a frequent iatrogenic event in modern medicine, resulting in significant morbidity and mortality, and remains grossly underdiagnosed. The process is enhanced gas diffusion from free phases to the venous blood flow for elimination through the lungs. Increasing pressure increases the outgassing gradient, and shrinks gas phases by Boyle contraction.
5. *Vasoconstriction* is an important spinoff of hyperbaric oxygen, manging intermediate compartment syndrome and other acute ischemias, as well as reducing interstitial edema in grafted tissues. Studies in burn wound applications indicate a significant decrease in fluid resuscitation requirements when HBOT is added to wound therapy.

6. *Reperfusion injury attenuation* is a recently discovered mechanism associated with hyperbaric oxygen. Leukocyte deactivation has been traced to high concentrations of oxygen in the blood, with the net effect the preservation of tissues that might otherwise be lost to ischemia-reperfusion injury. Reperfusion injury occurs with direct hypoxia and inappropriate activation of leukocytes.

## OXYGEN DOSE

### Oxygen Tolerance And Toxicity

Decompression sickness could be avoided by breathing just pure oxygen. And the usage of higher concentrations of oxygen in breathing mixtures not only facilitates metabolic function, but also aids in the washout of inert gases such as nitrogen and helium. Despite the beneficial effects of breathing oxygen at higher concentrations, oxygen proves to be toxic in excessive amounts, and over cumulative time intervals. Too little oxygen is equally detrimental to the diver. As discussed, limits to oxygen partial pressures in breathing mixtures range, 0.16 *atm* to 1.6 *atm*, roughly, but symptoms of hypoxia and hyperoxia are dose dependent. Or, in other words, symptom occurrences depend on oxygen partial pressures and exposure times, just like inert gas decompression sickness. The mixed gas diver needs to pay attention not only to helium and nitrogen in staged decompression, but also cumulative oxygen exposure over the dive, and possible underexposure on oxygen depleted breathing mixtures.

The neurotoxic actions of high pressure oxygen are thought to relate directly to biochemical oxidation of enzymes, either those linked to membrane permeability or metabolic pathways. The list below is not exhaustive, but includes the following mechanisms:

1. the inability of blood to remove carbon dioxide from tissue when hemoglobin is oxygen saturated;
2. inhibition of enzymes and coenzymes by lipid peroxides;
3. increased concentration of chemical free radicals which attack cells;
4. oxidation of membranes and structural deterioration reducing electrical permeability for neuron activation;
5. direct oxygen attack on smooth muscle fibres;
6. oxygen induced vasoconstriction in arterioles;
7. elevation of brain temperature due to lack of replacement of oxygen by carbopn dioxide in hemoglobin;
8. and, simple chemical kinetic redistribution of cellular carbon dioxide and oxygen with high surrounding oxygen tensions.

Fortunately for the diver, there are ways to avoid complications of hyperoxia. Careful attention to dose (depth-time) limitations for oxygen exposures is needed.

Despite the multiplicity and complexity of the above, limits for safe oxygen exposure are reasonably defined. Table 1 below lists NOAA oxygen exposure time limits,  $t_x$ , for corresponding oxygen partial pressures,  $p_{O_2}$ . Below 0.5 *atm*, oxygen toxicity is not really a problem.

Table 1. Oxygen Dose-Time Limits

oxygen partial pressure $p_{O_2}$ ( <i>atm</i> )	oxygen time limit $t_x$ ( <i>min</i> )	oxygen tolerance (OTU) $\Upsilon$ ( <i>min</i> )
1.6	45	87
1.5	120	213
1.4	150	244
1.3	180	266
1.2	210	278
1.1	240	279
1.0	300	300
0.9	360	299
0.8	450	295
0.7	570	266
0.6	720	189

The data in Table 1 is easily fitted to a dose time curve, using least squares, yielding,

$$t_x = \exp \left[ \frac{3.0 - p_{O_2}}{.36} \right] = 4160 \exp (-2.77 p_{O_2}) \quad (1)$$

or, equivalently,

$$p_{O_2} = 3.0 - .36 \ln (t_x) \quad (2)$$

in the same units, that is  $p_{O_2}$  and  $t_x$  in *atm* and *min* respectively. The last column tabulates an exposure dose,  $\Upsilon$ , for divers, called the oxygen tolerance unit (OTU), developed by Lambertsen and coworkers at the University of Pennsylvania. Formally, the oxygen toxicity,  $\Upsilon$ , is given by,

1. maintain single dive OTUs below 750 *min* on the liberal side, or allow for 550 *min* of that as possible full DCI recompression treatment on the conservative side;
2. maintain repetitive total dive OTUs below 300 *min*.

The expression is applied to each and all segments of a dive, and summed accordingly for total OTUs, and then benchmarked against the 750 *min* or 300 *min* rough rule. The 750 *min* and 300 *min* OTU rules are not cast in stone in the diving community, and 10% to 25% variations are common, in both conservative and liberal directions. For multiple exposures of dose,  $\Upsilon_n$ , for diving segments (multilevel, deco, repetitive),  $n$ , of duration,  $t_n$ , and oxygen exposure pressure,  $p_{nO_2}$ , the total dose,  $\Upsilon$ , is formally the sum of segment doses,

$$\Upsilon = \sum_{n=1}^N \Upsilon_n = \sum_{n=1}^N \left[ \frac{p_{nO_2} - 0.5}{0.5} \right]^{0.83} t_n \quad (3)$$

for  $N$  segments.

For exceptional and multiple exposures, the USN and University of Pennsylvania suggest the limits summarized in Table 2, where for multiple exposures,  $N$ , and segment times,  $t_{x_n}$ ,

$$T_x = \sum_{n=1}^N t_{x_n} \quad (4)$$

Table 2. Oxygen Exceptional Exposure Time Limits

oxygen partial pressure $p_{O_2}$ ( <i>atm</i> )	single exposure $t_x$ ( <i>min</i> )	multiple exposures $T_x$ ( <i>min</i> )
2.0	30	
1.9	45	
1.8	60	
1.7	75	
1.6	120	15
1.5	150	180
1.4	180	180
1.3	240	210
1.2	270	240
1.1	300	270
0.9	360	360
0.8	450	450
0.7	570	570
0.6	720	720

Note the severe reduction in multiple oxygen exposure time at 1.6 atm in Table 2. For this reason, technical divers generally restrict mixed gas diving exposures to  $p_{O_2} \leq 1.6 \text{ atm}$  throughout any sequence of dives.

A similar oxygen dose unit,  $\Phi$ , called the unit pulmonary toxicity dose (UPTD), is also used in the diving community, and is similar to the OTU,

$$\Phi = \left[ \frac{p_{O_2} - 0.5}{0.5} \right]^{1.2} t \quad (5)$$

but obviously weighs oxygen partial pressure more than time in estimating dose. Both measures have their proponents in oxygen exposure calculations.

### Oxygen Analyzers

There are many ways to measure oxygen, with devices called oxygen analyzers. They are employed in chemical plants and refineries, hyperbaric chambers, intensive care units, and nurseries. The paramagnetic analyzer is very accurate, and relies on oxygen molecular response to a magnetic field in displacing inert gases from collection chambers. Thermal conductivity analyzers differentiate oxygen and nitrogen conduction properties in tracking temperatures in thermistors, with difference in temperatures proportional to the oxygen concentration. Magnetic wind analyzers combine properties of paramagnetic and thermal analyzers. Polarographic analyzers measure oxygen concentration by resistance changes across permeable oxygen membranes. Galvanic cell analyzers are microfuel cells, consuming oxygen on touch and generating a small current proportional to the amount of oxygen consumed. In all cases, analyzer response is linear in oxygen concentration.

Although it is tempting to avoid problems of oxygen toxicity by maintaining oxygen partial pressures,  $p_{O_2}$ , far below toxic limits, this is not beneficial to inert gas elimination (free or dissolved state). Higher levels of inspired oxygen, thus correspondingly lower levels of inert gases, are advantageous in minimizing inert gas buildup and maximizing inert gas washout. Coupled to narcotic potency of helium and nitrogen, and molecular diffusion rates, balancing and optimizing breathing mixtures with decompression requirements is truly a complex and careful technical diving exercise.

### ADDITIONAL READING

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### BIOSKETCHES

Bruce Wienke is a Program Manager in the Nuclear Weapons Technology/ Simulation And Computing Office at the Los Alamos National Laboratory (LANL), with interests in computational decompression and models, gas transport, and phase mechanics. He authored *Physics, Physiology And Decompression Theory For The Technical And Commercial Diver, High Altitude Diving, Basic Diving Physics And Applications, Diving Above Sea Level, Basic Decompression Theory And Application*, and some 200 technical journal articles. Diving environs include the Caribbean, South Pacific, Asia, inland and coastal United States, Hawaii, and polar Arctic and Antarctic in various technical, scientific, military, and recreational activities. He functions on the LANL Nuclear Emergency Strategy Team (NEST), in exercises often involving Special Operations Units, above and underwater. He heads Southwest Enterprises, a consulting company for computer research and applications in wide areas of applied science and simulation.

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Wienke, a former dive shop owner in Santa Fe, presently works with DAN on applications of high performance computing and communications to diving, and is a Regional Data Coordinator for Project Dive Safety. SCUBAPRO, SUUNTO, ABYSMAL DIVING, and ATOMICS engage (or have) him as Consultant for meter algorithms. He is the developer of the Reduced Gradient Bubble Model (RGBM), a dual phase approach to staging diver ascents over an extended range of diving applications (altitude, nonstop, decompression, multiday, repetitive, multilevel, mixed gas, and saturation). The SUUNTO VYPER dive computer incorporates the RGBM into staging regimens, particularly for recreational diving (including nitrox). ABYSS, a commercial software product, features some of the RGBM dynamical diving algorithms developed by him for Internet users and technical divers. He is also Associate Editor for the International Journal Of Aquatic Research And Education, and is a former Contributing Editor of *Sources*, the NAUI Training Publication.

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