- Title: **Dysbaric Illness and its Treatment**
- Author(s) Alessandro Marroni (DAN Europe Foundation, Italy and Malta)
Frans J. Cronjé (DAN Southern Africa)
Danilo Cialoni (DAN Europe Foundation, Italy and Malta)
Massimo Pieri (DAN Europe Foundation, Italy and Malta)

- **Background :**

Dysbaric Illness (DI) – or decompression illness (DCI) [1] represents a broad range of complex bubble-related pathophysiological conditions associated with decompression [1-9]. Although the primary cause of DI is attributed to gas-phase separation and / or gas bubble migration within the body, many aspects of its etiology remain unclear [10-16]. The prevailing understanding is that, when ambient pressure drops (i.e., decompression) to a point that body tissue inert gas tensions exceed the ambient pressure (i.e. supersaturation), gas bubbles may appear (i.e., critical supersaturation). These bubbles may then cause local effects or enter the circulation as venous gas emboli. They may also eventually enter the systemic circulation as arterial emboli by passing through pulmonary or cardiac shunts. Alternatively, rapid decompression may precipitate arterial injection of alveolar gas bubbles as a result of pulmonary barotrauma. Given all these inter-related mechanisms, the pathophysiological effects of bubbles are both various and variable, as are their corresponding clinical manifestations. DI should therefore be considered as part of the differential diagnosis whenever individuals (1) develop immediate-onset neurological symptoms, even after breathing compressed gas at 100 cm depth (113 kPa) [17], or when they present with a range of abnormal clinical signs and symptoms at any time within 24 hours of (2) a significant exposure to compressed gas breathing (i.e., following compressed air / -gas diving; hyperbaric chamber attendant duties; or caisson work) [1] , or (3) after ascending from sea level pressure to altitudes greater than 3300 m / 11,000 ft (e.g., flying in an unpressurised aircraft) [18]. Although the management of all DI follows similar principles, this chapter focuses primarily on the consequences of compressed gas diving. In addition to the acute manifestations of DI, there are also concerns about chronic DI, particularly affecting the articular surface in long-bones [19].

Incidence of DI

The exact incidence of DI can only be estimated, because the total number of exposed individuals (i.e., commercial divers, hyperbaric attendants & recreational divers) and the number of dives performed, is unknown [20-23]. The international population of recreational divers is now estimated to be several million whereas there are probably less than 200,000 commercial and military divers. In lieu of a specific biochemical marker for DI, and with the sensitivity of radiological and nuclear medical examinations not exceeding clinical observation, diagnostic certainty of DI is also highly variable [1,16]. Fortunately, the risk of DI appears to be relatively small, particularly when appropriate decompression procedures are followed: For open water dives of

[1] In English-speaking countries, Decompression Sickness and Decompression Illness represent distinctly different terms as they are applied in different classifications of gas-bubble disease. This is potentially confusing when translated into other languages. The term - Dysbaric Illness (DI) - offers as some linguistic advantages in this regard. Therefore, in this chapter, DI it is used preferentially as a synonym for collective term Decompression Illness (DCI), which encompasses both Decompression Sickness (DCS) and Arterial Gas Embolism (AGE). Although DI conceivably also includes medical problems associated with compression, its use is strictly limited to the context of decompression following breathing from a compressed gas source.

moderate duration, the rate of occurrence (per dive) ranges slightly according to the diving population: 0·015% for scientific divers; 0·01–0·019% for recreational divers; 0·030% for US Navy divers; and 0·095% for commercial divers [13,24]. Other diving and hyperbaric populations include technical divers, for whom the incidence of DI is unknown, but seems to vary greatly according to the depth and duration of the dives performed; for commercial divers in the offshore oil industry DI is negligible due to slow decompressions from saturation; clinical hyperbaric chamber attendants, have a DI occurrence rate reported as 0·02% per exposure [20,21]. In altitude training or flight operations subjects, the rate of occurrence of decompression sickness is usually mild and below 0·1% per exposure although [25,26], anonymous surveys of high-altitude USAF pilots suggest higher rates and more serious symptoms [27-29]. DI incidence may also be affected by environmental conditions such as immersion (vs. 'dry' diving), exercise, and ambient temperature [13,30,31]. The effects of increasing age and BMI appear to favour venous gas emboli formation [13,32], whereas the role of gender remains controversial [33,34].

Clinical presentation of DI

DI can present with both a wide and variable range of signs and symptoms [1-3,35,36]. Certain types of diving or hyperbaric exposures may favor a specific range of presentations [1]. However, the vast majority of exposed subjects are recreational divers. As such, the manifestations of DI, as summarized in figure 1, are the predominant clinical findings of DI in recreational divers according to most common initial and eventual manifestations:

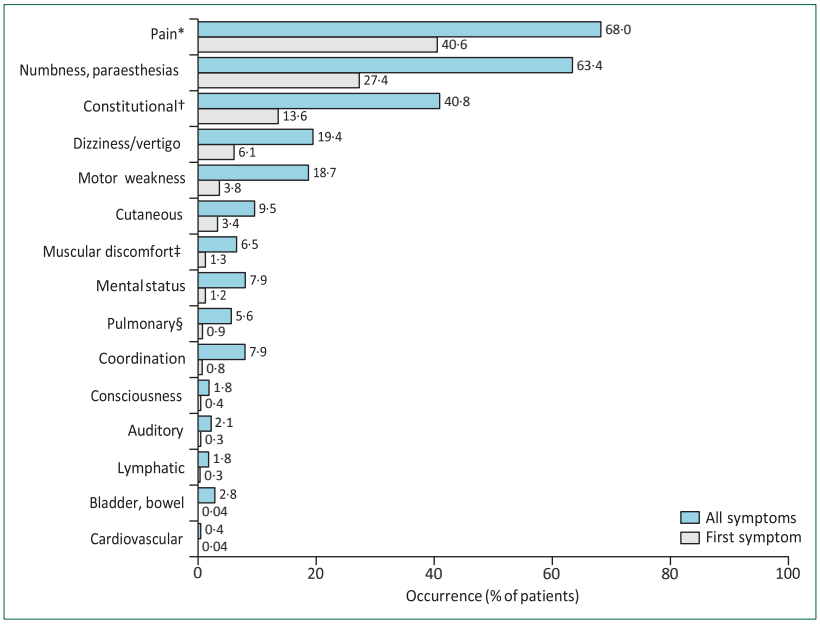

Figure 1: **Classification of initial and of all eventual manifestations of decompression illness in 2346 recreational diving accidents reported to the Divers Alert Network from 1998 to 2004.**

*For all instances of pain, 58% consisted of joint pain, 35% muscle pain, and 7% girdle pain. Girdle pain often portends spinal cord involvement.

†Constitutional symptoms included headache, light-headedness, inappropriate fatigue, malaise, nausea or vomiting, and anorexia.

‡Muscular discomfort included stiffness, pressure, cramps, and spasm but excluded pain.

§Pulmonary manifestations included dyspnoea and cough.

In special situations (e.g., in saturation diving) DI manifestations may occur during decompression. However, in recreational divers, most DI cases present shortly after surfacing. In a review of DI in military divers, 42% of DI symptoms appeared within 1 h of surfacing; 60% in 3 hrs; 83%

in 8 hrs; and all but 2% of cases within 24 hrs [37]. Central nervous system-related DI may present even sooner: In a series of 1070 patients, 56% already had symptoms within 10 min, whereas 90% presented within 4 hrs [38]. Altitude exposure after diving may cause the onset to be delayed beyond 24 hours [1,23,39].

Standard management (summary) and outcome

Although recompression therapy has been the mainstay of treatment for DI for the past 100 years [40,41], it may not always be available. Lack of access and delays to recompression have allowed the natural history of DI to be observed [42]: In general it seems that mild, joint-related pain-only DI abates eventually, although recompression does expedite resolution [43-46]. Constitutional manifestations – such as skin rashes and fatigue – seem to clear without residua unless more serious DI manifestations supervene [35,44-47]. Neurological forms of DI are less predictable, however: There are cases of spontaneous recovery (especially with cerebral manifestations) but there are a greater number of cases with permanent disability and paralysis when recompression is not performed promptly, or not at all [42]. On the other hand, recompression does not guarantee full recovery from neurological DI – particularly spinal DI – even when applied relatively promptly after the onset of symptoms [35,44-47].

Breathing 100% oxygen as a first aid measure is strongly recommended for the first-aid treatment of DI, and its use is supported by observation that it seems to lower the total number of recompression treatments required to achieve a clinical plateau [47,48]. Similarly, the infusion of crystalloid solutions (without glucose) is recommended, based largely on theoretical benefits and observed hemoconcentration following DI [1,40,49,50]. However, other measures and medications such as aspirin, colloid solutions, steroids, and heparin are not supported by strong evidence [1,40,49-51]. The use of lignocaine appears justified for serious neurological DI [51-53], whereas prophylaxis against deep venous thrombosis (using low molecular weight heparin and compression stockings) is recommended for paralyzed or immobile divers with DI [51].

Despite theoretical advantages for the head-down position, the consensus is in favour of horizontal, supine position for managing diving casualties with suspected DI. Oral rehydration should only be considered in stable, conscious patients with DI, although there is no strong evidence to support this practice; there is weak evidence, however, that good hydration has a role in prophylaxis of DI [1,51,54].

In-water recompression on *air* is not recommended, but there is growing support for the use of in-water recompression on oxygen under special circumstances [54].

• Rationale for HBO use

The primary purpose of HBO for the treatment of DI is to reduce the occlusive and compressive effects of bubbles; to prevent, treat or minimise secondary intra- and extravascular effects; and to eliminate the offending inert gas. To understand the role of HBO within evolutionary complexity and interrelated mechanisms involved, the pathophysiology of DI must be considered:

General Pathophysiology of DI:

With decreasing pressure, a threshold is eventually reached where bubbles start to form in the body; this depends on the amount of inert gas and the extent of decompression. At extreme altitudes, DI cannot be avoided, even after prolonged oxygen pre-breathing [55]. Although decompression bubbles are traditionally classified as intra- or extravascular, this division may be misleading as it does not describe the origin of bubbles but rather where they have been observed experimentally. In fact, there is no conclusive evidence that bubbles actually form directly within blood vessels. Rather, it is believed that they may be admitted through endothelial gaps as they develop within surrounding perivascular tissues [56].

Another mechanism for the intravascular appearance of bubbles is by traumatic introduction during pulmonary barotrauma [57]. As little as 10% over-expansion of the lungs is enough to cause gas embolism [17,58]. This would occur with an intra-tracheal pressure of 76-80 mm Hg (or 99.2-108 cm H2O), or during a breath-hold ascent (after breathing compressed gas) from only 3 feet (~1 meter) of seawater to the surface. Although traumatic injection of gas vs. bubbles released by inert gas supersaturation represent two completely different etiological mechanisms, they are often difficult to differentiate clinically: physical or radiological evidence of pulmonary injury is often absent in AGE [59], whereas arterialization of venous gas emboli containing inert gas may result in arterial gas embolization with clinically indistinguishable results. Over the last 10 years, the potential role of *a patent foramen ovale* (PFO) has enjoyed increasing attention. The potential contribution of a PFO towards the type and probability of DI remains controversial, although there is increasing support for the association between a large PFO and high cerebral or spinal DI, inner ear DI and cutis marmorata-like skin DI presentations [11,60-65].

Although the origin of bubbles may be ambiguous, their effects are more distinct. Intravascular bubbles embolize tissue causing ischemia [66]; they also traverse the microvasculature (so-called "transbolism") and injure endothelium [67]; they cause reperfusion injury and vasospasm [68]. Bubbles can cause venous stasis, hemorrhage and precipitate plasma protein interactions [69] Extravascular or tissue bubbles disrupt and tear delicate tissues and blood vessels; they can also increase tissue compartment pressures i.e., cause regional compartment syndromes [70].

The complexity and controversy regarding the pathophysiology of DI is exemplified by the division that still exists in the use of two classification systems: one pathological [5], and the other clinical [1,4]. While we do not always know the cause of DI, we must not ignore mechanisms altogether, thereby being unable to appreciate risk, determine probability of injury and prescribe effective and rational treatment. Astute clinical observation and focused research must remain the vital tools for unravelling the mysteries of DI.

Effects of Bubbles on various Tissues and Organ Systems

To consolidate the various mechanisms involved in DI into meaningful clinical entities, it is useful to observe their effects on known target organs: (1) blood and blood vessels; (2) the lungs; (3) the central and peripheral nervous systems; (4) the inner ear; (5) the skin and lymphatics, and (6) bones and joints.

Blood and blood vessels

Bubbles are biologically active. They interact with the cellular elements in blood as well as plasma protein cascades – coagulation, complement, kinin and plasmin. In addition, bubbles denature lipoproteins, liberating blood lipids [71-74]. Blood vessels, on the other hand, sustain damage through physical contact. This may range from minimal damage to bleeding [53,75].

***Blood**:* Upon appearance of a bubble in blood, the catalyzing event appears to be the formation of a plasma-protein coat around the bubble. This bubble "skin" is made up of plasma glycoproteins, fibrinogen and gamma globulins [76,77]. It is a biologically active interface that allows thrombocytes and white blood cells to become attached [78]. In time, activation of platelets leads to aggregation and coalescence around bubbles with entrapment of other blood constituents. Cellular blood elements – such as red blood cells – may become entangled in the growing fibrin web. This thickening of the bubble "skin" may reduce diffusion producing a mechanism for bubble stabilization and survival [79]. General platelet adhesiveness also increases in response to bubbles. Some studies have reported platelet depletion following decompression, even in the absence of symptoms [80]. However, thrombocytopenia or anti-platelet therapies do not appear to protect against DI. Also aggressive anticoagulation runs the risk of precipitating hemorrhage in DI affecting the spinal cord and inner ear [75,78,79,81]. On the other hand, DI does induce a hypercoagulable state with a high risk of thromboembolism aggravated by paralysis; this

should be actively prevented [51]. The activation of platelets and Hageman Factor also leads to activation of inflammatory cascades. Leukotrienes are released while the presence of gamma-globulin on the bubble skin, combined with the products of complement activation, attract white blood cells to the area [82]. Leukocytes may interact directly with the bubble or with damaged endothelium. The relevance of inflammation in DI underlies the recommended use of anti-inflammatory agents and, more recently, of lidocaine [83]. Lidocaine also has leukocyte anti-adherent properties [53,84]. DI has also been shown to result in elevations of blood lipid levels with as yet undefined clinical implications [85]. While the role of various elements in blood in DI has become downplayed in recent literature, the significance has not disappeared: The search continues to find safe and effective drugs or interventions that may attenuate the various pathophysiological events following exposure to bubbles. Recently research on nitric oxide donors and exercise have suggested that they may have a modifying role in vivo [86].

Blood vessels: The injection of 10-20µm bubbles into the carotid artery of a guinea pig has been shown to cause visible damage to the luminal surface surfactant layers of endothelial cells [73]. This form of injury may result in alterations in vasomotor tone, precipitate platelet or leukocyte adhesion, and cause failure of the blood-brain barrier. In more extreme cases endothelial cells may actually be stripped, exposing the basement membrane to plasma proteins and platelets as well as adding bioactive cell remnants to the blood [78].

The Lungs

Unlike pulmonary barotrauma, pulmonary DI is an intravascular occlusive bubble disease. It results from the passage of venous gas emboli through pulmonary capillaries. The peri-alveolar network of capillaries serves as a trap for venous gas emboli. However, if the amount of gas is excessive, it may cause cardiac air locking and pulmonary outflow obstruction or microvascular obstruction with vasoconstriction, endothelial damage, inflammation, capillary leak and pulmonary edema – "the chokes". The pulmonary "bubble trap" may also be overcome by massive embolization or be bypassed via broncho-pulmonary shunts, arterio-venous fistulae, or intra-cardiac shunts. A reduction in the diameter of circulating bubbles – such as by repetitive diving or "yoyo" diving – may allow bubble passage through the pulmonary capillary beds. All of these mechanisms may lead to arterialization of bubbles – so-called paradoxical gas embolism. The latter provides an attractive theoretical explanation for the poorly understood associations between "chokes", patent foramen ovale, and DI of the central nervous system and skin [87,88].

The Nervous System

Approximately two thirds of DI affects the nervous system [1,2]. Although clinical features may be ambiguous a distinction is made between three potential locations of injury: (1) the spinal cord, (2) brain and (3) peripheral nerves [38,89]. In each case, the primary mechanism may be vascular (embolic) or extra-vascular. A review of 1070 cases of neurological decompression sickness by Francis *et al* supports the probability of multiple mechanisms with varying latencies [38,89].

Spinal Cord: Four etiological theories have evolved to reconcile the varying observations of onset time, severity, response to therapy, and histopathology. They are (1) gas embolism; (2) venous infarction; (3) autochthonous ("in situ") bubbles; and (4) hemorrhage or inflammation [38,89]. *Gas Embolism:* The first theory for DI of the spinal cord was developed by Boycott and Damant. Lesions in the spinal cord of goats were found to consist, almost entirely, of white matter lesions [90]. Indeed human pathology, although rarely observed in this mostly non-fatal condition, has also shown similar punctate, white matter lesions and hemorrhage. However, embolic injury to the spinal cord is, generally speaking, very rare. This is believed to be due to the relative difference in blood flow favoring embolization of the brain. Experimental spinal cord embolism has also been shown to produce ischemic grey matter pathology rather than white matter lesions [91]. To confuse the matter further a type of DI

was identified that began as rapid onset cerebral arterial gas embolism but then evolved into a particularly resistant form of spinal injury. This has been called "combined", "concurrent" or "Type III decompression sickness" [14,92-94]. Although the exact mechanism is still unknown, the predominant theory is related to growth of arterial gas emboli in tissues saturated with inert gas. Recently a so-called ternary animal model has been proposed in an effort to reconcile these findings [95]. *Venous Infarction:* In 1975, based on Batson's experiments on tumor embolization via epidural veins [96], Hallenbeck et al postulated that DI of the spinal cord was due to bubble accumulation in the epidural venous plexus with subsequent venous infarction of the spinal cord. Although confirmed in extreme decompression [66,97-99], loss of function only occurred after several minutes and therefore did not offer an explanation for ultra-short-latency disease. In addition, the pattern of DI was different to that observed in other causes of venous infarction of the spinal cord that typically affects the central grey matter [100]. *Autochthonous Bubbles:* Francis *et al* proposed that rapid-onset spinal cord damage may be related to spontaneous bubble formation in the spinal cord white matter [89]. He felt that this was the only mechanism that could explain both the rapid onset and the distribution of lesions observed in the spinal cord. In his classic experiment, the spinal cord of decompressed dogs was rapidly perfusion-fixed at the moment of maximal disruption of somatosensory evoked potentials. He consistently found extravascular, non-staining space occupying lesions in the white matter which he attributed to gas that had evolved in the solid tissue – there are known as autochthonous bubbles [46,89]. The puzzling piece is how these small, scattered and isolated space occupying lesions (making up no more than 0.5% of the spinal cord and being no more than 20-200um in diameter) are able to produce such catastrophic clinical effects [101]. It has been postulated that autochthonous bubbles could account for loss of function if more than 30% of the axons became dysfunctional due to direct injury, stretching or compression, inflammation, biochemical injury or hemorrhage. In support of this, Hills et al has also shown that small lesions (able to increase the spinal cord volume by 14-31%) can cause an increase in tissue pressures with a resulting spinal compartment syndrome [102]. *Hemorrhage and Inflammation:* In his studies on autochthonous bubbles, Francis made three important additional observations [103]: (1) animals that only developed abnormalities after 30 minutes had no demonstrable space occupying lesions suggesting another mechanisms for the dysfunction; (2) animals sacrificed sometime after the development of rapid-onset dysfunction no longer had bubbles suggesting that they are temporary; and (3) the histological appearance of spinal cords from dogs with late-onset spinal symptoms was similar to that of spinal embolism or ischemic lesions [91]. Interestingly in the animals harvested sometime after rapid onset illness, hemorrhage and inflammation were observed in the same areas where autochthonous bubble injuries were seen in those harvested early. This could explain why some cases of rapid onset spinal cord DI appear resistant to recompression and would suggest caution in the use of anti-coagulants in DI of the spinal cord. Intriguingly, all of the mechanisms appear to converge within a particular area: a c-shaped area around the spinal cord grey matter. This area represents a watershed zone between the anterior and posterior spinal cord circulation and would therefore be susceptible to both inert gas accumulation as well as subsequent bubble-related ischemia. The cervical and lumbar enlargements are particularly vulnerable and also correspond to the areas of greatest clinical importance in DI. It is unlikely that one single mechanism can account for the wide variety of latencies and presentations of DI of the spinal cord and the decompression schedules leading to them. Rather it is probably the result of several interacting, compressive-ischemic mechanisms. DI of the spinal cord should be thought of as a spectrum of cause-and-effect over a 48-hour time-continuum. It is interplay between various distinct, yet synergistic pathophysiological processes - some of which are amenable to recompression and adjunctive medical therapy and some which, unfortunately, are not. Finally, in spite of the disturbing vulnerability of the spinal cord, it has a remarkable capacity of recovery. Many divers with residual deficits after recompression therapy continue to improve for years afterwards. However, this does not indicate that the injury has been reversed, only that the body has compensated for it [104,105].

Brain: Cerebral, cerebellar and brain stem-related decompression disorders differ from those of the spinal cord in that there is no experimental evidence suggesting autochthonous or venous stasis mechanisms. Accordingly, greater emphasis is placed on embolic and inflammatory mechanisms. Brain DI has a very short latency. In the review by Francis, 75% of the 311 cerebral DI cases became symptomatic within 10 minutes (even with all cases of overt pulmonary barotrauma specifically excluded) [38]. This leaves paradoxical gas embolization as an attractive alternative possibility. *Clinical Features Systemic Gas Embolism (SGE):* Gas embolism is by its nature a systemic disease although clinically it primarily affects the myocardium and the brain. While coronary embolism may account for some diving fatalities, it is not associated with long term morbidity. Cerebral events, on the other hand, are associated with both short term mortality and long term morbidity. SGE gain access to the cerebral circulation via the carotid and vertebral arteries that converge at the base of the brain forming the circle of Willis. Depending on the volume of gas and region of the brain involved the clinical outcome of gas embolism ranges from instant death to spontaneous uneventful recovery. Relapses have been reported in up to 30% of patients with arterial gas embolism following submarine escape, irrespective of preceding or concurrent recompression [106,107]. A subset of patients may also suffer subclinical damage only visualized by medical imaging [92]. Irrespective of the cause, the ultimate outcome of cerebral gas embolization appears to depend on the anatomical location, gas volume, delivery rate, pre-embolic gas saturation as well as co-morbid factors such as hypotension or dysfunction of vital centres.

Peripheral Nervous System: The peripheral nervous system may be affected by decompression injuries anywhere from the posterior horn of the spinal cord, to the mixed nerves, brachial or lumbar plexus, and cutaneous or muscular innervations. The most important considerations are differential diagnosis and prognosis. Clinically it is important to differentiate benign, peripheral sensory manifestations of possible DI from serious, spinal DI or from unrelated, compressive oligoneuropathies. The prognosis for peripheral manifestations is usually good.

Inner Ear

The inner ear appears to be uniquely vulnerable to DI, particularly in technical diving [11,12,108,109]. There are four dominant theories for the clinical and pathological findings associated with DI of the inner ear. They are: (1) explosive / hemorrhagic injuries; (2) counter diffusion; (3) gas induced osmosis; and (4) vascular emboli [94,95]. *Explosive / hemorrhagic injuries:* In 1980, Landolt *et al* found hemorrhage in the inner ear of squirrel monkeys subjected to rapid decompression from saturation [110]. Three years later Venter was able to show an implosive injury of the semi-circular canals as the cause for the hemorrhage [111]. The mechanism, they proposed, was one of gas accumulation in temporal bone osteoclast pockets that then explosively ruptured into the inner ear during decompression. Money subsequently found evidence of the same type of injury in a diver who died 56 days after left inner ear DI [112]. This mechanism is plausible for deep mixed gas diving, but less convincing for inner ear DI following shallower dives [11,12]. *Embolism:* Blood supply to the inner ear is end arterial and consequently prone to embolic or vascular injury. Embolic disturbance has been shown in cardiac bypass surgery, but how this relates to diving remains uncertain [113]. *Counter-diffusion:* This theory entertains the possibility that counter-diffusion can occur under conditions where the inert gas in the middle ear differs from that in the breathing mixture. Diffusion through the round or oval window could result in accumulation of inert gas with bubbling, resulting in deafness or vertigo. This theory has developed due to a high prevalence of inner ear DI in helium-oxygen and mixed gas divers [114]. Counter-diffusion may also occur within the partitions of the inner ear itself. The vascularity of the inner ear is not uniform: the *stria vascularis* supplies the endolymph directly and from there inert gas would diffuse to the perilymph. Therefore, with gas switching, it is possible that the endolymph could rapidly take up a new inert gas, e.g. helium, before the perilymph has had time to eliminate the former inert gas. Bubbles could then form within the endolymph with disruption of function and even rupture [114]. *Gas-induced Osmosis:* Finally, by a similar

mechanism, inert gas accumulation in the endolymph could result in gas-induced osmosis: an osmotic fluid shift towards the endolymph resulting in a form of *hydrops endolymphaticus* analogous to Meniere's disease [115].

Skin

Skin bends or DI of the skin may present in a variety of ways with varying etiologies and clinical significance. *"Diver's Lice"*: This erythematous rash usually presents in association with dry chamber dives or the use of dry suits. The hypothesis is that inert gas enters the skin directly and causes dermal bubbles with histamine release upon decompression. The condition can be avoided by not having gas skin contact, or by heating the skin during decompression. It is not considered serious in the absence of other findings, and does not require recompression. *Cutis Marmorata:* A more significant form of DI of the skin is called *cutis marmorata* or skin marbling. Although the condition itself is benign, its association with pulmonary and neurological DI requires careful consideration. Experimental work in pigs has shown that this pattern of illness is associated with venous congestion, inflammation, leukocyte adherence and endothelial damage [100]. No bubbles have been visualized, but the manifestations usually resolve promptly with recompression. *Counter-diffusion*: A rare type of DI may result from exposure to different inert gases, such as helium and nitrogen. Diffusion-related gas accumulation may occur when one gas is in contact with the skin, while another is breathed [116,117].

Musculoskeletal

Some of the first descriptions of DI or "the bends" involved painful joints [118]. Even today, musculoskeletal pain it is the most common presenting complaint [23]. There are two bone and joint conditions associated with DI: acute musculoskeletal DI and dysbaric osteonecrosis. *Acute Musculoskeletal DI:* Although joints, and musculo-tendinous attachments have similar blood supply, it is noteworthy that 'bends' pain only appears to affect long bones of the appendicular skeleton – not the axial skeleton. Adult long bones contain a fatty marrow cavity that could be a reservoir for inert gas and predispose to DI. Axial bones largely contain hemopoietic tissue which appears to be unaffected by decompression. Another interesting feature of 'bends' pain is that it is influenced by pre-morbid hyperbaric activity. In a review of more than 19,000 cases, Sowden found that bounce divers and pilots primarily developed shoulder pain, whereas saturation divers and caisson workers developed knee pain [119]. There are many theories but little evidence to explain this phenomenon. There are four theories for bubble-related pain in bones and joints. They involve stretching of nerve endings or inflammation occurring (1) within joints; (2) around the joints, such as within tendons and muscle; (3) within bone, due to gas expansion within fatty marrow, the medullary cavity and bone sinusoids (a phenomenon also associated with cancer-pain), and; (4) as a result of referred pain, either due to an injury to the nerves or nerve roots associated with the joint, or due to a generalized release of inflammatory modulators with flu-like symptoms and poly-arthralgia. Intra- and periarticular pain associated with decompression can usually be localized and is of a non-serious nature. There is a trend towards treating these conservatively although they respond well and promptly to recompression. Referred pain is part of the neurological spectrum of DI that has been considered elsewhere. What remains, is medullary pain. The discovery of sinusoid innervation has led to the concept of a venous congestive mechanism for cancer and osteoarthritic bone pain [120,121]. This sinusoid congestion pain theory is also attractive as an explanation for 'bends' pain as it addresses several clinical phenomena: (1) the deep, poorly localized, boring pain; (2) relief achieved by the local application of pressure (e.g., inflating a BP cuff over the affected area thereby achieving temporary relief as the inert gas bubbles are compressed a transient increase in tissue pressure); and (3) a gravity-related distribution of manifestations in the various patient subgroups. Although there is no scientific association between

medullary pain and dysbaric osteonecrosis, it is usually viewed as a more serious form of musculoskeletal DI and recompression is recommended.

Dysbaric Osteonecrosis (DO): DO appears to affect predominantly saturation divers and caisson workers[122-125], although cases have been reported in military and recreational divers, sometimes years after even a single exposure [123,124,126-129]. Again it appears to be the appendicular skeleton that is at risk, particularly the humoral head, femoral head and juxta-articular area of the distal femur and proximal tibia[123,127]. Lesions in proximity to the femoral and humeral head may be symptomatic and may eventually become disabling whereas femoral and tibial shaft lesions remain asymptomatic. The question remains why it is only certain types of diving that predispose to this disease, and why these areas are so uniquely vulnerable [123,126,127,130].

Recompression & HBO2:

For the purpose of clarity it is necessary to state that, although HBO2 is a form of recompression (i.e., elevation of ambient pressure), all recompression is not HBO2, technically speaking (i.e., breathing 100% oxygen under increased ambient pressure in a hyperbaric chamber): HBO2, by definition, is limited to 100% oxygen breathing between 1.5 and 3 atmospheres absolute; recompression can involve any pressure and any oxygen-gas mixture.

Depending on delay to recompression and the respective tissues affected by DI, recompression or HBO2 may offer different therapeutic effects: Generally speaking, prompt recompression commenced shortly after appearance of first DI manifestations is a direct, *bubble*-directed therapy. After 6 to 12 hours, recompression is still indicated, but by then it becomes more of an indirect, *bubble-damage*-directed therapy (i.e., anti-ischemic, anti-hypoxic, anti-reperfusion, anti-lipid peroxidation, anti-edema, anti-apoptotic, and anti-inflammatory).

Recompression on oxygen has been proposed for the treatment of DI in humans since 1939 [131]. It has been used extensively in animal models of DCI with superior outcomes[46,132-135].

Most hyperbaric facilities initially treat DI using the US Navy Treatment Table 5 (USN TT5) for mild, rapidly-resolving, joint pain-only DI or US Navy Treatment Table 6 (USN TT6) or its equivalent, with or without extensions, for all other forms of DI . USN TT5 has fallen into disfavor as a primary treatment due to several cases where undiagnosed neurological manifestations were inadvertently undertreated resulting in legal claims. Most DI cases also arrive at the recompression facilities hours after the onset of symptoms. As such, the secondary aspects of bubbles – such as inflammation – are more significant and less likely to respond adequately, and more likely produce a recurrence of symptoms when a short treatment is used. However, depending on the severity, it is quite acceptable to treat residual symptoms with USN TT5, USN TT6 or even HBO2 tables (e.g., USN TT9 or its equivalent) for the sake of convenience. More sophisticated recompression schedules (i.e., pressures greater than 3 atmospheres or gas mixtures) are recommended only under special conditions [136]. These may include situations where there is further deterioration of DI manifestations after recompression to 2.8 atmospheres (i.e., the diver is already on USN TT6); or if DI occurred due to very deep, technical diving [1,40,137]. Other situations may include inner-ear DI associated with Trimix (i.e., oxygen, nitrogen and helium mixtures) that are sometimes treated with 50:50 oxy-helium at 4 atmospheres on the COMEX 30 table [138], and the 6A1M table (i.e., a progressive recompression schedule starting on USN TT6 for 20 minutes, then transferring to Comex 30, and then USN TT4 due to ongoing deterioration) for e.g., severe spinal DI [139]. Saturation diving-related DI, requires completely different management [37] . However, for typical, surface-oriented, air or nitrogen-oxygen diving, there is no definitive evidence that HBO2 at 2.8 ATA in the form of USN TT6 (with or without extensions) is less effective than recompression at greater pressures and on different mixtures [1,40], although a recent workshop by the South Pacific Underwater Medicine Society

has issued conditional recommendations for the Comex 30 oxy-helium table [140,141]. There are very few rigorously-performed, comparative trials for different recompression schedules [1,40].

Delay to treatment potentially affects DI outcomes [35,36,47,142-146]: residual DI symptoms increase the longer recompression is delayed [36,147,148]. Nevertheless, good results are still recorded up to 12 hours after serious DI [144], and the routine use of recompression to 2.8 atmospheres on oxygen (i.e., USN TT6) is recommended even when the delay has been several days, though generally less than 1-month [1,41,149].

In-water recompression on oxygen may be justified in special situations when transport to a recompression facility is impractical, but on the condition that it can be performed safely [150-155]. The use of conservative treatment (i.e., non-recompression) may also be reasonable in mild, non-progressive cases of DI, if neurological manifestations have been excluded by proper medical assessment [154,156-161]. New therapies and technologies utilizing neuroprotection, perfluorocarbons or extracorporeal bypass for severe pulmonary problems are still under investigation [51,162-164].

- **Evidence-based review of HBO2 use:**

Essential Summary:

Medical literature is replete with animal studies, human cases, and case series of recompression for DI. Recompression has been considered the standard of care for DI for the past 100 years. As such, controlled trials on treatment of DI without recompression would be ethically questionable in much the same way a no-HBO2 trial for gas gangrene would be. However, it is ethically possible to compare DI outcomes utilizing different recompression pressures, durations, gas-mixtures and adjunctive therapies. The difficulty, though, is that DI is relatively rare and its presentation and evolution are highly variable. As such, achieving matched populations is challenging and requires an international, multi-centre trial. Even then, for this to be successful there would need to be a universally agreed, rigorously standardised, detailed categorization system for DI type and severity. Several attempts have been made and the process is ongoing. Unfortunately, not unlike the situation with multiple sclerosis, standardised assessment of DI has remained an elusive goal. One of the most promising adjunctive treatments for DI, lidocaine, eventually succumbed to the impracticability of achieving the required number of subjects at this level of consistency. Unless the situation changes, significant progress is unlikely.

The current state of evidence-based treatment for DI is summarised in the Cochrane Database for Systematic Review which has been updated twice [165-167]. The Cochrane review process included CENTRAL (The Cochrane Library, October 2011); MEDLINE (1966 to October 2011); CINAHL (1982 to October 2011); EMBASE (1980 to October 2011); the Database of Randomised Controlled Trials in Hyperbaric Medicine (October 2011); as well as hand-searched journals and texts. All randomized controlled trials – irrespective of language – that compared the outcome of any recompression schedules or adjunctive therapies with a standard recompression schedule, were included. The authors extracted the data independently and each trial was reviewed for internal validity. Ultimately, only two randomized controlled trials satisfied the inclusion criteria with a total of 268 patients [40,49,168]. Pooling of data was not possible, however, as the trials were completely different.

The risk of bias for the oxygen vs. oxy-helium trial was indeterminate as study was presented as an abstract [168]. The odds of multiple recompressions were lower with oxy-helium compared to an extended USN TT6 (Relative Risk [RR]: 0.56; 95% CI: 0.31-1.00; p = 0.05).

The trial comparing the effect of tenoxicam on recompression for pain-only DI was considered low risk for bias [49]. The impact of adding a non-steroidal anti-inflammatory drug (tenoxicam) to routine recompression therapy did not show improved outcome at 6 weeks (RR: 1.04; 95% CI: 0.90-1.20, p =

0.58), but the average number of recompressions was lowered from 3 to 2 when tenoxicam was added ($p = 0.01$; 95% CI: 0-1).

In summary, the author's conclusions were that, although recompression therapy is considered standard of care for the treatment of DI, there is no randomized controlled trial evidence for its use. The addition of a non-steroidal anti-inflammatory drug (NSAID) for pain-only DI, and the use of oxy-helium might reduce the number of recompressions required. However, neither improved the odds of recovery. The modest number of patients also imposes limitations. A rigorous, large randomized trial is recommended to assess different breathing gases and pressure profiles during recompression therapy within a framework of cost-effectiveness. Until then, either USN TT6 or oxy-helium tables remain appropriate for the initial treatment of DI in surface-oriented diving. Deeper tables should be used with caution and only in hyperbaric facilities capable of providing prolonged life-support.

Additional Background and summary of the current ECHM & UHMS Guidelines for recompression treatment and adjunctive treatment of DI [169,170]

- In 1994, the European Committee for Hyperbaric Medicine (ECHM) organized its first European Consensus Conference, where DI was one of the topics [3]. In 1996 a second, more specific Consensus Conference was organized [4], the theme of which was "The Treatment of Decompression Accidents in Recreational Diving". Their recommendations regarding recompression were as follows:
    - Decompression accidents are true medical emergencies that should receive the benefit of dedicated treatment in *specialized centres* as soon as possible. A *specialized centre* is considered a hospital-based recompression facility with permanent and adequately trained medical and paramedical staff.
    - After immediate stabilization and medical evaluation, the victims of a decompression accident should be immediately directed to the closest specialized centre – (*ECHM Type 1 recommendation: strongly recommended*)
    - In-water recompression should never be performed as the initial recompression - (*ECHM Type 1 recommendation: strongly recommended*)
    - Hyperbaric treatment, commenced as soon as possible, using 100% oxygen at pressures not exceeding 2.8 atmospheres absolute (ATA), achieves very good results in more than 80% of recreational DI cases.
    - The administration of adjunctive fluid therapy is usually recommended by diving/hyperbaric medicine specialists in Europe (*ECHM Type 1 recommendation: strongly recommended*), whereas the role of other drugs, such as steroids and anti-coagulants remains controversial *(Type 3: recommendation: optional)*.
    - Minor decompression accidents (pain only) can be treated with oxygen recompression tables at 18 meters depth maximum. (Note: this is based on the experience and the good results observed in commercial diving) - (*ECHM Type 1 recommendation: strongly recommended*)
    - For more serious decompression accidents (e.g., neurological and vestibular accidents), there are presently two acceptable protocols:
        - Oxygen recompression tables at 2.8 ATA (with or without extensions)
        - Hyper-oxygenated breathing mixtures at 4.0 ATA (50:50 oxy-helium or Nitrox as per Comex 30 Table or derivatives)
        - As for pressures exceeding 4 ATA: In lieu of scientific evidence, no specific recommendations can be made at this stage regarding the optimal PiO_2 (i.e., the range of 1.26 ATA [i.e., Air] to 3.0ATA [i.e., 50:50 Nitrox] at 6 ATA) nor on the preferred choice of diluent inert gas. Familiarity, availability and experience may affect decisions, but under no circumstances should the lack of availability of gas mixtures preclude or delay treatment by means of "low pressure oxygen tables" - (*ECHM Type 1 recommendation: strongly recommended*).
    - Compression to 6 ATA in case of Cerebral Arterial Gas Embolism is optional, with the proviso that this be performed using mixed gas (50:50 or 60:40 Nitrox) and not compressed air and only if the delay to recompression is no more than a few hours - (*ECHM Type 3 recommendation: optional*). Again there are no data guiding the maximum p_iO_2 or the maximum delay within which this therapy is still considered appropriate.

- In case of severe, persistent clinical signs, during the initial recompression, the continuation of treatment with a therapeutic saturation table may be useful – (*ECHM Type 3 recommendation: optional*)
- All decompression accidents should recorded in a standardized way for the purpose of compiling an epidemiological database.

- Adjunctive therapy (including first aid) began to be emphasized in the late 60's and 1970's. Then, in 1979 the Undersea Medical Society organized a workshop on the management of severe and complicated cases of DI, where the importance of hydration, steroids, heparin, aspirin and other agents were discussed [41,50,51,149,165]. Following the ECHM Consensus Conference in 2004, and after extensive presentations by leading international experts, the two International Juries brought forth the recommendations which have formed the current standards for the treatment of DI in Europe: The 7th ECHM Consensus Recommendations for Adjunctive Therapy and First Aid for DI are therefore as follows: [170]
  - On-site 100% oxygen first aid treatment (*ECHM Type 1*)
  - On-site fluid administration – oral (if appropriate) or IV – (*ECHM Type 1*)
  - Therapeutic recompression must be initiated as soon as possible (*ECHM Type 1*)
  - Adjunctive pharmacological treatment remain controversial (*ECHM Type 3*) but:
    - I.V. crystalloid fluid therapy is recommended (*ECHM Type 1*)
    - The use of steroids and anticoagulants is considered optional (*ECHM Type 3*)

Greater details of the ECHM 2004 Recommendations for Recompression & Adjunctive Treatment are summarised below in Table 1 [170]:

On Site		
First Aid	**Recommendation**	**Evidence level**
On Site First Aid – Oxygen 100%	Type 1	C
On Site First Aid – Fluids (oral)	Type 1	C
On Site First Aid – Fluids (IV)	Type 1	C
No In-Water Recompression	Type 1	C
Hospital-based Therapy		
HBO	**Recommendation**	**Evidence level**
Hyperbaric Tx Hyperoxygenated Tables	Type 1	C
Recompression with other Tables (USN 6A, Sat) for CAGE** or recalcitrant cases	Type 3	C
Fluids		
Fluid Therapy in General (Hospital Based)	Type 2	C
No Fluid Therapy D5W	Type 1	C
Fluid Therapy LR/crystalloids(Pain only/mild)	Type 2	C
Fluid Therapy LR/crystalloids (Chokes)	Type 2	B
Fluid Therapy LR/crystalloids (Neuro DCI)	Type 1	C
Fluid Therapy LR/crystalloids (AGE)	Type 2	B
Fluid Therapy Colloids (Pain)	Type 1	C
Fluid Therapy Colloids (Chokes)	Type 2	C
Fluid Therapy Colloids (Neuro)	Type 1	C
Fluid Therapy Colloids (AGE)	Type 2	C
Drug Therapy	**Recommendation**	**Evidence Level**
Life Support Drug Therapy	Type 1	C
Drug Therapy in General	Type 3	C
Aspirin	Type 3	C
NSAIDs (AGE and Chokes)	Type 3	C
NSAIDs (pain only & neurological)	Type 3	C
Anti-coagulants(AGE,Neurological)* Chokes)	Type 3	C
No Anticoagulants (pain only)	Type 1	C
Anticoagulants (DVT prevention leg immobility)*	Type 1	A
No Corticosteroids	Type 1	C
Lidocaine (AGE)	Type 2	B
Lidocaine (neuro DCS)	Type 3	C
No Lidocaine (pain only, chokes)	Type 1	C

* avoid complete decoagulation

** The use of USN 6A table should be limited to cases of CAGE caused by emergency ascent procedure without any previous compressed gas exposure leading to gas tissue supersaturation.

Table 1: ECHM 2004 Recommendations for Recompression & Adjunctive Treatment

- **Patients selection for HBO2**

The diagnosis of DI is based on a history of exposure to breathing compressed gas, and the appearance of clinical manifestations within 24-hours of the exposure [1,165]. Patients manifesting these manifestations may be selected for recompression or HBO2 [169,170]. Although the goal is to commence recompression as soon as possible, delays of several hours are not unusual, and there may be benefit in providing HBO2 even after several days [27,72].

- **Current protocol**

The current international consensus is that USN TT6 (4h45) should be used as the preferred initial treatment table for DI resulting from air or oxygen-nitrogen, surface-oriented diving [37,41,149,169,170].

For mild, non-neurological or joint-pain only DI, the shorter USN TT5 may be used if the delay to recompression has been brief (< 4 hours); if all pain-only or constitutional symptoms have disappeared completely within 10 minutes; and only if the presence of neurological DI manifestations have been

excluded by appropriate medical neurological examination. If not, the USN TT6 should be used as a minimum. USN TT5 is also appropriate for omitted decompression (i.e., violation of decompression schedules prior to the onset of probable DI) [37]. Minor decompression violations may be addressed adequately with 100% normobaric oxygen and oral rehydration.

If, on completion of the extended USN TT6 some residual neurological symptoms remain, additional recompression may be undertaken, typically within 4 to 24 hours depending on the situation [1,41,149,169]. If the residual neurological symptoms are significant, an additional 1 to 3 USN TT6's may be justified to achieve a clinical plateau. If there are neurological manifestations, extension of the table (up to 8h10) is appropriate. The option of using the COMEX 30 table has been mentioned previously [138].

The objective of recompression is to achieve the best, stable, functional level of recovery (i.e., mental-, psychomotor-, and bowel & bladder function), bearing in mind that compression and elimination of bubbles (which could be prompt if recompression is not delayed) may not necessarily reverse the bubble damage (e.g., bleeding, which may even be unresponsive to recompression or require time to heal).

Peer-review is recommended after 4 USN TT6's or more than 14 days of recompression therapy [169,170].

- **Cost impact**

The largest international experience with the cost of treatment of DI is that of Divers Alert Network [23]. On average treatment of DI approaches €3500 per case. This does not include the cost of transportation, aeromedical evacuation, hospitalization, and any special investigation.

- **Conclusion:**

Dysbaric Illness is generally considered a benign condition. If adequate treatment is started promptly, the success rate is in excess of 80 - 90%.

There is universal consensus that 100% oxygen should be administered immediately as the single most important first aid treatment of any DI case related to surface-oriented diving, and that rehydration is a very valuable first aid measure. Hyperbaric treatment should be started within the shortest possible delay from the onset of the first DI signs and symptoms.

Hyperbaric Treatment tables using 100% Oxygen at environmental pressures not exceeding 2.8 ATA ensure very good results in the vast majority of cases. There is no strong evidence that other more complex therapeutic schemes achieve better results in surface-oriented and particularly air diving.

For other forms of diving there are guidelines on the use of higher pressures and breathing gases other than 100% oxygen, but experience and appropriate infrastructure is required to perform this safely and effectively.

Although conclusive scientific evidence is lacking for many adjunctive modalities, the administration of fluid therapy is considered very important and generally recommended by diving and hyperbaric medicine specialists. The role of other drugs, such as steroids and anticoagulants, although widely used without any apparent adverse effects, is still controversial.

For neurological DI cases with significant residual deficits, continuation of hyperbaric oxygen therapy in combination with a dedicated rehabilitation protocol is considered important; there is growing scientific evidence that it can contribute significantly to achieving a better functional recovery.

The Consensus Conference System of the ECHM, over the last 10 years, has produced literature that is consistent with international evidence-based medical approaches on matters concerning diving medicine and the treatment of DI. These have now been adopted by the European Union Countries as the common standard of practice.

There are several important areas in need of research, namely: the relationship between gas separation and DI; the relationship between clinical symptoms and the severity of the disease; the relationship between initial clinical onset, treatment results and permanent sequelae; the reason for the large variation in individual susceptibility to DI; the life time of gas bubbles; and the actual incidence of DI. These questions will remain unanswered unless a focused, coordinated and concerted effort is made to solve them. It is hoped that Consensus Conferences and Workshops will continue to pave the way towards uniformity of practice and collaborative research efforts.

In closing, we:

- **recommend** the use of the supine position (*ECHM Type 2)*; 100% normobaric oxygen first aid (*ECHM Type 1*); intravenous fluid resuscitation with non-glucose containing crystalloid solutions (*ECHM Type 1*); hyperbaric oxygen therapy / recompression therapy tables (USN TT5 & 6 or equivalent) for the initial treatment of DI (*ECHM Type 1*); appropriate HBO2 / recompression tables for residual manifestations of DI (*ECHM Type 1*); and the use of low-molecular weight heparin for the prophylaxis of deep venous thrombosis for immobile or paralysed cases of DI (*ECHM Type 1*);
- **consider it reasonable** to use lignocaine / lidocaine and oxy-helium recompression tables for serious neurological DI (*ECHM Type 2*); and oral tenoxicam for appropriately selected DI cases (*ECHM Type 2*).

References

1. Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. *Lancet* 2011; **377**(9760): 153-64.
2. Marroni A. Clinical Aspects of Decompression Disorders. In: Bakker DJ, Cramer FS, eds. Hyperbaric Surgery - Perioperative Care. Flagstaff, AZ: Best Publishing Co; 2002: 177-206.
3. Marroni A. Decompression Illness, Final Report. In: Wattel F, Mathieu D, editors. First European Consensus Conference on Hyperbaric Medicine European Committee for Hyperbaric Medicine; 1994; University of Lille.: C.R.A.M. Nord-Picardie, Sécurité Social.; 1994. p. 28.
4. Francis TJR. Describing Decompression Sickness. In: Francis TJR, Smith DJ, editors. Fourty Second Undersea and Hyperbaric Medical Society Workshop: Describing Decompression Sickness; 1990 May 1991; Institute of Naval Medicine Alverstoke, Gosport, Hampshire, UK: Undersea and Hyperbaric Medical Society; 1990. p. 6-14.
5. Golding FC, Griffiths P, Hempleman HV, Paton WDM, Walder DN. Decompression sickness during construction of the Dartford tunnel. *Br J Ind Med* 1960; **17**: 167-80.
6. Moir EW. Tunnelling by compressed air. *Journal of the Society of Arts* 1896; (44): 567.
7. Moon RE. Classification of the decompression disorders: time to accept reality. *Undersea Hyperb Med* 1997; **24**(1): 2-4.
8. Pol M, Wattelle M. Memoire Sur Les Effets De La Compression De L'Air Applique Au Creusement Des Puits A Houille. *Ann D'Hygiene Publique Et De Medicine Legale* 1854; **Second Series**(1): 241.
9. Triger M. Letter to Monsieur Arago. *Comptes rendus de l'academie des sciences* 1845; **20**: 445-9.
10. Thom SR, Bennett M, Banham ND, et al. Association of microparticles and neutrophil activation with decompression sickness. *J Appl Physiol (1985)* 2015; **119**(5): 427-34.
11. Mitchell SJ, Doolette DJ. Pathophysiology of inner ear decompression sickness: potential role of the persistent foramen ovale. *Diving Hyperb Med* 2015; **45**(2): 105-10.
12. Mitchell SJ, Doolette DJ. Selective vulnerability of the inner ear to decompression sickness in divers with right-to-left shunt: the role of tissue gas supersaturation. *J Appl Physiol (1985)* 2009; **106**(1): 298-301.
13. Vann RD. Mechanisms and risks of decompression. In: Bove AA, ed. Bove and Davis' diving medicine. 4th Edn ed. Philidelphia, PA: Saunders; 2004: 127–64.
14. Neuman TS. Arterial gas embolism and decompression sickness. *News Physiol Sci* 2002; **17**: 77-81.
15. Buttolph TB, Dick EJ, Jr., Toner CB, et al. Cutaneous lesions in swine after decompression: histopathology and ultrastructure. *Undersea Hyperb Med* 1998; **25**(2): 115-21.
16. Moon RE, Vann RD, Bennett PB. The physiology of decompression illness. *Sci Am* 1995; **273**(2): 70-7.
17. Benton PJ, Woodfine JD, Westwood PR. Arterial gas embolism following a 1-meter ascent during helicopter escape training: a case report. *Aviat Space Environ Med* 1996; **67**(1): 63-4.
18. Kumar KV, Waligora JM, Calkins DS. Threshold altitude resulting in decompression sickness. *Aviat Space Environ Med* 1990; **61**(8): 685-9.
19. Gregg PJ, Walder DN. Caisson disease of bone. *Clin Orthop* 1986; (210): 43-54.
20. Cooper PD, Van den Broek C, Smart DR. Hyperbaric chamber attendant safety II: 14-year health review of multiplace chamber attendants. *Diving Hyperb Med* 2009; **39**(2): 71-6.
21. Doolette DJ, Goble SJ, Pirone CJ. Health outcome of hyperbaric chamber inside attendants following compressed-air exposure and oxygen decompression. *SPUMS J* 2004; **34**: 63-7.

22. Temple DJ, Ball R, Weathersby PK, Parker EC, Survanshi S. The dive profi les and manifestations of decompression sickness cases after air and nitrogen-oxygen dives. Volume I. Naval Medical Research Center, Washington, DC: NMRC, 1999.
23. Buzzacott P, Trout BM, Caruso JL, et al. DAN Annual Diving Report 2012-2015 Edition. Durham, NC., 2015.
24. Ladd G, Stepan V, Stevens L. The Abacus Project: establishing the risk of recreational scuba death and decompression illness. *SPUMS J* 2002; **32**: 124–28.
25. Bason R, Yacavone D. Decompression sickness: U.S. Navy altitude chamber experience 1 October 1981 to 30 September 1988. *Aviat Space Environ Med* 1991; **62**(12): 1180-4.
26. Chisholm DM, Billings CE, Bason R. Behavior of naive subjects during decompression: an evaluation of automatically presented passenger oxygen equipment. *Aerosp Med* 1974; **45**(2): 123-27.
27. Bendrick GA, Ainscough MJ, Pilmanis AA, Bisson RU. Prevalence of decompression sickness among U-2 pilots. *Aviat Space Environ Med* 1996; **67**(3): 199-206.
28. Jersey SL, Jesinger RA, Palka P. Brain magnetic resonance imaging anomalies in U-2 pilots with neurological decompression sickness. *Aviat Space Environ Med* 2013; **84**(1): 3-11.
29. Pickard BJ. Altitude decompression sickness in a pilot wearing a pressure suit above 70,000 feet. *Aviat Space Environ Med* 2003; **74**(4): 357-9.
30. Vann RD. Exercise and circulation in the formation and growth of bubbles. In: Brubakk A, Hemmingsen BB, Sundnes G, eds. Supersaturation and bubble formation in fluids and organisms. Trondheim: Royal Norwegian Society; 1989b: 235-58.
31. Van Der Aue OE, Kellar RJ, Brinton ES. The effect of exercise during decompression from increased barometric pressures on the incidence of decompression sickness in man. Washington, DC: US Navy Experimental Diving Unit,, 1949.
32. Dunford RG, Vann RD, Gerth WA, et al. The incidence of venous gas emboli in recreational diving. *Undersea Hyperb Med* 2002; **29**(4): 247-59.
33. Webb JT, Kannan N, Pilmanis AA. Gender not a factor for altitude decompression sickness risk. *Aviat Space Environ Med* 2003; **74**(1): 2-10.
34. St Leger Dowse M, Bryson P, Gunby A, Fife W. Comparative data from 2250 male and female sports divers: diving patterns and decompression sickness. *Aviat Space Environ Med* 2002; **73**(8): 743-9.
35. Haas RM, Hannam JA, Sames C, et al. Decompression illness in divers treated in Auckland, New Zealand, 1996-2012. *Diving Hyperb Med* 2014; **44**(1): 20-5.
36. Xu W, Liu W, Huang G, Zou Z, Cai Z, Xu W. Decompression illness: clinical aspects of 5278 consecutive cases treated in a single hyperbaric unit. *PLoS One* 2012; **7**(11): e50079.
37. US Navy Diving Manual. Revision 6. Washington, DC: Naval Sea Systems Command: Navy Department. Diving Medicine and Recompression Chamber Operations; 2008.
38. Francis TJ, Pearson RR, Robertson AG, Hodgson M, Dutka AJ, Flynn ET. Central nervous system decompression sickness: latency of 1070 human cases. *Undersea Biomed Res* 1988; **15**(6): 403-17.
39. Freiberger JJ, Denoble PJ, Pieper CF, Uguccioni DM, Pollock NW, Vann RD. The relative risk of decompression sickness during and after air travel following diving. *Aviat Space Environ Med* 2002; **73**(10): 980-4.
40. Bennett M, Mitchell SJ, Lehm JP, Wasiak J. Recompression and adjunctive therapy for decompression illness: a systematic review of randomised controlled trials. *Diving Hyperb Med* 2008; **38**(2): 91-8.
41. Moon RE. Hyperbaric oxygen treatment for decompression sickness. *Undersea Hyperb Med* 2014; **41**(2): 151-7.
42. Dunford RG, Mejia EB, Salbador GW, Gerth WA, Hampson NB. Diving methods and decompression sickness incidence of Miskito Indian underwater harvesters. *Undersea Hyperb Med* 2002; **29**(2): 74-85.
43. Doolette DJ, Gault KA, Gutvik CR. Sample size requirement for comparison of decompression outcomes using ultrasonically detected venous gas emboli (VGE): power calculations using Monte Carlo resampling from real data. *Diving Hyperb Med* 2014; **44**(1): 14-9.
44. Gempp E, Blatteau JE. Risk factors and treatment outcome in scuba divers with spinal cord decompression sickness. *J Crit Care* 2010; **25**(2): 236-42.
45. Kelleher PC, Pethybridge RJ, Francis TJ. Outcome of neurological decompression illness: development of a manifestation-based model. *Aviat Space Environ Med* 1996; **67**(7): 654-8.
46. Francis TJ, Dutka AJ, Flynn ET. Experimental determination of latency, severity, and outcome in CNS decompression sickness. *Undersea Biomed Res* 1988; **15**(6): 419-27.
47. Lee J, Kim K, Park S. Factors associated with residual symptoms after recompression in type I decompression sickness. *Am J Emerg Med* 2015; **33**(3): 363-6.
48. Longphre JM, Denoble PJ, Moon RE, Vann RD, Freiberger JJ. First aid normobaric oxygen for the treatment of recreational diving injuries. *Undersea Hyperb Med* 2007; **34**(1): 43-9.
49. Bennett M, Mitchell S, Dominguez A. Adjunctive treatment of decompression illness with a non-steroidal anti-inflammatory drug (tenoxicam) reduces compression requirement. *Undersea Hyperb Med* 2003; **30**(3): 195-205.
50. Adjunctive Therapy for Decompression Illness (DCI): Summary of Undersea and Hyperbaric Medical Society Guidelines. Bethesda: UHMS; 2002.
51. Moon RE. Adjunctive therapy for decompression illness: a review and update. *Diving Hyperb Med* 2009; **39**(2): 81-7.
52. Weenink RP, Hollmann MW, Zomervrucht A, van Ooij PJ, van Hulst RA. A retrospective cohort study of lidocaine in divers with neurological decompression illness. *Undersea Hyperb Med* 2014; **41**(2): 119-26.
53. Cogar WB. Intravenous lidocaine as adjunctive therapy in the treatment of decompression illness. *Ann Emerg Med* 1997; **29**(2): 284-6.
54. Mitchell SJ, Pyle R, Moon RE. Therapy for decompression illness. In: Vann RD, Mitchell SJ, Denoble PJ, Anthony TG, eds. Technical diving proceedings of the divers alert network 2008 January 18–19 conference Durham, NC: Divers Alert Network; 2009: 178–203.
55. Waligora JM, Horrigan DJ, Conkin J. The effect of extended O2 pre-breathing on altitude decompression sickness and venous gas bubbles. *Av Space Environ Med* 1987; **58**(9, Sect. II): A10-A112.
56. Smith-Silvertsen J. The origin of intravascular bubbles produced by decompression of rats killed prior to hyperbaric exposure. In: Lambertsen CJ, ed. Underwater Physiology V. Bethesda: FASEB; 1976: 303-9.

57. Leitch DR, Green RD. Pulmonary barotrauma in divers and the treatment of cerebral arterial gas embolism. *Aviat Space Environ Med* 1986; 57(10 Pt 1): 931-8.
58. Malhotra MS, Wright HC. The effects of a raised intrapulmonary pressure on the lungs in fresh unchilled cadavers. *J Path Bact* 1961; **82**: 198-202.
59. Harker CP, Neuman TS, Olson LK, Jacoby I, Santos A. The roentgenographic findings associated with air embolism in sport scuba divers. *J Emerg Me.* 1993; **11**: 443-9.
60. Wilmshurst PT, Morrison WL, Walsh KP. Comparison of the size of persistent foramen ovale and atrial septal defects in divers with shunt-related decompression illness and in the general population. *Diving Hyperb Med* 2015; **45**(2): 89-93.
61. Tremolizzo L, Malpieri M, Ferrarese C, Appollonio I. Inner-ear decompression sickness: 'hubble-bubble' without brain trouble? *Diving Hyperb Med* 2015; **45**(2): 135-6.
62. Smart D, Mitchell S, Wilmshurst P, Turner M, Banham N. Joint position statement on persistent foramen ovale (PFO) and diving. South Paci fi c Underwater Medicine Society (SPUMS) and the United Kingdom Sports Diving Medical Committee (UKSDMC). *Diving Hyperb Med* 2015; **45**(2): 129-31.
63. Kemper TC, Rienks R, van Ooij PJ, van Hulst RA. Cutis marmorata in decompression illness may be cerebrally mediated: a novel hypothesis on the aetiology of cutis marmorata. *Diving Hyperb Med* 2015; **45**(2): 84-8.
64. Reiter R, Bertog SG, Vaskelyte L, et al. PFO closure: rational, procedure and devices. *Minerva Cardioangiol* 2014; **62**(1): 83-97.
65. Sykes O, Clark JE. Patent foramen ovale and scuba diving: a practical guide for physicians on when to refer for screening. *Extrem Physiol Med* 2013; **2**(1): 10.
66. Hallenbeck JM, Obrenovitch T, Kumaroo K, Thompson C, Leitch DR. Several new aspects of bubble-induced central nervous system injury. *Philos Trans R Soc Lond B Biol Sci* 1984; **304**(1118): 177-84.
67. Warren BA, Philp RB, Inwood MJ. The ultrastructural morphology of air embolism: platelet adhesion to the interface and endothelial damage. *Br J Exp Pathol* 1973; **54**(2): 163-72.
68. Broome JR. Aspects of neurological decompression illness: a view from Bethesda. *J R Nav Med Serv* 1995; **81**(2): 120-6.
69. Eckenhoff RG, Hughes JS. Hematologic and hemostatic changes with repetitive air diving. *Aviat Space Environ Med* 1984; **55**(7): 592-7.
70. Hills BA. Mechanical vs. ischemic mechanisms for decompression sickness. *Aviat Space Environ Med* 1979; **50**(4): 363-7.
71. Balestra C, Germonpre P, Marroni A. Intrathoracic pressure changes after Valsalva strain and other maneuvers: implications for divers with patent foramen ovale. *Undersea Hyperb Med* 1998; **25**(3): 171-4.
72. Boussuges A, Blanc P, Molenat F, Bergmann E, Sainty JM. Haemoconcentration in neurological decompression illness. *Int J Sports Med* 1996; **17**(5): 351-5.
73. Boussuges A, Succo E, Juhan-Vague I, Sainty JM. Activation of coagulation in decompression illness. *Aviat Space Environ Med* 1998; **69**(2): 129-32.
74. Levin LL, Stewart GJ, Lynch PR, Bove AA. Blood and blood vessel wall changes induced by decompression sickness in dogs. *J Appl Physiol* 1981; **50**(5): 944-9.
75. Philp RB, Gowdey CW. Platelets as an etiological factor in experimental decompression sickness. *J Occup Med* 1969; **11**(5): 257-8.
76. Lehto VP, Kantola I, Tervo T, Laitinen LA. Ruthenium red staining of blood-bubble interface in acute decompression sickness in rat. *Undersea Biomed Res* 1981; **8**(2): 101-11.
77. Lehto VP, Laitinen LA. Scanning and transmission electron microscopy of the blood-bubble interface in decompressed rats. *Aviat Space Environ Med* 1979; **50**(8): 803-7.
78. Philp RB, Inwood MJ, Warren BA. Interactions between gas bubbles and components of the blood: implications in decompression sickness. *Aerosp Med* 1972; **43**(9): 946-53.
79. Philp RB. A review of blood changes associated with compression-decompression: relationship to decompression sickness. *Undersea Biomed Res* 1974; **1**(2): 117-50.
80. Martin KJ, Nichols G. Observations on platelet changes in man after simulated diving. *Aerosp Med.* 1972; **43**: **827-30**.
81. Philp RB, Bennett PB, Andersen JC, et al. Effects of aspirin and dipyridamole on platelet function, hematology, and blood chemistry of saturation divers. *Undersea Biomed Res* 1979; **6**(2): 127-46.
82. Ersson A, Linder C, Ohlsson K, Ekholm A. Cytokine response after acute hyperbaric exposure in the rat. *Undersea Hyperb Med* 1998; **25**(4): 217-21.
83. Stransky A, Szereda-Przestaszewska M, Widdicombe JG. The effects of lung reflexes on laryngeal resistance and motoneurone discharge. *J Physiol* 1973; **231**: 417-38.
84. Molvaer OI, Natrud E. Ear damage due to diving. *Acta Otolaryngol Suppl* 1979; **360**: 187-9.
85. Kitano M, Hayashi K. Acute decompression sickness. *Acta Pathol Jap* 1981; **31**: 269-76.
86. Wisloff U, Richardson RS, Brubakk AO. Exercise and nitric oxide prevent bubble formation: a novel approach to the prevention of decompression sickness? *J Physiol* 2004; **555**(Pt 3): 825-9.
87. Germonpre P, Dendale P, Unger P, Balestra C. Patent foramen ovale and decompression sickness in sports divers. *J Appl Physiol* 1998; **84**(5): 1622-6.
88. Wilmshurst P, Allen C, Parish T. Incidence of decompression illness in amateur scuba divers. *Health Trends* 1994; **26**(4): 116-8.
89. Francis TJR. The pathophysiology of decompression sickness. In: Bennett PB, Moon RE, eds. Diving accident management: UHMS; 1990: 38-56.
90. Boycott AE, Damant GCC. Experiments on the influence of fatness on susceptibility to caisson disease. *J Hyg* 1908; **8**: 445-56.
91. Francis TJ, Pezeshkpour GH, Dutka AJ. Arterial gas embolism as a pathophysiologic mechanism for spinal cord decompression sickness. *Undersea Biomed Res* 1989; **16**(6): 439-51.
92. Neuman TS, Bove AA. Severe refractory decompression sickness resulting from combined no-decompression dives and pulmonary barotrauma: type III decompression sickness. . In: Bove AA, Bachrach AJ, Greenbaum Jr LJ, editors. *9th International Symposium on Underwater and Hyperbaric Physiology*. p 1987; Bethesda, MD: UHMS; 1987.
93. Neuman TS, Bove AA. Combined arterial gas embolism and decompression sickness following no-stop dives. *Undersea Biomed Res* 1990; **17**(5): 429-36.

94. Neuman TS, Hallenbeck JM. Barotraumatic cerebral air embolism and the mental status examination: a report of four cases. *Ann Emerg Med* 1987; **16**(2): 220-3.
95. Buzzacott P, Lambrechts K, Mazur A, et al. A ternary model of decompression sickness in rats. *Comput Biol Med* 2014; **55**: 74-8.
96. Batson O. The function of the vertebral veins and their role in the spread of metastases. *Ann Surg* 1940; **112**: 138-49.
97. Hallenbeck JM. Cinephotomicrography of dog spinal vessels during cord-damaging decompression sickness. *Neurology* 1976; **26**(2): 190-.
98. Hallenbeck JM, Bove AA, Elliott DH. Mechanisms underlying spinal cord damage in decompression sickness. *Neurology* 1975; **25**(4): 308-16.
99. Hallenbeck JM, Elliott DH, Bove AA. Decompression sickness studies in the dog. In: Lambertsen CJ, ed. Underwater Physiology V. Bethesda: Fed Am Soc Exp Biol; 1975
100. Hughes JT. Venous infarction of the spinal cord. *Neurology* 1971; **21**(8): 794-800.
101. Francis TJ, Griffin JL, Homer LD, Pezeshkpour GH, Dutka AJ, Flynn ET. Bubble-induced dysfunction in acute spinal cord decompression sickness. *J Appl Physiol* 1990; **68**(4): 1368-75.
102. Hills BA, James PB. Spinal decompression sickness: mechanical studies and a model. *Undersea Biomed Res* 1982; **9**(3): 185-201.
103. Francis TJ, Pezeshkpour GH, Dutka AJ, Hallenbeck JM, Flynn ET. Is there a role for the autochthonous bubble in the pathogenesis of spinal cord decompression sickness? *J Neuropathol Exp Neurol* 1988; **47**(4): 475-87.
104. Calder IM. The pathology of spinal cord DCS. In: Francis TJR, Smith DJ, editors. *Describing decompression illness*; 1990; Institute for Naval Medicine, Alverstoke, Gosport, Hampshire, UK: UHMS; 1990. p. 29-45.
105. Linaweaver PG, Greer HD. Paralysis in divers: the natural history of decompression sickness. In: Miller N.J., J.L. P, editors. The Thirtieth Undersea Medical Society Workshop: Rehabilitation of the paralyzed diver; 1984 1 July 1985; Point Clear, Alabama: Undersea Medical Society; 1984. p. 7-23.
106. Palanzo DA, Kurusz M, Butler BD. Surface tension effects of heparin coating on arterial line filters. *Perfusion* 1990; **5**(4): 277-84.
107. Prevention of Dysbaric Injuries in Diving and Compressed Air Work. Sixth European Consensus Conference on Hyperbaric Medicine; 2003; Geneva: European Committee for Hyperbaric Medicine; 2003.
108. Doolette DJ, Mitchell SJ. Biophysical basis for inner ear decompression sickness. *J Appl Physiol (1985)* 2003; **94**(6): 2145-50.
109. Doolette DJ, Mitchell SJ. Recreational technical diving part 2: decompression from deep technical dives. *Diving Hyperb Med* 2013; **43**(2): 96-104.
110. Landolt JP, Money KE, Topliff ED, Nicholas AD, Laufer J, Johnson WH. Pathophysiology of inner ear dysfunction in the squirrel monkey in rapid decompression. *J Appl Physiol* 1980; **49**(6): 1070-82.
111. Venter RD, Ward CA, Ho S, Johnson WR, Fraser WD, Landolt JP. Fracture studies on a mammalian semicircular canal. *Undersea Biomed Res* 1983; **10**(3): 225-40.
112. Money KE, Buckingham IP, Calder IM, et al. Damage to the middle ear and the inner ear in underwater divers. *Undersea Biomed Res* 1985; **12**(1): 77-84.
113. Walsted A, Andreassen UK, Berthelsen PG, Olesen A. Hearing loss after cardiopulmonary bypass surgery. *Eur Arch Otorhinolaryngol* 2000; **257**: 124-7.
114. Farmer JC, Thomas WG, Youngblood DG, Bennett PB. Inner ear decompression sickness. *Laryngoscope* 1976; **86**(9): 1315-27.
115. Edmonds C, Lowry C, Pennefather J. The ear and diving. In: Edmonds C, Lowry C, Pennefather J, eds. Diving and subaquatic medicine. 3rd ed. Oxford: Butterworth-Heineman; 1992: 362-74.
116. Lambertsen CJ. Relations of isobaric gas counterdiffusion and decompression gas lesion diseases. In: Vann RD, ed. The physiological basis of decompression. 38 ed. Bethesda: UHMS; 1989: 87-106.
117. Lambertsen CJ, Indicula J. A new gas lesion in man, induced by "isobaric gas counterdiffusion". *J Appl Physiol* 1975; **39**: 434-43.
118. Woodward C. A history of the St. Louis Bridge. St. Louis: GI Jones; 1881.
119. Sowden LM, Kindwall EP, Francis TJ. The distribution of limb pain in decompression sickness. *Aviat Space Environ Med* 1996; **67**(1): 74-80.
120. Dey A, Sarma UC, Dave PK. Effect of high tibial osteotomy on upper tibial venous drainage: study by intraosseous phlebography in primary osteoarthritis of knee joint. *Ann Rheum Dis* 1989; **48**: 188-93.
121. Walder D. The pain and mechanism of bends. In: Nashimoto I, Lanphier EH, editors. *43rd UHMS Workshop: What is Bends*; 1990; Shimizu, Japan: UHMS; 1990. p. 58-62.
122. Uguen M, Pougnet R, Uguen A, et al. Dysbaric osteonecrosis in professional divers: two case reports. *Undersea Hyperb Med* 2015; **42**(4): 363-7.
123. Sharareh B, Schwarzkopf R. Dysbaric osteonecrosis: a literature review of pathophysiology, clinical presentation, and management. *Clin J Sport Med* 2015; **25**(2): 153-61.
124. Kenney IJ, Sonksen C. Dysbaric osteonecrosis in recreational divers: a study using magnetic resonance imaging. *Undersea Hyperb Med* 2010; **37**(5): 281-8.
125. Uzun G, Toklu AS, Yildiz S, et al. Dysbaric osteonecrosis screening in Turkish Navy divers. *Aviat Space Environ Med* 2008; **79**(1): 44-6.
126. Gempp E, Louge P, de Maistre S. Predictive factors of dysbaric osteonecrosis following musculoskeletal decompression sickness in recreational SCUBA divers. *Joint Bone Spine* 2015.
127. Uguen M, Pougnet R, Uguen A, Lodde B, Dewitte JD. Dysbaric osteonecrosis among professional divers: a literature review. *Undersea Hyperb Med* 2014; **41**(6): 579-87.
128. Kuang XY, Chen LJ, Li HL, et al. A study on dysbaric osteonecrosis in caisson workers. *Undersea Hyperb Med* 2014; **41**(3): 229-33.
129. Gempp E, Blatteau JE, Simon O, Stephant E. Musculoskeletal decompression sickness and risk of dysbaric osteonecrosis in recreational divers. *Diving Hyperb Med* 2009; **39**(4): 200-4.
130. Uzun G. Dysbaric osteonecrosis in divers: an editorial perspective. *Undersea Hyperb Med* 2014; **41**(6): 493-4.
131. Yarbrough OD, Behnke AR. The treatment of compressed-air illness utilizing oxygen. *J Ind Hyg Tox* 1939; **21**: 213-8.
132. Arieli R, Svidovsky P, Abramovich A. Decompression sickness in the rat following a dive on trimix: recompression therapy with oxygen vs. heliox and oxygen. *J Appl Physiol (1985)* 2007; **102**(4): 1324-8.

133. Shupak A, Melamed Y, Ramon Y, Bentur Y, Abramovich A, Kol S. Helium and oxygen treatment of severe air-diving-induced neurologic decompression sickness. *Arch Neurol* 1997; **54**(3): 305-11.
134. Broome JR, Dick EJ, Jr. Neurological decompression illness in swine. *Aviat Space Environ Med* 1996; **67**(3): 207-13.
135. Sykes JJ, Hallenbeck JM, Leitch DR. Spinal cord decompression sickness: a comparison of recompression therapies in an animal model. *Aviat Space Environ Med* 1986; **57**(6): 561-8.
136. Nikolaev VP, Sokolov GM, Komarevtsev VN. [Theoretical analysis of recompression-based therapies of decompression illness]. *Aviakosm Ekolog Med* 2011; **45**(4): 47-54.
137. Bennett MH, Mitchell SJ, Young D, King D. The use of deep tables in the treatment of decompression illness: the Hyperbaric Technicians and Nurses Association 2011 Workshop. *Diving Hyperb Med* 2012; **42**(3): 171-80.
138. Ignatescu M, Bryson P, Klingmann C. Susceptibility of the inner ear structure to shunt-related decompression sickness. *Aviat Space Environ Med* 2012; **83**(12): 1145-51.
139. Lee HC. Therapeutic effects of different tables on Type II DCS. *J Hyperb Med* 1991; **6**(1): 34-9.
140. Bennett MH, Mitchell SJ, Young D, King DA. The use of deep tables in the treatment of decompression illness: the Hyperbaric Technicians and Nurses Association 2011 Workshop. *Diving Hyperb Med* 2012; **42**(3): 171-80.
141. van Hulst RA. Treatment of decompression illness with heliox: the best of both worlds? *Diving Hyperb Med* 2014; **44**(2): 101.
142. Guan YD, Wang Z, Li DS, Fang YQ, Huang ZQ. [A study of recompression treatment schedule for treating type I decompression illness with medical hyperbaric chamber pressurized]. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi* 2011; **29**(5): 374-6.
143. Hadanny A, Fishlev G, Bechor Y, et al. Delayed recompression for decompression sickness: retrospective analysis. *PLoS One* 2015; **10**(4): e0124919.
144. Kizer KW. Neurological decompression illness (DCI) responds favorably to hyperbaric oxygen treatment (HBOT) even when treatment is substantially delayed. *Undersea Hyperb Med* 2008; **35**(6): 455-6; author reply 6.
145. Kot J, Sicko Z. Delayed treatment of bubble related illness in diving--review of standard protocol. *Int Marit Health* 2004; **55**(1-4): 103-20.
146. Weaver LK. Hyperbaric medicine for the hospital-based physician. *Hosp Pract (1995)* 2012; **40**(3): 88-101.
147. Bessereau J, Genotelle N, Brun PM, et al. Decompression sickness in urban divers in France. *Int Marit Health* 2012; **63**(3): 170-3.
148. Wilson CM, Sayer MD. Transportation of divers with decompression illness on the west coast of Scotland. *Diving Hyperb Med* 2011; **41**(2): 64-9.
149. Moon RE. Hyperbaric oxygen treatment for air or gas embolism. *Undersea Hyperb Med* 2014; **41**(2): 159-66.
150. Blatteau JE, Pontier JM, Buzzacott P, et al. Prevention and treatment of decompression sickness using training and in-water recompression among fisherman divers in Vietnam. *Inj Prev* 2015.
151. Blatteau JE, Hugon J, Gempp E, Castagna O, Peny C, Vallee N. Oxygen breathing or recompression during decompression from nitrox dives with a rebreather: effects on intravascular bubble burden and ramifications for decompression profiles. *Eur J Appl Physiol* 2012; **112**(6): 2257-65.
152. Wendling J, Nussberger P, Wolfel C. Problems of a preclinical treatment algorithm for diving accidents: analysis of the Swiss hyperbaric situation. *Diving Hyperb Med* 2009; **39**(2): 100-3.
153. Blatteau JE, Pontier JM. Effect of in-water recompression with oxygen to 6 msw versus normobaric oxygen breathing on bubble formation in divers. *Eur J Appl Physiol* 2009; **106**(5): 691-5.
154. Blatteau JE, Jean F, Pontier JM, et al. [Decompression sickness accident management in remote areas. Use of immediate in-water recompression therapy. Review and elaboration of a new protocol targeted for a mission at Clipperton atoll]. *Ann Fr Anesth Reanim* 2006; **25**(8): 874-83.
155. Gold D, Geater A, Aiyarak S, Juengprasert W, Chuchaisangrat B, Samakkaran A. The indigenous fisherman divers of Thailand: in-water recompression. *Int Marit Health* 1999; **50**(1-4): 39-48.
156. Sayer MD, Kupper FC, van West P, Wilson CM, Brown H, Azzopardi E. Managing scientific diving operations in a remote location: the Canadian high Arctic. *Diving Hyperb Med* 2013; **43**(4): 239-43.
157. Wilkinson D, Goble S. A review of 17 years of telephone calls to the Australian Diver Emergency Service (DES). *Diving Hyperb Med* 2012; **42**(3): 137-45.
158. Marroni A. Acute management of Decompression Accidents in normal and remote locations Proceedings of the XXVI Annual Scientific Meeting of the EUBS; 2000; Malta; 2000. p. 127.
159. Vann RD, Denoble PJ, Howle LE, Weber PW, Freiberger JJ, Pieper CF. Resolution and severity in decompression illness. *Aviat Space Environ Med* 2009; **80**(5): 466-71.
160. Vann RE, Wise LE, Varvel SA, Philibin SD, Walentiny DM, Porter JH. Route of administration influences substitution patterns in rats trained to discriminate methadone vs. vehicle. *Drug Alcohol Depend* 2009; **103**(3): 124-30.
161. Management of mild or marginal decompression illness in remote locations: workshop proceedings. . Durham, NC Divers Alert Network, 2005.
162. Kondo Y FM, Kukita I. Extracorporeal membrane oxygenation therapy for pulmonary decompression illness 9. *Crit Care* 2014**;18:**438.
163. Spiess BD. The potential role of perfluorocarbon emulsions in decompression illness. *Diving Hyperb Med* 2010; **40**(1): 28-33.
164. Wright JL, Durieux ME, Groves DS. A brief review of innovative uses for local anesthetics. *Curr Opin Anaesthesiol* 2008; **21**(5): 651-6.
165. Bennett MH, Lehm JP, Mitchell SJ, Wasiak J. Recompression and adjunctive therapy for decompression illness. *Cochrane Database Syst Rev* 2012; **5**: CD005277.
166. Bennett MH, Lehm JP, Mitchell SJ, Wasiak J. Recompression and adjunctive therapy for decompression illness: a systematic review of randomized controlled trials. *Anesth Analg* 2010; **111**(3): 757-62.
167. Bennett MH, Lehm JP, Mitchell SJ, Wasiak J. Recompression and adjunctive therapy for decompression illness. *Cochrane Database Syst Rev* 2007; (2): CD005277.
168. Drewry A, Gorman DF. A progress report on the prospective randomised double blind controlled study of oxygen and oxygen-helium in the treatment of air-diving decompression illness. . *Undersea Hyperb Med* 1994; **21**: 98.
169. Hyperbaric Oxygen Therapy Indications. North Palm Beach, FL: Undersea and Hyperbaric Medical Society (UHMS), 2014.

170. 7th European Consensus Conference on Hyperbaric Medicine. Lille, France: Best Publishing Company; 2004.