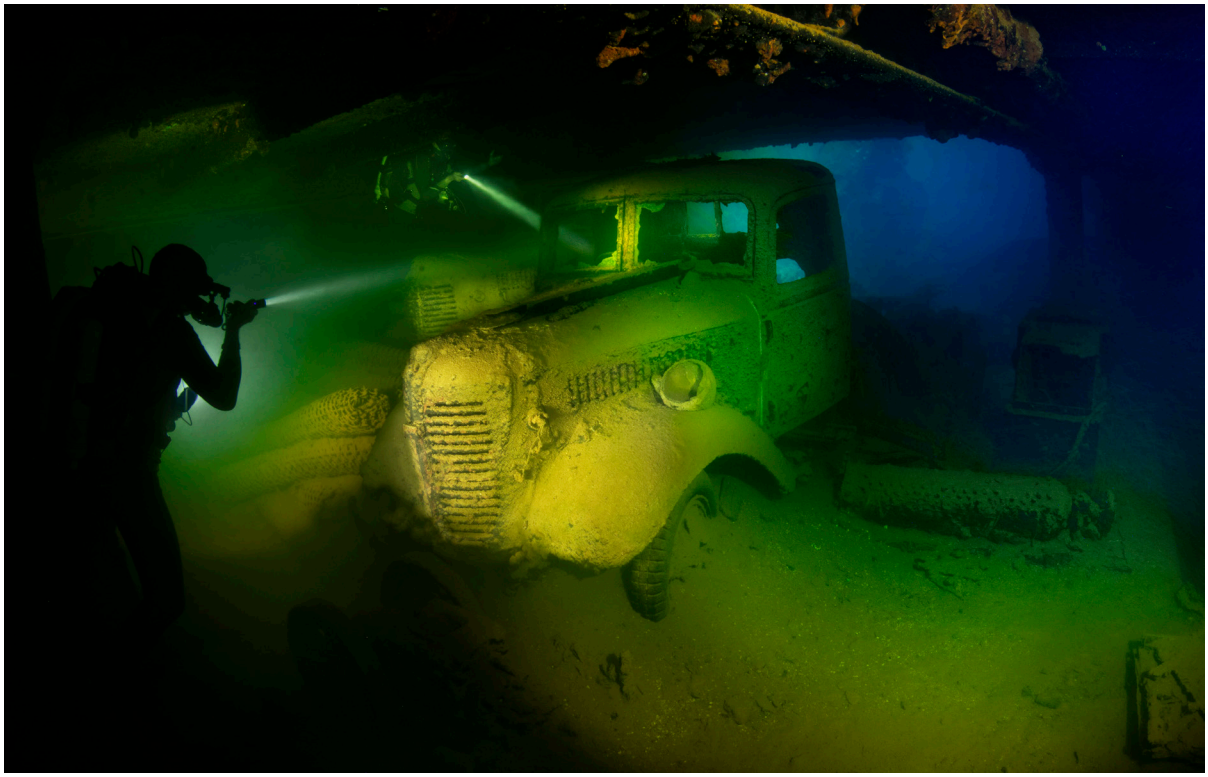
Diving and Hyperbaric Medicine

The Journal of the South Pacific Underwater Medicine Society and the European Underwater and Baromedical Society©

SPUMS *Volume 54 No. 1 Supplement March 2024* EUBS



Decompression illness: a comprehensive overview

Diving and Hyperbaric Medicine is indexed on MEDLINE, Web of Science® and Embase/Scopus
Articles from 2017 are deposited in PubMed Central®

E-ISSN 2209-1491 **ABN 29 299 823 713**

PURPOSES OF THE SOCIETIES

To promote and facilitate the study of all aspects of underwater and hyperbaric medicine
To provide information on underwater and hyperbaric medicine
To publish a journal and to convene members of each Society annually at a scientific conference

---

DIVING AND HYPERBARIC MEDICINE

https://www.dhmjournal.com/

***Diving and Hyperbaric Medicine* is published online jointly by the South Pacific Underwater Medicine Society and the European Underwater and Baromedical Society**
E-ISSN 2209-1491; ABN 29 299 823 713

Decompression illness: a comprehensive overview

Simon J Mitchell[1,2,3]

[1] *Department of Anaesthesiology, School of Medicine, University of Auckland, Auckland, New Zealand*
[2] *Department of Anaesthesia, Auckland City Hospital, Auckland, New Zealand*
[3] *Slark Hyperbaric Medicine Unit, North Shore Hospital, Auckland, New Zealand*

Corresponding author: *Professor Simon Mitchell, Department of Anaesthesiology, School of Medicine, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand*
ORCiD: *0000-0002-5149-6371*
sj.mitchell@auckland.ac.nz

Keywords
Arterial gas embolism; Decompression sickness; Pathophysiology; Prevention; Pulmonary barotrauma; Symptoms; Treatment

Abstract

(Mitchell SJ. Decompression illness: a comprehensive overview. Diving and Hyperbaric Medicine. 2024 31 March;54(1 Supp):1–53. doi: 10.28920/dhm53.4.supp.1-53. PMID: 38537300.)
Decompression illness is a collective term for two maladies (decompression sickness [DCS] and arterial gas embolism [AGE]) that may arise during or after surfacing from compressed gas diving. Bubbles are the presumed primary vector of injury in both disorders, but the respective sources of bubbles are distinct. In DCS bubbles form primarily from inert gas that becomes dissolved in tissues over the course of a compressed gas dive. During and after ascent ('decompression'), if the pressure of this dissolved gas exceeds ambient pressure small bubbles may form in the extravascular space or in tissue blood vessels, thereafter passing into the venous circulation. In AGE, if compressed gas is trapped in the lungs during ascent, pulmonary barotrauma may introduce bubbles directly into the pulmonary veins and thence to the systemic arterial circulation. In both settings, bubbles may provoke ischaemic, inflammatory, and mechanical injury to tissues and their associated microcirculation. While AGE typically presents with stroke-like manifestations referrable to cerebral involvement, DCS can affect many organs including the brain, spinal cord, inner ear, musculoskeletal tissue, cardiopulmonary system and skin, and potential symptoms are protean in both nature and severity. This comprehensive overview addresses the pathophysiology, manifestations, prevention and treatment of both disorders.

Background

This account of decompression illness (DCI) was written for a chapter in the pending Oxford Handbook of Diving and Hyperbaric Medicine. It has proven too long and excessively referenced for that purpose and will be reoriented and substantially abridged when published in the handbook. Rather than lose the detail and linkages to source literature, the Oxford publishers have graciously consented to publication of the original work as a supplement to *Diving and Hyperbaric Medicine* Journal.

Introduction and terminology

'Decompression illness' (DCI) is a collective term for two diving disorders, decompression sickness (DCS) and arterial gas embolism (AGE).[1] These disorders are related in having bubbles as the presumed primary vector of injury, potentially some symptoms in common and similar treatment protocols, but the origins of the bubbles are different and many aspects of pathophysiology and presentation are distinct. Detailed accounts of DCS and AGE appear in this review, but brief summaries, and an explanation of potentially confusing terminology that has arisen around these disorders are given here first.

Decompression sickness is caused by bubbles formed primarily from inert gas (nitrogen in air-breathing divers) that is dissolved in tissues during a dive on which compressed gas is breathed. During and after ascent ('decompression') elimination of dissolved nitrogen takes time, and if the sum of gas partial pressures in solution exceeds the ambient pressure (a condition referred to as 'supersaturation') bubbles may form in tissues or the blood passing through them. Bubbles forming in blood appear in the veins and are typically tiny (most < 50 μm)[2] yet large enough to be filtered by the pulmonary capillary bed which uaually prevents bubbles from reaching the arterial circulation.[3] These tissue and vascular bubbles can incite a complex chain of mechanical, ischaemic, haematologic and inflammatory events with symptoms varying from minor to life-threatening, and potentially involving many organ systems.[4] A common presentation is the onset of musculoskeletal pain or a skin rash over minutes or hours after a dive. Such mild presentations have been referred to as 'Type I DCS'.[5] Less commonly there may be serious

neurological manifestations such as paraplegia or vertigo suggesting spinal cord or inner ear involvement respectively. These typically appear in a progressive fashion early (within an hour) after a dive. Neurological manifestations have often been referred to as 'Type II DCS',[5] but some neurological presentations (such as patchy dermal paraesthesiae) are relatively common and less consequential, so the boundary between 'Type I' ('mild') and 'Type II' ('serious') is ill-defined and this terminology is now less often used.

Arterial gas embolism is caused by pulmonary barotrauma when respired compressed gas becomes trapped in the lungs during ascent and expands as ambient pressure falls, causing damage to the pulmonary parenchyma and potentially introducing bubbles directly into the arterial circulation.[4] These bubbles may be very large and capable of causing ischaemia in significant vascular territories or even air-locking the central circulation. The principal target organ is the brain, with onset of multifocal stroke-like symptoms immediately or within five minutes of surfacing being the most common presentation.[6]

The above summaries reflect the 'traditional' view of DCS and AGE, and the basis for a prior long-standing belief that they could be distinguished clinically. This belief was challenged in the late 1980s with the discovery of a strong association between serious neurological DCS (such as inner ear, spinal cord, and cerebral involvement) and the presence of a right-to-left shunt, such as a patent foramen ovale (PFO).[7,8] This finding implied that tiny venous nitrogen bubbles cross the right-to-left shunt and play a role in causing these DCS manifestations in a manner described in more detail later. It also challenged the belief that AGE and DCS could be easily distinguished clinically. For example, how would a clinician know whether early onset cerebral symptoms were caused by bubbles introduced to the arterial circulation by pulmonary barotrauma or by arterialisation of venous bubbles formed from dissolved gas? This difficulty was illustrated by a lack of diagnostic concordance among experts when presented with ambiguous hypothetical cases.[9]

This situation led to a proposal that DCS and AGE be collectively grouped under the umbrella term 'decompression illness' (DCI) which carried no implication about the source of bubbles. An associated descriptive taxonomy containing terms for progression and organ system was proposed.[10] For example, worsening post-dive musculoskeletal pain would be diagnosed as 'progressive musculoskeletal DCI', and a diver who became unconscious on arrival at surface, then recovered consciousness shortly after would be diagnosed with 'remitting neurological DCI'.

This approach gained popularity in the 1990s. However, as memories of its origins fade or are not taught, the terminology has become increasingly chaotic. The terms 'DCS' and 'DCI' are so similar that they are used interchangeably, with 'DCI' commonly used when the user's clear intention is to refer specifically to the consequences of bubbles formed from dissolved gas (i.e., DCS). It is not uncommon to see 'DCI' and 'AGE' used to imply separate disorders in the same article even though AGE is technically a subset of DCI. Another common problem is labelling the clinical consequences of tiny nitrogen bubbles crossing a right-to-left shunt as 'AGE' whereas this is an important component of the pathophysiology of DCS.

There must now also be some doubt about whether the potential diagnostic ambiguity between DCS and AGE is as real as believed at the time the 'DCI classification' was proposed. Subsequent widespread PFO testing using bubble contrast, which opacifies the right heart with small venous bubbles of similar size to venous bubbles formed from dissolved nitrogen after decompression,[2,11] only rarely results in cerebral symptoms even when the test is strongly positive and large showers of small bubbles enter the arterial circulation.[12] Any related symptoms are typically evanescent or mild, with only very rare exceptions where serious focal signs have occurred.[13,14] These symptoms are thus dissimilar to the stroke-like manifestations of AGE that may follow pulmonary barotrauma, presumably because the latter often introduces much larger bubbles to the circulation. The fate of tiny arterialised bubbles entering the cerebral circulation after diving is unlikely to be materially different to the PFO testing scenario because the brain washes out nitrogen very quickly, and is unlikely to be supersaturated early after a dive;[15] a condition that might otherwise cause tiny arriving bubbles to grow. Thus, although diagnostic ambiguity remains possible, the symptoms, symptom latency, and details of the incident dive allow many cases exhibiting cerebral symptoms after diving to be diagnosed as DCS or AGE with reasonable confidence.

One argument for using the collective / descriptive ('DCI') terminology is that the management of DCS and AGE is the same (see later) and so the distinction may be clinically unimportant. This is the rationale for recommendations that the collective term be used in clinical commentary, with reversion to the original DCS and AGE terminology for pathophysiological discussions. That approach is largely adopted in the present work, with the pathophysiology, manifestations and prevention of DCS and AGE described separately but both considered collectively as 'DCI' in the section on treatment.

Pathophysiology of decompression sickness

Decompression sickness is caused by bubble formation from dissolved inert gas during or after a reduction in ambient pressure ('decompression'). Relevant decompressions may occur on ascent from an underwater dive, exiting a pressurised workspace, ascent to high altitude in an unpressurised aircraft, and during extravehicular activity in space. Compressed gas diving is now by far the most common scenario in which DCS is seen, though historically

it was workers performing underwater work in pressurised caissons in whom the problem first became apparent.[4] For completeness, although not discussed further here, repetitive deep breath hold diving may also result in sufficient nitrogen uptake to provoke bubble formation and DCS.[16] The process of gas uptake and elimination during diving, the formation of bubbles during or after decompression, and the complex mechanical and inflammatory effects that may result are described below.

UPTAKE AND ELIMINATION OF INERT GAS

During a compressed gas dive, underwater breathing apparatus supplies the diver with gas at an inspired pressure essentially equivalent to the surrounding water pressure. Therefore, the inspired partial pressure of gases in the breathing mix increases in direct proportion to the ambient pressure. For example, a diver breathing air at 30 metres of seawater (msw) where the ambient pressure is 405.2 kPa (4 atmospheres absolute [atm abs]) will inspire nitrogen at 0.79 (the fraction of nitrogen in air) x 405.2 kPa = 320.1 kPa (3.2 atm abs), compared to 80.0 kPa (0.79 atm abs) at sea level pressure. Such considerations are applicable to any of the inert gases used in diving, but since air is by far the most common diving gas, and for simplicity, this narrative will routinely refer to nitrogen. Nitrogen is relatively insoluble in blood so the alveolar and arterial pressures of nitrogen (PN_2) rapidly equilibrate with the inspired pressure.[17]

During the period at depth nitrogen diffuses into tissues from the arterial blood. The rate at which tissues equilibrate with the arterial PN_2 is variable between tissues and is substantially dependent on tissue perfusion and the blood-tissue partition coefficient for nitrogen. Thus, the PN_2 in a well perfused 'fast' tissue such as the brain will equilibrate quickly, whereas a less well perfused 'slow' tissue with a high solubility for nitrogen (such as adipose tissue) will equilibrate more slowly. For the purposes of predicting inert gas pressure uptake and elimination, the most widely employed models assume the body to be composed of parallel well stirred perfusion-limited 'compartments' with a range of time constants in which the arterial-tissue PN_2 difference declines monoexponentially.[17] Clearly, the longer the period at depth, the smaller that difference will become across a wider range of tissues with longer time constants, and the deeper the dive, the higher the tissue PN_2 will be at the point of initiating the ascent.

During ascent toward the surface ambient pressure falls, the PN_2 in the inspired and alveolar gas falls, and once again there is rapid equilibration between the arterial and alveolar PN_2. The perfusion of tissues with arterial blood with a lower PN_2 than dissolved in the tissue establishes a gradient for outward diffusion of nitrogen. Upon reaching the surface all tissues should be washing out nitrogen in this manner though very fast tissues may have equilibrated with inspired PN_2 almost immediately whereas very slow tissues may, depending on the duration of the dive, have absorbed very little excess nitrogen.

BUBBLE FORMATION

During ascent and after arrival at the surface, unless ascent is conducted extremely slowly, the sum of the partial pressures of dissolved gases (nitrogen, oxygen carbon dioxide and water vapour) in at least some tissues will exceed the ambient pressure; a state referred to as 'supersaturation' (Figure 1). Supersaturation is the fundamental requirement for a bubble to form in solution from dissolved gas.

Interestingly, in pure solutions the supersaturation required for a nascent spherical bubble to overcome the surface tension of the surrounding fluid is immense and far larger than achieved in diving decompressions. Even in blood, the supersaturation required for de novo formation of a bubble of 10 nm radius exceeds 11.2 MPa.[18] In contrast, venous bubbles have been detected in humans after saturation exposures at depths as shallow as 3.4 msw (135 kPa) implying that the maximum possible supersaturation in these subjects was just over 30 kPa.[19]

Attempts to explain this discrepancy between predicted and observed supersaturation thresholds for bubble formation have focused on the likely existence of micron-scale micronuclei in blood, on blood vessel walls, or in tissues, and although not definitively proven, there is circumstantial evidence for their presence.[20] More recently there has been further discussion of nano-scale micronuclei[21] or bubble formation on hydrophobic surfaces in blood vessels,[22] but the clinical relevance of these mechanisms is unproven.

Bubble formation from dissolved gas occurs in supersaturated tissues and associated microcirculation during and after

Figure 1

Changes in the ambient pressure (P_{depth}), arterial pressure of nitrogen (PaN_2) and the pressure of nitrogen dissolved in a notional tissue ($P_{tis}N_2$) during and after a dive to 30 msw (405 kPa, 4 atm abs) for 25 minutes. The area occupied by the blue arrows represents supersaturation of the tissue, that is, where the pressure of gas dissolved in the tissue is greater than the ambient pressure

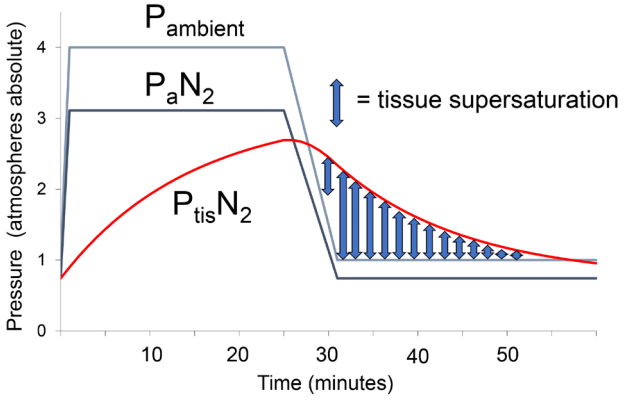


Figure 2

Four chamber transthoracic echocardiography showing the heart as it might appear with a high venous gas emboli load. The right heart is opacified with bubbles, and there are multiple small hyperechoic signals in the left heart representing bubbles that have crossed a right to left shunt. A – atrium; L – left; R – right; V – ventricle; VGE – venous gas emboli. Reproduced with permission from Blogg SL, et al. Ultrasound detection of vascular decompression bubbles: the influence of new technology and consider-ations on bubble load. Diving Hyperb Med. 2014;44(1):35–44

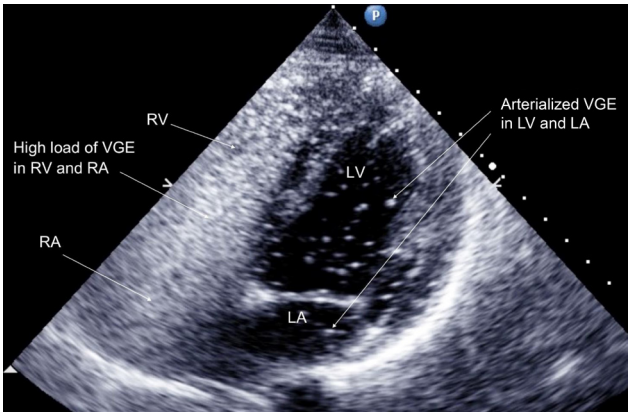
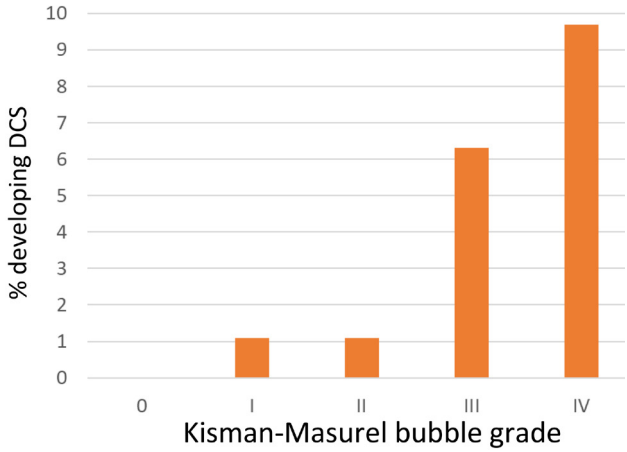


Figure 3

Percentage of test dive subjects developing symptoms of DCS at different venous gas emboli grades measured using Doppler ultrasound. Data from Nishi et al. (2003)[33]



decompression. Little is known about the formation of bubbles in the extravascular tissue space because tiny stationary bubbles are difficult to detect or study. Arguably the best characterised tissue bubbles are 20–200 µm diameter 'non-staining space occupying lesions' formed in spinal cord white matter in canine models of spinal DCS,[23,24] whose number and distribution were a plausible explanation for the neurological impairment exhibited by experimental animals.[25] Bubbles in soft tissue, anatomically distributed in approximate concordance with symptoms of musculoskeletal DCS, have recently been detected in computed tomography scans following recompression treatment.[26]

Much more is known about intravascular bubbles because these appear in the veins, presumably after forming in the capillaries or venules passing through supersaturated tissues. Gas tensions in arterial blood equilibrate in a single pass with alveolar gases, so supersaturation (and bubble formation) does not occur in the arterial blood unless there is an explosive decompression. Venous bubbles can be safely detected using Doppler ultrasound or echocardiographic techniques (see Figure 2).[27,28] In a canine model these venous gas emboli (VGE) ranged from 19–700 µm in diameter though most measured 20–40 µm.[2] In humans VGE typically appear within 15 minutes of surfacing and continue to appear for several hours post-dive.[29] Venous gas emboli grades are the most widely reported, albeit imperfect, outcome measure in human decompression studies.[27,30,31] There is a correlation between VGE grades and risk of DCS in both animals and humans,[32,33] but the positive predictive value of high VGE grades for DCS symptoms is nevertheless poor. For example, in one large air dive series less than 10% of subjects developing the highest VGE grade (using Doppler detection) exhibited symptoms (see Figure 3).[33] Studies using VGE as a measure of decompression stress must be carefully designed to ensure the methods and timing of VGE detection are valid.[31]

It is convenient to describe the pathophysiological effects of VGE in relation to their simple presence in blood, and then in relation to their distribution in the circulatory system.

EFFECTS OF THE PRESENCE OF VGE IN BLOOD

Bubbles in blood appear capable of initiating a variety of inflammatory and pro-thrombotic responses. It is difficult to be sure whether it is the mere presence of bubbles, or mechanical harm they may cause (for example, to blood vessel endothelium),[34] or both, that is responsible for these interactions. Bubbles have been shown to activate platelets,[35,36] and the complement,[37] kinin,[38] and coagulation systems.[39] Leucocytes may aggregate on bubbles,[35] and are activated by endothelial damage caused by bubbles.[40] Another relevant activation associated with DCS is a rise in circulating pro-inflammatory microparticle numbers.[41] There is some evidence that elevation of microparticles may be caused by bubbles,[42] though there appear to be other relevant mechanisms by which microparticles are generated in diving. The role of microparticles as potential vectors of harm in DCS is discussed in more detail later.

Although specific evidence is lacking, it is speculated that inflammatory activations may contribute to 'constitutional' symptoms of DCS such as fatigue or malaise. It also seems likely that inflammatory mechanisms underpin the haemoconcentration and shock occasionally seen in very severe DCS, and activation of coagulation explains disseminated intravascular coagulation and coagulopathy occasionally seen in such cases.[43] Thankfully DCS of this severity is rare (see Manifestations of DCS below). Local

activation of coagulation is proposed as one mechanism by which the spinal cord may be injured. Bubbles forming in the epidural vertebral venous plexus may cause coagulation, flow stasis and a venous infarction of the spinal cord.[44] This mechanism plausibly explains spinal DCS cases that are non-responsive to recompression.

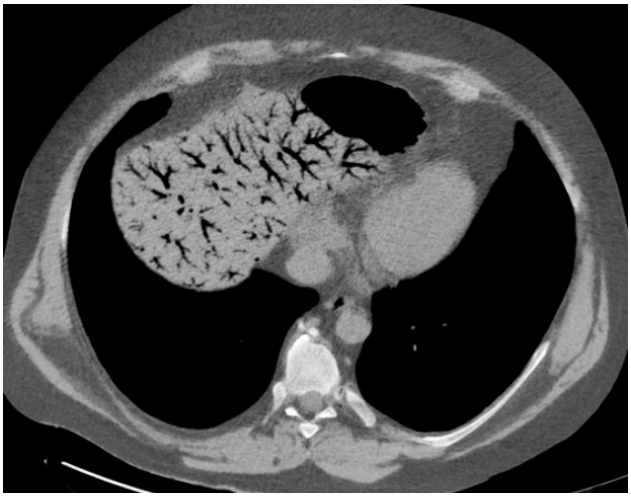
There are inconsistencies in relation to these putative mechanisms of harm by VGE-mediated inflammatory activations, not least being (as alluded to above) the fact that high grade VGE are detected frequently in divers who do not suffer any symptoms.[45] There is yet no clear explanation for this, except to speculate about individual variability in responses to the presence of VGE, which could be genetically based. For example, it has been possible to selectively breed DCS-resistant rats, and the principal phenotypic characteristics that differ between vulnerable and resistant rats identified to date relate to haematologic, clotting and haemodynamic indices.[46,47] Work continues to identify the key DCS-resistant genotypes or phenotypes.

EFFECTS OF VGE DISTRIBUTING IN THE CIRCULATION

VGE entering the systemic circulation at the venous end of tissue capillary beds will pass into larger veins and eventually to the right heart. The first microcirculation they encounter is the pulmonary capillaries. This low-pressure microcirculation interfaced with a gas exchange system is a remarkably efficient filter for microbubbles,[3,48] typically preventing VGE from entering the arterial circulation. Moreover, there is substantial evidence from post-dive monitoring that this filtering function usually occurs without producing either acute pulmonary symptoms, or obvious short- or long-term harm in the diver in the vast majority of cases. Nevertheless, if post-dive VGE formation exceeds a poorly defined threshold, symptoms such as chest pain, cough and dyspnoea may occur as this larger volume of venous gas enters the pulmonary circulation. No relevant investigations have been performed during a case in humans, but experimental boluses or infusions of gas in dogs show a gas-dose-dependent increase in pulmonary artery pressure and acute right heart failure if the dose is excessive.[49] In addition, VGE passing into the pulmonary circulation seem capable of causing endothelial disruption,[34] and in the rat lung, can produce significant inflammation and leukocytic infiltrates.[50] So-called 'cardiopulmonary DCS' provoked by such mechanisms is rare but can be rapidly fatal.

One exception to bubbles formed in veins passing in the first instance to the pulmonary microcirculation are those bubbles arising in the portal venous system. The first microcirculation those bubbles encounter is in the liver, and this occasionally produces congestion of the portal venous system with gas (see Figure 4);[51] sometimes accompanied by abdominal pain and occasionally liver injury.[52]

Figure 4
Axial abdominal CT scan showing portal venous gas in a diver with severe DCS. Reproduced with permission from Siaffa R, Luciani M, Grandjean B, Coulange M. Massive portal venous gas embolism after scuba diving. Diving Hyperb Med. 2019;49(1):61–3



Right-to-left shunting of VGE

The last three decades have produced a mass of evidence that right-to-left shunting of VGE into the arterial circulation is strongly associated with an increased risk of DCS;[7,8,53] specifically the cutaneous, inner ear, cerebral and spinal manifestations.[54–62] Most of the relevant studies have associated the presence of a 'large' persistent (patent) foramen ovale (PFO), easily provoked into shunting blood from the venous to arterial circulations (e.g., by lifting, straining, bending or a Valsalva manoeuvre), with one or more of these particular manifestations of DCS. A PFO is relatively common, being found in approximately 25% of middle age adults,[63] although it is the larger defects present in less than 2% of the population that are most likely to be associated with DCS cases.[64]

The only plausible explanation for the association between PFO and DCS is that VGE that would normally be filtered by the lungs become 'arterialised' across the shunt, and injure target organs in the manner described below. An alternative hypothesis, that shunting of blood renders inert gas elimination less efficient, is not plausible because the shunt fraction with these lesions is typically too small (< 2%) to materially affect inert gas kinetics,[65] and nor would this explain why only certain forms of DCS are selectively promoted by the presence of a PFO.

A simplistic interpretation of the association between PFO and DCS would hold that small arterialized VGE 'embolise' the target organ and produce harm accordingly. However, tiny VGE have a predicted lifespan of only seconds when exposed to non-supersaturated arterial conditions.[66] Moreover, very small bubbles typically redistribute through non-supersaturated tissue into the venous circulation.[67] It is

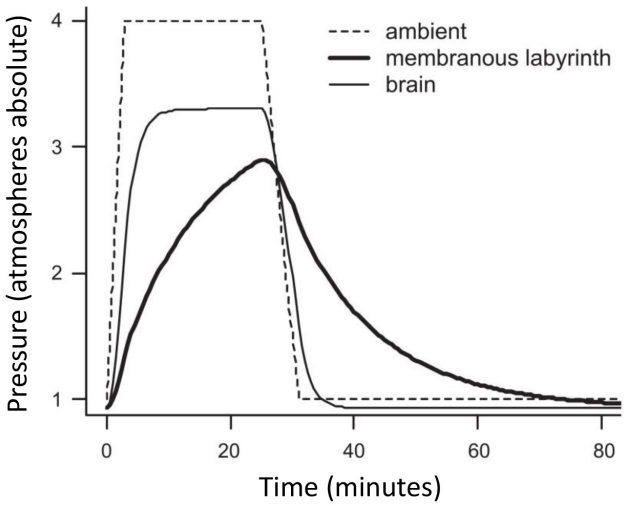
therefore not surprising that thousands of strongly positive investigations for PFO using bubble contrast have never resulted in the inner ear, cutaneous or spinal symptoms that are associated with PFO in DCS even though these positive tests result in the arterial circulation being showered with tiny bubbles that are a similar size to VGE produced by decompression.[11] It follows that those associations require additional explanation beyond the simple arrival of tiny bubbles.

The likely explanation is that tiny bubbles arriving in the microcirculation of a tissue that is functionally sensitive (or visible in the case of skin) and that remains supersaturated, will grow by inward gas diffusion,[55] fail to redistribute, and potentially cause ischaemia, mechanical injury and inflammatory activations. This hypothesis is supported by observed growth of bubbles introduced into supersaturated spinal cord white matter *in vivo*.[68] Further support comes from studies of inner ear DCS. Modelling of the inert gas kinetics of the inner ear predict it remains supersaturated for about 30 minutes after surfacing,[69] a period in which 75% of inner ear DCS symptoms begin (with almost all arising within 60 minutes).[70] Moreover, this paradigm is consistent with the apparent selective vulnerability of the inner ear compared to the brain. Approximately 75% of inner ear DCS cases exhibit no other symptoms, despite the fact that if arterial bubbles are reaching the inner ear via the labyrinthine artery, they must be arriving in the brain in much larger numbers via the basilar artery.[70] One relevant difference between the inner ear and brain is that the brain is an extremely 'fast' tissue and will exhibit little or no post-dive supersaturation as illustrated in Figure 5.[15] Tiny bubbles arriving in the brain early after diving will not grow, and will continue to rapidly involute or redistribute.

This paradigm in which arterialised VGE grow on reaching supersaturated tissue is also plausibly relevant to cutaneous and spinal DCS, but not (as mentioned above) to cerebral DCS which is also associated with PFO. In the brain, as with the lung described earlier, the development of symptoms in response to arrival of tiny bubbles may depend on synchronous arrival of high numbers of bubbles. This simple explanation is consistent with the occasional occurrence of transient cerebral symptoms in strongly positive bubble contrast investigations for PFO.[71] Exactly how large numbers of small bubbles passing through the cerebral microvasculature cause harm is unknown, but bubble redistribution (while notionally preferable to obstruction and ischaemia) is not a completely benign process. The passage of small bubbles through the cerebral microvasculature may cause transient ischaemia, and is known to compromise endothelium and the blood-brain barrier,[72,73] provoke leukocyte activation and cause reduced cerebral perfusion.[74] There is now evidence from a human study that the passage of small bubbles may impair cerebral vasoreactivity and autoregulation.[75] These effects provide a plausible explanation for the global dysexecutive symptoms

Figure 5

Changes in the ambient pressure, and compartment gas tensions in the membranous labyrinth of the inner ear and the brain during and after an air dive to 30 msw (405 kPa, 4 atm abs) for 25 minutes. The brain takes up and eliminates nitrogen very quickly with almost no supersaturation after decompression, whereas the inner ear remains supersaturated for some 40 minutes after surfacing. Reproduced with permission from 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. 2009;106: 298–301



and subtle transient focal events seen in cerebral DCS (see Manifestations of decompression sickness). These 'small bubble effects' are less likely to include the dense focal stroke-like events that can follow the introduction of large arterial bubbles by pulmonary barotrauma (see Pathophysiology of arterial gas embolism). However, it is acknowledged that if many small VGE have the opportunity to coalesce before or after crossing a PFO and passing to the brain as a larger bubble, a stroke-like picture could arise.[14]

A curious feature of the role of PFO in DCS is that affected divers may complete many dives before suffering a related problem, yet they presumably have had the PFO throughout their diving career. There are several potential explanations for this. One is that the predilection of the PFO for left-to-right shunting increases over time. There is some evidence from a diving population that this may occur.[76] Another possibility is that diving activity becomes more provocative (e.g., more advanced deeper dives that are more likely to produce higher numbers of VGE) over the course of an evolving diving career. It is also possible that all the necessary events described above for a PFO to contribute to DCS have not previously occurred simultaneously. These events include forming large numbers of VGE, having a provokable PFO, provoking significant right-to-left shunting while there are large numbers of VGE in the right atrium, and timing this such that arterialised VGE

arrive in a target tissue while it remains supersaturated so that arriving bubbles grow. This potentially codependent sequence of events required for PFO-related DCS to occur could explain both the poor positive predictive value of high grade VGE and what Moon and Bove (2004) characterised as a "*fundamental disconnection*";[77] that VGE and PFO are both common, yet the serious neurological DCS associated with a PFO remains rare.

A PFO is not the only potential route for right-to-left shunting of VGE. It is recognised that this can also happen via intrapulmonary shunts, sometimes referred to as intrapulmonary arteriovenous anastomoses (IPAVA).[78] These are less well understood, but are potentially present in most people and dynamic in nature; that is, they are frequently not detected at rest but 'open' during exercise.[79] It is possible that those forms of DCS associated with PFO that arise in divers without a PFO could have their origins in VGE arterialised across an IPAVA.

EFFECTS OF EXTRAVASCULAR BUBBLES

The formation of bubbles in extravascular tissue after decompression and their related effects are less well studied than intravascular bubbles, primarily because there is no widely available validated research tool that can detect them. However, their presence has been proven in some injured tissues (such as spinal cord white matter)[24] and can be inferred from the lack of any association between PFO and some DCS symptoms such as musculoskeletal pain; implying that intravascular bubbles are not involved. The very rapid response of pain to early recompression[80] supports a bubble-related pathophysiology.

The means by which bubbles forming in tissue might produce harm or symptoms are unproven and speculative and include: direct mechanical damage to surrounding tissue; indirect mechanical damage through stretching or distortion; ischaemia through external compression on adjacent blood vessels; haemorrhage due to external disruption of adjacent blood vessels; stimulation of pain or other sensory receptors in sensitive tissues; and incitement of inflammatory responses secondary to these injurious processes. At least some of these proposed mechanisms have been circumstantially validated in relation to bubble formation in the spinal cord white matter.[25,81]

MICROPARTICLES

Over the last 15 years there has been substantial interest in the potential role of microparticles in the pathophysiology of DCS. Microparticles are sub-micron size fragments of cell membrane potentially arising from erythrocytes, leukocytes, platelets and endothelium, that circulate in blood. They carry surface marker proteins and pro-inflammatory cytokines such as interleukin 1ß from the parent cell, and are elevated in a variety of disease states where their role may involve modulation of inflammation, coagulation, immune responses and other pathophysiological mechanisms.[82]

It was first reported that circulating microparticles increased after diving in 2009,[83] and soon after, that decompression-induced microparticles could activate neutrophils and mediate perivascular inflammation,[84] thus identifying a potential role for microparticles in DCS pathophysiology. An obvious question was whether microparticle generation was precipitated by bubble formation. *In vitro* studies supported this idea,[42] but a human study did not support this idea.[85] It has become clear that microparticles can increase during pressure exposure,[86,87] before decompression and therefore before any opportunity for bubble formation. Moreover, it has also been shown that some microparticles contain gas and these could act as previously described 'micronuclei', that is, as a nidus for supersaturated gas to form bubbles after decompression.[88] Interestingly, microparticle elevations are greater post-dive in divers developing DCS compared to those without,[41] though given the known proclivity for microparticles numbers to increase in many disease states, that finding is perhaps not surprising.

There is no disputing that these findings (and others not reported in this non-exhaustive review) suggest a role for microparticles as potential vectors of harm in DCS, perhaps even independently of parallel effects by bubbles. However, although the idea has occasionally been raised, microparticles are extremely unlikely to be the primary vector of injury in DCS for multiple reasons, not least being the indisputable association between PFO and relevant forms of DCS. If microparticles were primarily responsible for DCS symptoms, a PFO would be unimportant because the lungs do not filter microparticles. In addition, induction of microparticle shedding by exposures to pressure, hyperbaric inert gases, and oxidative stress cannot possibly be part of the pathophysiology of DCS caused by rapid ascent from sea level to high altitude. Research to better understand the role of microparticles in DCS continues.

DCS PATHOPHYSIOLOGY BY ORGAN SYSTEM

The above discussion identifies a range of organ systems that can be injured by an array of interacting physical and inflammatory mechanisms in DCS, with multiple injurious processes being potentially relevant to any one organ system. In an attempt to summarise this complex picture, the organ systems affected by DCS are listed in Table 1 with a synopsis of relevant pathophysiological processes and other points of interest.[14,50,69,86,89-96]

Risk factors for decompression sickness

With the above pathophysiology in mind, at least some risk factors for DCS are predictable.

Table 1

Putative mechanisms of injury to commonly affected organs in decompression sickness (DCS) with other points of pathophysiological interested noted; some of these matters are discussed more fully in the text. PFO – patent foramen ovale; VGE – venous gas emboli

Organ	Potential DCS injury mechanisms	Other points of interest
Musculoskeletal tissue	Bubble formation and secondary inflammatory effects in pain-sensitive structures like tendon, ligament, periosteum, joint capsule. Bubble formation in bone marrow may cause sub-cortical tissue injury that results in delayed cortical bone breakdown (dysbaric osteonecrosis). May be symptomatic and disabling if underlying articular cartilage.	Musculoskeletal DCS has never been associated with presence of a PFO, suggesting that arterialised VGE are not involved.
Skin	The association of DCS-induced rashes with PFO implicates arterialised VGE which may grow on arrival if skin is supersaturated. Histopathological studies of cutis marmorata report endothelial disruption and perivasculitis consistent with a vascular injury caused by transiting bubbles.[89] Extravascular bubble formation is also plausible especially if skin becomes cold and vasoconstricted after gas uptake at depth, impairing gas elimination during and after ascent. Extravascular cutaneous bubble formation may explain 'patchy tingling' symptoms. Such 'tingling' has not been associated with presence of a PFO.[90]	Intravascular bubbles have been detected in dermal vessels underlying cutis marmorata rash in divers with a large PFO.[91] A proposal that sympathetic outflow in response to cerebral injury in DCS (or arterial gas embolism) may cause such rashes[92] is plausible in divers with significant cerebral symptoms (as seen in other serious brain injury), but implausible in explaining the much more common scenario of DCS rash that appears with no cerebral symptoms. Rashes are never seen in strongly positive bubble contrast studies for PFO, even though many arterial bubbles must pass to the brain in this setting. This also implies that skin supersaturation is required for small incoming arterial bubbles to cause symptoms.
Brain	Extremely well-perfused 'fast' tissue very unlikely to form bubbles in-situ from supersaturated gas. Association of cerebral DCS with PFO implicates arterialised VGE. Arriving bubbles won't grow because the brain is not supersaturated. However, redistributing bubbles can incite vasculitic change which may become symptomatic if sufficient bubbles enter the cerebral circulation.	The brain receives ~20% of cardiac output so will receive a similar proportion of any VGE crossing a right-to-left shunt. It is possible that small venous bubbles might coalesce into a larger embolus prior to arterialising across a PFO, and so could cause a stroke-like event.[14] Based on the extremely rare nature of such events in bubble contrast testing for PFO, such events are probably also rare in diving.
Spinal cord	The association of spinal DCS with PFO implicates arterialised VGE arriving and growing if tissue is sup ersaturated.[8,55]Extravascular bubble formation has also been demonstrated in spinal white matter.[24,25] Bubble-induced coagulation in the epidural vertebral venous plexus leading to venous infarction of the cord has also been proposed based on animal model findings.[44]	White matter is more vulnerable than grey matter because it is less well perfused, has slower gas elimination, and is therefore more likely to form bubbles in situ, and to be supersaturated if arterialised VGE arrive early after a dive. It is speculated that the venous infarction mechanism may explain cases that are unresponsive to recompression even when treated relatively early.
Inner ear	The association of inner ear DCS with PFO[57,59] implicates arterialised VGE arriving and growing if tissue is supersaturated. Extravascular bubble formation has also been proposed as a cause of bony injury in the semi-circular canals of decompressed monkeys.[93]	Typically follows deeper repetitive dives.[94] The inner ear has unique anatomy in which perilymph and endolymph may represent diffusion-limited reservoirs of inert gas that exchange with blood via the vascular labyrinth. During decompression, a helium-to-nitrogen breathing gas switch may transiently enhance vascular labyrinth supersaturation as nitrogen diffuses inward from blood and helium tension is maintained by diffusion from perilymph. This may increase risk of tissue bubble formation and may help explain cases that occur during decompression (before surfacing) from deep dives.[69]

Table 1 continued.

Lungs	The lungs efficiently filter substantial numbers of VGE but if arriving VGE exceed some poorly defined threshold this can cause an acute rise in pulmonary artery pressure, acute right heart strain or failure, and haemodynamic instability.[49] High bubble loads cause pulmonary vasculitic changes in animal models.[50]	Typically follows a dive where an error or problem has occurred e.g., omitting substantial periods of decompression time, or a rapid ascent thus provoking formation of many VGE. Potentially a rapidly fatal form of DCS, although dyspnoea may occur and then resolve spontaneously (especially if oxygen is given), presumably as bubbles obstructing the pulmonary circulation are cleared.
Lymphatics	It is assumed but not proven that bubbles may form either within or adjacent to lymph channels causing obstruction to flow, lymph accumulation and subcutaneous swelling.	There is an anecdotal association between DCS-induced rash and underlying swelling suggestive of lymphatic involvement. This is logical because both manifestations have local tissue bubble formation as a potential mechanism in common.
Blood	Bubbles merely being present in blood, and bubbles causing damage to endothelium, seem capable of activating platelets, white cells, complement, and the coagulation cascade (see text). This may cause vasculitic inflammation at a local or general level, potentially causing local tissue damage, or more general effects such as malaise, disseminated intravascular coagulation, coagulopathy, and haemoconcentration. These processes may stimulate microparticle shedding and/or be amplified by circulating pro-inflammatory microparticles.	The role of circulating microparticles in mediating inflammation and tissue injury in DCS is still being elucidated. As discussed in the text, it is possible that oxidative stress arising from respiration of gases at hyperbaric pressures during the dive may provide a stimulus to shedding of pro-inflammatory microparticles that occurs prior to decompression and any bubble formation,[86,95] thus creating an inflammatory process that is 'parallel' to bubble-induced pathology. It is also possible that gas-containing microparticles are one form of micronuclei that facilitate bubble formation by supersaturated gas.
Liver and kidneys	VGE formed in the portal system can cause congestion of the portal inflow to the liver, manifest as reversible transaminitis and abdominal pain. Rarely, acute kidney injury occurs in DCS.[96] The mechanism is uncertain, but may include vasculitic injury by arterialised VGE or other circulating pro-inflammatory mediators such as microparticles. In serious DCS hypotension / shock may cause pre-renal impairment.	Involvement of the liver and kidney in DCS seems rare, although it is not looked for in most cases. Asymptomatic portal venous gas may be more common than currently perceived.

DEPTH / TIME / ASCENT PROFILES

Arguably the most obvious risk factor is failure to adhere to time / depth / ascent rate limits prescribed by so-called 'dive tables' or computers that are intended to prevent excessive supersaturation and limit bubble formation. Failure to complete prescribed decompression stops or ascending too quickly both increase the risk of DCS, although such breaches of protocol do not guarantee it will occur. Similarly, adherence to the prescribed time / depth limits or ascent protocols does not guarantee that it won't. For example, in one series of 52 mainly mild cases arising from dives planned using dive tables, 20 divers had dived profiles compliant with their table.[97] Further perspective on dive tables and computers as strategies for managing risk of DCS is provided in the section on 'Prevention of decompression sickness'.

FLYING AFTER DIVING

A reduction in barometric pressure associated with flight soon after diving (most passenger aircraft are pressurised to an equivalent altitude of 2400 m ~ 0.74 atm abs) will increase supersaturation in tissues that have not completed gas washout, potentially enabling formation of new bubbles and encouraging any existing bubbles to expand. This may make existing symptoms worse, or precipitate DCS in a previously asymptomatic diver.[98] The risk associated with flight after diving decreases over time after diving as tissues wash out inert gas.[99] Evidence-based recommendations for pre-flight surface intervals have been developed.[100] In most recreational diving scenarios a 24-hour pre-flight surface interval is recommended.

RIGHT-TO-LEFT SHUNT

The presence of a right-to-left shunt is a well-established risk factor whose pathophysiological relevance was discussed in detail above. Such shunts are most commonly a PFO. Further perspective on managing PFO as a risk factor for DCS is provided in the section on 'Prevention of decompression sickness' below.

TEMPERATURE

There is strong evidence from human experiments which used DCS as the primary outcome measure that becoming cooler during decompression can markedly increase risk.[101] This is presumably because tissue cooling and associated vasoconstriction with reduced perfusion may hinder washout of inert gas after it was taken up while the tissue was warm. Conversely, the lowest risk was in exposures involving a transition from cooler to warmer water at the beginning of ascent with a plausible explanation being that better perfusion of warm tissues during decompression facilitated gas washout. The difference in risk between the warmer at depth – cooler during ascent and cooler at depth – warmer during ascent exposures was at least an order of magnitude illustrating the potential importance of this risk factor.

EXERCISE AT DEPTH AND AFTER DECOMPRESSION

Work during the bottom phase of a dive can increase the risk of DCS compared to a resting dive with otherwise identical time / depth parameters.[102,103] This almost certainly occurs because exercise increases perfusion and inert gas wash-in during the bottom phase of the dive, whereas decompression is typically undertaken in a resting state with lower perfusion during gas washout. Gas wash-in and washout therefore become asymmetric processes, increasing the risk of greater tissue supersaturation during and after decompression.

Exercise after decompression, particularly work that involves lifting or straining may also increase risk. Post-dive exercise could open intrapulmonary shunts[79] and promote right-to-left shunting of VGE via this route. Lifting and straining may reproduce the transient increase in right atrial pressure seen with a Valsalva manoeuvre, and promote shunting of VGE via a PFO.[104]

DEHYDRATION

Divers commonly cite dehydration as a risk factor for DCS. Although there are supportive data from animal studies, human data are largely lacking. It is known that normal scuba air diving does produce a small but measurable degree of haemoconcentration.[105] Dehydration during exercise reduces tissue perfusion,[106] thus raising the possibility that dehydration toward the end of a dive could compromise inert gas washout from tissues. One study using a swine model of severe DCS in which one group was normally hydrated and another was deprived of water and given a diuretic during a simulated dive, showed that dehydrated pigs exhibited greater incidence and severity of DCS. Another study showed that purposive pre-hydration reduced the incidence and severity of DCS in rats.[107] In contrast, a second rat study did not show a difference in VGE after a simulated dive in control (normally hydrated) and dehydrated rats.[108]

In humans, one small study has demonstrated that pre-dive hydration (~1300 ml oral fluid over 60 minutes) reduced VGE formation, particularly in divers who appeared prone to forming VGE.[58] There are no relevant human studies in which DCS was used as an outcome measure. The status of hydration as a risk factor for DCS is widely accepted but not strongly proven.

OBESITY

Since nitrogen is very soluble in fat it has been suggested that obesity may enhance uptake of nitrogen and increase the risk of DCS. Although bubble formation in fat *per se* would likely not be harmful, it is possible that increased bubble formation in adipose tissue might contribute to greater numbers of VGE over a prolonged period after a dive, making right-to-left shunt-related DCS more likely. Observational studies in humans generally support this hypothesis,[109–111] but not universally.[112,113]

FEMALE GENDER

Although difficult to pinpoint the belief's origin, it has previously been hypothesised that women may be at higher risk of DCS than men for various reasons including a higher percentage body fat. The existing data do not support this notion.[114] There are, however, data suggesting that the menstrual phase of the female reproductive cycle may be associated with higher risk of DCS.[115,116]

PREVIOUS DCS

Based on the observation that individual divers have sometimes suffered the same symptoms in serial events, it has been suggested that a prior episode of DCS may predispose to another. While this must be acknowledged as a possibility, serial similar events may also arise from a predisposition that predated the first one. This would certainly be true of right-to-left shunt-related DCS. The role of DCS events predisposing to subsequent episodes remains unclear.

Incidence of DCS

Most epidemiologic studies lump DCS and AGE together under the umbrella term 'DCI' but the vast majority of cases are DCS. For example, in two recent series totalling 3,018 cases and which distinguished between DCS and AGE, 93% of cases were attributed to DCS.[94,117] The reported incidence of DCS is heavily influenced by multiple factors such as methodology (e.g., prospective versus retrospective studies), the definition of DCS (e.g., 'confirmed' cases undergoing recompression versus 'possible' cases on the basis of self-reported symptoms), and the type of diving undertaken by the studied population (e.g., normal recreational scuba air divers versus 'technical divers'). 'Technical divers' are recreational divers who use techniques such as tailored gases

(e.g., helium for very deep dives and oxygen rich mixtures for decompression) and rebreather devices to facilitate deeper longer dives.[118] Prospective studies of 'confirmed' cases suggest that for recreational diving scuba air diving the incidence of DCS is about 1/10,000 dives.[119] In contrast, in a retrospective survey of technical divers diving in cold water the incidence of self-reported and self-treated symptoms was 91/10,000 dives.[120] The latter study suggests that because divers often self-treat and don't report them, the incidence of mild DCS symptoms is probably much higher than generally acknowledged, particularly among so-called technical divers.

Manifestations of DCS

With multiple organ systems potentially affected it is no surprise that DCS has many potential presenting symptoms, most of which are non-specific and arise much more commonly from other causes. This creates considerable potential for misdiagnosis when divers are seen acutely by physicians with little or no training in diving medicine. If someone has been compressed air diving and is acutely sick, then the potential for DCS should be kept front of mind.

The symptoms most commonly associated with DCS are presented in Table 2. Symptoms can occur singly (especially rash, musculoskeletal pain and inner ear manifestations) or in combinations particularly in serious cases. The prevalence estimates for the various symptoms among DCS cases in Table 2 pertain primarily to cases arising from typical scuba air diving.[121]

Different symptom patterns are recognised in particular scenarios. For example, inner ear and spinal symptoms are more common after deeper dives or decompression dives.[94] In another example, decompressions from saturation dives must be conducted very slowly to protect tissues with slow inert gas washout from excessive supersaturation. Faster tissues (such as neurological organs) are comparatively protected in such scenarios, thus when symptoms are seen they almost always involve those slower exchanging tissues, with musculoskeletal pain the most common symptom.[122]

'SEVERE' DCS

Decompression sickness cases considered 'severe' are generally those that are potentially life threatening (such as cardiovascular or cardio-pulmonary cases) or associated with a risk of long-term disability (such as inner ear, spinal and cerebral cases). There has been a tradition of referring to severe cases as 'Type II DCS' though this is an imprecise term, and citing the organ system(s) involved when describing cases is a more useful approach.

All of the severe manifestations can occur singly; indeed, this is common with inner ear DCS which presents as an isolated entity in about 75% of cases.[70] However, 'fulminant' cases with multisystem involvement such as a combination of haemoconcentration, hypotension, coagulopathy, hypoxia, quadriplegia, impaired consciousness and rash are also seen.[43] In the past these were typically limited to circumstances where air divers undertaking deep dives had performed unplanned rapid ascents to the surface. With the rise of technical diving such cases have been seen in divers who have completed uneventful carefully planned dives with no adverse events, though typically as part of a pattern of multiday deep decompression diving. These cases can be extremely challenging to manage may require intensive care as well as recompression (see 'Treatment of decompression illness' later).

'MILD' DCS

The manifestations falling under the 'mild' designation do so because their natural history is toward eventual spontaneous resolution even if not recompressed, although resolution may be slower in the absence of recompression.[123] There has been a tradition of referring to mild cases as 'Type I DCS' though, as above, this is an imprecise term, and referring to the organ system(s) involved is a more useful approach.

In 2005, an international consensus designated limb pain (but not girdle, chest, back or abdominal pain), rash, constitutional symptoms, and patchy (non-dermatomal) paraesthesiae as 'mild' forms of DCS.[123] The relevant qualifications were that the 'mild' designation could not be finalised if symptoms were progressive and unless a competent neurological examination had been performed to exclude more serious signs. In 2018, an updated consensus added lymphatic symptoms to the 'mild' definition and specified that a diving medicine physician may apply the 'mild' designation in the absence of a neurological examination under appropriate circumstances.[124] This definition of a 'mild' form of DCS in 2005 (revised in 2018) resulted in a paradigm shift in decision-making around evacuation and recompression of divers whose symptoms met the definition. This is described further under 'Treatment of decompression illness'.

A common point of confusion in defining 'mild DCS' relates to the cutis marmorata form of skin rash because it is sometimes a harbinger of development of more serious DCS symptoms. Moreover, a similar rash was demonstrated in pigs experimentally subject to significant arterial gas embolism leading to a proposal that cutis marmorata may be a sign of central nervous system involvement.[92] However, there were signs of significant brain injury in these pigs whereas most cases of cutis marmorata in human DCS occur in the absence of any obvious neurological involvement. It seems plausible that a sympathetic surge recorded in these pigs precipitated the rash, as may be seen in analogous human injuries such as shock or activated phaeochromocytoma.[125] Thus, if not accompanied by non-mild manifestations, a cutis marmorata rash is still considered a mild symptom of DCS.

Table 2

Symptoms of decompression sickness (DCS) by organ system; the approximate prevalence of symptoms among DCS cases is based on data from several sources, and the experience of the authors of the parent publication. Adapted from New England Journal of Medicine, Mitchell SJ, Bennett MH, Moon RE, Decompression Illness, 386, 1254-64, Copyright © 2022 Massachusetts Medical Society. Reproduced with permission

Organ system	Manifestations	% of all DCS cases	Comments
Musculoskeletal	Pain	50–65%	Often described as a 'deep boring ache' in shoulder, elbow, hip, or knee area and unaffected by joint movement, usually without local tenderness. May be multifocal, poorly localised (not necessarily perceived in a joint *per se*), and may fluctuate in severity. Delayed onset (weeks to months later) of arthritic joint pain may be due to dysbaric osteonecrosis..
Skin	Rash	10–20%	Several morphologies: erythematous poorly demarcated patch, often itchy; or a more clearly circumscribed reticular cyanotic discoloration termed 'cutis marmorata' or 'livedo racemosa'. Usually a truncal / proximal distribution. Often associated with underlying subcutaneous swelling.
	Paraesthesiae	40–50%	Patchy, non-dermatomal distribution. Often described by divers as 'tingling'.
Lymphatic	Subcutaneous swelling	5-10%	Similar truncal distribution to skin rash, particularly upper chest and shoulders. May be subtle or conspicuous. Sometimes perceived as 'skin tightness'.
Spinal cord	Motor weakness	20–25%	Typically, para- or quadriplegias with upper motor neuron signs. Range in severity from subtle to dense.
	Numbness or dense paraesthesiae	20–30%	The dorsal columns seem vulnerable and proprioception may be affected resulting in an abnormal 'stomping' gait despite normal muscle power.
	Bladder and sphincter dystonia	1–5%	Bladder also becomes insensate and urinary retention may occur.
	Girdle, chest, back or abdominal pain	1–5%	May be a premonitory referred pain symptom that precedes other spinal symptoms. Abdominal pain may also be caused by portal venous gas (Figure 4).
Inner ear	Vestibular – nausea, vertigo, ataxia	10–20%	There may be nystagmus and extremely poor balance. 75% of inner ear DCS cases have no other DCS symptoms.
	Cochlear - hearing loss, tinnitus	1–5%	Cochlear symptoms are less common than vestibular symptoms in DCS,[121] and more common in inner ear barotrauma.
Brain ('cerebral')	Cognitive impairment, scotomata, visual field changes, dysarthria, focal weakness, ataxia	5–10%	Typically, mild dysexecutive symptoms e.g., concentration or memory difficulty. Sometimes transient focal symptoms like scotomata or visual aura. Gross focal lesions are possible but less likely in DCS than AGE.
Cardiopulmonary	Dyspnoea, cough, chest pain, hypotension, cardiac arrest	1–5%	Typically, very early onset after provocative events such as rapid ascent or omitted decompression after deep dives. May progress to cardiovascular collapse, but more subtle spontaneously remitting dyspnoea or cough are also seen.
Cardiovascular	Haemoconcentration, shock, coagulopathy	< 1%	Rare. Typically associated with provocative events such as rapid ascent or omitted decompression after deep dives, and multiple other DCS symptoms.
Uncertain	Constitutional including fatigue, malaise, headache	20–40%	Often described as similar to a viral infection. A very non-specific constellation of symptoms. Fatigue is very common after diving.

EVOLUTION OF SYMPTOMS

In typical recreational scuba air diving, symptoms of DCS typically arise after surfacing, but in decompression dives onset may occur during decompression stops while still in the water.[69] In symptoms arising after surfacing latency is generally short, especially if serious manifestations occur. In one large series of more than 5,000 cases, most developed symptoms within one hour including 73% of cases considered mild and 98% of cases considered severe, with 99% of all cases appearing with six hours.[126] These findings were confluent with an earlier study of 1,070 cases of neurological DCS which reported that 50% became symptomatic within 10 minutes and only 15% after one hour.[127] It is possible that cases can present later, especially is there is an associated precipitating event such as an ascent to altitude on high roads or in a plane. Symptoms attributable to DCS have occurred in divers taking flights more than 24 hours after diving.[98]

It is relevant that during history taking, divers may exaggerate symptom latency in order not to be judged for failure to report their problems earlier. Delayed reporting is a consequence of a strong tendency to denial and symptom rationalization among divers, many of whom still associate a certain stigma with DCS. There have also been cases in which divers have slept and woken up with new symptoms making the latency uncertain. At least partly for these reasons it would be injudicious to state a latency threshold beyond which it is 'impossible' for DCS to appear. However, if the true latency is greater than six hours, then there should be a high index of suspicion for alternative diagnoses.

The natural history of symptoms is highly variable. Mild symptoms as defined above almost always eventually resolve even in the absence of any intervention.[120,123] More serious symptoms such as cardiopulmonary manifestations and paraplegia occasionally resolve spontaneously or with first aid oxygen administration, but more typically are progressive or static and require recompression (see 'Treatment of decompression illness').

Diagnostic approach in decompression sickness

Decompression sickness is primarily a clinical diagnosis.[4] The history and examination provide the most important information. Investigations usually contribute little.

HISTORY

To begin, many diving physicians take a brief history of the diver's career (years of diving, qualification, number of dives, previous DCS) because this provides valuable contextualising information. Thereafter, the key diagnostic elements of the history in suspected DCS are the history of dives performed and their notional 'provocation' for DCS, the symptom latency after diving, and the compatibility of the symptoms with DCS.

The history of diving and its interpretation is fundamental in diagnosing DCS. The depth and duration of the dive(s) performed in the lead up to development of symptoms should be considered, along with any relevant events such as rapid ascents or missed decompression stops. The presence of risk factors described earlier, such as a hard-working dive, cold and dehydration is relevant. In a case following use of technical diving methods,[118] an informed history taker might ask about the gases used at depth and during decompression, the inspired PO_2 set point if a rebreather was used, breathing gas switches, and the decompression algorithm employed. The objective is to evaluate whether the dives were compliant with time / depth / ascent prescriptions provided by the diver's chosen algorithm. It can be difficult to interpret an actual dive profile, which may include multiple changes in depth, against limits prescribed by 'dive tables' which specify allowable times at single depths before decompression stops are required during the ascent. In addition, almost all modern recreational divers use 'dive computers' which monitor depth and time, and recalculate allowable durations with each change in depth. Often the best that can be achieved by a history taker is to establish whether there was compliance (or not) with the recommendations of the dive computer worn during the dive. Non-compliance is suggested by notifications such as rapid ascent rate or missed decompression warnings.

Dives that are overtly non-compliant, for example, involving a rapid ascent or missed decompression stops, are often referred to as 'provocative' for DCS. The 'provocative' label might also be applied to diving patterns that are technically algorithm-compliant but very close to prescribed limits, especially across multiple dives in one day and consecutive days with multiple dives. In contrast, dives well within limits are considered 'non-provocative'. Defining an invariably safe boundary of the 'non-provocative' diving range where DCS is 'impossible' is imprecise, but there is some evidence that dives to depths shallower than 6 msw are extremely unlikely to result in DCS irrespective of duration.[128]

The symptoms of DCS with key characteristics and associations are described in Table 2. Typical patterns of latency are described above (see 'Evolution of symptoms'). Although somewhat obvious (because DCS requires a 'decompression'), it is important to establish that the symptom(s) did, in fact, arise after diving and not prior to or during the dive. Some important differential diagnoses frequently onset during the period at depth, before decompression. Potential differential diagnoses and some of their distinguishing features are described in Table 3.[129] Plausible alternative explanations for some symptoms may become apparent from the history, such as pre-existing problems, or mechanical injuries. Other important features of the symptom history include enquiry about the present state of symptom evolution (are they static, worsening or remitting) and response to any first aid measures such as oxygen administration. Progression of symptoms at the

time of evaluation is predictive of incomplete recovery,[130] and response to first aid oxygen is generally accepted as supportive (albeit not pathognomonic) of the diagnosis of DCS.

EXAMINATION

In rare cases of very severe DCS with cardiopulmonary or cardiovascular manifestations (see Table 2) the early interaction with the patient will involve simultaneous diagnosis and treatment on an emergent basis where resuscitation interventions may take priority (see 'Treatment of decompression illness'). In the vast majority of cases there is time for a careful examination, though divers with serious neurological symptoms must be assessed expeditiously with a view to recompression as quickly as possible.

Examination involves measurement of vital signs, brief examination of the respiratory and cardiac systems, and a focus on the neurological system. All elements of the neurological examination are potentially important including cranial nerves, tone and power in the limbs, tests of upper and lower limb coordination, sensation and reflexes. Simple cognitive function screens are sometimes applied, particularly if the diver is complaining of related difficulties. Because the dorsal columns can be selectively affected, lower limb proprioception should be tested. In that regard, integrative tests of multiple neurological sub-system function such as assessment of the gait or the Romberg or sharpened Romberg tests are sensitive to dysfunction in DCS.[131,132] All the latter tests require the subject to stand upright and this should not be done prior to recompression in cases where cerebral arterial gas embolism is suspected because occasional re-embolisation events associated with moving from the supine to upright positions have been reported.[14]

INVESTIGATIONS

Divers with fulminant forms of DCS including cardiopulmonary or cardiovascular manifestations require intensive care level investigation and monitoring on arrival in an emergency room. Investigations may include: arterial blood gas assay looking for hypoxia, haemoconcentration and acidosis; renal function tests; liver function tests; coagulation studies; electrocardiogram and chest X-ray.

However, for the vast majority of cases the diagnosis and management of DCS typically does not rely on any investigation. There are no biomarkers that aid in diagnosis. Even modern radiology seems relatively insensitive to early changes producing significant neurological impairment in DCS. For example, magnetic resonance imaging (MRI) is insensitive to spinal cord DCS acutely despite significant functional impairment.[133] There is some evidence that newer MRI technology may be more sensitive,[134] and that negative findings may be prognostically useful.[135] Nevertheless, radiological investigations are not routinely undertaken prior to recompression in neurological DCS. In circumstances where there is a strongly suspected alternative diagnosis, appropriate investigations may be justified.[136] In cases potentially involving pulmonary barotrauma a supine chest radiograph or ultrasound to exclude pneumothorax is advised prior to recompression because untreated pneumothorax is dangerous in the hyperbaric environment.

DIAGNOSIS

Integrating all the above information to derive a diagnosis can be challenging, especially for a practitioner who does not see divers regularly. In some cases, particularly in serious cases, the diagnosis is relatively straight forward but in others it is not, as illustrated by the following hypothetical (but typical) examples.

A scuba air diver completed the second of two 35 msw dives one hour apart, both with 15 minutes at the maximum depth. His computer indicated he should do 10 minutes of decompression stops on the second dive, but he ran out of air and surfaced without completing these stops. Five minutes after surfacing he developed transient shortness of breath and 'tingling' and weakness in his legs which 15 minutes later felt numb and very weak. Examination at an emergency room two hours later reveals grade 3/5 paraplegia and a sensory level at T12.

This is a provocative dive history with short latency symptoms that are relatively specific for remitting cardiopulmonary and progressive spinal DCS. Given the serious nature of the symptoms and potential for long term disability, it is an uncomplicated decision that this diver requires urgent recompression. In contrast:

A diver completed a single air dive to 18 msw for 35 minutes with no unusual events. Five hours later and soon after un-loading heavy equipment from his car he noticed moderate pain in his left elbow. He has had pain in the same elbow unrelated to diving in the distant past. Examination (including a neurological examination) at a local clinic eight hours after the dive is unremarkable.

This could be musculoskeletal DCS, but the dive history is relatively non-provocative, the symptom arose after a long latency and is non-specific, and there is a plausible alternative explanation. Even if the cause is DCS it will almost certainly resolve spontaneously and it is much less clear whether recompression should be pursued, particularly if it is difficult to access. Further discussion of management of such cases appears in 'Treatment of decompression illness'.

These cases illustrate the paradox that the most challenging diagnosis and management decisions in DCS often arise in milder cases because the diagnosis may be uncertain and

Table 3

Differential diagnoses in decompression sickness (DCS). Adapted from New England Journal of Medicine, Mitchell SJ, Bennett MH, Moon RE, Decompression Illness, 386, 1254-64, Copyright © 2022 Massachusetts Medical Society. Reproduced with permission

DCS variant and key features	Differentials	Distinguishing features of the differential
Inner ear DCS: Cochlear symptoms are less common (33%) than vestibular (92%). Symptoms begin during ascent or early after surfacing (85% within 60 min). More common after dives ≥ 30 msw. Vertigo is typically sustained	Inner ear barotrauma	Can occur on shallow dives that are unprovocative for DCS (and breath-hold dives). May be associated with ear pain during descent and > 50% symptoms begin before surfacing. Cochlear symptoms are more common in barotrauma (94%) than in DCS.[129]
	Vestibular migraine	History of previous episodes unrelated to diving. Often followed by typical headache.
	Alternobaric vertigo	Caused by differing middle ear pressures during ascent or descent. Is always transient (< 1 min) and does not persist after surfacing.
	Benign paroxysmal positional vertigo	Typically recurrent (history of previous episodes unrelated to diving) and transient (< 1 min).
	Seasickness	Common self-misdiagnosis or rationalisation for vestibular symptoms. Does not cause true vertigo or hearing loss.
Spinal DCS: Symptoms usually evolve relatively rapidly (within one hour of surfacing)	Epidural hematoma or abscess	Rare. Onset early after surfacing from a dive is a possible but unlikely coincidence. Prior anticoagulation is a risk for haematoma. Abscess usually produces systemic symptoms of infection, likely present before diving.
	Transverse myelitis, Guillain-Barré, multiple sclerosis	These conditions typically evolve slowly (potentially over days). There is often a history of previous events unrelated to diving in multiple sclerosis.
Cardiopulmonary DCS: Onset within 30 minutes of surfacing. Provocative dives e.g., deep, fast ascent, omitted decompression	Immersion pulmonary oedema	Symptoms often begin before decompression (ascent) and may occur on shallow dives that are unprovocative for DCS.
	Near drowning	History of panic or water aspiration during the dive or at surface after dive.
	Myocardial infarction	History of angina or risk factors. Symptoms may onset at depth before ascent.
Musculoskeletal DCS: Pain may be multifocal	Musculoskeletal injury	Usually unifocal and associated with a history of trauma or an activity such as lifting or straining likely to cause injury. May be stereotypic of a recurrent injury.
	Myocardial infarction	Could account for left shoulder or arm pain. History of angina or risk factors. Symptoms may onset at depth before ascent.
Constitutional DCS: (fatigue, malaise, headache)	Viral / bacterial infection	Often associated with other symptoms such as coryza and fever.
	Carbon dioxide retention	Common cause of headache after diving, particularly dives involving hard work.
Cerebral DCS: Often reported late with dysexecutive symptoms. Gross focal symptoms less likely than after pulmonary barotrauma	Carbon monoxide toxicity	May cause confusion and unconsciousness, but often with onset at depth before ascent.
	Arterial gas embolism after pulmonary barotrauma	Can occur on shallow dives that are unprovocative for DCS. Onset immediately or within minutes of surfacing. Multifocal stroke-like symptoms. Approximately 50% have symptoms of the underlying pulmonary barotrauma (e.g., haemoptysis).
Mixed neurological and constitutional DCS	Toxic seafood ingestion	Ciguatera, paralytic shellfish poisoning, puffer fish. May cause nausea and vomiting, perioral paraesthesiae, and progressive, relatively slow onset of weakness.
Cutaneous DCS: Rash, itch and sometimes painful. Proximal / truncal distribution	Allergic reaction	History of previous reactions and / or obvious precipitant such as contact with marine life. Potentially wider distribution including periphery.
	Arterial gas embolism after pulmonary barotrauma	Rash has occurred in animal models of severe arterial gas embolism. If rash is due to the arterial gas embolism it will be accompanied by stroke-like symptoms. Can occur on shallow dives that are unprovocative for DCS.
Lymphatic DCS: Truncal distribution, particularly upper trunk	Allergic reaction	History of previous reactions and / or obvious precipitant. May affect upper airway which is never seen in lymphatic DCS. Potentially wider distribution including periphery which is very unusual in lymphatic DCS.

the merit of pursuing an intervention (recompression) of uncertain benefit at a distant location is debatable. These difficulties are widely recognised and part of the reason that 24 hour on-call diving emergency resources are available worldwide to provide advice to divers and doctors unfamiliar with diving medicine (see https://dan.org/health-medicine/medical-services/emergency-assistance/)

Prevention of decompression sickness

Since bubble formation from supersaturated dissolved gas is considered the key precipitating event in DCS, the most fundamental preventative strategies focus on limiting supersaturation during and after ascent. Other strategies focus on modifying those risk factors for DCS identified earlier in the discussion on pathophysiology. It is germane to acknowledge that prospective experimental research into the efficacy of preventative measures using DCS as an outcome measure is challenging for obvious reasons, and most studies have used VGE as a surrogate index of 'decompression stress'. Venous bubble grades are an imperfect surrogate in this role,[30] but guidelines exist to optimise their use.[31]

DEPTH / TIME / ASCENT PROFILE

Controlling the time at depth and the ascent protocol has been the central focus in attempts to prevent DCS. The goal of decompression algorithms is to prevent levels of tissue supersaturation that result in symptomatic bubble formation. The limits and ascent protocols described below are provided by so-called 'dive tables'. There are various dive tables based on different decompression algorithms or models and there is variation in the depth / time / ascent profile guidance provided.[137] Very few studies compare different approaches. In addition, very few modern divers use 'hard copy' or 'paper' tables as a guide to their decompression status during a dive. Instead, wearable 'dive computers' programmed with a decompression algorithm automatically calculate decompression status and provide updated no decompression limits or decompression plans (as required) to the diver in real time.

No-decompression diving

The vast majority of recreational scuba air divers, practice 'no-decompression diving' In this paragdigm, time at depth is limited such that a direct ascent to the surface, not exceeding a prescribed rate but without decompression stops, can be made at any point in the dive without (it is assumed) provoking dangerous levels of tissue supersaturation. For each depth there is a 'no-decompression limit'; the maximum allowable duration (typically including descent) at that depth. These no-decompression limits become shorter as depth increases because at deeper depths there is greater capacity to absorb nitrogen. Beyond approximately 40 msw it is virtually impossible to conduct no-decompression diving because the no-decompression limits are very short.

Several ascent-related strategies have been introduced aimed at enhancing the safety of 'no-decompression diving'.

First, there has been widespread adoption of the practice of inserting a five minute 'safety stop' at 3–5 msw just prior to surfacing, even though the algorithm employed predicts that decompression stops are unnecessary. Although not supported by definitive evidence of efficacy, it seems plausible that 'safety stops' should be effective in slowing ascent and reducing risk of DCS.

Second, one group demonstrated that insertion of a single 'deep safety stop' at 15 msw during ascent from a 25 msw no-decompression dive in addition to a shallow safety stop at 6 msw reduced VGE formation after surfacing.[138] However, in another study where deep and shallow safety stops were compared in dives where the total ascent time was kept constant, the deep stops were found to result in more VGE.[139] The practice of inserting deep safety stops in 'no-decompression' dives is of uncertain benefit and has not become widespread.

Decompression diving

A second diving paradigm is so-called 'decompression diving' in which the 'no-decompression limits' are exceeded necessitating 'decompression stops' during the ascent. Decompression stops are pauses in the ascent made at fixed depths so that ambient pressure does not change and supersaturation therefore does not continue to increase. The pause gives time for nitrogen washout from tissues and for supersaturation to reduce before the ascent is resumed. A variation on the 'decompression stop' approach is to follow a continuous decompression 'ceiling' without actual stops.[140] This slightly accelerates decompression, but is effort intensive, not widely adopted, and the effect on risk of DCS has not been evaluated.

JS Haldane is credited with the first attempt to model gas uptake and elimination during a dive in order to prescribe safe decompression practices.[141] Haldane's multicompartment perfusion-limited model assumed that different tissues ('compartments') would equilibrate with the inhaled pressure of nitrogen at different rates based on their perfusion and tissue:blood partition coefficient for nitrogen. He modelled that process for five notional tissues with equilibration half times of 5, 10, 20, 40 and 75 minutes. Haldane developed a decompression rule based on assumptions about supersaturations required for bubble formation, partly informed by experimentation in goats. The resulting 'decompression tables' were very successful in reducing the rate of DCS in diving operations. Haldane's algorithm was widely adopted with empirical adjustment over time by other groups; particularly the US Navy.[142] They introduced a wider range of tissue half times and a different approach to interpreting maximum allowable supersaturation based on depth-dependent decompression

rules unique to each notional tissue compartment. The US Navy air decompression tables were also widely adopted.

Subsequently several other related models based on Haldanian principles (referred to as 'gas content models') have emerged, most famously the ascent rules for 16 notional tissues proposed by Swiss physiologist AA Bühlmann.[143] The Bühlmann model (and related manipulations that are briefly described later) is programmed into many contemporary dive planning software packages and dive computers worn by divers and is arguably the most widely used decompression planner among technical divers.[144]

These multicompartmental gas content models estimate supersaturation in each notional tissue compartment during ascent, and the tissue coming closest to its maximum allowable supersaturation at any particular point in the ascent is said to be the 'leading' or 'controlling tissue'. Decompression stops are inserted when the controlling tissue reaches its supersaturation limits, which allows time for nitrogen washout. In general, faster tissues are more likely to be supersaturated and therefore controlling early in the ascent, and slower tissues are likely to be supersaturated and controlling later in the ascent. A relevant characteristic of models such as the Bühlmann algorithm is that they assume faster tissues are more tolerant of supersaturation because fast gas washout ensures supersaturation is relatively transient. A related consequence is that these models tolerate moderate levels of fast tissue supersaturation during a relatively long ascent to the first decompression stop.

Bubble models and related controversy

In the late 1980s and early 1990s evidence from ultrasound studies showed that dives controlled by gas content models resulted in VGE formation, and DCS sometimes occurred. Although in the present era it is well understood that these are virtually inevitable consequences of decompression using any model, at that time these findings were interpreted as a failing of the gas content models. So-called 'bubble models' were proposed as a potentially superior alternative.[145,146]

Bubble models use identical calculations as gas content models to track uptake and elimination of inert gas during a dive and ascent, but their treatment of derived supersaturation values during ascent is different. Bubble model algorithms attempt to predict the size range of bubble micronuclei that will grow for a given level of supersaturation (it takes more supersaturation to induce growth in smaller micronuclei) and a decompression strategy can be based on such calculations. For example, the varying permeability model (VPM) assumes a population of spherical gas nuclei with a particular size distribution, and calculates the number of bubbles that will be formed for a given supersaturation.[146] An extension of this approach is to calculate a bubble index that, by multiplying bubble numbers by the time integral of supersaturation, accounts for bubble growth in addition to the number of bubbles formed. Target values for this bubble index are set and supersaturation values controlled so it is not exceeded.[17]

It is a characteristic of bubble models that they protect faster tissues from supersaturation early in the ascent by prescribing initial decompression stops at deeper depths than a gas content model for the same depth and duration of dive. The models assume that this controls bubble formation from an earlier point in the ascent, and as a consequence, the deeper stops do not generally necessitate longer overall decompressions compared to a gas content model decompression for the same dive. This emphasis on deeper initial decompression stops has seen the term 'deep stop decompression' become synonymous with bubble models.

The notion of explicitly controlling bubble formation using a bubble model rather than just limiting supersaturation when using a gas content model had considerable appeal among technical divers in the late 1990s, and by the early 2000s the use of bubble models became almost ubiquitous. It is fascinating to reflect on how this occurred in the almost complete absence of any data comparing gas content and bubble models in respect of any relevant outcome measure after actual dives. The almost universal adoption of bubble models was driven by assumptions of superiority grounded primarily on theoretical attraction.

As bubble models became more popular, those who preferred the relative mathematical simplicity of the Bühlmann algorithm began to apply 'gradient factors (GF)' to related decompression planning.[147] The usual intent was to make a decompression based on Bühlmann's limits look more like a bubble model decompression with deeper initial stops. The GF user is required to choose two numbers, 'GF Low' and 'GF High'. GF Low is the percentage of the Bühlmann supersaturation limit allowed in the leading / controlling tissue at the first decompression stop. For example, GF Low = 20 would dictate that the first decompression stop should occur when the most supersaturated tissue reaches only 20% of its allowable Bühlmann limit. Clearly, this will mean the imposition of a much deeper first decompression stop than the unaltered Bühlmann supersaturation limits would allow.[144] GF High is the percentage of the Bühlmann supersaturation limit allowed in the leading / controlling tissue on arrival at the surface. For example, choosing GF High = 80 would dictate that the final ascent from the last decompression stop should not occur until the most supersaturated tissue has outgassed sufficiently that it will not exceed 80% of its allowable Bühlmann limit on arrival at the surface. Since the slower tissues become controlling late in the ascent, and since they are by definition 'slow' to outgas, a lower GF High will impose longer shallow stops in the decompression. Allowable supersaturations during the ascent at points between GFs Low and High are

essentially defined by a line interpolated between them. As implied above, the principal strategy employed to make the Bühlmann algorithm behave more like a bubble model (with deeper initial decompression stops) was to choose a low GF Low value such as 10% or 20%.

The first indication that assumptions of bubble model superiority might be incorrect came when Blatteau et al. (2005) compared post-dive VGE in mixed gas decompression dives planned using French military bubble and gas content models.[148] The outcomes were generally equivalent in some profiles, but in others the bubble model algorithm resulted in more VGE. This study emerged at the height of popularity of bubble models and was largely ignored.

Subsequently, a landmark US Navy Experimental Diving Unit (NEDU) study comparing rates of DCS following air decompression dives of identical duration planned using a US Navy gas content (shallower stops) and bubble model (deeper stops), showed higher rates of DCS (and more VGE) following the bubble model profile.[149] This study provoked considerable controversy among bubble model users in the technical diving community because it involved air dives and employed a different bubble model to those used by technical divers. However, multiple re-analysis of the results has suggested that the bubble model deep stops profile failed for two reasons: first, slower tissues continued to absorb inert gas during deep stops and became more supersaturated later in the ascent and after surfacing,[150] leading to greater and more sustained VGE formation; and second, the total integrated value for supersaturation over time across all tissues was greater in the bubble model decompression, despite it being of exactly the same length as the gas content model decompression.

Despite claims from bubble model afficionados that the NEDU study has no relevance to technical diving, these same two apparently disadvantageous features can be demonstrated in modelling decompression from indisputably real-world technical dives using a technical diving bubble model compared to a GF decompression with less emphasis on deep stops to produce decompressions of identical length. It is therefore difficult to conceive why a large study comparing such dives would not result in the same conclusion as the NEDU study. Indeed, one subsequent study in real world technical diving to 50 msw comparing a decompression with heavy emphasis on deep stops to another with shallower initial stops showed greater inflammatory activation after the deep stops decompression, despite it being some 20% longer than the shallower stops profile.[151]

As a consequence of this emerging evidence, technical divers performing deep dives have progressively shifted away from initial stops as deep as prescribed by bubble models. This is typically achieved using GF manipulation (for example, choosing a GF Low around 50 or 60 instead of 10 or 20). The principal challenge is a lack of hard evidence guiding how far to walk back from stops as deep as prescribed by bubble models. Nevertheless, the weight of available evidence suggests that if the goal is to achieve the least risk for a given duration of decompression, then bubble models are not optimal because they over-emphasize deep stops. Unfortunately, the path of optimal decompression is still not established. More research is occurring that space.

Probabilistic decompression models

The above approaches to formulating ascent rules based on calculating and controlling tissue supersaturation levels are often referred to as 'deterministic' methods. A different 'probabilistic' approach is based on fitting a biophysical risk function such as a time integral of supersaturation or calculated bubble volume to large databases of dives of accurately known profile and outcome to allow generation of time / depth profiles with a predicted risk of DCS. Using this approach, the amount of required decompression for a particular time / depth exposure is based largely on the risk of DCS that is acceptable to the user. Greater acceptable risk will result in shorter decompressions and vice versa. This approach has become popular in military settings, perhaps because of its adaptability in relation to risk levels. It must be noted that there are a number of published examples of dive profile tests where the actual risk of DCS has proven greater than the risk predicted by a previously established probabilistic model.[149,152]

Personalised decompression

Whichever modelling approach is used to calculate the limits of no-decompression or decompression diving, it is recognised that these models are inevitably only an approximation of gas uptake, gas elimination, supersaturation, and bubble formation at an individual diver level. This has generated interest in developing methods to personalise decompression. At the present time, there is one relevant device designed for use by 'everyday' divers in the field. This device is used to monitor post-dive VGE in the subclavian vein[153] and based on those VGE data and the time / depth profile of the dive, the device and its associated app provides both an index of 'dive quality' and recommendations on how it might be improved in a future dive.[154]

There have been several challenges to the legitimacy of this strategy. Recent studies suggest that the correlation of VGE grades obtained using this device and the gold-standard echocardiography is only fair.[155,156] This finding, of itself, does not invalidate use of the device in improving dive outcomes. However, another recent landmark study from the NEDU group examined within-diver variability in post-dive venous gas emboli (VGE) production after identical dives.[157] The authors extracted relevant data from their large databases of experimental dives that included recording of post-

dive bubble grades and clinical outcomes. These datasets included many instances of individual divers repeating identical dives multiple times. Importantly, these dives were typically closely controlled for important variables that might influence bubbling like depth, time, decompression, temperature, thermal protection, and exercise levels. The defining finding was that the same diver commonly produced markedly variable bubble grades after essentially identical dives. The study also showed that when decompression sickness occurred it was almost always on those occasions when the victims produced high bubble grades. Considered together, these results suggest that seeking strategies to reduce post-dive bubbling remains an important goal in prevention of decompression sickness, but they also demonstrate that factors other than the dive profile *per se* strongly influence bubble formation and making changes to a dive profile for the next dive based on VGE outcome of the previous one is confounded by the potential for remarkable variability in VGE measurements even when dive profiles remain unchanged. Further research into the basis for this VGE variability between identical dives is required.

Perspective on dive profile control in preventing DCS

It has long been recognised that it is possible to suffer DCS despite adherence to time/depth/ascent profile prescriptions provided by dive tables or computers. This is hardly surprising because those limits do not define a binary outcome (DCS vs no DCS); rather, they represent a point on a continuum of risk considered acceptable to the table's designer. This has been brought into even sharper focus by the above-mentioned study by Doolette and Murphy which demonstrated marked variability in VGE formation in the same diver performing an identical dive profile multiple times.[157] This finding is a signal to the community that although dive profiles matter, there are clearly other factors that may significantly influence bubble formation after diving and therefore have an important bearing on risk. It is likely that the Doolette and Murphy study will renew interest in identifying and (potentially) manipulating these factors in conjunction with profile adjustment to reduce risk of DCS.

PATENT FORAMEN OVALE

The pathophysiological significance of a large PFO in DCS was discussed earlier. Given the apparent importance of these lesions, it is not surprising that considerable attention has been given to who should be tested for one, and what to do if one is found in order to reduce the risk of DCS.

Screening / testing for a PFO

It is the conclusion of two major consensus initiatives that screening for a PFO in all diving candidates is inappropriate.[158,159] This recognises the fact that PFO is common and the serious forms of DCS associated with a PFO are nevertheless relatively rare. There is not a significant proliferation of 'shunt-related' DCS (cerebral, spinal, inner ear, cutaneous forms) among recreational divers, and a requirement for universal screening for a PFO prior to diver training would add significant cost, inconvenience, and some risk (see below) to the diver training journey. It is difficult to escape the conclusion that requiring PFO testing for every prospective diver would effectively destroy the recreational diving industry.

Testing for a PFO is advocated if one[158] or two[159] episodes of apparently shunt-related DCS occur. One consensus also advocates PFO testing for diver candidates with a history of migraine headache with aura, cryptogenic stroke, or a history of PFO or atrial septal defect in a first degree relative.[159] Physicians will occasionally be approached by divers who meet none of these criteria but who have self-researched the matter and who want to be tested. This is a relatively common request among technical divers who perform more provocative dives and have greater motivation to eliminate DCS risk factors. Such requests can be accommodated, though divers must understand that bubble contrast echocardiography for a PFO (see below) is not risk-free, and may provoke transient mild[71] or, extremely rarely, serious neurological complications.[14] Divers must also understand that absence of a PFO does not imply 'resistance' to DCS, nor does discovery of a PFO after a DCS event constitute definitive proof that the PFO was contributory.

Detection of a PFO is most effectively achieved using bubble contrast transthoracic echocardiography in which saline is agitated to produce many tiny bubbles that are injected into a peripheral vein. A four-chamber view of the heart is simultaneously obtained using echocardiography, and the operator looks for passage of bubbles across the interatrial septum. Spontaneous right-to-left shunting of bubbles indicates a significant PFO, but the test must also include provocative manoeuvres that transiently increase right atrial pressure relative to the left. Performance and release of a Valsalva or sniffing against a partially occluded nose are relevant examples. Cardiologists recognise that transoesophageal echocardiography provides the best structural images of the heart, and this frequently leads to an assumption that it is also the optimal technique for bubble contrast investigations. In fact, transthoracic echocardiography is usually preferred because the subjects do not require sedation and are able to fully cooperate with Valsalva or sniffing at the key moment when the right heart is opacified with bubbles.[159,160]

Options if a PFO is found

Very small PFOs that shunt only a few bubbles during provocation probably have little or no effect on the risk of DCS. In contrast, spontaneously shunting PFOs or those that can be easily provoked into shunting large numbers of

bubbles do materially increase risk.[60] Decision-making if such a PFO is discovered can be complex. Broadly, there are three options: cease diving; modify diving practice to reduce VGE formation and the chance of right to left shunting; and have the PFO repaired.

Strategies to make diving less provocative for VGE formation might include depth limitation, a one dive per day limit, staying well within no-decompression limits, use of nitrox with an air dive planning tool, and longer safety stops.[159] Avoiding exercise or lifting / straining for at least three hours after diving would also reduce the chance of 'shunting' any VGE that do form.[159] Such 'conservative diving' approaches appear to have reduced risk of DCS divers with unrepaired PFOs in several observational studies.[161–163] Conservative diving is a legitimate option and might best suit those divers whose PFO does not shunt large numbers of bubbles even when provoked (a feature known to be related to lower risk),[60] and who do not mind the consequent limitations on the scope of their diving.

The conservative diving option is not likely to appeal to divers on a more ambitious trajectory, for example, a technical diver who undertakes decompression diving. Such divers with a PFO that shunts spontaneously or readily after provocation may consider PFO closure. In the modern era closure can be achieved with transvenous catheter techniques and risk is low but certainly not absent.[164] For example, new onset atrial fibrillation was reported in 29/441 (6.6%) of patients (mean age 45) undergoing transvenous closure (Søndergaard et al. 2017).[165] Failure to achieve complete closure can also occur,[164] and this may contribute to subsequent DCS in affected divers.[166] Nevertheless, there is accumulating evidence, mainly from small observational studies, that closure of a large PFO prevents shunting of VGE generated by decompression[167] and reduces the risk of DCS.[161,163,168–171]

TEMPERATURE MANAGEMENT

The increased risk of DCS associated with becoming cold during decompression after being warm during time at depth was described in the pathophysiology section. The obvious implication for reducing risk of DCS is to avoid becoming progressively colder during a dive. This is challenging under many circumstances. In some occupational settings the diver's temperature can be maintained by constantly circulating warm water through specially designed exposure suits. Battery powered drysuit heating systems are also available for free-swimming divers and are popular among technical divers diving in cold water. A common strategy with the goal of improving peripheral perfusion and gas washout during decompression is to switch on the heating system only during the ascent and decompression stops, but the effect of this on decompression efficiency has not been evaluated. Some technical divers performing long decompressions in cold water cave systems install small 'habitats' which allow the divers to remove themselves from the water thus reducing peripheral cooling for periods during decompression.

The majority of divers wearing wetsuits or drysuits do not use active heating options and the strategies to mitigate cooling include optimising the fit and thickness of a wetsuit, and the nature of the undergarments worn under a drysuit.

EXERCISE

Exercise has a complex relationship with risk of DCS which hinges on its intensity and timing. In the earlier pathophysiology section it was noted that exercise during the bottom phase of the dive (that is, during gas wash-in) is a risk factor for DCS because increased perfusion will accelerate tissue gas uptake. It follows that minimising work at depth may reduce risk. For example, divers may utilise diver propulsion vehicles to reduce the exercise associated with swimming.

In contrast, there is some evidence that even a single bout of aerobic exercise within 24 hours prior to diving may reduce DCS risk. This finding was initially reported in rats exercised 20 hours before simulated provocative dives. Exercised rats exhibited a survival advantage.[172] Human studies subsequently demonstrated reduced VGE formation in subjects aerobically exercised as early as 24 hours[173] and as late as two hours[174] or even (ending) 15 minutes prior to diving.[175] High intensity pre-dive exercise also reduced post-dive microparticle production and neutrophil activation.[176] The exact mechanism of these phenomena has not been elucidated but it seems likely to be related to endothelial conditioning and / or reducing numbers of micronuclei.[177] Despite the strong observational evidence, pre-dive exercise for reduction of DCS risk has not been subject to a large prospective controlled study, or systematically taught in training courses for divers undertaking provocative dives (such as technical divers).

There is also limited evidence that mild exercise during decompression can reduce post-dive detection of VGE.[178] This effect is assumed attributable to improved perfusion of tissues and accelerated inert gas washout during decompression. In contrast, exercise after arrival back at the surface is generally discouraged out of concern that it might promote right to left shunting of VGE either through a PFO or intra-pulmonary shunt.

HYDRATION

Among divers pre-dive hydration is widely considered a valid strategy to reduce the risk of DCS. Relevant studies were discussed earlier in the section on DCS risk factors. There are no human studies demonstrating that purposive

pre-dive hydration reduces DCS, but there is general agreement that dehydration should be avoided, while taking care not to over-hydrate which may increase the risk of immersion pulmonary oedema.[179]

OTHER PRECONDITIONING STRATEGIES

A variety of pre-dive interventions characterised as 'preconditioning' strategies have been subject to limited experimentation. Although the aim is ultimately reduction in risk of DCS, at this point in time none have been studied in a manner that would allow demonstration of this. The outcome measures employed have typically been VGE grades or other physiological phenomena such as changes in arterial flow-mediated dilation.

Pre-dive exercise, discussed above, is arguably the most comprehensively studied preconditioning strategy. Other pre-dive interventions which have exerted potentially positive effects in humans include oxygen breathing,[180,181] exogenous nitric oxide administration,[182] whole body vibration,[183,184] heat exposure in a sauna,[183] dark chocolate ingestion,[183] and bouncing on a mini trampoline.[185] All of these potential interventions require further research and evaluation of efficacy before promotion into mainstream practice.

Causes of arterial gas embolism

Arterial gas embolism (AGE) in diving is a consequence of pulmonary barotrauma which can introduce large bubbles directly into the pulmonary veins and thence into the systemic arterial circulation via the left heart. As discussed earlier, the term AGE is generally avoided in describing arterialisation of much smaller VGE across a right to left shunt, because those tiny bubbles, evolved primarily from dissolved inert gas, typically produce different manifestations that are part of the DCS clinical syndrome described above. Arterial gas emboli can arise from iatrogenic pulmonary barotrauma and a variety of accidental and iatrogenic sources that do not involve pulmonary barotrauma.

PULMONARY BAROTRAUMA

Ascent from a compressed gas dive

Pulmonary barotrauma may occur during ascent from scuba diving if compressed gas becomes trapped in the lungs. Expansion of trapped gas as ambient pressure decreases can rupture alveoli and disrupt surrounding vascular structures, potentially introducing gas to the pulmonary blood vessels. The most obvious cause for gas trapping is failure to breathe normally or overt breath-holding; a potential consequence of ascent in a panicking diver. It may also occur in other diving scenarios known to carry a risk of such events, such as submarine escape training ascents[186] or controlled emergency ascent training in scuba courses[187] in which divers attempt to empty the lungs progressively during a single-breath ascent. Rarely, breath-hold divers have breathed from compressed gas carried by another diver at depth and then forgotten to exhale during ascent.[188,189] Gas trapping may also occur as a result of abnormalities in pulmonary anatomy such as bullae (Figure 6).[190] There is speculation that scarring of the pulmonary parenchyma resulting from previous injury or infection may either cause gas trapping or heterogeneity in compliance between adjacent areas of lung. This might lower the threshold for barotraumatic damage if gas spaces expand at different rates in these adjacent areas during an ascent.

It is germane that pulmonary barotrauma and AGE can occur during ascent from depths as shallow as 1m.[191,192] This 'shallow depth risk' exemplifies the fact that the greatest proportional volume change in an expanding gas space occurs during transit through the shallowest depths.

Decompression in a hyperbaric chamber

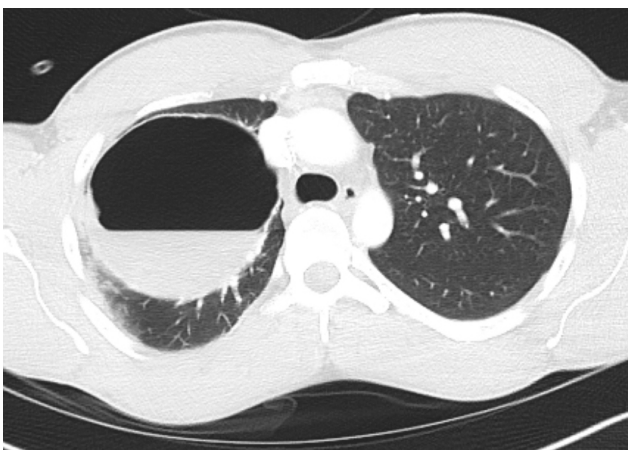
Expansion of trapped compressed gas can also occur during decompression in a hyperbaric chamber. However, since these decompressions are typically very slow, breath-holding is not a risk factor. Pulmonary barotrauma and AGE is extremely rare in this setting and based on reporting to date, only occurs in situations where there is underlying lung disease or a predisposing anatomical abnormality.[193–195]

Ascent to altitude during flight

Ascent to altitude during flight is a similar scenario to hyperbaric chamber decompressions, though the relative pressure changes are even smaller and given the number of passenger flights and small number of relevant reports, pulmonary barotrauma during flight can be considered

Figure 6

Axial CT scan showing a large primary bulla in the right lung of a diver who suffered AGE. Reproduced with permission from Goffinet CMJ, Simpson G. Cerebral arterial gas embolism in a scuba diver with a primary lung bulla. Diving Hyperb Med. 2019;49(2):141–144



extremely rare. Nevertheless, pulmonary barotrauma and AGE in passengers with predisposing pulmonary lesions have been reported.[196,197]

Mechanical ventilation

Pulmonary barotrauma can occur during mechanical (positive pressure) ventilation, particularly in patients with predisposing anatomic lesions (such as bullae) or intercurrent pulmonary pathology such as asthma or acute respiratory distress syndrome. There is some evidence that peak inflation pressures higher than 30–35 cmH_2O should be avoided to reduce risk if possible.[198]

Unregulated compressed gas

There have been several published cases of pulmonary barotrauma and AGE resulting from attempts to breathe from hoses connected directly to unregulated high pressure helium cylinders (to produce the voice-altering effects of helium).[199–201]

OTHER ACCIDENTAL AND IATROGENIC SOURCES

There are many medical (and some non-medical) scenarios in which gas may be introduced accidentally to the vascular space. These can be usefully divided into scenarios resulting in introduction of gas directly into the arterial circulation, and those introducing gas to the venous circulation from whence bubbles may arterialise in the same way as VGE in diving (across pulmonary or intracardiac shunts).[202] Detailed discussion of individual sources is beyond the scope of this review, but a summary appears in Table 4.[203–224]

Table 4

Causes of iatrogenic arterial gas embolism. Adapted with permission from Moon RE. Hyperbaric treatment for air or gas embolism. Undersea Hyperb Med. 2019;46:673–83

Source of gas	Reference
Direct arterial air entry	
Accidental injection of air into a radial artery catheter	Dube et al. 2004[203]
Alveolar-capillary injury due to necrotising pneumonia	Ceponis et al. 2017[204]
Bronchoscopy	Wherrett et al. 2022[205]
Cardiopulmonary bypass accident	Malik et al. 2017[206]
Needle biopsy of the lung	Rehwald et al. 2016[207]
Penetrating chest trauma	
Venous gas embolism with secondary arterial entry	
Accidental intravenous air injection	Sakai et al. 1998[208]
Blowing air into the vagina during orogenital sex	Bernhardt et al. 1988[209]
Cardiopulmonary resuscitation	Hwang et al. 2005[210]
Central venous catheter placement or disconnection	Vesely et al. 2001[211]
Caesarean section	Nims et al. 2006[212]
Chest tube placement	Berlot et al. 2018[213]
Endoscopic vein harvesting	Lin et al. 2003[214]
Endoscopic retrograde cholangiography	Berlot et al. 2018[213]
Gastrointestinal endoscopy	Ghannam et al. 2019[215]
Haemodialysis catheter accident	Lau et al. 2018[216]
Hydrogen peroxide ingestion	Berlot et al. 2018[213]
Hydrogen peroxide irrigation	Jones et al. 2004[217]
Laparoscopy	Kawahara et al. 2017[218]
Liver resection	Foo et al. 2012[219]
Liver transplantation	Badenoch et al. 2017[220]
Hysteroscopy	Groenman et al. 2008[221]
Sexual intercourse after childbirth	Batman et al. 1998[222]
Sitting craniotomy	Mammoto et al. 1998[223]
Spine surgery	Bapteste et al. 2021[224]

Pathophysiology of arterial gas embolism

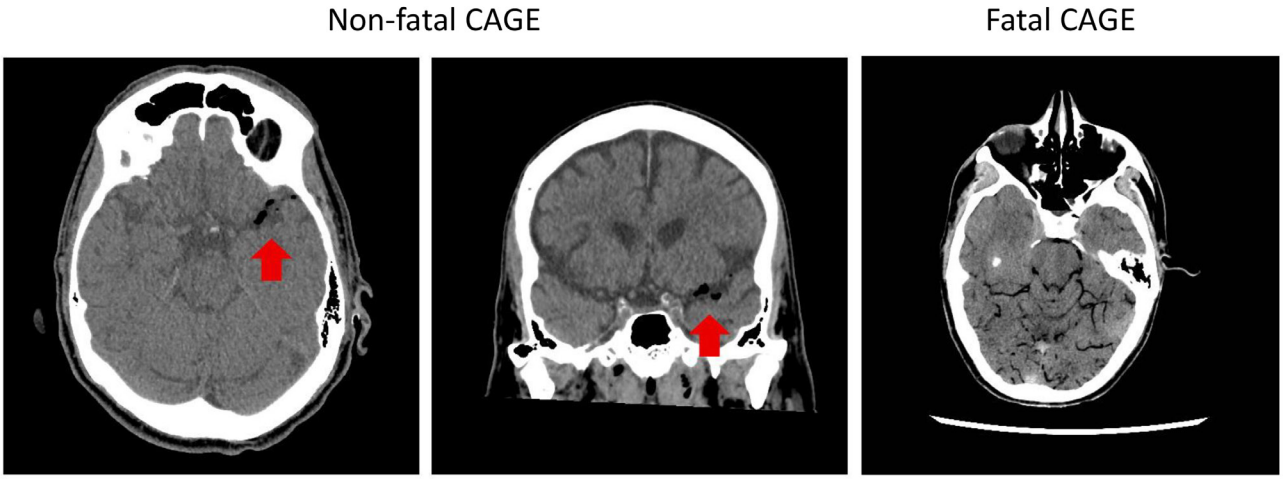
The primary focus of this discussion is on arterial gas embolism arising from pulmonary barotrauma in diving. In this setting, the volume of gas introduced into the arterial circulation is extremely variable. It can range from massive volumes that may obstruct the central circulation with air or extensively displace blood from arteries in target organs, to smaller discrete bubbles that freely distribute into the systemic circulation. The former scenario would invariably result in sudden death whereas the latter may result in survival with symptomatic target organ damage that reflects bubble size and distribution (Figure 7). Unlike many of the tiny arterialised VGE described earlier in relation to DCS, 'macrobubbles' arising from pulmonary barotrauma will not involute during passage to target organs.

TARGET ORGANS

Bubbles introduced to the left heart almost certainly distribute widely in the arterial circulation. However, the brain is the most important target organ because it receives a significant proportion of any gas entering the central arteries, and because of its poor tolerance of the consequences and the clinically important symptoms that result (see below). Bubbles leaving the left ventricle may also enter the coronary circulation though the extent to which this accounts for cardiac arrest or arrhythmias in AGE is uncertain, with

Figure 7

Axial and coronal CT images of a patient who survived iatro-genic cerebral AGE, showing a small amount of gas (red arrows); and an axial image of a diver who suffered fatal cerebral AGE showing wide distribution of intravascular gas in the cerebral vessels. Reproduced with permission from Banham NDG, Lippmann J. Fatal air embolism in a breath-hold diver. Diving Hyperb Med. 2019;49(4):304–305, and Banham ND, Saw J, Hankey GJ, Ghia D. Cerebral arterial gas embolism proven by computed tomography following transthoracic echocardiography using bubble contrast. Diving Hyperb Med. 2020;50(3):300–2



physical obstruction of the central circulation in massive AGE and cerebrally mediated dysrhythmia being competing explanations.[225,226] Other organs are almost certainly impacted by bubbles and there may be biochemical evidence of their involvement. For example, creatinine kinase is commonly elevated in AGE, suggesting injury to skeletal muscle.[227] Elevation of liver enzymes and derangement of renal function have also been reported.[228,229] Nevertheless, it is unusual for injuries to organs other than the brain to declare themselves as clinically important in AGE.

BUBBLE DISTRIBUTION AND REDISTRIBUTION

The distribution of bubbles in the arterial blood is primarily influenced by flow.[230] The distribution of larger bubbles in large blood vessels may also be influenced by buoyancy. It is therefore no surprise that in an upright (surfacing) diver the introduction of air into the pulmonary veins will likely result in cerebral arterial gas embolism since large bubbles may track superiorly in the aortic arch and the cerebral vessels received approximately 20% of cardiac output.[231] A recent study in cardiac surgery found that the right cerebral circulation was preferentially entered by bubbles which perhaps reflects the fact that the vessels passing to the right brain arise most proximally in the aortic arch.[232]

When a larger bubble enters an arterial territory with branching vessels of lesser diameter it will contact the vessel walls, form a cylinder, and continue to move forward (at least initially). This ability of bubbles to adapt to vessel geometry and progress forward distinguishes them pathophysiologically from solid thrombi that cause most strokes. Depending primarily on bubble volume and also other factors such as the blood pressure driving the bubble forward, bubbles may redistribute from arterial to venous circulations without causing prolonged flow stasis. However, if the bubble is large enough to occupy several generations of branching arterioles, the very high surface tensions at the hemispherical leading bubble ends located in branch vessels of small diameter will generate increasing force opposing forward movement. This may exceed the mean arterial pressure and surface tension of the hemispherical trailing end of the bubble which tend to drive the bubble forward.[67] A larger bubble will also generate greater frictional forces through a greater contact area with the vessel wall. Under these circumstances the bubble may obstruct flow through the vessel. Size thresholds for trapping or redistribution are poorly defined. However, one study in feline mesentery showed that bubbles < 15 µm diameter transit the microvasculature with little or no interruption to microcirculatory flow whereas bubbles ≥ 15 µm produce transient flow interruption.[233] Another study showed that bubbles larger than 200 µm often trap in cerebral arterioles at least transiently.[234] Trapping is most likely in arterioles of 20–50 µm diameter[235] typical of those found in watershed areas of the brain.[236] This region appears particularly vulnerable to ischaemia during experimental AGE.[237]

Dynamic factors other than those mentioned above may also influence redistribution of bubble lodged in cerebral vessels. Both hypo- and hypertensive responses may be seen in AGE; the former promoting obstruction and latter promoting redistribution.[238] Embolised vessels tend to dilate which may help promote redistribution.[239] In living tissue gas is resorbed from bubbles gradually. As its volume declines the bubble cylinder will shorten potentially to a point where the competing forces described above may favour redistribution.[240] This will be accelerated by oxygen breathing and also recompression (see 'Treatment of decompression illness').

HARMFUL EFFECTS OF ARTERIAL BUBBLES

Massive AGE may cause physical obstruction of the central circulation and sudden death. However, most cases involve more modest gas loads where the most important effects of AGE mostly arise from obstruction of or redistribution through cerebral vessels.

Bubbles obstructing a cerebral vessel will cause ischaemia in the downstream territory. The detail of pathophysiological consequences of neuronal ischaemia are beyond the scope of this review, but briefly, the interruption of energy metabolism causes a loss of transmembrane ion homeostasis, sodium influx, neuronal depolarisation and a subsequent cascade of events involving release of excitotoxins, calcium fluxes and neuronal death or apoptosis.[241] Bubbles large enough to cause obstruction can thus act in much the same way as thrombi or other solid emboli causing downstream ischaemia and strokes. One common difference is that bubbles are seldom discrete single emboli, and the injuries caused to the brain tend to be multifocal.

Another difference, as described above, is that bubbles may redistribute immediately or soon after impacting in an arteriolar territory, thus restoring flow. Although a notionally better outcome than complete vessel obstruction, redistribution of bubbles is not a benign process. Bubbles transiting through blood vessels cause damage to vessel walls including disruption of the surfactant coating on endothelial cells or damage to the endothelial cells themselves.[72,242,243] Functionally relevant evidence of this has been detected in the form of blood brain barrier incompetence following transit of small bubbles.[242]

This damage seems capable of inciting inflammatory processes with particular involvement of leucocytes. Two independent groups using different animal models demonstrated a progressive decline in cerebral blood flow over several hours after the redistribution of bubbles. In both models this could be prevented by rendering the animals leucopenic prior to the embolic event.[40,74,244] These findings may imply that physical accumulation of leucocytes at sites of damaged endothelium causes a secondary impairment of blood flow and distal ischaemia. It is also possible that release of pro-inflammatory cytokines, proteases and oxygen free radicals by activated leucocytes may injure surrounding tissue.[245] Given that endothelium is an important transducer and effector of vasoreactivity it is not surprising that these injurious processes would impair cerebral autoregulation. A recent human study suggested that patients who were exposed to greater numbers of arterial bubbles exhibited impairment of cerebral vasoreactivity / autoregulation after cardiac surgery.[75]

Another potential source of harm in AGE arising from diving is the growth of bubbles entering a tissue that remains supersaturated with gas after surfacing. This is analogous to the mechanism of harm proposed for arterialised VGE in the earlier discussion of DCS pathophysiology. This mechanistic hypothesis arose from cases in which focal cerebral symptoms typical of AGE occurred immediately after a dive, followed a short time later by symptoms more typical of (for example) spinal DCS.[246] Such cases were sometimes referred to as 'Type III DCS'. These early observations of 'Type III' cases followed no-decompression dives considered unlikely to provoke spinal DCS, leading to the suggestion that AGE bubbles may have provided 'seeds' for bubble amplification by inward diffusion of supersaturated gas. However, it is also possible that the simultaneous occurrence of AGE and DCS may be coincidental; with DCS provoked by risk factors that are now better understood, such as arterialisation of VGE across a PFO.

Manifestations of arterial gas embolism

DIVING-RELATED CASES

In diving related cases a key characteristic of AGE is the short latency between surfacing and onset of symptoms. In a series of 117 cases, 10 (8.6%) exhibited symptoms during the ascent, and a further 97 (83.6%) showed symptoms within 5 minutes of surfacing.[6] The remaining 10 cases all developed their symptoms within 10 minutes of surfacing.

Symptoms are most commonly referrable to cerebral involvement. Based on the series (n = 117) reported by Leitch and Green (1986) the most common symptoms are loss of consciousness and sensory change (both occurring in 39% of cases), confusion (37%), dizziness and pre-syncope (30%), hemiplegia (27%), visual changes (21%), headache (20%), dysphasia (11%), and seizures (11%).[6] In another series (n = 31) cited by Neuman (2003), 25 (81%) exhibited loss of consciousness.[226] Cardiac symptoms are also sometimes seen. In the series cited by Neuman;[226] nine (29%) complained of chest pain (which could also arise from pulmonary barotrauma) and cardiac arrest occurred in five (16%).

Since AGE has such a rapid and disabling onset which may occur while the victim is still immersed, it is not surprising that a significant proportion of victims also exhibit signs of water aspiration. Other important associations include symptoms or signs of the underlying pulmonary barotrauma such as haemoptysis, dyspnoea, chest pain, pneumothorax and mediastinal emphysema. These pulmonary signs are not invariably present, occurring in 58% of the large Leitch and Green series.[6] It follows that the diagnosis of AGE should never be discounted simply on the basis that signs of pulmonary barotrauma are absent.

Another feature of the manifestations of AGE is a tendency toward spontaneous improvement, including dramatic changes like spontaneous recovery of consciousness. In the large Leitch and Green series 59/117 (50.4%) of

cases spontaneously improved, with 25/117 (21.4%) recovering completely.[6] A small number relapse after spontaneous recovery. Spontaneous improvements may represent the clinical correlate of bubble redistribution and restoration of flow. Gradual relapse may correlate to the progressive reduction in cerebral blood flow that occurs after redistribution of bubbles as described earlier. Precipitous relapse may be caused by re-embolisation induced by postural changes (particularly supine to upright) that release bubbles trapped in the pulmonary veins or left heart chambers.[14]

As in DCS, radiological investigations are of limited diagnostic utility in AGE, although they may help in excluding other diagnoses (see below). In this modern age of rapidly available computed tomography (CT) in emergency departments, divers presenting to such facilities are often scanned prior to recompression, though where the diagnosis seems clear, recompression should not be delayed to facilitate this. This may show gas in the cerebral vessels (Figure 7), signs of pulmonary barotrauma (e.g., pneumothorax, mediastinal emphysema, subcutaneous emphysema) or a predisposing pulmonary lesion (Figure 6). These would be useful confirmatory findings, but all may be absent despite florid AGE symptoms. Notwithstanding the limitations of radiology in diagnosis of suspected diving-related AGE, these cases, by definition, involve pulmonary barotrauma and a supine chest radiograph or ultrasound examination to exclude pneumothorax is advised prior to initiating recompression because untreated pneumothorax is dangerous in the hyperbaric environment.[4]

Haematologic and biochemical investigations are of limited diagnostic value, though as noted earlier, creatine kinase levels are often elevated in AGE.[227] These investigations are, however, routinely undertaken for the purposes of managing a patient requiring the intensive levels of care likely to be required after an AGE event.

ACCIDENTAL AND IATROGENIC CASES

The manifestations of arterial gas embolism arising from accidental or iatrogenic causes are fundamentally no different to diving cases but because of the circumstances under which such events often occur, the diagnosis is far more easily overlooked. For example, many of the medical procedures in which AGE can occur (see Table 4) take place with the patient sedated or anaesthetised. There may be no sign that an AGE has occurred during the procedure, but subsequently there may be failure to wake, new neurological signs, or delirium. These symptoms have many potential explanations in (for example) an elderly comorbid patient. Even when patients are awake when undergoing at-risk procedures, it is easy to misdiagnose the onset of confusion or new focal neurological signs as caused by mechanisms more familiar to the procedural clinicians, such as stroke. Clinicians undertaking procedures with a known risk of AGE must keep the possibility front-of-mind so that it is considered in the differential for such events.

DIFFERENTIAL DIAGNOSES

The manifestations of cerebral AGE are similar to those caused by other diving- or non-diving-related disorders that can acutely affect the brain or cranial nerves. Those potential differentials, primarily for AGE arising during diving, are listed in Table 5. Cerebral AGE is often misdiagnosed as stroke in centres not accustomed to seeing divers, despite the low probability of a stroke coincidentally arising within five minutes of surfacing from a dive.

Prevention of arterial gas embolism

Prevention of arterial gas embolism in diving equates with the prevention of pulmonary barotrauma. This, in turn, relies on avoiding gas trapping in the lungs during ascent from a compressed gas dive. Hence, it is not surprising that scuba diver training agency literature emphasises that "the most important rule in scuba diving" is to breathe normally and never hold your breath at any time. This dictum aims to avoid gas trapping from the most obvious source (breath holding). Secondary preventative strategies in diver training include the teaching of strong buoyancy control skills and conservative gas supply management strategies in an attempt to minimise the risk of rapid uncontrolled or panicked ascents. Awareness of the hazards of taking breaths from a compressed gas source such as another diver's scuba equipment while breath-hold diving needs to be improved.[189] This includes taking breaths from gas trapped at depth in pockets in overhead environments ('air bubbles' in caves).

There is attention given to screening for divers who may have predispositions to pulmonary barotrauma, such as bullae (indicated by a history of spontaneous pneumothorax) and significant asthma. In recreational diving initial screening is typically by questionnaire with medical consultation and investigation only required if there is relevant positive history. In occupational diving, periodic investigations like spirometry or chest X-rays may be routine.[247] Similar principles are recommended in assessing patients prior to hyperbaric oxygen treatment for medical (non-diving) indications.[248]

There has been substantial recent focus on the implications for risk of pulmonary barotrauma when diving after COVID-19 infection. There is no doubt that COVID-19 infection can cause lung lesions that plausibly increase the risk of pulmonary barotrauma.[249] However, it also seems clear that infections with trivial symptoms generally don't. Over the course of the pandemic, guidelines evolved to a consensus that infections which fit a definition of 'very mild' do not require further investigation, but more serious infections would justify pulmonary investigation prior to diving.[250–252] These guidelines are still evolving.

Table 5

Differential diagnoses in arterial gas embolism (AGE) following diving. DCS – decompression sickness; TIA – transient ischaemic attack. Adapted from New England Journal of Medicine, Mitchell SJ, Bennett MH, Moon RE, Decompression Illness, 386, 1254–64, Copyright © 2022 Massachusetts Medical Society. Reproduced with permission

	Differentials	Comments / distinguishing features of the differential
Arterial gas embolism: Onset within seconds to minutes of surfacing. Can occur even in very shallow dives not provocative for DCS. Often follows a rapid or panic ascent. Often exhibit loss of consciousness and multifocal cerebral signs. ~50% exhibit signs of underlying pulmonary barotrauma e.g., chest pain or haemoptysis.[6]	Stroke or subarachnoid haemorrhage (SAH)	Occurrence within minutes of surfacing from a compressed gas dive is a possible but unlikely coincidence. A history of previous TIAs or other risk factors may be elicited. First symptom of SAH is often a 'thunderclap headache'
	Seizure disorder	A history of previous seizures (epilepsy) may be elicited. May occur during the dive (before ascending)
	Aura prior to migraine	A history of previous stereotypic events unrelated to diving may be elicited. Often followed by the typical headache
	Facial nerve baroparesis	Barotrauma to facial nerve in middle ear. A history of middle ear pain during dive may be elicited. Upper and lower face involved whereas AGE spares the upper face. Symptoms limited to the facial nerve (unilateral weakness)
	Carotid or vertebral dissection	Occurrence within minutes of surfacing from a compressed gas dive is a possible but unlikely coincidence. There may be a history of neck trauma or strain and there may be anterior or posterior neck pain
	Cerebral DCS	Often slower onset and less likely to cause gross focal signs. Usually after deeper dives e.g., > 25 m. Other DCS symptoms are likely to be present. A potentially difficult distinction

Treatment of decompression illness

With few exceptions, the approach to treatment of DCS and AGE is essentially identical. It follows that in the following clinical discussion the collective term decompression illness (DCI) is frequently employed, with DCS and AGE used in any situations where it is necessary to discriminate between these conditions.

FIRST AID FOR DECOMPRESSION ILLNESS

Divers may present to first responders in a variety of situations that reflect varying degrees of acuity. For example, a diver might present to a family medicine practitioner one or more days after diving complaining of symptoms that fit the definition of 'mild DCS' (see earlier). In contrast, a diver could present with increasing numbness and weakness in the lower limbs on a dive boat only minutes after surfacing. In the former scenario the urgent institution of first aid measures is unnecessary whereas in the latter acute early-presentation scenario appropriate first aid is critically important. This account of first aid for decompression illness is therefore largely applicable to those acute early presentation scenarios.

The key steps in first aid management of early-presenting DCI are immediate life support, positioning of the patient, oxygen administration, administration of fluids, and information gathering and reporting to a knowledgeable remote expert. In delayed presentation with mild symptoms, intervention is less urgent, and information gathering and reporting may be all that is required in the first instance.

Immediate life support

Application of advanced life support (ALS) is necessary if there is respiratory or cardiac arrest. Description of relevant skills such as cardiopulmonary resuscitation (CPR) and administration of resuscitation drugs is beyond the scope of this review, but approaches follow standard teaching for any ALS scenario. Where this occurs in the field (such as on a dive boat) the prognosis for recovery is poor.

Positioning

A diver presenting with symptoms of DCI within the first few hours of a dive should be placed in the supine position and, if possible, maintained in that position during evacuation. This advice has evolved from a previous recommendation that divers, particularly those suspected of suffering from AGE, be placed in the Trendelenburg (head down) position. That advice arose from early work which showed that the head down position helped prevent arterial bubbles from entering the cerebral circulation.[253] However, this finding was subsequently challenged,[230] and the head down position was associated with worse cerebral outcomes in AGE *in vivo*.[254] Moreover, head down positioning proved technically difficult to achieve in the field, and contemporary advice on DCI first aid is to place the victim supine.[124] The lateral

decubitus ('recovery position') can be used if consciousness is compromised. There is one study showing that inert gas washout in humans is enhanced when supine compared to sitting, presumably because of enhanced venous return, increased cardiac output and increased tissue perfusion.[255]

Oxygen administration

The purpose of oxygen breathing in DCI is to accelerate the involution of bubbles that contain mainly nitrogen (or any other inert gas the diver was breathing). Pure oxygen breathing will reduce the inert gas fraction in the alveoli toward zero thus markedly reducing inert gas tensions in arterial blood. This, in turn, creates a substantial diffusion gradient for removal of inert gas from tissue and bubbles.

There is evidence from *in vivo* studies that first aid oxygen is effective in reducing post-decompression bubble formation. For example, in one study of goats undergoing a decompression designed to emulate escape from a sunken submarine, when compared to air breathing, oxygen breathing caused a much more rapid decline in VGE grades after surfacing.[256] There are no randomised human studies of the efficacy of first aid oxygen in DCI. However, in one retrospective observational study, divers who received early first aid oxygen often improved in temporal relation of oxygen administration, and required fewer recompressions to reach complete recovery or plateau in clinical condition.[257] Another retrospective study suggested that first aid oxygen administration ameliorated the outcome disadvantage associated with delay to recompression.[258]

The aim is to provide oxygen in an inspired fraction of one (100% inspired oxygen). Failure to achieve this is a common error in first aid for DCI. It is very important for divers to understand that simple 'Hudson masks' (which have no reservoir) do not provide 100% inspired oxygen even at high oxygen flow rates. In a conscious spontaneously breathing subject the simplest way to achieve 100% oxygen administration is using a demand valve regulator system connected to a cylinder of oxygen. This has the advantage of being familiar and intuitive to divers (given they use similar two-stage regulator systems in diving). However, the interface between the diver and second stage regulator can significantly influence oxygen delivery; a mouthpiece and nose clip is most efficient, and an oronasal mask lacking an inflatable sealing cushion is least efficient.[259] This almost certainly reflects failure to achieve a complete seal during use of an oronasal mask; an even more difficult task if the diver has a beard.

In a spontaneously breathing but unconscious diver who cannot cooperate with the use of a mouthpiece, the options for 100% oxygen administration are more limited for first aiders. An oronasal mask connected to a demand valve or 'bag mask reservoir' system can be held on the face by a trained user. Alternatively, a so-called 'non-rebreather' mask which has a reservoir can be used. There is some evidence that when used with a constant oxygen flow rate of 15 $L \cdot min^{-1}$ these deliver oxygen nearly as efficiently as a demand regulator with a mouthpiece. However, at lower flow rates efficiency declines.[260] In an unconscious diver who is not breathing or is hypoventilating, 100% oxygen can be administered using positive pressure / assisted ventilation via a bag-mask-reservoir system with a constant oxygen inflow rate greater than minute volume, or a demand valve with a positive pressure ventilation function. These configurations of equipment require skilled users.

A common mistake in field oxygen treatment for DCI is failure to carry enough oxygen for an evacuation to an appropriate receiving facility or to last until further oxygen resources can be obtained. Planning of this nature should be emphasised in advanced diver and oxygen provision courses. Efficiency in oxygen usage while maintaining delivery of 100% oxygen can be markedly enhanced using rebreather devices; either diving rebreathers or circle circuit devices designed specifically for first aid.[260]

Divers are sometimes taught to insert air-breathing 'breaks' during administration of first aid oxygen in DCI. This may be appropriate depending on the circumstances and expected duration of evacuation. However, in the early stages of first aid treatment, air breaks are not necessary and oxygen delivery should be maintained at least until the initial discussion with an expert authority (see later) who can advise on the necessity for breaks.

Fluid administration

Hypotension, haemoconcentration and shock may be a feature of fulminant DCS (see Manifestations of DCS). In this setting aggressive intravenous (IV) fluid resuscitation may be lifesaving.[43,124] If available, IV fluids should be administered as discussed under 'Definitive management' below. However, IV fluids are unlikely to be available in the first aid setting, and shocked, extremely unwell divers are unlikely to absorb fluids taken orally. Oral fluids should also not be administered to a victim with compromised or deteriorating consciousness.

The value of fluid administration in DCI cases without haemodynamic instability is less certain. There is human evidence that routine scuba diving causes a mild degree of dehydration, particularly through immersion diuresis.[105] Dehydration, in turn, might reduce tissue perfusion and inert gas washout. There is some evidence that dehydration worsens DCS *in vivo*,[261] and some human evidence that purposive pre-dive hydration reduces post-dive bubble formation.[58] These studies contribute to a general sense that ensuring good hydration in a DCI victim is a clinically sensible goal. It follows that oral hydration is recommended in DCI first aid but should be avoided if the patient is not fully conscious. Fluids should be non-carbonated, non-

caffeinated, non-alcoholic, and ideally isotonic (but drinking water is acceptable).[124] There are no specific guidelines regarding oral fluid volumes in the first aid setting.

Other first aid strategies

Several human studies have found that warm subjects exhibit faster inert gas washout than subjects allowed to become cool.[255,262] Another study found greater post-dive VGE formation subjects exposed to a cold environment compared to a warm environment.[263] It therefore seems sensible to ensure that a diver being treated for DCS does not become cold, though hyperthermia should also be avoided because of its potentially deleterious effects on an injured central nervous system.[264] Moreover, attempts to precipitously re-warm post-dive should probably be avoided; three of four subjects exposed to cold conditions after a significant gas-loading hyperbaric exposure (12 hours at 30 feet of seawater [fsw]) who then took a hot shower developed mild DCS symptoms.[263]

The use of drugs in the treatment of DCI will be discussed further below. Of the potential options only one, oral administration of a non-steroidal anti-inflammatory drug (NSAID), is considered supported by evidence for use by first responders in the field.

Another potential field intervention is recompression in-water. This will also be discussed under 'Recompression treatment for DCI' below.

REPORTING AND TRIAGE

Following the institution of first aid measures, a priority for any individual or group responding acutely to a diver with DCI symptoms should be to contact a remote expert for advice on further management and (if necessary) evacuation. It is extremely fortunate that through the auspices of the Divers Alert Network (DAN), there is an international network of emergency contact numbers through which such advice can be obtained 24/7. Some jurisdictions have their own diver emergency hotlines.

In preparation for contact with a remote expert, the referring party (which may be the diver themselves) should gather the following information: current location (place, boat name etc); contact number for return calls; name, age and gender of diver; notable past medical history; history of incident dive(s) including depth, time, surface intervals, compliance (or not) with dive computer, any adverse events like a rapid ascent; latency of symptoms after surfacing; nature of symptoms and order in which they occurred; current status of symptoms (e.g., stable, worsening, improving, resolved); any relevant functional observations (e.g., 'tried to stand but can't'); first aid measures used and any apparent response; logistics of accessing the nearest opportunity for medical assessment and for recompression from the current location. The remote expert might also ask for a very brief history of the victim's diving career such as years of diving, number of dives, any previous DCI. If technical or rebreather diving was involved, a knowledgeable responder might ask about breathing gases (open circuit diving), diluent gas and PO_2 set point (rebreather diving), gas switches, and the decompression algorithm employed. There may be other contextually relevant questions.

This information is intended to provide the remote expert with a basis for judging how likely the symptoms are to represent DCI or another diving disorder, and the severity of the problem. The answers to these questions will strongly influence what happens at this point. If symptoms are severe and seem likely to represent DCI then urgent evacuation for recompression will be advised largely irrespective of the diver's location. In a very severe case such as fulminant DCS or an unconscious AGE victim, the need for intensive care facilities to be co-located with a recompression chamber will likely influence the decision about where to send the diver.

DECISION-MAKING IN MILD DCS

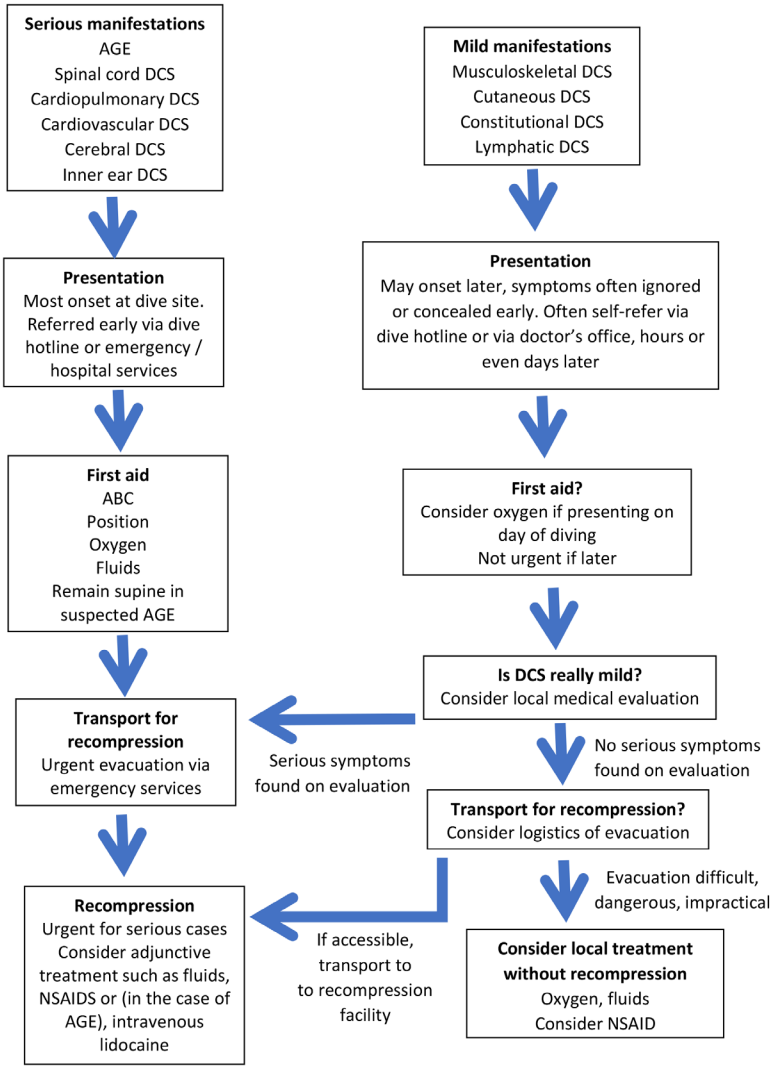
If symptoms seem mild or even equivocal for DCI then decision-making is nuanced and, paradoxically, often more challenging than for serious cases. The 2005 'remote workshop' consensus and its 2018 revision defined 'mild' symptoms and signs (see 'Manifestations of DCS' earlier) and legitimised the option of not recompressing cases that met the definition, particularly if recompression would be logistically difficult to access from the diver's location.[123,124] However, it was acknowledged that recovery might be slower in the absence of recompression, and so if a recompression chamber is readily accessible (e.g., over a reasonable distance by road transport), then mild DCS cases should still be transported to that facility and recompressed.[265]

Where a recompression facility is logistically difficult to access and treatment without recompression is contemplated, the remote workshop and its 2018 revision recommended a competent medical examination (particularly a neurological examination) to confirm the absence of manifestations that would not comply with the 'mild' definition.[123,124] It follows that where possible in such situations, a medical evaluation near the diver's location is often sought. If this were to reveal concerning findings, then the diver would be evacuated for recompression. If there were no positive findings this would provide further reassurance that local treatment without recompression is an appropriate option. These various pathways are summarised in Figure 8. Note that in respect of the 'mild' definition, although the 2005 remote workshop refered to 'mild DCI', AGE is never considered mild, and thus all 'mild DCI' cases are actually mild DCS cases as previously defined.

Local treatment of a mild DCS case without recompression involves continuation of the first aid measures described

Figure 8

Illustrative clinical pathways for divers with AGE, or DCS of serious or mild severity. Evacuation is advisable for AGE cases even after spontaneous recovery. Mild DCS cases may paradoxically involve more complex decisions about whether evacuation is justified as indicated. Adapted from New England Journal of Medicine, Mitchell SJ, Bennett MH, Moon RE, Decompression Illness, 386, 1254–64, Copyright © 2022 Massachusetts Medical Society. Reproduced with permission



above. There are no evidence-based guidelines on an appropriate duration of oxygen breathing. Anecdotally, 4–6 hours of 100% oxygen breathing is generally effective in treatment of cutaneous manifestations, and often resolves musculoskeletal pain, especially combined with administration of a NSAID. Reduced, fluctuating residual musculoskeletal pain that gradually settles over a day or two is common. Longer periods on oxygen may be utilised depending on local resources. Divers undergoing such treatment should be periodically checked over the first 24 hours to ensure no new 'non-mild' symptoms emerge. In practice, such late deteriorations seem extremely rare.

It is worth reflecting on the substantial paradigm-shift in DCS management precipitated by the 2005 remote workshop findings. Prior to 2005 there was a general perception that recompression was a standard of care for all DCS cases irrespective of severity. However, the workshop's examination of the natural history of cases conforming with the mild definition suggested that they typically resolve spontaneously without harm, and that while recompression is still desirable for effecting rapid resolution, requiring recompression of all such cases irrespective of the logistics, costs and hazards of evacuation was excessively conservative. Moreover, as dive travel to increasingly remote locations became more popular, mild or equivocal cases with non-specific symptoms were common and increasingly problematic for remote experts triaging diving emergencies. The remote workshop guidelines have legitimised sensible decision making by such experts, but emphasise that all relevant decisions are made by or discussed with practitioners with appropriate training and experience-based expertise.[124]

It is germane that the option of managing mild cases without recompression has now been in place and invoked extensively for some 19 years. There has been no large-scale formal investigation of outcomes for divers managed according to the workshop's guidelines, but one observational study of apparently mild cases managed without recompression reported invariable recovery.[120] Moreover, there is no prevalent anecdote or signal in the literature that the guidelines were flawed. Indeed, after 13 years of experience in application, the absolute requirement for a neurological examination in all cases prior to designating a case 'mild' was conditionally moderated in the 2018 revision.[124]

One concern occasionally expressed about musculoskeletal pain as a 'mild' symptom is its potential role as a harbinger of dysbaric osteonecrosis (DON). DON is a delayed consequence of what is thought to be bubble-induced injury in bone which manifests as cortical bone necrosis.[266] It only becomes symptomatic if affected bone underlies an articular surface (usually shoulders or hips) leading to breakdown of articular cartilage and arthritis. Since DON does not manifest as part of acute DCS it is not addressed in detail in this review, but it is a relevant consideration here because musculoskeletal pain in DCS may reflect a disease process that might lead to DON. There is occasionally concern about whether failure to recompress such cases because they are considered 'mild' increases the risk of subsequently developing DON.

There are several relevant points. First, one study using acute magnetic resonance imaging (MRI) showed bone marrow changes in 14/42 divers diagnosed with musculoskeletal DCS. All were subsequently recompressed, but 11/14 still developed MRI-detected bone infarction (as distinct from symptomatic DON). Thus, recompression did not seem particularly effective in preventing bone infarction in this cohort.[267] Second, when divers in the same study were stratified for delay to recompression, the odds of developing DON were 8.2 times greater if recompression was delayed by more than six hours. This is confluent with the findings of animal studies which suggested that the efficacy of recompression in preventing DON declines significantly after eight hours.[268] The remote workshop guidelines sanction treatment without recompression if access to a chamber is logistically difficult. Accessing recompression from remote locations where evacuation is 'logistically difficult' would almost certainly take longer than six or eight hours (many cases are not even reported until much later) and recompression after such long delays would therefore be of unlikely benefit in preventing DON. Finally, despite the high proportion of acutely symptomatic divers with sub-clinical bone change detectable by MRI in the Gempp study,[267] the association between musculoskeletal DCS and symptomatic DON seems tenuous. Cases of DON have occurred in the complete absence of any history of musculoskeletal DCS.[269] Moreover, non-recompressed musculoskeletal DCS is almost certainly common and under-reported. For example, among 55 technical divers who prospectively logged symptoms of DCS over one year, there were 22 instances of musculoskeletal symptoms, but none of the divers reported these symptoms at the time, nor were they recompressed.[120] Despite the likelihood that this reflects common behaviour, particularly in the technical diving community, clinically symptomatic DON among recreational and technical divers seems very rare.

With these points in mind, divers with musculoskeletal DCS managed according to the remote workshop guidelines will either have access to a nearby chamber in which case they should definitely be offered recompression, potentially within six hours, or they will be located in remote situations where pre-recompression evacuation would involve delays longer than the interval within which recompression might help prevent DON. In the latter scenario they may be managed without recompression and are unlikely to be at higher risk of developing clinically symptomatic DON as a result.

EVACUATION OF DCI PATIENTS

The transport of DCI patients to a recompression facility draws on basic principles that apply to transport of patients in many clinical settings. The receiving facility must be available, aware that the diver is coming, suitable for the clinical status of the diver, and safe. Application of these seemingly simple considerations is not always straight forward.

In some regions such as the United States there has been a steady decline in the number of centres offering 24-hour cover for diving emergencies. This almost certainly reflects the fact that such services are expensive to provide and the costs are difficult to recoup from the small number divers treated. In general, experts providing advice on diving emergency hotlines will have an awareness of resources available in their jurisdictions, and the quality / safety of the facilities. Such knowledge may be incomplete however, and circumstances in some locations may be variable. For example, there are some chamber facilities in the South Pacific whose readiness depends on the availability of staff which is unpredictable. The key, as in all patient transfer scenarios, is to ensure direct contact with clinicians in the receiving facility before initiating patient transport.

Another important goal is to avoid mismatch between the condition of the patient and the clinical skills and / or resources available at the receiving centre. This is particularly true for a condition like DCI which is characterised by a vast range of potential severity. Virtually any safely operational recompression facility should be able to manage a case of mild DCS, but some would lack the expertise or resources to manage an unconscious AGE patient or a shocked diver with fulminant DCS. The condition of the patient should be clearly described to the receiving clinician who must decide

whether his or her facility is appropriate. In (rare) cases, it may be appropriate for a very sick diver to be stabilised at a nearby non-hyperbaric hospital, and then transported to a hyperbaric facility for recompression.

In choosing a mode of transport there is considerable scope for pragmatism. Over short distances late-presenting divers with mild symptoms have been transported to hospital using private cars, or public transport options. Earlier presenting divers, especially with more serious symptoms would usually justify road ambulance transport.

Over long distances, air transport is typically used. Avoidance of significant ambient pressure reduction is an important goal to minimise bubble growth and any increase in tissue supersaturation. The gold standard in this regard is a one atmosphere pressurised fixed wing air ambulance for very long evacuations. However, helicopters are more adaptable both for patient uplift at locations without a runway, and for landing directly at a hospital. When helicopters are used, altitudes greater than 150–300 m are avoided if possible. There is a theoretical concern that vibration in a helicopter might provoke increased VGE formation but to date this has not been adequately studied to allow conclusions to be drawn.[270] Divers are commonly transported in helicopters. It is also acknowledged that rare situations with no other options evacuation by commercial airliner (typically pressurised to ~2400 m altitude) has been utilised. There is some evidence that doing so at least 24 hours after surfacing is associated with better outcomes.[271]

Most DCI cases requiring long distance evacuation will have significant symptoms and it is usually appropriate to maintain 100% oxygen administration throughout transport. This might not be possible in a commercial airliner, but some form of oxygen supplementation is usually possible and recommended. Periods of air breathing ('air breaks') to reduce the possibility of pulmonary oxygen toxicity are usually not necessary unless evacuations (including time spent organising them) are very long. There are no clear guidelines but, for example, in the New Zealand / South Pacific region, if an evacuation is likely to take more than six hours, a recurring pattern of two hours on oxygen and 30 minutes off oxygen is instituted, beginning with an air break after the first four hours of 100% oxygen administration. To avoid relapse induced by bubble mobilisation after postural change in cases suspected of having suffered cerebral AGE, it is recommended that the patient remains supine throughout the evacuation, even where there has been some degree of spontaneous recovery.

Delay to recompression

Recompression and hyperbaric oxygen administration is the definitive treatment for DCI (see below). The effect of delay to recompression on outcome is of relevance in evacuation planning. Indeed, the effect of delay may also influence decisions on how urgently to institute recompression when available. It is generally believed that in treating DCI (with DCS being by far the more common malady), the shorter the delay to recompression the better the response to the treatment. However, it is only in AGE or the more serious DCS cases with potentially disabling long term sequelae in which the eventual outcome may be materially affected by delay to recompression. Studies evaluating the effect of recompression delay without stratification of case severity are flawed because mild DCS cases (which are usually numerically superior) tend to spontaneously recover irrespective of delay, or indeed, irrespective of being recompressed or not.

In respect of patients defined as suffering serious DCS there are several datasets that suggest a measurable inflection in the risk of incomplete recovery on completion of all recompression treatment if the delay to recompression exceeds six hours.[130,258,272] The change in risk is around 20%; that is, incomplete recovery after completion of recompression treatment is seen in 40% of divers treated within six hours, and 60% of divers treated later than six hours. A recent and more comprehensive update to one of those studies shifts the inflection point earlier to three hours although the outcome difference was not dramatic (29% of patients recompressed within 3 hours had sequelae vs 42% after a delay of more than 3 hours).[273] This study also confirmed that the outcome disadvantage of delay was only apparent in more severely affected divers.

In respect of patients suffering AGE, a recent meta-analysis of observational studies of iatrogenic AGE provided strong evidence of a benefit from earlier compression. Patients with favourable (vs poor) outcomes were compressed on average 2.4 hours earlier. The proportion of favourable outcome decreased from approximately 65% when compression was started immediately, to 30% if compression was delayed for 15 hours.[274]

On balance, these studies are generally supportive of the concept that 'earlier is better' in recompression for AGE or serious DCS, but the measured advantage across the range of typical delays is not dramatic (particularly for DCS). One potential explanation for this is that even the shorter recompression delays in patients included in real-world clinical studies exceed a threshold where recompression will reliably make a substantial difference. There is some support for this hypothesis. In a recent evaluation of the potential utility of in-water recompression whose singular advantage is immediate recompression, one review documented extremely good outcomes (essentially complete recovery in all cases) for DCS arising after US Navy experimental dives where a recompression chamber was on site and divers with symptoms were recompressed with little or no delay.[80] Some of these cases had serious symptoms. Thus, it seems likely that the window of opportunity for 'ensuring' a good outcome in AGE or serious DCS may be measured

in minutes rather than hours, and that the effect of longer delays is more subtle.

Although efficacy may be reduced, it also seems clear that recompression may still be effective after relatively long delays.[275–277] This is perhaps not surprising given that bubbles seem capable of persisting in tissue for protracted periods after diving (even after recompression),[26] and that hyperbaric oxygen may have relevant anti-inflammatory effects which are discussed further below. There is no clear delay threshold beyond which recompression for DCI is considered of no use.

RECOMPRESSION FOR TREATMENT OF DECOMPRESSION ILLNESS

Definitive treatment of DCI can be subdivided into recompression and adjunctive treatment, the latter includes the use of fluids and drugs and will be discussed further below. Recompression involves returning the diver to a pressurised environment; usually in a hyperbaric chamber. In the modern context this invariably also involves breathing 100% oxygen, that is, the administration of hyperbaric oxygen (HBO). Recompression protocols will be discussed in greater detail below, but as a point of early clarification, 284 kPa (2.8 atm abs, 18 msw / 60 feet of seawater [fsw] equivalent) is considered the greatest pressure at which 100% oxygen can be safely breathed in a hyperbaric chamber environment before the risk of oxygen toxicity becomes unacceptably high. It follows that 284 kPa is adopted as the initial recompression pressure in the most commonly used protocols used for treating DCI.

There are several mechanisms by which HBO may be of added benefit.

Compression of bubbles

The volume of a bubble in the blood or tissues of a diver compressed to elevated pressure in a hyperbaric chamber will be reduced in direct proportion to the increase in pressure. However, volume change is asymptotic as pressure increases, with the greatest proportional volume changes occurring at the lower pressures.[272] Moreover, reductions in actual bubble dimension (such as diameter) are proportionally less than the changes in volume. Nevertheless, bubble volume reduction is of potential benefit if bubbles are occupying space and distorting structures in pain sensitive tissues such as periosteum, ligaments, tendons, joint capsules, or functionally sensitive tissues such as the inner ear or spinal cord white matter. Similarly, a cylindrical bubble in an arteriole occupying several generations of branching arterioles to produce obstruction will shorten when its volume reduces in response to recompression. Shortening will reduce bubble contact with the vessel wall thus reducing associated frictional forces, and may also reduce the number of branching arterioles occupied. These effects may increase the likelihood of the bubble redistributing.

Enhanced bubble redistribution provided a theoretical basis for use of recompressions to higher pressure such as 608 kPa (6 atm abs, 50 msw / 165 fsw equivalent), especially when treating divers suspected of suffering from AGE.[6] However, as noted above, the proportional change in bubble volume diminishes at progressively higher pressures, and compression beyond 284 kPa requires switching from breathing 100% oxygen to a mixture containing inert gas thus reducing the diffusion gradient for inert gas washout. It is perhaps not surprising that neither studies of AGE[278,279] nor DCS[280] *in vivo*, nor a retrospective review of human case outcomes[281] have found evidence of enhanced bubble redistribution or better outcomes in treatments beginning with an initial pressure exposure greater than 284 kPa. As discussed below, 'deeper' recompressions are now much less commonly used, and certainly not considered a standard of care.[282]

Preventing further growth of bubbles

A particular advantage of early recompression is preventing further growth of bubbles. Early after a dive, a bubble in supersaturated tissue will tend to grow through inward diffusion of supersaturated inert gas down a partial pressure gradient from tissue to bubble. In first aid, breathing 100% oxygen at surface pressure accelerates tissue inert gas washout and reduces tissue supersaturation as previously discussed, but it does not immediately stop bubbles from growing while tissue supersaturation exists. In contrast, if the diver is recompressed to a pressure greater than the dissolved gas partial pressure in the tissue, the tissue is no longer supersaturated because compression does not increase the partial pressure of the dissolved gas in incompressible tissue. In contrast, in a compressible bubble present in the tissue, the inert gas partial pressure increases in direct proportion to the compression pressure, reversing the previous tissue to bubble diffusion gradient such that gas now moves from bubble to tissue. To be of real value, compression is combined with oxygen breathing which not only prevents further inert gas uptake, but (as in first aid oxygen administration) also markedly increases the diffusion gradient for movement of gas from tissue to arterial blood and thence to the alveoli.

Oxygenation of compromised tissues

Hyperbaric oxygen markedly increases the PO_2 of dissolved oxygen in arterial blood and increases diffusion distances of oxygen through tissue.[283] The resulting potential for enhancement of oxygenation in vascular territories with compromised microcirculation is often cited as a generic advantage in many of the indications for HBO including DCI. To what extent enhanced oxygenation per se accounts for benefit in AGE or the various forms of DCS is unknown.

Anti-inflammatory action of HBO

Given that HBO administration inevitably induces a degree of oxidative stress, an anti-inflammatory / tissue repair effect

seems counterintuitive, but there is a substantial body of literature describing complex cell signalling effects and biochemical consequences that have anti-inflammatory outcomes and enhance tissue repair.[284] A detailed account is beyond the scope of this review, but some of these effects seem relevant to suppression of injurious processes, such as activation of pro-inflammatory microparticles or leucocyte accumulation at sites of bubble induced endothelial injury, that may be important in the pathophysiology of DCI.[285,286]

Evidence of efficacy

Recompression and HBO have achieved a 'standard-of-care' status for AGE and serious DCS in the absence of any randomised trials. Such trials would now be considered unethical because the supporting observational evidence is strong. This situation had its origins in the dramatic improvement in outcomes observed when recompression was introduced for the treatment of DCS arising during tunnelling and bridge building projects in New York and the UK.[287–290] Those recompressions were conducted using air rather than oxygen as the breathing gas, yet despite the shortcomings associated with this approach they were associated with marked reductions of mortality[289] and morbidity[290] when outcomes were compared to management without recompression. Nevertheless, there were still failures. Moreover, the air recompression protocols that evolved for treating divers were often started at high pressures, run over long durations, logistically difficult and risked DCS in chamber attendants. This prompted development of recompression using oxygen as the breathing gas by US Navy researchers in the 1960s.[291] Initial trials of so-called 'short oxygen tables' with a starting compression pressure of 284 kPa met with considerable success in treating DCS arising from US Navy experimental dives.[292] There remains, however, a paucity of data comparing different recompression strategies. Given the significant heterogeneity of DCI cases in terms of severity, organ system involvement, delay to recompression and other factors that may influence outcome, and the relatively small number of cases seen at most individual facilities, comparing outcomes following different recompression approaches in a large high-quality human study would be extremely difficult.

Multiplace vs monoplace hyperbaric chambers

In the narrative below there are references to the role of the inside attendant who accompanies the diver in a multiplace chamber. It is therefore germane at this point to briefly elaborate on the difference between multiplace and monoplace chambers in treatment of DCI.

Multiplace chambers are large enough for two or more occupants. They usually also have multiple interlinked compartments so that someone from outside could 'lock in' to the treatment compartment without changing its pressure. The chamber is pressurised with air and the patient breathes oxygen through a specialised delivery system. In multiplace chamber recompressions for DCI the patient is invariably accompanied by an inside attendant; typically a nurse with hyperbaric training or a diving medical technician. In contrast, a monoplace chamber accommodates only the patient. Some monoplace chambers are pressurised with oxygen and the patient simply breathes the chamber atmosphere.

There has been long standing controversy over whether it is appropriate to treat DCI in a monoplace chamber. Critics of using monoplace chambers for this purpose have pointed out an inability to compress to pressures greater than 284 kPa, to easily conduct air breaks, to conduct objective assessments of patient progress, and to manage seizures, excreta, and the needs of an intensive care patients. Virtually all of these concerns are either now less relevant or have been mitigated in various ways.[293] In the modern context, a capability to conduct recompressions to greater than 284 kPa is no longer considered mandatory for a therapeutic chamber. Higher pressure recompressions are rarely used and their use continues to decline. Monoplace chambers have evolved with many now having 'built in breathing systems' (BIBS) to allow the patient to breathe a gas other than the chamber atmosphere. Air breaks are therefore possible.

Some disadvantages of monoplace chambers are real but can be adequately mitigated to allow their use in treating DCI in selected patients. For example, patient response to treatment can be assessed subjectively, a seizure can be safely managed by decompressing the chamber to surface pressure once the seizure has passed, and toileting issues can be managed with urinal bottles, bedpans or catheterisation.[293] Intensive care patients are a challenge in either monoplace or multiplace settings. A multiplace chamber may offer a more readily adaptable environment, but experience has proven that practiced and appropriately equipped units can manage intensive care patients in monoplace chambers.[294]

Many modern monoplace chambers are capable of running standard treatment protocols for DCI such as a US Navy Treatment Table 6 (see below). Nevertheless, modified recompression protocols (sometimes shorter), have been developed for recompressing divers in monoplace chambers.[295–297] Outcomes using these protocols have been positively reported, even in cases with significant delays to recompression.[275] It is notable that a recent randomised comparison of a slightly modified Table 6 (duration 275 minutes) with a 160-minute protocol designed specifically for a monoplace chamber found that the shorter monoplace treatment resulted in a lower median number of treatments to reach recovery plateau or full recovery. The final outcomes were equivalent in the two groups which is not surprising because most of the treated cases suffered mild DCS.[298]

Preparation for recompression

Once a diver has arrived at a hyperbaric unit, DCI is diagnosed, and a decision made to recompress, there are some steps to take in preparation for recompression.

Recompression is a medical intervention with risks, and prior informed consent should be obtained from the patient if possible. As in any clinical situation, if a diver is unable to provide consent, then the treatment can be discussed with a guardian or close relative. Consent follows the same principles as used for any medical intervention. Patients should be informed of risks, benefits, alternative treatments and the implications of the null option (no treatment).

Risks of recompression include all forms of barotrauma that are possible in diving, however the risks are typically lower in a recompression because of the slower pressure changes. The most likely is middle ear barotrauma if there is failure to adequately equalise volume in the middle ear during compression.[299] This is rarely a problem with divers because they are very practiced at ear equalisation. Another relevant risk is oxygen toxicity. Cerebral oxygen toxicity occurs in about 0.56% (1:178) of US Navy Table 6 treatments.[300] It is reasonable to characterise these seizures as almost always benign and self-limiting though biting of the tongue or lips is possible, and recently the first report of a fatal oxygen toxic seizure emerged.[301] The latter case involved a morbidly obese patient who probably suffered airway management difficulties after a seizure. Subtle symptoms of pulmonary oxygen toxicity such as dry cough and mild retrosternal chest discomfort are likely after a Table 6, particularly if there has been prolonged first aid oxygen administration and / or the table is extended (see below). These symptoms usually spontaneously resolve over 24 hours after the treatment. Claustrophobia and anxiety are potential risks, but rarely a problem with divers. Fatal hyperbaric chamber accidents such as fire have occurred (see 'Safety and briefings' below) but are extremely rare.

The benefit of recompression is that it is the most effective means of treating DCI, and the most likely intervention to result in a cure. However, it is important to remind divers that recompression is not invariably successful, and residual symptoms after completion of all treatment are possible, especially in cases with serious neurological manifestations.

Alternative treatments and the null option are unlikely to be a plausible or sensible choice in AGE or serious DCS, but are legitimate topics to discuss in a diver with mild DCS. Nevertheless, as previously discussed, if readily available, recompression is recommended in mild DCS cases to improve the speed of recovery and possibly reduce risk of DON in musculoskeletal DCS if administered within 6–8 hours. Divers who have suffered cerebral AGE with apparent spontaneous recovery may legitimately question the need for recompression, but in that particular scenario the null option carries a risk of return of symptoms[6,302] and a poorly quantified risk of re-embolisation of the cerebral circulation with gas trapped in locations like the pulmonary veins and heart chambers. Therefore, recompression is still recommended.

Safety and briefings

It is important that the supervising clinician briefs the chamber operator and nursing staff on the diver's condition and the treatment plan. The diver themselves should also be briefed on what to expect during the recompression, including the need to equalise the ears as in diving, the purpose of air breaks, the possibility of extensions to the table, and what assessments are likely to be undertaken during the treatment. The diver should be reminded to notify the inside attendant if having trouble with ear equalisation during compression, or if developing any premonitory symptoms of oxygen toxicity such as muscle spasms, visual changes, tinnitus, or nausea. If the treatment is taking place in a multiplace chamber and the inside attendant is going to monitor certain signs for progress toward resolution, it is important that the supervising clinician demonstrate those signs to the attendant to ensure a shared common baseline.

Although fasting is not considered a pre-requisite for HBO, some clinicians prefer patients not to eat or drink immediately prior to or during the period at 284 kPa when the risk of cerebral oxygen toxicity is highest. Insertion of an intravenous cannula for IV fluid administration (see later) may be appropriate, and some clinicians prefer to have an IV cannula in situ for the initial recompression irrespective of the patient's need for IV fluid.

If the patient has spinal DCS or compromised consciousness they are likely to need catheterisation prior to recompression. A patient not requiring catheterisation may usefully be advised to attend to toileting matters prior to entering the chamber for a long recompression.

Other generic HBO safety strategies include ensuring the patient is dressed in non-flammable, pocketless clothing, and has been clearly warned about banned items that constitute a fire risk in a hyperbaric chamber. This includes most electrical devices such as phones and tablets.

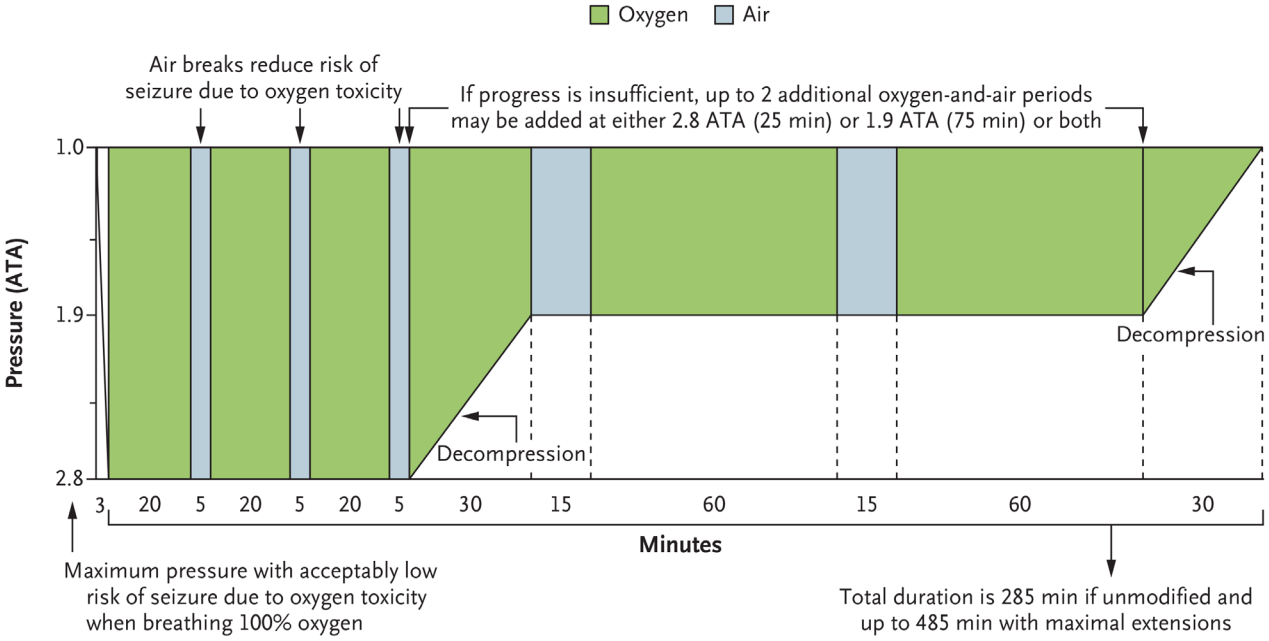
RECOMPRESSION PROTOCOLS FOR INITIAL TREATMENT

US Navy Treatment Table 6

The US Navy Treatment Table 6[303] (Figure 9) is the most commonly used initial recompression protocol for DCI[265]. This involves compression to 284 kPa (2.8 atm abs) with three oxygen breathing periods of 20 minutes separated by

Figure 9

Pressure / time / gas profile of the US Navy Treatment Table 6. ATA – atmospheres absolute pressure. Reproduced from New England Journal of Medicine, Mitchell SJ, Bennett MH, Moon RE, Decompression Illness, 386, 1254–64, Copyright © 2022 Massachusetts Medical Society. Reproduced with permission



five-minute air breaks, decompression to 193 kPa (1.9 atm abs) over 30 min, a 15 minute air break, two one hour oxygen breathing periods separated by a 15 minute air break, and finally, a 30 min decompression to surface pressure. The air breaks were inserted primarily to reduce the risk of cerebral oxygen toxicity; a strategy recently validated in a large human observational study.[304] The air breaks also offer an opportunity for conversations with the patient unimpeded by oxygen administration equipment, and for conducting assessments of symptoms and signs.

Table 6 can be lengthened up to two additional 25-minute periods at 284 kPa (20 minutes on oxygen and 5 minutes on air), or up to two additional 75-minute periods at 193 kPa (15 minutes on air and 60 minutes on oxygen), or both.[303] These 'extensions' are inserted at the discretion of the supervising clinician if there has been inadequate resolution of symptoms. There are no relevant definitive guidelines, but extensions are usually reserved for cases exhibiting serious symptoms. Mild DCS cases undergoing recompression are typically treated with a standard non-extended US Navy Table 6 or sometimes a US Navy Treatment Table 5 (see below).

Decision making about extending the table usually occurs for the first time at the second or third air break at 284 kPa. Related assessment may be undertaken by asking the patient about subjective symptoms, and through eliciting of signs by the inside attendant. If a twin-lock multiplace chamber is used, a medical supervisor may choose to be locked in briefly to perform the assessment themselves. Persistence of disabling symptoms like paraplegia are the strongest indication for extending the treatment. In contrast, in treating a diver for musculoskeletal pain that is reduced but not completely resolved after three oxygen periods at 284 kPa, most clinicians would not extend but rather continue with the decompression to 193 kPa with a confident expectation that the pain would continue to diminish over the remainder of the table.

In a multiplace chamber treatment, the inside attendant breathes oxygen for the last 30 minutes at 193 kPa and during the 30-minute decompression to surface pressure. If there has been more than one extension at either pressure the attendant breathes oxygen for the last 60 minutes at 193 kPa and during the decompression.

US Navy Treatment Table 5

US Navy Treatment Table 5 is a shorter recompression; it has two 20-minute oxygen breathing periods at 284 kPa and one short 20-minute period at 193 kPa.[303] As with the Table 6, the decompressions from 284 kPa to 193 kPa and from 193 kPa to surface pressure each take place over 30 minutes with the patient breathing oxygen. Table 5 can be used in the treatment of mild DCS or as a follow-up treatment (see below). Given Tables 5 and 6 begin identically, when treating mild DCS some clinicians take the approach of conducting the first two oxygen breathing periods. If there is complete or near complete resolution of the symptoms

after the second period at 284 kPa, they proceed with a Table 5 but if symptoms are persistent, the patient completes a Table 6. When conducted in a multiplace chamber, the inside attendant breathes oxygen for the final 30-minute decompression to surface pressure.

Other initial recompression protocols

Prior accounts of recompression for DCI are replete with diagrams of historic protocols, often involving initial 'deep' exposures during air breathing.[272] One that persisted into recent practice was the US Navy Treatment Table 6A which imposed an initial compression to 608 kPa for 30 minutes breathing air (or a treatment gas containing an oxygen fraction not greater than 50% so as to not exceed an inspired PO_2 greater than 304 kPa (3 atm abs)).[303] This was followed by a 35-minute decompression to 284 kPa where a standard Table 6 protocol would begin. This strategy was designed for use in immediate treatment of cerebral AGE with the aim of reducing bubble volume to a greater degree than achieved in a 284 kPa compression, and thereby enhancing bubble redistribution. As discussed above several studies failed to find evidence of an outcome advantage[280,281] and Table 6A has gradually fallen into disuse.

There are many other protocols, including so-called 'air saturation' tables which, in one example (the US Navy Treatment Table 7),[303] the diver was compressed to 284 kPa and remained there for at least 12 hours but potentially longer, breathing mainly air with short bouts of oxygen. This was followed by a very slow decompression and the entire treatment would take at least 36 hours and potentially several days. These treatments are logistically taxing, potentially hazardous for attendants, and often not successful. They were intended for use in serious DCS cases with little or no improvement during the early stages of a Table 6 at 284 kPa, or exhibiting relapse during decompression from 284 to 193 kPa. There is, however, no evidence that this strategy is any more successful than the more modern approach of completing a maximally extended Table 6 in refractory serious cases and instituting follow-up treatments (see below).

One 'deeper' treatment which has persisted into contemporary practice is the so-called Comex-30 table. The protocol for this table is inconsistently reported in the literature with various subtle differences between versions. In general terms, it combines a modest increase in pressure beyond 284 kPa (to 405 kPa, 4 atm abs, 30 msw equivalent) with breathing of a 50:50 oxygen-helium mixture for those initial portions of the protocol conducted at a higher pressure than 284 kPa. After periods at 405 kPa and 344 kPa breathing 50:50 oxygen-helium the patient is decompressed to 284 kPa and the table continues with oxygen breathing and air breaks in a pattern similar to a Table 6, although in some versions the lowest pressure period is spent at 222 kPa rather than 193 kPa.

In those places where it is used, the Comex 30 table is usually reserved for early presenting cerebral AGE or serious neurological DCS. The perceived advantage accrues from greater bubble compression and possibly the use of helium as a breathing gas. Non-diving studies have reported helium to have neuroprotective and anti-inflammatory properties.[305,306] This is an under-researched area in diving medicine, though one recent study comparing air versus trimix (oxygen, helium, nitrogen) as breathing gases during dives found no post-dive difference in inflammatory markers.[307] Helium breathing may also influence post-dive bubble evolution. In a series of studies in the early 1990s Hyldegaard and colleagues showed *in vivo* that exposure of bubbles containing principally nitrogen in spinal cord white matter, fat, and musculoskeletal tissue shrank more quickly during helium-oxygen breathing than during air or 100% oxygen breathing.[68,308,309] The biophysical explanation for these observations involves a complex interplay between gas diffusivity and solubility in blood and the various tissues involved, and is beyond the scope of this review. This work generated considerable enthusiasm about the potential for helium as a treatment gas in DCI. One very small non-randomised study showed equivalent outcomes for divers treated for neurological DCS with an initial T6 or 6A versus a helium-oxygen protocol despite the fact that the helium group appeared sicker at presentation.[310] However, a recent comprehensive study in a severe swine DCS model incorporated oxygen-helium breathing into T6 and T6A protocols and compared outcomes to treatment with standard T6 and T6A protocols. There was no outcome advantage in the helium (or higher pressure) groups.[280] There are no relevant randomised studies in humans. Despite its theoretical attraction and the early support from *in vivo* studies, the use of helium combined with higher pressure in recompression for DCI is not strongly supported by evidence and cannot be considered a standard of care.[282]

Decompression sickness occurring in specialised diving scenarios such as decompression from saturation diving and in unpressurised flights to high altitude is treated using specific protocols. Mild symptoms occurring at altitude may resolve simply with return to ground level, but at least two hours breathing 100% oxygen is recommended irrespective of recovery. Patients with pain who recover during oxygen breathing at ground level prior to recompression should be observed for 24 hours and may not require recompression. Patients with symptoms that persist at ground level should be recompressed, generally using a US Navy Treatment Table 5 or 6. Cardiopulmonary symptoms or progressive symptoms at ground level require 100% oxygen, IV hydration and urgent recompression using Table 6.[265]

Decompression sickness occurring during the very slow decompressions from saturation dives almost always manifests as musculoskeletal pain. Pausing the decompression, recompressing to or beyond depth of relief before resuming the de-compression, and administration

of a higher inspired fraction of oxygen are all potential interventions.[311] Detailed discussion is beyond the scope of this review.

Initial treatment by in-water recompression (IWR)

The question of whether divers should recompress themselves in-water after appearance of DCI symptoms has been extremely controversial, with the medical community generally not in favour until recently. This is because there are well-recognised risks such as an oxygen toxic seizure, worsening patient condition, hypothermia and drowning, whereas the benefit of the singular putative advantage (very rapid recompression) had not been convincingly demonstrated by data available in the public domain. Moreover, it was unclear whether the shorter, 'shallower' recompressions (compared to a Table 6) achievable in-water were actually effective. There was supportive anecdote for IWR using oxygen,[312,313] with most failures occurring when IWR was attempted using air.[314,315]

A recent review of this issue found evidence that allayed some relevant concerns and answered important relevant questions.[80] Review of US Navy experimental diving databases revealed an extensive history of very early recompression for DCS (including serious symptoms) following experimental dives, with outcomes clearly superior to those reported for later-presenting recreational divers.[80] In addition, US Navy trials to develop the short oxygen tables in the 1960s demonstrated that short, 'shallow' (for example, 203 kPa, 2 atm abs, 10 msw / 33 fsw equivalent for 30 minutes) recompression was effective in most cases.[292] In relation to the risk of drowning if a seizure occurs, recent data imply that mouthpiece retaining devices[316] or full-face masks[317] may be effective in protecting to airway to allow safe surfacing. Heated dry suits and the use of habitats in caves can help reduce the risk of hypothermia in cold environments.[318] A final development that has influenced perception of IWR is the emergence of technical divers who are explicitly trained and equipped for the use of 100% oxygen in-water as part of their decompression protocols.[118]

This confluence of evidence suggesting that the advantage of IWR is real and that the risks can be mitigated has resulted in cautious and conditional endorsement of IWR by the medical community.[124] The conditional recommendations are that IWR using oxygen be performed only if recompression in a chamber will take longer than two hours to access, if there are no contraindications, if all involved (patient, buddy, supervisor) are trained to decompression procedures level (which includes the use of 100% oxygen) or above, if a stable under-water platform (shot line or decompression stage) is used, if a mouth-piece retainer or full-face mask is employed, along with other recommendations. There are various protocols described,[80] but none involve exposure to oxygen deeper than 193 kPa (9 msw). IWR using air is not recommended. IWR is best seen as a first aid procedure, and on completion, divers may require evacuation for more definitive recompression. At the very least this should be discussed with a diving medicine expert.

FOLLOW-UP RECOMPRESSIONS

In the event that there are residual symptoms following the initial recompression, further recompressions are typically recommended. The pathophysiological basis for further recompression is that bubbles may still persist,[26] and the anti-inflammatory effect[284–286] or oxygen delivery enhancement[283] achieved in HBO may continue to be relevant.

The usual approach to follow-up recompression is once daily treatment using a shorter protocol than the initial recompression until there is either complete recovery or no sustained improvement over two consecutive days.[4,265] There are many protocols used for follow-up recompression, but in general they involve compression to between 243 and 284 kPa (2.4 to 2.8 atm abs) for 60 to 120 minutes of oxygen breathing. The US Navy Table 5 described earlier is one potential choice as is US Navy Table 9 (a compression to 243 kPa with three 30-minute oxygen breathing periods separated by 5-minute air breaks).[303] In facilities where logistics demand it, DCI patients requiring follow-up recompressions have been included in routine multiplace chamber treatments of patients with non-diving indications for HBO.[272] There are no data establishing superiority of one approach compared to another.

Apart from the differing nature of follow-up treatment protocols, there are other occasional variations from this paradigm. In serious AGE or DCS cases with a poor response to (or significant relapse after) the initial treatment, some clinicians choose to repeat the initial table (such as a Table 6) as the first follow-up recompression. In these scenarios the timing of the first follow-up is sometimes pushed forward to earlier than 'the next day' depending on logistic factors and the patient's tolerance of the oxygen exposure. Another variation is the policy of some units to give one further follow-up recompression after full resolution of symptoms; a practice sometimes referred to as 'one for the road'. Users justify this practice with anecdotal reports of reduced post-discharge relapse of symptoms. None of these variations are validated with human data.

ADJUNCTS TO RECOMPRESSION FOR DECOMPRESSION ILLNESS

The administration of fluids and drugs, and other miscellaneous interventions are potentially part of the definitive management of DCI.

Fluids in treatment of decompression illness

Intravenous and oral fluids were mentioned earlier in discussion of first aid for DCI. The importance of their role

in definitive management is largely dictated by the severity of the patient's condition.

In mild DCS IV fluids are unnecessary, but in initial recompression of any diver it is the author's personal preference to place an IV cannula and run 1000 ml of a balanced electrolyte (non-glucose containing) crystalloid fluid over the course of a Table 6. This may have little or no therapeutic benefit, but it ensures that the IV is functioning.

In AGE or DCS with more serious symptoms there is *in vivo* evidence that dehydration is disadvantageous,[261] and purposive rehydration may therefore be beneficial. In this setting it is recommended to provide IV fluids. A common approach is to give 1000 ml of crystalloid fluid reasonably quickly, and then titrate further fluids to maintain an hourly urine output greater than 0.5–1 $ml \cdot kg^{-1} \cdot h^{-1}$. In fulminant DCS with haemoconcentration and shock, intensive care including aggressive IV fluid resuscitation is required as a life-saving intervention.[43] Large bore IV access, arterial and central venous cannulation, and urethral catheterisation are strongly recommended. Vital signs and serial arterial blood gas measurement of haemoglobin will help guide fluid resuscitation. High volumes of fluid given rapidly and inotropic and vasopressor support may be required to achieve haemodynamic stability. There is no evidence of superiority for crystalloid or colloid fluid in fulminant DCS. The CHEST randomised study of saline vs hydroxyethyl starch for fluid resuscitation in 'all comers' to intensive care reported no difference in mortality, but a higher proportion of patients receiving starch required renal replacement therapy.[319] Sedation, intubation and mechanical ventilation may be required.[43] Although clinicians are invariably motivated to initiate recompression as soon as possible, when dealing with a shocked unstable patient a process of expeditious resuscitation / stabilisation with establishment of lines and monitoring etc is often advisable before recompression because some interventions are difficult or hazardous once compressed.

Drugs in the treatment of decompression illness

Many drugs have been proposed for use in treatment of DCI, usually on the basis of theoretical attraction or the results of *in vivo* experiments. Only one has actually undergone formal testing in human DCI. A summary of relevant drugs is provided in Table 6[320–343] and several drugs are discussed in greater detail below.

Non-steroidal anti-inflammatory drugs (NSAIDS)

The only randomised double blind trial of any pharmacologic intervention in human DCS to date involved the use of the NSAID tenoxicam as an adjunct to recompression (20 mg once daily for seven days starting with the initial recompression) in mainly mild DCS.[320] Patients who received tenoxicam required fewer follow-up recompressions to achieve full recovery or plateau than patients who received the placebo. There was no difference in final outcome. The number need to treat to prevent one recompression was five. Tenoxicam was chosen for the study because of its once daily dosing regimen; considered likely to result in better participant compliance in the study. It is likely that the measured difference in recovery trajectory is a class effect and could be achieved with any NSAID. These drugs are widely accepted as an adjunct to recompression in DCS, or as part of the treatment without recompression measures for mild DCS. There is no widely accepted protocol for their use, but sustained use over a week after onset as in the published study seems sensible.

Fractionated heparin

Like any immobile patient, a diver with paraplegia from spinal DCS is at high risk of venous thrombosis and consequent thromboembolic events. Although it has no known role in modifying the course of DCS, prophylactic anticoagulation should be started as soon as possible for any diver likely to be confined to bed for a protracted period. Compression stockings, and automatic pneumatic calf compressors or foot pumps are other strategies that should be considered in this setting.

Lignocaine (lidocaine)

Lignocaine, an amide local anaesthetic and anti-arrhythmic drug which acts by sodium channel blockade, is neuroprotective, particularly if present at the onset of transient neuronal hypoxia. Hypoxia results in interruption of energy metabolism, a loss of transmembrane ion homeostasis, sodium influx, neuronal depolarisation and a subsequent cascade of events involving release of excitotoxins, calcium fluxes and neuronal death or apoptosis. Lignocaine may delay these processes by preventing sodium influx. It also has significant anti-inflammatory properties, particularly in relation to leucocyte-mediated processes.[322] It is perhaps not surprising that early animal studies suggested that lignocaine was neuroprotective in animal models of arterial gas embolism; an injury potentially involving transient ischaemia and leucocyte activation. There is extensive evidence based on *in vitro* and *in vivo* work that demonstrates lignocaine in clinically relevant plasma levels to be neuroprotective in a variety of injury models.[322]

Lignocaine has been investigated as a neuroprotective agent in human randomised trials, primarily in the setting of cardiac surgery in which one potential mechanism of brain injury is an almost invariable exposure to small arterial bubbles.[232,344] There have been mixed results but a recent meta-analysis suggests benefit (Habibi et al. 2018).[323] On the basis of this evidence, lignocaine has been accepted as a potentially useful intervention in early management of AGE,[4,321] but it is not promoted as a standard of care. None of the relevant animal or human studies have been in

Table 6

Drugs proposed as potentially useful in treatment of decompression illness. COX – cyclooxygenase; DCS – decompression sickness; NSAID – non-steroidal anti-inflammatory drug. Adapted from New England Journal of Medicine, Mitchell SJ, Bennett MH, Moon RE, Decompression Illness, 386, 1254–64, Copyright © 2022 Massachusetts Medical Society. Reproduced with permission

Drug	Action	Comments
Acceptable in DCS		
Tenoxicam	Non-specific COX inhibitor	Reduced number of recompressions to reach recovery or plateau in a human trial in DCS.[320] Probably a class effect, and similar effect likely for other NSAIDs. Used as an adjunct to recompression
Fractionated heparin	Anticoagulant	Recommended after first recompression for deep venous thrombosis prevention in immobile spinal DCS patients[321]
Acceptable in AGE		
Lignocaine (Lidocaine)	Sodium channel blocker Anti-inflammatory	Neuroprotective when given prophylactically in many animal models of neuronal injury including arterial gas embolism.[322] Investigated in human cardiac surgery patients who are exposed to cerebral arterial bubbles. Meta-analysis suggests some neuroprotective benefit in humans.[323] Possibly useful early after AGE.[4] Not tested in DCS. Not a standard of care
Experimental		
Aspirin	Antiplatelet	Mild reduction of severity in DCS in rats when given prophylactically.[324,325] No human evidence, but used clinically in some jurisdictions
Clopidogrel, Abciximab, Tirofiban	Potent antiplatelet	Substantial reduction of severity[32,324,325] and lung inflammation[326] in DCS in rats when given prophylactically. No human evidence
Methyl-prednisolone, Dexamethasone	Steroids Anti-inflammatory	In canine AGE prophylactic dexamethasone was marginally beneficial, but no effect when given therapeutically.[327] Methylprednisolone given therapeutically worsened outcome in two animal models of spinal DCS.[328,329] No human evidence but used clinically in some jurisdictions
Perfluoro-carbon emulsions	Enhancement of gas transport	Animal studies in DCS suggest benefit when given prophylactically[330] or therapeutically.[331,332] Some negative studies.[333,334] No human evidence and currently not available for human use
Ulinastatin	Anti-inflammatory	Mortality and severe DCS reduced in rabbits[335]
Xuebijing	Anti-inflammatory	Composite herbal medicine. Reduced lung injury in rabbits with severe DCS when administered after decompression[336]
Escin	Anti-inflammatory	Prophylactic administration reduced mortality, severity and endothelial dysfunction in rats with severe DCS.[337]
Enalapril	ACE-inhibitor	Prophylactic administration reduced mortality and incidence of DCS in rats[338]
Fluoxetine	Selective serotonin reuptake inhibitor	Prophylactic administration reduced incidence of DCS and improved motor and sensory recovery in mice and rats[339,340]
Nitroglycerine	Vasodilator	Prophylactic administration reduced venous bubble formation in decompressed swine.[341] One negative study in rats[342]
1,3-butanediol acetoacetate diester	Antioxidant Anti-inflammatory	Prophylactic administration reduced incidence of DCS and inflammatory response to DCS in rats[343]

neurological DCS and despite positive case reporting in that setting, lignocaine is not recommended. When used in AGE, the goal is to use a bolus plus infusion regimen to establish plasma levels considered useful for antiarrhythmic purposes. There are no definitive guidelines on the appropriate duration of the infusion, but a 12–24 hour infusion is a plausible goal.

Other drugs

The use of other drugs explicitly for treating DCI cannot be justified on the basis of evidence at this time. Nevertheless, as noted in Table 6 there are a number of 'agents of interest' and considerable regional variation in practice. For example, in some European centres it appears routine to administer

aspirin and methylprednisolone to DCS cases (Blatteau et al. 2020).[136] The use of other drugs may be required to achieve particular therapeutic goals. For example, inotropes and vasopressors may be required in managing haemodynamic instability, and anaesthetic agents, opiates and muscle relaxants may be required if a patient requires intubation and ventilation.

Other adjunctive interventions

In patients with severe neurological manifestations of DCI general principles of neurological intensive care should apply. Hypotension should be avoided, with support of blood pressure using fluids and vasopressors if necessary. Patients should be kept normothermic, and even mild hyperthermia should be actively suppressed. Normoglycaemia should be maintained. These patients also typically require urethral catheterisation for bladder atonia. Immobile patients should be managed in beds designed for spinal care to avoid pressure areas. The importance of thrombosis prophylaxis was discussed above. Physiotherapists should be involved early to maintain limb mobility.

Oxygen administration is discontinued between recompression treatments unless there is another indication for its continuation such as hypoxia from concurrent near drowning. In divers with mild symptoms it can be appropriate for them to leave the hospital between treatments, for example, if they live in the same city.

ADVICE ON COMPLETION OF TREATMENT

On completion of all hyperbaric treatment there are various issues that need to be addressed and advice provided. A diver with serious DCI who has not fully recovered and is disabled in some manner may require discharge or referral to a rehabilitation service of the type that normally deals with spinal injury patients. Thankfully this is an uncommon scenario and is not discussed further. The rest of this narrative pertains to the much more common scenario of a fully or near fully recovered patient fit to return home.

There are several elements of essentially generic advice for discharging patients. Recently recovered DCI patients should be advised to report any relapse of significant symptoms. This can be a nuanced conversation, and the clinician should aim to avoid engendering hypervigilance for trivial sensations that occur in everyday life. Patients who have been recompressed for mild symptoms like musculoskeletal pain can be reassured that fleeting aches in the same distribution as their original pain are common, and usually not an indication for further recompression. Fatigue is also common after treatment for DCI. Related advice is to transition back into normal activity (especially exercise) slowly. Excessive exercise can easily produce symptoms that might be interpreted by the patient as a relapse.

Flying after recompression for DCI

A common pressing issue for the DCI patient, given that recompression treatment may have occurred at a location distant from their home, is ‘when can I fly’? To a lesser extent the same question is relevant to driving over high hills (notionally > 300 m). The concern is that the hypobaric exposure occurring during flight may cause relapse by allowing any residual bubbles to expand, or through some other un-known mechanism.

This issue is very poorly informed by data and there is considerable variation in the advice given. In a 2004 survey of US hyperbaric facilities and treated divers, facilities reported median recommended pre-flight wait times of three days (range 1–7) and five days (range 2–7) after treatment for mild and serious DCS respectively. Responding divers reported a median recommended pre-flight wait time of three days (range 1–30).[345] With those recommendations in mind, it was reported that three divers who relapsed during flight had waited 14 hours, three days and 10 days preflight. This illustrates the difficulty in formulating reliable advice. Interestingly, responding divers reported similar rates of post-recompression relapse whether they flew or not. These data reveal a confused picture of highly variable advice, relapses occurring despite adherence to that advice, and some uncertainty over the true magnitude of the risk.

Another observational study examining relapse rates in divers who waited (after recompression) less than three days versus three or more days found that whether the diver had experienced complete resolution of symptoms or not before flying was a more robust predictor of symptom relapse or worsening during flight than preflight wait time.[346] The latter results suggest that the preflight wait time might best be tailored to the injured diver’s circumstances as opposed to a reflex application of the popular 3–5 day recommendation. Thus, a diver recompressed for mild DCS with a rapid and complete recovery on the initial recompression might be recommended a wait time of three days. In contrast, a diver with residual leg weakness and lower limb proprioceptive impairment that was slow to respond to recompression might be advised to wait for at least a week or more. The arbitrary nature of these recommendations, the likelihood that risk reduces with time, and the impossibility of guaranteeing risk-free travel within realistic time frames would form the basis of a risk vs benefit discussion with the patient so they can make a choice about when to fly as an informed risk acceptor.

RETURN TO DIVING AFTER RECOMPRESSION FOR DCI

There are three criteria frequently applied to the question of whether it is appropriate for a diver to return to diving after treatment for DCI.

First, the diver should have made a full recovery. With particular reference to the neurological system, this recommendation has its roots in the concept of organ system reserve. Thus, it is possible that a diver with residual neurological dysfunction may be more likely to exhibit greater permanent functional impairment if injured again in another episode of DCI. In addition, a diver with residual functional limitation after DCI may be less able to cope with the functional requirements of diving.

Second, there should be no suspicion that pulmonary barotrauma was part of the pathophysiological process. Such suspicion would obviously be present in any case of AGE. The concern is that pulmonary barotrauma may have arisen because of an underlying pulmonary abnormality. An additional, albeit poorly validated concept, is that a barotraumatic event may create 'scarring' in the lung parenchyma that could predispose to a further event. In divers fully recovered after suspected AGE who are highly motivated to return to diving, one option is to undertake a high-resolution chest CT scan to look for any pre-existing or secondarily induced predispositions. If none are found, the diver could choose to return to diving after a careful explanation that no guarantees against a repeat event can ever be given. A problem with this approach is that high resolution CT is very sensitive and may detect lesions of uncertain significance.[248]

Third, there should be no suspicion that a DCS event fits a pattern suggesting a predisposition. For example, the occurrence of DCS symptoms associated with a right-to-left shunt (see earlier) after a relatively non-provocative dive would raise suspicion of a PFO or pulmonary shunt. In such situations the path to return to diving for a motivated diver might involve investigation using bubble contrast echocardiography (see earlier). The results would facilitate a risk versus benefit discussion of closing a PFO (if one is found), adopting more conservative diving practices, or ceasing diving altogether. Once again, it needs to be made clear to any diver returning to diving after DCS that no matter what risk mitigation strategies are employed, recurrence is always a possibility.

In reality, the majority of DCS cases recover fully, meet the above criteria, and many elect to return to diving. This raises the question of how long they should wait. There are no evidence-based guidelines. A popular recommendation is not to resume diving for at least a month after completion of treatment and full recovery of symptoms. A longer period may be recommended for divers who have suffered serious neurological DCS, especially where full recovery was slow. Anecdotally, many divers have opted to return to diving much more quickly following mild DCS events.

References

1 Mitchell SJ. DCS or DCI? The difference and why it matters. Diving Hyperb Med. 2019;49:152–3. doi: 10.28920/dhm49.3.152-153. PMID: 31523788. PMCID: PMC6881199.

2 Hills BA, Butler BD. Size distribution of intravascular air emboli produced by decompression. Undersea Biomed Res. 1981;8:163–70. PMID: 7292785.

3 Butler BD, Hills BA. The lung as a filter for microbubbles. J Appl Physiol Respir Environ Exerc Physiol. 1979;47:537–43. doi: 10.1152/jappl.1979.47.3.537. PMID: 533747.

4 Mitchell SJ, Bennett MH, Moon RE. Decompression sickness and arterial gas embolism. N Eng J Med. 2022;386:1254–64. doi: 10.1056/NEJMra2116554. PMID: 35353963.

5 Golding FC, Griffiths P, Hempleman HV, Paton WD, Walder DN. Decompression sickness during construction of the Dartford tunnel. Br J Ind Med. 1960;17:167–80. doi: 10.1136/oem.17.3.167. PMID: 13850667. PMCID: PMC1038052.

6 Leitch DR, Green RD. Pulmonary barotrauma in divers and the treatment of cerebral arterial gas embolism. Aviat Space Environ Med 1986;57:931–8. PMID: 3778391.

7 Moon RE, Camporesi EM, Kisslo JA. Patent foramen ovale and decompression sickness in divers. Lancet. 1989; 333(8637):513–4. doi: 10.1016/s0140-6736(89)90064-0. PMID: 2564057.

8 Wilmshurst PT, Byrne JC, Webb-Peploe MM. Relation between interatrial shunts and decompression sickness in divers. Lancet. 1989;334(8675):1302–6. doi: 10.1016/s0140-6736(89)91911-9. PMID: 2574256.

9 Smith DH, Francis TJR, Pethybridge RJ, Wright JM, Sykes JJW. Concordance: a problem with the current classification of diving disorders. Undersea Biomed Res. 1992;18(Supp):40.

10 Francis TJR, Smith DH, editors. Describing Decompression Illness: The Forty-second Undersea and Hyperbaric Medical Society Workshop. Bethesda (MD): Undersea and Hyperbaric Medical Society; 1991.

11 Sastry S, Daly K, Chengodu T, McCollum C. Is transcranial Doppler for the detection of venous-to-arterial circulation shunts reproducible? Cerebrovasc Dis. 2007;23:424–9. doi: 10.1159/000101466. PMID: 17406112.

12 Bommer WJ, Shah PM, Allen H, Meltzer R, Kisslo J. The safety of contrast echocardiography: report of the committee on contrast echo-cardiography for the American Society of Echocardiography. J Am Coll Cardiol. 1984;3:6–13. doi: 10.1016/s0735-1097(84)80423-4. PMID: 6690558.

13 Romero JR, Frey JL, Schwann LH, Demaerschalk BM, Chaliki HP, Parikh G, et al. Cerebral ischemic events associated with 'bubble study' for identification of right to left shunts. Stroke. 2009;40:2343–8. doi: 10.1161/STROKEAHA.109.549683. PMID: 19498192.

14 Banham ND, Saw J, Hankey GJ, Ghia D. Cerebral arterial gas embolism proven by computed tomography following transthoracic echocardiography using bubble contrast. Diving Hyperb Med. 2020;50:300–2. doi: 10.28920/dhm50.3.300-302. PMID: 32957135. PMCID: PMC7819724.

15 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;106:298–301. doi: 10.1152/japplphysiol.90915.2008. PMID: 18801958.

16 Blogg SL, Tillmans F, Lindholm P. The risk of decompression illness in breath-hold divers: a systematic review. Diving Hyperb Med. 2023;53:31–41. doi: 10.28920/dhm53.1.31-41. PMID: 36966520. PMCID: PMC10106275.

17 Doolette DJ, Mitchell SJ. The physiological kinetics of nitrogen and the prevention of decompression sickness. Clin Pharmacokinetics. 2001;40:1–14. PMID: 11236806.

18 Doolette DJ. Gas micronuclei that underlie decompression

bubbles and decompression sickness have not been identified. Diving Hyperb Med. 2019;49:64. doi: 10.28920/dhm49.1.64. PMID: 30856670. PMCID: PMC6526047.

19 Eckenhoff RG, Olstad CS, Carrod G. Human dose-response relation-ship for decompression and endogenous bubble formation . J Appl Physiol. 1990;69:914–8. doi: 10.1152/jappl.1990.69.3.914. PMID: 2246178.

20 Blatteau J-E, Souraud J-B, Gempp E, Boussuges A. Gas nuclei, their origin, and their role in bubble formation. Aviat Space Environ Med 2006;77:1068–76. PMID: 17042253.

21 Arieli R. Nanobubbles form at active hydrophobic spots on the luminal surface of blood vessels: consequences for decompression illness in diving and possible implications for autoimmune disease – an overview. Front Physiol. 2017;8:591. doi: 10.3389/fphys.2017.00591. PMID: 28861003. PMCID: PMC5559548.

22 Arieli R, Marmur A. Decompression sickness bubbles: are gas micronuclei formed on a flat hydrophobic surface? Respir Physiol Neurobiol. 2011;177:19–23. doi: 10.1016/j.resp.2011.02.013. PMID: 21376842.

23 Burns BA, Hardman JM, Beckman EL. In situ bubble formation in acute central nervous system decompression sickness. J Neuropathol Exp Neurol 1988;47:371.

24 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;47:475–87. doi: 10.1097/00005072-198807000-00008. PMID: 3385440.

25 Francis TJ, Griffin JL, Homer LD, Pezeshkpour GH, Dutka AJ, Flynn ET. Bubble-induced dysfunction in acute spinal cord decompression sickness. J Appl Physiol (1985). 1990;68:1368–75. doi: 10.1152/jappl.1990.68.4.1368. PMID: 2347778.

26 Dapena JC, Lansdorp CA, Mitchell SJ. Persistent extravascular bubbles on radiologic imaging after recompression treatment for decompression sickness; a case report. Diving Hyperb Med. 2020;50:424–30. doi: 10.28920/dhm50.4.424-430. PMID: 33325027. PMCID: PMC8026230.

27 Blogg SL, Gennser M, Møllerløkken A, Brubakk AO. Ultrasound detection of vascular decompression bubbles: the influence of new technology and considerations on bubble load. Diving Hyperb Med. 2014;44:35–44. PMID: 24687484. [cited 2024 Jan 12]. Available from: https://dhmjournal.com/images/IndividArticles/44March/Blogg_dhm.44.1.35-44.pdf.

28 McCune EP, Le DQ, Lindholm P, Nightingale KR, Dayton PA, Papadopoulou V. Perspective on ultrasound bioeffects and possible implications for continuous post-dive monitoring safety. Diving Hyperb Med. 2022;52:136–48. doi: 10.28920/dhm52.2.136-148. PMID: 35732286. PMCID: PMC9522608.

29 Blogg SL, Gensser M. The need for optimisation of post-dive ultra-sound monitoring to properly evaluate the evolution of venous gas emboli. Diving Hyperb Med. 2011;41:139–46. [cited 2024 Jan 12]. Available from: https://dhmjournal.com/images/IndividArticles/41Sept/Blogg_dhm.41.3.139-146.pdf.

30 Doolette DJ. Venous gas emboli detected by two-dimensional echocardiography are an imperfect surrogate endpoint for decompression sickness. Diving Hyperb Med. 2016;46:4–10. PMID: 27044455. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/46March/Doolette_dhm.46.1.4-10.pdf.

31 Møllerløkken A, Blogg SL, Doolette DJ, Nishi RY, Pollock NW. Consensus guideline for the use of ultrasound in diving research. Diving Hyperb Med. 2016;46:26–32. PMID: 27044459. [cited 2024 Jan 31]. Available from: https://www.dhmjournal.com/images/IndividArticles/46March/Mollerlokken_dhm.46.1.26-32.pdf.

32 Lambrechts K, de Maistre S, Abraini JH, Blatteau J-E, Risso J-J, Vallee N. Tirofiban, a glycoprotein IIb/IIIa antagonist, has a protective effect of decompression sickness in rats: is the crosstalk between platelet and leukocytes essential? Front Physiol. 2018:00906. doi: 10.3389/fphys.2018.00906. PMID: 30050468. PMCID: PMC6050390.

33 Nishi RY, Brubakk AO, Eftedal OS. Bubble detection. In: Brubakk AO, Neuman TS, editors. Bennett and Elliott's physiology and medicine of diving. Edinburgh: Saunders; 2003. p. 501–29.

34 Nossum V, Koteng S, Brubakk AO. Endothelial damage by bubbles in the pulmonary artery of the pig. Undersea Hyperb Med. 1999;26:1–8. PMID: 10353178.

35 Philp RB. A review of blood changes associated with compression-decompression: relationship to decompression sickness. Undersea Biomed Res. 1974;1:117–50. PMID: 4469186.

36 Pontier JM, Vallee N, Bourdon L. Bubble-induced platelet aggregation in a rat model of decompression sickness. J Appl Physiol (1985). 2009;107:1825–9. doi: 10.1152/japplphysiol.91644.2008. PMID: 19850726.

37 Ward CA, Koheil A, McCullough D, Johnson WR, Fraser WD. Activation of complement at plasma-air or serum-air interface of rabbits. J Appl Physiol (1985). 1986;60:1651–8. doi: 10.1152/jappl.1986.60.5.1651. PMID: 3710983.

38 Ogston D, Bennett B. Surface mediated reactions in the formation of thrombin, plasmin and kallikrein. Br Med Bull. 1978;34:107–12. PMID: 148934.

39 Hallenbeck JM, Bove AA, Moquin RB, Elliott DH. Accelerated coagulation of whole blood and cell-free plasma by bubbling in vitro. Aerosp Med. 1973;44:712–4. PMID: 4715083.

40 Helps SC, Gorman DF. Air embolism of the brain in rabbits pre-treated with mechlorethamine. Stroke. 1991;22:351–4. doi: 10.1161/01.str.22.3.351. PMID: 2003304.

41 Thom SR, Bennett M, Banham ND, Chin W, Blake DF, Rosen A, et al. Association of microparticles and neutrophil activation with decompression sickness. J Appl Physiol (1985). 2015;119:427–34. doi: 10.1152/japplphysiol.00380.2015. PMID: 26139218.

42 Yu X, Xu J, Liu W, Xu W. Bubbles induce endothelial microparticle formation via a calcium-dependent pathway involving flippase inactivation and rho kinase activation. Cell Physiol Biochem. 2018;46:965–74. doi: 10.1159/000488825. PMID: 29669319.

43 Trytko B, Mitchell SJ. Extreme survival: a deep technical diving accident. SPUMS Journal. 2005;35:23–7. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/35March/Trytko_dhm.35.1.23.27.pdf.

44 Hallenbeck JM, Bove AA, Elliott DH. Mechanisms underlying spinal cord damage in decompression sickness. Neurology. 1975;25:308–16. doi: 10.1212/wnl.25.4.308. PMID: 1168317.

45 Dunford RG, Vann RD, Gerth WA, Pieper CF, Huggins K, Wachholz C, et al. The incidence of venous gas emboli in recreational diving. Undersea Hyperb Med. 2002;29:247–59. PMID: 12797666.

46 Lautridou J, Dugrenot E, Amérand A, Guernec A, Pichavant-Rafini K, Goanvec C, et al. Physiological characteristics associated with increased resistance to decompression sickness in male and female rats. J Appl Physiol (1985). 2020;129:612–25. doi: 10.1152/japplphysiol.00324.2020. PMID: 32702269.

47 Dugrenot E, Orsat J, Guerrero F. Blood pressure in rats selectively bred for their resistance to decompression sickness. Diving Hyperb Med. 2022;52:119–25. doi: 10.28920/dhm52.2.119-125. PMID: 35732284. PMCID: PMC9522594.

48 Verstappen FT, Bernards JA, Kreuzer F. Effects of pulmonary gas embolism on circulation and respiration in the dog. III. Excretion of venous bubbles by the lung. Pflugers Arch. 1977;370:67–70. doi: 10.1007/BF00707947. PMID: 561384.

49 Verstappen FT, Bernards JA, Kreuzer F. Effects of pulmonary gas embolism on circulation and respiration in the dog. I. Effects on circulation. Pflugers Arch. 1977;368:89–96. doi: 10.1007/BF01063459. PMID: 558602.

50 Zhang K, Wang D, Jiang Z, Ning X, Buzzacott P, Xu W. Endothelial dysfunction correlates with decompression bubbles in rats. Sci Rep. 2016;6:33390. doi: 10.1038/srep33390. PMID: 27615160. PMCID: PMC5018851.

51 Siaffa R, Luciani M, Grandjean B, Coulange M. Massive portal venous gas embolism after scuba diving. Diving Hyperb Med. 2019;49:61–3. doi: 10.28920/dhm49.1.61-63. PMID: 30856669. PMCID: PMC6526053.

52 Oh SH, Kang HD, Jung SK, Choi S. Successful treatment of decompression sickness complicated with acute hepatic infarction and acute kidney injury; a case report. Undersea Hyperb Med. 2019;46:81–5. PMID: 31154689.

53 Honěk J, Šrámek M, Šefc L, Januška J, Fiedler J, Horváth M, et al. High-grade patent foramen ovale is a risk factor of unprovoked decompression sickness in recreational divers. J Cardiol. 2019;74:519–23. doi: 10.1016/j.jjcc.2019.04.014. PMID: 31255461.

54 Germonpré P, Dendale P, Unger P, Balestra C. Patent foramen ovale and decompression sickness in sports divers. J Appl Physiol (1985). 1998;84:1622–6. doi: 10.1152/jappl.1998.84.5.1622. PMID: 9572808.

55 Wilmshurst P, Bryson P. Relationship between the clinical features of neurological decompression illness and its causes. Clin Sci (Lond). 2000;99:65–75. PMID: 10887059.

56 Wilmshurst PT, Pearson MJ, Walsh KP, Morrison WL, Bryson P. Relationship between right-to-left shunts and cutaneous decompression illness. Clin Sci (Lond). 2001;100:539–42. PMID: 11294694.

57 Cantais E, Louge P, Suppini A, Foster PP, Palmier B. Right-to-left shunt and risk of decompression illness with cochleovestibular and cerebral symptoms in divers: Case control study in 101 consecutive dive accidents. Crit Care Med. 2003;31:84–8. doi: 10.1097/00003246-200301000-00013. PMID: 12544998.

58 Gempp E, Blatteau J-E, Pontier J-M, Balestra C, Louge P. Preventive effect of pre-dive hydration on bubble formation in divers. Br J Sports Med. 2009;43:224–8. doi: 10.1136/bjsm.2007.043240. PMID: 18308884.

59 Klingmann C, Benton PJ, Ringleb PA, Knauth M. Embolic inner ear decompression illness: correlation with a right to left shunt. Laryngoscope 2003;113:1356–61. doi: 10.1097/00005537-200308000-00017. PMID: 12897559.

60 Torti S, Billinger M, Schwerzmann M, Vogel R, Zbinden R, Windecker S, et al. Risk of decompression illness among 230 divers in relation to the presence and size of patent foramen ovale. Eur Heart J. 2004;25:1014–20. doi: 10.1016/j.ehj.2004.04.028. PMID: 15191771.

61 Hartig F, Reider N, Sojer M, Hammer A, Ploner T, Muth C-M, et al. Livedo racemosa - the pathophysiology of decompression-associated cutis marmorata and right/left shunt. Front Physiol. 2020;11:994. doi: 10.3389/fphys.2020.00994. PMID: 33013436. PMCID: PMC7497564.

62 Germonpré P, Lafere P, Portier W, Germonpré FL, Marroni A, Balestra C. Increased risk of decompression sickness when diving with a right-to-left shunt: results of a prospective single-blinded observational study (The "Carotid Doppler" Study). Front Physiol. 2021;12:763408. doi: 10.3389/fphys.2021.763408. PMID: 34777020. PMCID: PMC8586212.

63 Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc. 1984;59:17–20. doi: 10.1016/s0025-6196(12)60336-x. PMID: 6694427.

64 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;45:89–93. PMID: 26165530. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/45June/Wilmshurst_dhm.45.2.89-93.pdf.

65 Lovering AT, Stickland MK, Amann M, O'Brien MJ, Hokanson JS, Eldridge MW. Effect of a patent foramen ovale on pulmonary gas exchange efficiency at rest and during exercise. J Appl Physiol (1985). 2011;110:1354–61. doi: 10.1152/japplphysiol.01246.2010. PMID: 21372097. PMCID: PMC3290103.

66 Doolette DJ, Mitchell SJ. Extended lifetimes of bubbles at hyperbaric pressure may contribute to inner ear decompression sickness during saturation diving. J Appl Physiol (1985). 2022;133:517–23. doi: 10.1152/japplphysiol.00121.2022. PMID: 35834629.

67 Gorman DF, Browning DM, Parsons DW, Traugott FM. The distribution of arterial gas emboli in the pial circulation. SPUMS Journal 1987;17:101–15. [cited 2024 Jan 31]. Available from: https://www.dhmjournal.com/images/IndividArticles/17Sept/Gorman_SPUMSJ.17.3.101-116.pdf.

68 Hyldegaard O, Moller M, Madsen J. Effect of He-O_2, O2, and N_2O-O_2 breathing on injected bubbles in spinal white matter. Undersea Biomed Res. 1991;18:361–71. PMID: 1746064.

69 Doolette DJ, Mitchell SJ. A biophysical basis for inner ear decompression sickness. J Applied Physiol (1985). 2003;94:2145–50. PMID: 12562679.

70 Mitchell SJ, Doolette DJ. Pathophysiology of inner ear decompression sickness: potential role of the persistent foramen ovale. Diving Hyperb Med. 2015;45:105–10. PMID: 26165533.

71 Sorensen SG, Aguilar H, Reichert W, Goldstein M, Thoen D, Thomas H, et al. Transient neurological symptoms during contrast transcranial doppler right-to-left shunt testing in patients with cryptogenic neurological disease. J Intervent Cardiol. 2010;23:284–90. doi: 10.1111/j.1540-8183.2010.00557.x. PMID: 20636850.

72 Hills BA, James PB. Microbubble damage to the blood brain barrier: relevance to decompression sickness. Undersea Biomed Res. 1991;18:111–6. PMID: 2042262.

73 Kaakkola S, Lehtosalo J, Laitinen LA. Changes in blood brain barrier permeability to drugs in decompressed rats. Undersea Biomed Res. 1982;9:233–40. PMID: 6890252.

74 Helps SC, Parsons DW, Reilly PL, Gorman DF. The effect of gas emboli on rabbit cerebral blood flow. Stroke. 1990;21:94–9. doi: 10.1161/01.str.21.1.94. PMID: 2300997.

75 Jabur GNS, Merry AF, McGeorge A, Cavadino A, Donnelly J, Mitchell SJ. A prospective observational study on the effect of emboli exposure on cerebral autoregulation in cardiac surgery

requiring cardiopulmonary bypass. Perfusion. 2022;38:1045–52. doi: 10.1177/02676591221094696. PMID: 35676779.
76 Germonpré P, Hastir F, Dendale P, Marroni A, Nguyen AF, Balestra C. Evidence for increasing patency of the foramen ovale in divers. Am J Cardiol. 2005;95:912–5. doi: 10.1016/j.amjcard.2004.12.026. PMID: 15781033.
77 Moon RE, Bove AA. Transcatheter occlusion of patent foramen ovale: A prevention for decompression illness? Undersea Hyperb Med. 2004;31:271–4. PMID: 15568413.
78 Madden D, Ljubkovic M, Dujic Z. Intrapulmonary shunt and SCUBA diving: another risk factor? Echocardiography. 2015;32 Suppl 3:S205–10. doi: 10.1111/echo.12815. PMID: 25693625.
79 Eldridge MW, Dempsey JA, Haverkamp HC, Lovering AT, Hokanson JS. Exercise-induced intrapulmonary arteriovenous shunting in healthy humans. J Appl Physiol (1985). 2004;97:797–805. doi: 10.1152/japplphysiol.00137.2004. PMID: 15107409.
80 Doolette DJ, Mitchell SJ. In water recompression. Diving Hyperb Med. 2018;48:84–95. doi: 10.28920/dhm48.2.84-95. PMID: 29888380. PMCID: PMC6156824.
81 Broome JR, Dick EJ, Dutka AJ. Multifocal CNS hemorrhage as a cause of recompression treatment failure in a pig model of neurological decompression illness (DCI). Undersea Hyperb Med. 1994;21(Supp):69.
82 Barteneva NS, Fasler-Kan E, Bernimoulin M, Stern JNH, Ponomarev ED, Duckett L, et al. Circulating microparticles: square the circle. BMC Cell Biol. 2013;14:23. doi: 10.1186/1471-2121-14-23. PMID: 23607880. PMCID: PMC3651414.
83 Vince RV, McNaughton LR, Taylor L, Midgley AW, Laden G, Madden LA. Release of VCAM-1 associated endothelial microparticles following simulated SCUBA dives. Eur J Appl Physiol. 2009;105:507–13. doi: 10.1007/s00421-008-0927-z. PMID: 19002703.
84 Thom SR, Yang M, Bhopale VM, Huang S, Milovanova TN. Micro-particles initiate decompression-induced neutrophil activation and subsequent vascular injuries. J Appl Physiol (1985). 2011;110:340–51. doi: 10.1152/japplphysiol.00811.2010. PMID: 20966192.
85 Thom SR, Milovanova TN, Bogush M, Bhopale VM, Yang M, Bushmann K, et al. Microparticle production, neutrophil activation, and intravascular bubbles following open-water SCUBA diving. J Appl Physiol (1985). 2012;112:1268–78. doi: 10.1152/japplphysiol.01305.2011. PMID: 22323646.
86 Bhullar J, Bhopale VM, Yang M, Sethuraman K, Thom SR. Microparticle formation by platelets exposed to high gas pressures - An oxidative stress response. Free Radic Biol Med. 2016;101:154–62. doi: 10.1016/j.freeradbiomed.2016.10.010. PMID: 27751909.
87 Brett KD, Nugent NZ, Fraser NK, Bhopale VM, Yang M, Thom SR. Microparticle and interleukin-1β production with human simulated compressed air diving. Sci Rep. 2019;9(1):13320. doi: 10.1038/s41598-019-49924-1. PMID: 31527725. PMCID: PMC6746808.
88 Thom SR, Yang M, Bhopale VM, Milovanova TN, Bogush M, Buerk DG. Intramicroparticle nitrogen dioxide is a bubble nucleation site leading to decompression-induced neutrophil activation and vascular injury. J Appl Physiol (1985). 2013;114:550–8. doi: 10.1152/japplphysiol.01386.2012. PMID: 23264541.
89 Buttolph TB, Dick Jr EJ, Toner CB, Broome JR, Williams R, Kang YH, Wilt NL. Cutaneous lesions in swine after decompression: histopathology and ultrastructure. Undersea Hyperb Med. 1998;25:115–21. PMID: 9670437.
90 Koch AE, Kirsch H, Reuter M, Warninghoff V, Rieckert H, Deuschl G. Prevalence of patent foramen ovale (PFO) and MIR-lesions in mild neurological decompression sickness (Type B-DCS/AGE). Undersea Hyperb Med. 2008;35:197–205. PMID: 18619115.
91 Garcia E, Mitchell SJ. Bubbles in the skin microcirculation underlying cutis marmorata in decompression sickness: preliminary observations. Diving Hyperb Med. 2020;50:173–7. doi: 10.28920/dhm50.2.173-177. PMID: 32557421. PMCID: PMC7481116.
92 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;45:84–8. PMID: 26165529. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/45June/Kemper_dhm.45.2.84-88.pdf.
93 Venter RD, Ward CA, Ho S, Johnson WR, Fraser WD, Landolt JP. Fracture studies on a mammalian semicircular canal. Undersea Biomed Res. 1983;10:225–40. PMID: 6636347.
94 Azzopardi CP, Caruana J, Matity L, Muscat S, Meintjes WAJ. Increasing prevalence of vestibulo-cochlear decompression illness in Malta – an analysis of hyperbaric treatment data from 1987–2017. Diving Hyperb Med 2019;49:161–6. doi: 10.28920/dhm49.3.161-166. PMID: 31523790. PMCID: PMC6881197.
95 Thom SR, Bhopale VM, Yang M. Neutrophils generate microparticles during exposure to inert gases due to cytoskeletal oxidative stress. J Biol Chem. 2014;289(27):18831–45. doi: 10.1074/jbc.M113.543702. PMID: 24867949. PMCID: PMC4081925.
96 Chishti EA, Edgington TL, Chishti AA, Ortiz-Soriano V, Neyra JA. Severe acute kidney injury caused by decompression sickness syndrome. Clin Nephrol. 2022;97:298–304. doi: 10.5414/CN110662. PMID: 35006071.
97 Gardner M, Forbes C, Mitchell S. One hundred divers with DCI treated in New Zealand during 1995. SPUMS Journal 1996;26:222–6. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/26Dec/Gardiner_SPUMSJ264222-226.pdf.
98 St Leger Dowse M, Howell S, Smerdon GR. Flying after diving: a questionnaire-based evaluation of pre-flight diving behaviour in a recreational diving cohort. Diving Hyperb Med. 2021;51:361–7. doi: 10.28920/dhm51.4.361-367. PMID: 34897601. PMCID: PMC8920893.
99 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;73:980–4. PMID: 12398259.
100 Vann RD, Gerth WA, Denoble PJ, Pieper CF, Thalmann ED. Experimental trials to assess the risks of decompression sickness in flying after diving. Undersea Hyperb Med. 2004;31:431–44. PMID: 15686274.
101 Gerth WA, Ruterbusch VL, Long ET. The influence of thermal expo-sure on diver susceptibility to decompression sickness. NEDU TR 06-07. Panama City (FL): Navy Experimental Diving Unit; 2007.
102 van der Aue OE, Kellar RJ, Brinton ES. Surface decompression: derivation and testing of decompression tables with safety limits for certain depths and exposures. NEDU Report 5-45. Panama City (FL): US Navy Experimental Diving Unit; 1945.

103 Doolette DJ, Vann RD. Risk factors for decompression sickness. In: Vann RD, Mitchell SJ, Denoble PJ, Anthony TG, editors. Technical diving. Proceedings of the Divers Alert Network 2008 Conference. Durham (NC): Divers Alert Network; 2009. p. 119–37. [cited 2024 Jan 31]. Available from: http://www.swiss-cave-diving.ch/PDF-dateien/2008TechDiverReport.pdf.

104 Balestra C, Germonpré P, Marroni A. Intrathoracic pressure changes after Valsalva strain and other maneuvers: implications for divers with patent foramen ovale. Undersea Hyperb Med. 1998;25:171–4. PMID: 9789337.

105 Williams STB, Prior FGR, Bryson P. Hematocrit change in tropical scuba divers. Wilderness Envrion Med. 2007;18:48–53. doi: 10.1580/06-weme-br-009r.1. PMID: 17447715.

106 Gonzalez-Alonso J, Calbet JA, Nielsen B. Muscle blood flow is reduced with dehydration during prolonged exercise in humans. J Physiol. 1998;513:895–905. doi: 10.1111/j.1469-7793.1998.895ba.x. PMID: 9824726. PMCID: PMC2231307.

107 Wang Q, Guerrero F, Theron M. Pre-hydration strongly reduces decompression sickness occurrence after a simulated dive in the rat. Diving Hyperb Med. 2020;50:288–91. doi: 10.28920/dhm50.3.288-291. PMID: 32957132. PMCID: PMC7819728.

108 Skogland S, Stuhr LB, Sundland H, Olsen RE, Hope A. Venous gas emboli in normal and dehydrated rats following decompression from a saturation dive. Aviat Space Environ Med. 2008;79:565–9. doi: 10.3357/asem.2199.2008. PMID: 18581939.

109 Carturan D, Boussuges A, Vanuxem P, Bar-Hen A, Burnet H, Gardette B. Ascent rate, age, maximal oxygen uptake, adiposity, and circulating venous bubbles after diving. J Appl Physiol (1985). 2002;93:1349–56. doi: 10.1152/japplphysiol.00723.1999. PMID: 12235035.

110 Lam TH, Yau KP. Analysis of some individual risk factors for decompression sickness in Hong Kong. Undersea Biomed Res. 1989;16:283–92. PMID: 2773160.

111 Mendez-Dominguez N, Huchim-Lara O, Chin W, Carrillo-Arceo L, Camara-Koyoc I, Cárdenas-Dajdaj R, et al. Body mass index in association with decompression sickness events: cross-sectional study among small-scale fishermen-divers in southeast Mexico. Undersea Hyperb Med. 2018;45:445–51. PMID: 30241124.

112 Hagberg M, Ornhagen H. Incidence and risk factors for symptoms of decompression sickness among male and female dive masters and instructors – a retrospective cohort study. Undersea Hyperb Med. 2003;30:93–102. PMID: 12964853.

113 Schellart NAM, van Rees Vellinga TP, van Hulst RA. Body fat does not affect venous bubble formation after air dives of moderate severity: theory and experiment. J Appl Physiol (1985). 2013;114:602–10. doi: 10.1152/japplphysiol.00949.2012. PMID: 23305985.

114 Webb JT, Kannan N, Pilmanis AA. Gender not a factor for altitude decompression sickness risk. Aviat Space Environ Med. 2003;74:2–10. PMID: 12546293.

115 Lee V, St Leger Dowse M, Edge C, Gunby A, Bryson P. Decompression sickness in women: a possible relationship with the menstrual cycle. Aviat Space Environ Med. 2003;74:1177–82. PMID: 14620475.

116 Rudge FW. Relationship of menstrual history to altitude chamber decompression sickness. Aviat Space Environ Med. 1990;61:657–9. PMID: 2386454.

117 Denoble PJ, editor. DAN annual diving report 2019 edition: a report on 2017 diving fatalities, injuries, and incidents. Durham (NC): Divers Alert Network; 2019. p. 113.

118 Mitchell SJ, Doolette DJ. Recreational technical diving part 1: an introduction to technical diving methods and activities. Diving Hyperb Med. 2013;43:86–93. PMID: 23813462. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/43June/Mitchell_dhm.43.3.86-93.pdf.

119 Hubbard M, Davis FM, Malcolm K, Mitchell SJ. Decompression illness and other injuries in a recreational dive charter operation. Diving Hyperb Med. 2018;48:218–23. doi: 10.28920/dhm48.4.218-223. PMID: 30517953. PMCID: PMC6355312.

120 Tuominen LJ, Sokolowski S, Lundell RV, Räisänen-Sokolowski AK. Decompression illness in Finnish technical divers: a follow-up study on incidence and self-treatment. Diving Hyperb Med. 2022;52:78–84. doi: 10.28920/dhm52.2.74-84. PMID: 35732278. PMCID: PMC9527095.

121 Mason JS, Buzzacott P, Gawthrope IC, Banham ND. A retrospective review of divers treated for inner ear decompression sickness at Fiona Stanley Hospital hyperbaric medicine unit 2014–2020. Diving Hyperb Med. 2023;53:243–50. doi: 10.28920/dhm53.3.243-250. PMID: 37718299.

122 Berghage TE. Decompression sickness during saturation dives. Undersea Biomed Res. 1976;3:387–98. PMID: 10897865.

123 Mitchell SJ, Doolette DJ, Wacholz CJ, Vann RD, editors. Management of mild or marginal decompression illness in remote locations: workshop proceedings. Durham (NC): Divers Alert Network; 2005

124 Mitchell SJ, Bennett MH, Bryson P, Butler FK, Doolette DJ, Holm JR, et al. Pre-hospital management of decompression illness: expert review of key principles and controversies. Diving Hyperb Med. 2018;48:45–55. doi: 10.28920/dhm48.1.45-55. PMID: 29557102. PMCID: PMC6467826.

125 Wilmshurst P. Cutis marmorata and cerebral arterial gas embolism. Diving Hyperb Med. 2015;45:261. PMID: 26687315. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/45Dec/Wilmshurst_dhm.45.4.261.pdf.

126 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. doi: 10.1371/journal.pone.0050079. PMID: 23185538. PMCID: PMC3503765.

127 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;15:403–17. PMID: 3067433.

128 Van Liew HD, Flynn ET. Direct ascent from air and N_2-O_2 saturation dives in humans: DCS risk and evidence of a threshold. Undersea Hyperb Med. 2005;32:409–19. PMID: 16509283.

129 Lindfors OH, Räisänen-Sokolowski AK, Hirvonen TP, Sinkkonen ST. Inner ear barotrauma and inner ear decompression sickness: a systematic review on differential diagnostics. Diving Hyperbaric Med. 2021;51:328–37. doi: 10.28920/dhm51.4.328-337. PMID: 34897597. PMCID: PMC8923696.

130 Blatteau JE, Gempp E, Simon O, Coulange M, Delafosse B, Souday V, et al. Prognostic factors of spinal cord decompression sickness in recreational diving: retrospective and multicentric analysis of 279 cases. Neurocrit Care. 2011;15:120–7. doi: 10.1007/s12028-010-9370-1. PMID: 20734244.

131 Fitzgerald B. A review of the sharpened Romberg test in diving medicine. SPUMS Journal 1996;26:142–6. [cited 2024 Jan

31]. Available from: https://www.dhmjournal.com/images/IndividArticles/26Sept/Fitzgerald_SPUMSJ.26.3.142-146.pdf.
132 Lee CT. Sharpening the sharpened Romberg. South Pacific Underwater Medicine Society Journal. 1998;28:125–32. [cited 2024 Jan 31]. Available from: https://www.dhmjournal.com/images/IndividArticles/28Sept/Lee_SPUMSJ.28.3.125-131.pdf.
133 Saadi A, Ferenczi EA, Reda H. Spinal decompression sickness in an experienced scuba diver: a case report and review of literature. Neurohospitalist. 2019;9:235–8. doi: 10.1177/1941874419828895. PMID: 31534615. PMCID: PMC6739671.
134 Kamtchum Tatuene J, Pignel R, Pollak P, Lovblad KO, Kleinschmidt A, Vargas MI. Neuroimaging of diving-related decompression illness: current knowledge and perspectives. AJNR Am J Neuroradiol. 2014;35:2039–44. doi: 10.3174/ajnr.A4005. PMID: 24924550. PMCID: PMC7965165.
135 Chung JM, Ahn JY. Relationship between clinical and radiologic findings of spinal cord injury in decompression sickness. Undersea Hyperb Med. 2017;44:57–62. doi: 10.22462/1.2.2017.9. PMID: 28768086.
136 Blatteau J-E, Morin J, Roffi R, Druelle A, Sbardella F, Castagna O. Clinical problem solving: mental confusion and hypoxaemia after scuba diving. Diving Hyperb Med. 2020;50:181–4. doi: 10.28920/dhm50.2.181–4. PMID: 32557423. PMCID: PMC7481123.
137 Sayer MDJ, Azzopardi E, Sieber A. Decompression management by 43 models of dive computer: single square-wave exposures to between 15 and 50 metres' depth. Diving Hyperb Med. 2014;44:193–201. PMID: 25596832. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/44Dec/Sayer_dhm.44.4.193-201.pdf.
138 Marroni A, Bennett PB, Cronje FJ, Cali-Corleo R, Germonpré P, Pieri M, et al. A deep stop during decompression from 82 fsw (25 m) significantly reduces bubbles and fast tissue gas tensions. Undersea Hyperb Med. 2004;31:233–43. PMID: 15485086.
139 Schellart NA, Corstius JJ, Germonpré P, Sterk W. Bubble formation after a 20-m dive: deep-stop vs. shallow-stop decompression profiles. Aviat Space Environ Med. 2008;79:488–94. doi: 10.3357/asem.2164.2008. PMID: 18500045.
140 Angelini SA, Tonetto L, Lang MA. Ceiling-controlled versus staged decompression: comparison between decompression duration and tissue tensions. Diving Hyperb Med. 2022;52:7–15. doi: 10.28920/dhm52.1.7-15. PMID: 35313367. PMCID: PMC9016140.
141 Boycott AE, Damant GC, Haldane JS. The prevention of compressed-air illness. J Hyg (Lond). 1908;8:342–443. doi: 10.1017/s0022172400003399. PMID: 20474365. PMCID: PMC2167126.
142 Workman RD. American decompression theory and practice. In: Bennett PB, Elliott DH, editors. The physiology and medicine of diving and compressed air work. 1st ed. London: Ballière Tindall and Cassell; 1969.
143 Bühlmann AA. Die [Computation of low-risk compression. Computation model and results of experimental decompression research]. Schweiz Med Wochenschr. 1988;118:185–97. PMID: 3363309. German.
144 Doolette DJ, Mitchell SJ. Recreational technical diving part 2: decompression from deep technical dives. Diving Hyperb Med. 2013;43:96–104. PMID: 23813463. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/43June/Doolette_dhm.43.3.96-104.pdf.
145 Wienke BR. Numerical phase algorithm for decompression computers and application. Comput Biol Med. 1992;22:389–406. doi: 10.1016/0010-4825(92)90039-p. PMID: 1458851.
146 Yount DE, Hoffman DC. On the use of a bubble formation model to calculate diving tables. Aviat Space Environ Med. 1986;57:149–56. PMID: 3954703.
147 Mitchell SJ. Decompression sickness: prevention. In: Edmonds C, Bennett M, Lippmann J, Mitchell SJ. Diving and subaquatic medicine. 5th ed. Boca Raton: CRC Press; 2015. p. 153–66.
148 Blatteau J-E, Hugon M, Gardette B, Sainty J-M, Galland F-M. Bubble incidence after staged decompression from 50 or 60 msw: effect of adding deep stops. Aviat Space Environ Med. 2005;76:490–2. PMID: 15892549.
149 Doolette DJ, Gerth WA, Gault KA. Redistribution of decompression stop time from shallow to deep stops increases incidence of decompression sickness in air decompression dives. Technical Report No. 11-06. Panama City (FL): Navy Experimental Diving Unit; 2011.
150 De Ridder S, Pattyn N, Neyt X, Germonpré P. Selecting optimal air diving gradient factors for Belgian military divers: more conservative settings are not necessarily safer. Diving Hyperb Med. 2023;53:251–8. doi: 10.28920/dhm53.3.251-258. PMID: 37718300.
151 Spisni E, Marabotti C, De Fazio L, Valerii MC, Cavazza E, Brambilla S, Hoxha K, L'Abbate A, Longobardi P. A comparative evaluation of two decompression procedures for technical diving using inflammatory responses: compartmental versus ratio deco. Diving Hyperb Med. 2017;47:9–16. doi: 10.28920/dhm47.1.9-16. PMID: 28357819. PMCID: PMC6147226.
152 Hjelte C, Plogmark O, Silvanius M, Ekström M, Frånberg O. Risk assessment of SWEN21 a suggested new dive table for the Swedish armed forces: bubble grades by ultrasonography. Diving Hyperb Med. 2023;53:299–305. doi: 10.28920/dhm53.4.299-305. PMID: 38091588.
153 Hugon J, Metelkina A, Barbaud A, Nishi R, Bouak F, Blatteau JE, et al. Reliability of venous gas embolism detection in the subclavian area for decompression stress assessment following scuba diving. Diving Hyperb Med. 2018;48:132–40. doi: 10.28920/dhm48.3.132-140. PMID: 30199887. PMCID: PMC6205931.
154 Germonpré P, Van der Eecken P, Van Renterghem E, Germonpré F-L, Balestra C. First impressions: use of the Azoth Systems O'Dive sub-clavian bubble monitor on a liveaboard dive vessel. Diving Hyperbaric Med. 2020;50:405–12. doi: 10.28920/dhm50.4.405-412. PMID: 33325023. PMCID: PMC7872790.
155 Karimpour K, Brenner RJ, Dong GZ, Cleve J, Martina S, Harris C, et al. Comparison of newer hand-held ultrasound devices for post-dive venous gas emboli quantification to standard echocardiography. Front Physiol. 2022;13:907651. doi: 10.3389/fphys.2022.907651. PMID: 35755430. PMCID: PMC9222333.
156 Plogmark O, Hjelte C, Ekström M, Frånberg O. Agreement between ultrasonic bubble grades using a handheld self-positioning Doppler product and 2D cardiac ultrasound. Diving Hyperb Med. 2022;52:281–5. doi: 10.28920/dhm52.4.281-285. PMID: 36525686. PMCID: PMC10017197.
157 Doolette DJ, Murphy FG. Within-diver variability in venous gas emboli (VGE) following repeated dives. Diving Hyperb

Med. 2023;53:333–9. doi: 10.28920/dhm53.4.333-339. PMID: 38091593.

158 Moon RE, Mitchell SJ, Bove AA. PFO statement. In: Denoble PJ, Holm JR, editors. Patent foramen ovale and fitness to dive consensus workshop proceedings. Durham (NC): Divers Alert Network; 2016. p. 141–4.

159 Smart D, Mitchell SJ, Wilmshurst P, Turner M, Banham N. Joint position statement on persistent (patent) foramen ovale and diving. South Pacific Underwater Medicine Society (SPUMS) and the United Kingdom Sports Diving Medical Committee (UKSDMC). Diving Hyperbaric Med. 2015;45:129–31. PMID: 26165538. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/45June/Smart_dhm.45.2.129-131.pdf.

160 Azzopardi CP, Magri K, Borg A, Schembri J, Sammut J. Echocardiography – techniques and pitfalls whilst diagnosing persistent (patent) foramen ovale as a risk factor in divers with a history of decompression sickness. Diving Hyperb Med. 2021;51:98–102. doi: 10.28920/dhm51.1.98-102. PMID: 33761549. PMCID: PMC8313782.

161 Anderson G, Ebersole D, Covington D, Denoble PJ. The effectiveness of risk mitigation interventions in divers with persistent (patent) foramen ovale. Diving Hyperb Med. 2019;49:80–7. doi: 10.28920/dhm49.2.80-87. PMID: 31177513. PMCID: PMC6704009.

162 Klingmann C, Rathmann N, Hausmann D, Bruckner T, Kern R. Lower risk of decompression sickness after recommendation of conservative decompression practices in divers with and without vascular right-to-left shunt. Diving Hyperb Med. 2012;42:146–50. PMID: 22987461. [cited 2024 Jan 31]. Available from: https://dhmjournal.com/images/IndividArticles/42Sept/Klingmann_dhm.42.3.146-150.pdf.

163 Scarff CW, Lippmann J, Fock AW. A review of diving practices and outcomes following the diagnosis of a patent foramen ovale in com-pressed air divers with a documented episode of decompression illness. Diving Hyperb Med. 2020;50:363–9. doi: 10.28920/dhm50.4.363-369. PMID: 33325017. PMCID: PMC8026231.

164 Iskander B, Anwer F, Oliveri F, Fotios K, Panday P, Arcia Francini AP, Hamid P. Amplatzer patent foramen ovale occluder device-related complications. Cureus. 2022;14(4): e23756. doi: 10.7759/cureus.23756. PMID: 35402119. PMCID: PMC8980243.

165 Søndergaard L, Kasner SE, Rhodes JF, Andersen G, Iversen HK, Nielsen-Kudsk JE, et al; Gore REDUCE Clinical Study Investigators. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. N Engl J Med. 2017;377:1033–42. doi: 10.1056/NEJMoa1707404. PMID: 28902580.

166 Vanden Eede M, Van Berendoncks, De Wolfe D, De Maeyer C, Vanden Eede H, Germonpré P. Percutaneous closure of patent foramen ovale for the secondary prevention of decompression illness in sports divers: mind the gap. Undersea Hyperb Med. 2019;46:625–32. PMID: 31683360.

167 Honěk J, Srámek M, Sefc L, Januška J, Fiedler J, Horváth M, et al. Effect of catheter-based patent foramen ovale closure on the occurrence of arterial bubbles in scuba divers. JACC Cardiovasc Interv. 2014;7:403–8. doi: 10.1016/j.jcin.2013.12.199. PMID: 24630875.

168 Billinger M, Zbinden R, Mordasini R, Windecker S, Schwerzmann M, Meier B, et al. Patent foramen ovale closure in recreational divers: effect on decompression illness and ischaemic brain lesions during long-term follow-up. Heart. 2011;97:1932–7. doi: 10.1136/heartjnl-2011-300436. PMID: 21917666.

169 Koopsen R, Stella PR, Thijs KM, Rienks R. Persistent foramen ovale closure in divers with a history of decompression sickness. Neth Heart J. 2018;26:535–9. doi: 10.1007/s12471-018-1153-x. PMID: 30178210. PMCID: PMC6220018.

170 Honěk J, Šrámek M, Honěk T, Tomek A, Šefc L, Januška J, et al. Patent foramen ovale closure is effective in divers: long-term results from the DIVE-PFO registry. J Am Coll Cardiol. 2020;76:1149–50. doi: 10.1016/j.jacc.2020.06.072. PMID: 32854848.

171 Edvinsson B, Thilén U, Nielsen NE, Christersson C, Dellborg M, Eriksson P, et al. Does persistent (patent) foramen ovale closure reduce the risk of recurrent decompression sickness in scuba divers? Diving Hyperb Med. 2021;51:63–7. doi: 10.28920/dhm51.1.63-67. PMID: 33761542. PMCID: PMC8313773.

172 Wisløff U, Brubakk AO. Aerobic endurance training reduces bubble formation and increases survival in rats exposed to hyperbaric pressure. J Physiol. 2001;537(Pt 2):607–11. doi: 10.1111/j.1469-7793.2001.00607.x. PMID: 11731590. PMCID: PMC2278955.

173 Dujic Z, Duplancic D, Marinovic-Terzic I, Bakovic D, Ivancev V, Valic Z, et al. Aerobic exercise before diving reduces venous gas bubble formation in humans. J Physiol. 2004;555(Pt 3):637–42. doi: 10.1113/jphysiol.2003.059360. PMID: 14755001. PMCID: PMC1664874.

174 Blatteau JE, Gempp E, Galland FM, Pontier JM, Sainty JM, Robinet C. Aerobic exercise 2 hours before a dive to 30 msw decreases bubble formation after decompression. Aviat Space Environ Med. 2005;76:666–9. PMID: 16018350.

175 Castagna O, Brisswalter J, Vallee N, Blatteau JE. Endurance exercise immediately before sea diving reduces bubble formation in scuba divers. Eur J Appl Physiol. 2011;111:1047–54. doi: 10.1007/s00421-010-1723-0. PMID: 21107599.

176 Madden D, Thom SR, Yang M, Bhopale VM, Ljubkovic M, Dujic Z. High intensity cycling before SCUBA diving reduces post-decompression microparticle production and neutrophil activation. Eur J Appl Physiol. 2014;114:1955–61. doi: 10.1007/s00421-014-2925-7. PMID: 24917356.

177 Doolette DJ. Exercise fizzy-ology. J Physiol. 2001;537(Pt 2):330. doi: 10.1111/j.1469-7793.2001.00330.x. PMID: 11731566. PMCID: PMC2278978.

178 Jankowski LW, Tikuisis P, Nishi RY. Exercise effects during diving and decompression on postdive venous gas emboli. Aviat Space Environ Med. 2004;75:489–95. PMID: 15198273.

179 Shupak A, Weiler-Ravell D, Adir Y, Daskalovic YI, Ramon Y, Kerem D. Pulmonary oedema induced by strenuous swimming: a field study. Respir Physiol. 2000;121:25–31. doi: 10.1016/s0034-5687(00)00109-2. PMID: 10854620.

180 Castagna O, Gempp E, Blatteau J-E. Pre-dive normobaric oxygen reduces bubble formation in scuba divers. Eur J Appl Physiol. 2009;106:167–72. doi: 10.1007/s00421-009-1003-z. PMID: 19219451.

181 Bosco G, Yang ZJ, Di Tano G, Camporesi EM, Faralli F, Savini F, et al. Effect of in-water oxygen prebreathing at different depths on decompression-induced bubble formation and platelet activation. J Appl Physiol (1985). 2010;108:1077–83. doi: 10.1152/japplphysiol.01058.2009. PMID: 20185629.

182 Dujić Z, Palada I, Valic Z, Duplancić D, Obad A, Wisløff U, et al. Exogenous nitric oxide and bubble formation in divers. Med Sci Sports Exerc. 2006;38:1432–5. doi: 10.1249/01.mss.0000228936.78916.23. PMID: 16888456.

183 Germonpré P, Balestra C. Preconditioning to reduce decompression stress in scuba divers. Aerosp Med Hum Perform. 2017;88:114–20. doi: 10.3357/AMHP.4642.2017. PMID: 28095955.
184 Elia A, Eiken O, Ånell R, Grönkvist M, Gennser M. Whole-body vibration preconditioning reduces the formation and delays the manifestation of high-altitude-induced venous gas emboli. Exp Physiol. 2021;106: 1743–51. doi: 10.1113/EP089522. PMID: 34142740.
185 Lambrechts K, Germonpré P, Vandenheede J, Delorme M, Lafère P, Balestra C. Mini Trampoline, a new and promising way of SCUBA diving preconditioning to reduce vascular gas emboli? Int J Environ Res Public Health. 2022;19(9):5410. doi: 10.3390/ijerph19095410. PMID: 35564805. PMCID: PMC9105492.
186 Edgar M, Franco MA, Dainer HM. Case series of arterial gas embolism incidents in U.S. Navy pressurized submarine escape training from 2018 to 2019. Mil Med. 2021;186(5-6):e613–e618. doi: 10.1093/milmed/usaa233. PMID: 33038246.
187 Banham N, da Silva E, Lippmann J. Cerebral arterial gas embolism (CAGE) during open water scuba certification training whilst practising a controlled emergency swimming ascent. Diving Hyperb Med. 2023;53:345–50. doi: 10.28920/dhm53.4.345–50. PMID: 38091595.
188 Toklu AS, Hobek A, Toker A. Pulmonary barotrauma in a free diver who breathed compressed air at depth: case report. Turkiye Klinikleri J Med Sci. 2012;32:255–9. [cited 2024 Jan 31]. Available from: https://www.turkiyeklinikleri.com/article/tr-pulmonary-barotrauma-in-a-free-diver-who-breathed-compressed-air-at-depth-case-report-61650.html.
189 Banham NDG, Lippmann J. Fatal air embolism in a breath-hold diver. Diving Hyperb Med. 2019;49:304–5. doi: 10.28920/dhm49.4.304-305. PMID: 31828750. PMCID: PMC7039776.
190 Goffinet CM, Simpson G. Cerebral arterial gas embolism in a scuba diver with a primary lung bulla. Diving Hyperb Med. 2019;49:141–4. doi: 10.28920/dhm49.2.141-144. PMID: 31177521. PMCID: PMC6704005.
191 Hampson NB, Moon RE. Arterial gas embolism breathing compressed air in 1.2 metres of water. Diving Hyperb Med. 2020;50:292–4. doi: 10.28920/dhm50.3.292-294. PMID: 32957133. PMCID: PMC7819734.
192 Lindblom U, Tosterud C. Pulmonary barotrauma with cerebral arterial gas embolism from a depth of 0.75–1.2 metres of fresh water or less: a case report. Diving Hyperb Med. 2021;51:224–6. doi: 10.28920/dhm51.2.224-226. PMID: 34157741. PMCID: PMC8349688.
193 Rivalland G, Mitchell SJ, van Schalkwyk JM. Pulmonary barotrauma and cerebral arterial gas embolism during hyperbaric oxygen therapy. Aviat Space Environ Med. 2010;81:888–90. doi: 10.3357/asem.2783.2010. PMID: 20824998.
194 Tetzlaff K, Reuter M, Kampen J, Lott C. Hyperbaric chamber-related decompression illness in a patient with asymptomatic pulmonary sarcoidosis. Aviat Space Environ Med. 1999;70:594–7. PMID: 10373052.
195 Wolf HK, Moon RE, Mitchell PR, Burger PC. Barotrauma and air embolism in hyperbaric oxygen therapy. Am J Forensic Med Pathol. 1990;11:149–53. doi: 10.1097/00000433-199006000-00009. PMID: 2343842.
196 Almeida FA, Desouza BX, Meyer T, Gregory S, Greenspon L. Intrapulmonary bronchogenic cyst and cerebral gas embolism in an aircraft flight passenger. Chest. 2006;130:575–7. doi: 10.1378/chest.130.2.575. PMID: 16899861.
197 Edwardson M, Wurth D, Lacy JM, Fink J, Becker K. Cerebral air embolism resulting in fatal stroke in an airplane passenger with a pulmonary bronchogenic cyst. Neurocrit Care. 2009;10:218–21. doi: 10.1007/s12028-008-9126-3. PMID: 18696271.
198 Esteban A, Anzueto A, Frutos F, Alía I, Brochard L, Stewart TE, et al. Mechanical Ventilation International Study Group. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. JAMA. 2002;287:345–55. doi: 10.1001/jama.287.3.345. PMID: 11790214.
199 Pao BS, Hayden SR. Cerebral gas embolism resulting from inhalation of pressurized helium. Ann Emerg Med. 1996;28:363–6. doi: 10.1016/s0196-0644(96)70039-2. PMID: 8780487.
200 Mitchell SJ, Benson M, Vadlamudi L, Miller P. Cerebral arterial gas embolism by helium: an unusual case successfully treated with hyperbaric oxygen and lidocaine. Ann Emerg Med. 2000;35:300–3. doi: 10.1016/s0196-0644(00)70086-2. PMID: 10692202.
201 Morales G, Fiero M, Albert J, Di Gennaro J, Gerbino A. Cerebral arterial gas embolism due to helium inhalation from a high-pressure gas cylinder. Case Rep Emerg Med. 2022;2022:1847605. doi: 10.1155/2022/1847605. PMID: 35311225. PMCID: PMC8924607.
202 Moon RE. Hyperbaric treatment of air or gas embolism: current recommendations. Undersea Hyperb Med. 2019;46:673–83. PMID: 31683367.
203 Dube L, Soltner C, Daenen S, Lemarieé J, Asfar P, Alquier P. Gas embolism: an exceptional complication of radial arterial catheterization. Acta Anaesthesiol Scand. 2004;48:1208–10. doi: 10.1111/j.1399-6576.2004.00476.x. PMID: 15352970.
204 Ceponis PJ, Fox W, Tailor TD, Hurwitz LM, Amrhein TJ, Moon RJ. Non-dysbaric arterial gas embolism associated with chronic necrotizing pneumonia, bullae and coughing: a case report. Undersea Hyperb Med. 2017;44:73–7. doi: 10.22462/1.2.2017.16. PMID: 28768088.
205 Wherrett CG, Mehran RJ, Beaulieu MA. Cerebral arterial gas embolism following diagnostic bronchoscopy: delayed treatment with hyperbaric oxygen. Can J Anaesth. 2002;49:96–9. doi: 10.1007/BF03020427. PMID: 11782337.
206 Malik N, Claus PL, Illman JE, Kligerman SJ, Moynagh MR, Levin DL, et al. Air embolism: diagnosis and management. Future Cardiol. 2017;13:365–78. doi: 10.2217/fca-2017-0015. PMID: 28644058.
207 Rehwald R, Loizides A, Wiedermann FJ, Grams AE, Djurdjevic T, Glodny B. Systemic air embolism causing acute stroke and myocardial infarction after percutaneous transthoracic lung biopsy – a case report. J Cardiothorac Surg. 2016;11(1):80. doi: 10.1186/s13019-016-0478-z. PMID: 27154545. PMCID: PMC4859960.
208 Sakai O, Nakashima N, Shinozaki T, Furuse M. Air bubbles in the subclavian or internal jugular veins: a common finding on contrast-enhanced CT. Neuroradiology. 1998;40:258–60. doi: 10.1007/s002340050580. PMID: 9592800.
209 Bernhardt TL, Goldmann RW, Thombs PA, Kindwall EP. Hyperbaric oxygen treatment of cerebral air embolism from orogenital sex during pregnancy. Crit Care Med. 1988;16:729–30. doi: 10.1097/00003246-198807000-00017. PMID: 3371050.
210 Hwang SL, Lieu AS, Lin CL, Liu GC, Howng SL, Kuo TH. Massive cerebral air embolism after cardiopulmonary

resuscitation. J Clin Neurosci. 2005;12:468–9. doi: 10.1016/j.jocn.2004.03.041. PMID: 15925785.
211 Vesely TM. Air embolism during insertion of central venous catheters. J Vasc Interv Radiol. 2001;12:1291–5. doi: 10.1016/s1051-0443(07)61554-1. PMID: 11698628.
212 Nims M, Hallonquist H, Camann W. Coronary arterial air embolus occurring during cesarean delivery. Int J Obstet Anesth. 2006;15:166–9. doi: 10.1016/j.ijoa.2005.08.003. PMID: 16431100.
213 Berlot G, Rinaldi A, Moscheni M, Ferluga M, Rossini P. Uncommon occurrences of air embolism: description of cases and review of the literature. Case Rep Crit Care. 2018;2018:5808390. doi: 10.1155/2018/5808390. PMID: 30073096. PMCID: PMC6057342.
214 Lin SM, Chang WK, Tsao CM, Ou CH, Chan KH, Tsai SK. Carbon dioxide embolism diagnosed by transesophageal echocardiography during endoscopic vein harvesting for coronary artery bypass grafting. Anesth Analg. 2003;96:683–5. doi: 10.1213/01.ANE.0000049687.38081.95. PMID: 12598243.
215 Ghannam M, Beran A, Ghazaleh D, Ferderer T, Berry B, Al Banna M, et al. Cerebral air embolism after esophagogastroduodenoscopy: insight on pathophysiology, epidemiology, prevention and treatment. J Stroke Cerebrovasc Dis. 2019;28(12):104403. doi: 10.1016/j.jstrokecerebrovasdis.2019.104403. PMID: 31563566.
216 Lau L, London K. Cortical blindness and altered mental status following routine hemodialysis, a case of iatrogenic cerebral air embolism. Case Rep Emerg Med. 2018;2018:9496818. doi: 10.1155/2018/9496818. PMID: 29732225. PMCID: PMC5872667.
217 Jones PM, Segal SH, Gelb AW. Venous oxygen embolism produced by injection of hydrogen peroxide into an enterocutaneous fistula. Anesth Analg. 2004;99:1861–3. doi: 10.1213/01.ANE.0000135411.96718.AD. PMID: 15562087.
218 Kawahara T, Hagiwara M, Takahashi H, Tanaka M, Imai K, Sawada J, et al. Cerebral infarction by paradoxical gas embolism during laparoscopic liver resection with injury of the hepatic vessels in a patient without a right-to-left systemic shunt. Am J Case Rep. 2017;18:687–91. doi: 10.12659/ajcr.903777. PMID: 28630395. PMCID: PMC5484459.
219 Foo E, Williams D, Singh H, Bridgman PG, McCall J, Connor S. Successful management of a large air embolus during an extended right hepatectomy with an emergency cardiopulmonary bypass. HPB (Oxford). 2012;14(12):871–3. doi: 10.1111/j.1477-2574.2012.00550.x. PMID: 23134190. PMCID: PMC3521917.
220 Badenoch A, Srinivas C, Al-Adra D, Selzner M, Wasowicz M. A case report of paradoxical air embolism caused by intrapulmonary shunting during liver transplantation. Transplant Direct. 2017;3(3):e134.
221 Groenman FA, Peters LW, Rademaker BM, Bakkum EA. Embolism of air and gas in hysteroscopic procedures: pathophysiology and implica-tion for daily practice. J Minim Invasive Gynecol. 2008;15:241–7. doi: 10.1016/j.jmig.2007.10.010. PMID: 18313001.
222 Batman PA, Thomlinson J, Moore VC, Sykes R. Death due to air embolism during sexual intercourse in the puerperium. Postgrad Med J. 1998;74:612–3. doi: 10.1136/pgmj.74.876.612. PMID: 10211360. PMCID: PMC2361003.
223 Mammoto T, Hayashi Y, Ohnishi Y, Kuro M. Incidence of venous and paradoxical air embolism in neurosurgical patients in the sitting position: detection by transesophageal echocardiography. Acta Anaesthesiol Scand. 1998;42:643–7. doi: 10.1111/j.1399-6576.1998.tb05295.x. PMID: 9689268.
224 Bapteste L, Kamar Z, Mazaud A, Balança B. Air embolism during lumbar surgery in the prone position. Diving Hyperb Med. 2021;51:303–5. doi: 10.28920/dhm51.3.303-305. PMID: 34547783. PMCID: PMC8608445.
225 Evans DE, Kobrine AI, Weathersby PK, Bradley ME. Cardiovascular effects of cerebral air embolism. Stroke 1981;12:338–44. PMID: 7245300.
226 Neuman TS. Arterial gas embolism and pulmonary barotrauma. In: Brubakk AO, Neuman TS. Bennett and Elliott's physiology and medicine of diving. Edinburgh: Saunders; 2003. p. 557–77.
227 Smith RM, Neuman TS. Elevation of serum creatine kinase in divers with arterial gas embolism. New Eng J Med. 1994;330:19–24. doi: 10.1056/NEJM199401063300104. PMID: 8259140.
228 Smith RM, Neuman TS. Abdominal serum biochemistries in association with arterial gas embolism. J Emerg Med. 1997;15:285–9. doi: 10.1016/s0736-4679(97)00007-3. PMID: 9258775.
229 Viecelli A, Jamboti J, Waring A, Banham N, Ferrari P. Acute kidney injury due to decompression illness. Clin Kidney J. 2014;7:380–2. doi: 10.1093/ckj/sfu048. PMID: 25852912. PMCID: PMC4377796.
230 Butler BD, Laine GA, Leiman BC, Warters D, Kurusz M, Sutton T, et al. Effect of the Trendelenburg position on the distribution of arterial air emboli in dogs. Ann Thorac Surg. 1988;45:198–202. doi: 10.1016/s0003-4975(10)62437-x. PMID: 3341824.
231 Mitchell S, Gorman D. The pathophysiology of cerebral arterial gas embolism. J Extra Corpor Technol. 2002;34:18–23. PMID: 11911624.
232 Jabur GN, Donnelly J, Merry AF, Mitchell SJ. A prospective observational study of emboli exposure in open versus closed chamber cardiac surgery. Perfusion. 2022;37:715–21. doi: 10.1177/02676591211023897. PMID: 34112049.
233 Feinstein SB, Shah PM, Bing RJ, Meerbaum S, Corday E, Chang BL, et al. Microbubble dynamics visualized in the intact capillary circulation. J Am Coll Cardiol. 1984;4:595–600. doi: 10.1016/s0735-1097(84)80107-2. PMID: 6470341.
234 Gorman DF, Browning DM. Cerebral vasoreactivity and arterial gas embolism. Undersea Biomed Res. 1986;13:317–35. PMID: 3095973.
235 Francis TJR, Gorman DF. Pathogenesis of the decompression disorders. In Bennett PB, Elliott DH, editors. The physiology and medicine of diving. 4th ed. London: Saunders; 1993. p. 454–80.
236 De Reuck J. The corticoangioarchitecture of the human brain. Acta Neurol Belg. 1972;72:323–9. PMID: 4653787.
237 Dutka AJ, Kochanek PM, Hallenbeck JM, Storey JR. Air embolism may cause unrecognised ischemia of the grey-white matter junction. Undersea Biomed Res. 1988;15:99–106. PMID: 3363756.
238 Dutka AJ, Mink R, McDermott J, Clark JB, Hallenbeck JM. Effect of lidocaine on somatosensory evoked response and cerebral blood flow after canine cerebral air embolism. Stroke. 1992;70:1515–21. doi: 10.1161/01.str.23.10.1515. PMID: 1412590.
239 Helps SC, Meyer-Witting M, Reilly PL, Gorman DF. Increasing doses of intracarotid air and cerebral blood flow in rabbits. Stroke. 1990;21:1340–5. doi: 10.1161/01.str.21.9.1340. PMID: 2396272.
240 Dexter F, Hindman BJ. Computer simulation of microscopic

cerebral air emboli during cardiac surgery. Undersea Hyperb Med. 1998;25:43–50. PMID: 9566086.
241 Siesjo BK, Hu B, Kristian T. Is the cell death pathway triggered by the mitochondrion or the endoplasmic reticulum. J Cereb Blood Flow Metab. 1999;19:19–26. doi: 10.1097/00004647-199901000-00002. PMID: 9886351.
242 Nohara A, Yusa T. Reversibility in blood brain barrier, microcirculation, and histology in rat brain after decompression. Undersea Hyperb Med. 1997;24:15–21. PMID: 9068151.
243 Warren BA, Philp PB, Inwood MJ. The ultrastructural morphology of air embolism: platelet adhesion to the interface and endothelial damage. Br J Exp Pathol. 1973;54:163–72. PMID: 4121722. PMCID: PMC2072572.
244 Dutka AJ, Kochanek PM, Hallenbeck JM. Influence of granulocytopenia on canine cerebral ischaemia induced by air embolism. Stroke. 1989;20:390–5. doi: 10.1161/01.str.20.3.390. PMID: 2922779.
245 Boyle Jr EM, Pohlman TH, Johnson MC, Verrier ED. Endothelial cell injury in cardiovascular surgery: the systemic inflammatory response. Ann Thorac Surg. 1997;63:277–84. doi: 10.1016/s0003-4975(96)01061-2. PMID: 8993292.
246 Neuman TS, Bove AA. Combined arterial gas embolism and decompression sickness following no-stop dives. Undersea Biomed Res. 1990;17:429–36. PMID: 2219551.
247 Meintjes WAJ, Davids L, van Wijk CH. A retrospective review of the utility of chest X-rays in diving and submarine medical examinations. Diving Hyperb Med. 2023;53:237–42. doi: 10.28920/dhm53.3.237-242. PMID: 37718298. PMCID: PMC10735703.
248 Brenna CT, Khan S, Djaiani G, Buckey Jr JC, Katznelson R. The role of routine pulmonary imaging before hyperbaric oxygen treatment. Diving Hyperb Med. 2022;52:197–207. doi: 10.28920/dhm52.3.197-207. PMID: 36100931. PMCID: PMC9731143.
249 Mirasoglu B, Yetis G, Erelel M, Toklu AS. Post COVID-19 fitness to dive assessment findings in occupational and recreational divers. Diving Hyperb Med. 2022;52:35–43. doi: 10.28920/dhm52.1.35-43. PMID: 35313371. PMCID: PMC9177431.
250 Sadler C, Alvarez-Villela M, Van Hoesen K, Grover I, Lang M, Neuman T, et al. Diving after SARS-CoV-2 (COVID-19) infection: Fitness to dive assessment and medical guidance. Diving Hyperb Med. 2020;50:278–87. doi: 10.28920/dhm50.3.278-287. PMID: 32957131. PMCID: PMC7755459.
251 Sadler C, Alvarez Villela M, Van Hoesen K, Grover I, Lang M, Neuman T, et al. Diving after COVID-19: an update to fitness to dive assessment and medical guidance. Diving Hyperb Med. 2022;52:66–7. doi: 10.28920/dhm52.1.66-67. PMID: 35313377. PMCID: PMC9016139.
252 Smart D. Validation of very mild COVID-19 illness criteria to guide successful return to occupational diving. Diving Hyperb Med. 2022;52:222–3. doi: 10.28920/dhm52.3.222-223. PMID: 36100936. PMCID: PMC9722341.
253 Van Allen CM, Hrdina LS, Clark J, Air embolism from the pulmonary vein. Arch Surg. 1929;19:567–99.
254 Polychronidis JE, Dutka AJ, Mink RB, Hallenbeck JM. Head down position after cerebral air embolism: effects on intracranial pressure, pressure volume index and blood-brain barrier. Undersea Biomed Res. 1990;17(Suppl):99.
255 Balldin U. Effects of ambient temperature and body position on tissue nitrogen elimination in man. Aerospace Med. 1973;44:365–70.
256 Gensser M, Loveman G, Seddon F, Thacker J, Blogg SL. Oxygen and carbogen breathing following simulated submarine escape. Undersea Hyperb Med. 2014;41:387–92. PMID: 25558547.
257 Longphre JM, Denoble PJ, Moon RE, Vann RD, Frieberger JJ. First aid normobaric oxygen for the treatment of recreational diving injuries. Undersea Hyperb Med. 2007;34:43–9. PMID: 17393938.
258 Stipp W. Time to treatment for decompression illness. Research Report 550. UK Health and Safety Executive; 2007. [cited 2024 Jan 31]. Available from: https://www.hse.gov.uk/Research/rrpdf/rr550.pdf.
259 Blake DF, Crowe M, Lindsay D, Brouff A, Mitchell SJ, Pollock NW. Comparison of tissue oxygenation achieved breathing oxygen from a demand valve with four different mask configurations. Diving Hyperbaric Med. 2018;48:209–17. doi: 10.28920/dhm48.4.209-217. PMID: 30517952. PMCID: PMC6355319.
260 Blake DF, Crowe M, Lindsay D, Brouff A, Mitchell SJ, Leggat PA, Pollock NW. Comparison of tissue oxygenation achieved breathing oxygen using different delivery devices and flow rates. Diving Hyperb Med. 2020;50:34–42. doi: 10.28920/dhm50.1.34-42. PMID: 32187616. PMCID: PMC7276271.
261 Fahlman A, Dromsky DM. Dehydration effects on the risk of severe decompression sickness in a swine model. Aviat Space Environ Med. 2006;77:102–6. PMID: 16491576.
262 Pendergast DR, Senf CJ, Fletcher MC, Lundgren CEG. Effects of ambient temperature on nitrogen uptake and elimination in humans. Undersea Hyperb Med. 2015;42:85–94. PMID: 26094308.
263 Mekjavic IB, Kakitsuba N. Effect of peripheral temperature on the formation of venous gas bubbles. Undersea Biomed Res. 1989;16:391–401. PMID: 2800052.
264 Minamisawa H, Smith ML, Siesjö BK. The effect of mild hyperthermia and hypothermia on brain damage following 5, 10, and 15 minutes of forebrain ischemia. Ann Neurol. 1990;28:26–33. doi: 10.1002/ana.410280107. PMID: 2375631.
265 Moon RE, Mitchell SJ. Hyperbaric oxygen for decompression sickness. Undersea Hyperb Med. 2021;48:195–203. PMID: 33975411.
266 Coleman B, Davis FM. Dysbaric osteonecrosis in technical divers: The new 'at-risk' group? Diving Hyperb Med. 2020;50:295–9. doi: 10.28920/dhm50.3.295-299. PMID: 32957134. PMCID: PMC7819721.
267 Gempp E, Louge P, de Maistre S. Predictive factors of dysbaric osteonecrosis following musculoskeletal decompression sickness in recreational SCUBA divers. Joint Bone Spine. 2016;83:357–8. doi: 10.1016/j.jbspin.2015.03.010. PMID: 26454506.
268 Lehner CE, Kunchur MG, Dueland RT, Wilson MA, Nordheim EV, Crump PM, Markel MD. Effectiveness of delayed recompression treatment in limb bends cases for the prevention of dysbaric osteonecrosis. Undersea Hyperb Med. 1997;24(supp):28.
269 Jones JP, Neuman TS. Dysbaric osteonecrosis. In: Brubakk AO, Neuman TS. Bennett and Elliott's physiology and medicine of diving. Edinburgh: Saunders; 2003. p. 659–79.
270 Blake DF, Crowe M, Mitchell SJ, Aitken P, Pollock NW. Vibration and bubbles: a systematic review of the effects of helicopter retrieval on injured divers. Diving Hyperb Med. 2018;48:241–51. doi: 10.28920/dhm48.4.241-251. PMID: 30517957. PMCID: PMC6355309.
271 Vann RD, Wachholz CJ, Nord D, Denoble PJ, Macris G. Can divers with mild symptoms of DCI fly on commercial airliners? In: Mitchell SJ, Doolette DJ, Wacholz CJ, Vann

RD, editors. Management of mild or marginal decompression illness in remote locations workshop proceedings. Durham (NC): Divers Alert Network; 2005. p. 90–9. [cited 2024 Jan 31]. Available from: https://world.dan.org/wp-content/uploads/2021/06/remotewrkshpfinal05-1.pdf.

272 Moon RE, Gorman DF. Treatment of the decompression disorders. In: Brubakk AO, Neuman TS, editors. Bennett and Elliott's physiology and medicine of diving. 5th ed. London: Harcourts; 2003. p. 600–50.

273 Andre S, Lehot H, Morin J, Louge P, de Maistre S, Roffi R, et al. Influence of prehospital management on the outcome of spinal cord decompression sickness in scuba divers. Emerg Med J. 2022. Feb 7: Online ahead of print. doi: 10.1136/emermed-2021-211227. PMID: 35135892.

274 Fakkert RA, Karlas N, Schober P, Weber NC, Preckel B, van Hulst RA, et al. Early hyperbaric oxygen therapy is associated with favorable outcome in patients with iatrogenic cerebral arterial gas embolism: systematic review and individual patient data meta-analysis of observational studies. Crit Care. 2023;27(1):282. doi: 10.1186/s13054-023-04563-x. PMID: 37434172. PMCID: PMC10337083.

275 Cianci P, Slade Jr JB. Delayed treatment of decompression sickness with short, no-air-break tables: review of 140 cases. Aviat Space Environ Med. 2006;77:1003–8. PMID: 17042243.

276 Hadanny A, Fishlev G, Bechor Y, Bergan J, Friedman M, Maliar A, Efrati S. Delayed recompression for decompression sickness: retrospective analysis. PLoS One. 2015;10(4):e0124919. doi: 10.1371/journal.pone.0124919. PMID: 25906396. PMCID: PMC4408070.

277 Sokolowski SA, Räisänen-Sokolowski AK, Tuominen LJ, Lundell RV. Delayed treatment for decompression illness: factors associated with long treatment delays and treatment outcome. Diving Hyperb Med. 2022;52:271–6. doi: 10.28920/dhm52.4.271-276. PMID: 36525684. PMCID: PMC10026386.

278 Leitch DR, Greenbaum LJ, Hallenbeck JM. Cerebral arterial air embolism: III. Cerebral blood flow after decompression from various pressure treatments. Undersea Biomed Res. 1984;11:249–63. PMID: 6506337.

279 Leitch DR, Greenbaum LJ Jr, Hallenbeck JM. Cerebral arterial air embolism: II. Effect of pressure and time on cortical evoked potential recovery. Undersea Biomed Res. 1984;11:237–48. PMID: 6506336.

280 Rainey Johnson W, Roney NG, Zhou H, Ciarlone GE, Williams BT, Green WT, et al. Comparison of treatment recompression tables for neurologic decompression illness in swine model. PLoS One. 2022;17(10):e0266236. doi: 10.1371/journal.pone.0266236. PMID: 36197931. PMCID: PMC9534405.

281 Howsare CR, Rocca AF, Morrison LJ, Jackson RL. Comparison of USN TT-6 vs TT-6A for the treatment of AGE in the US Navy. A retrospective study. Undersea Hyperb Med. 1997;24(supp):33.

282 Bennett MH, Mitchell SJ, Young D, King D. The use of deep tables in the treatment of decompression illness. Diving Hyperb Med. 2012;24:171–80. PMID: 22987463. [cited 2024 Jan 12]. Available from: https://dhmjournal.com/images/IndividArticles/42Sept/Bennett_dhm.42.3.171-180.pdf.

283 Saltzman HA. Rational normobaric and hyperbaric oxygen therapy. Ann Internal Med. 1967:67:843–52. doi: 10.7326/0003-4819-67-4-843. PMID: 4861210.

284 Fosen KM, Thom SR. Hyperbaric oxygen, vasculogenic stem cells, and wound healing. Antioxid Redox Signal. 2014;21:1634–47. doi: 10.1089/ars.2014.5940. PMID: 24730726. PMCID: PMC4175035.

285 Buras JA, Stahl GL, Svoboda KK, Reenstra WR. Hyperbaric oxygen down regulates ICAM-1 expression induced by hypoxia and hypoglycemia: the role of NOS. Am J Physiol Cell Physiol. 2000:278:C292–302. doi: 10.1152/ajpcell.2000.278.2.C292. PMID: 10666024.

286 Thom SR, Bhopale VM, Yang M. Microparticle-induced vascular injury in mice following decompression is inhibited by hyperbaric oxygen: effects on microparticles and interleukin-1β. J Appl Physiol (1985). 2019;126:1006–14. doi: 10.1152/japplphysiol.01109.2018. PMID: 30763157.

287 Smith AH. Effects of high atmospheric pressure, including the caisson disease. Brooklyn: Eagle Print; 1873.

288 Snell EH. Compressed air illness: or, so-called caisson disease. London: HK Lewis; 1896.

289 Moir EW. Tunnelling by compressed air. J Soc Arts 1896;44:567–86.

290 Keays FL. Compressed-air illness, with a report of 3692 cases. Publications of Cornell University Medical College 1909;2:1–55.

291 Goodman MW, Workman RD. Minimal recompression oxygen-breathing approach to treatment of decompression sickness in divers and aviators. Washington (DC): US navy Experimental Diving Unit Report 5-65; 1965.

292 Thalmann ED. Principles of U.S. Navy recompression treatments for decompression sickness. In: Moon RE, Sheffield PJ, editors. Treatment of decompression illness. Proceedings of the 45th Undersea and Hyperbaric Medical Society workshop 1995. Kensington (MD): Undersea and Hyperbaric Medical Society; 1996. p. 75–95.

293 Clarke R. Monoplace chamber treatment of decompression illness: Review and commentary. Diving Hyperb Med. 2020;50:264–72. doi: 10.28920/dhm50.3.264-272. PMID: 32957129. PMCID: PMC7755460.

294 Weaver LK. Operational use and patient care in the monoplace hyperbaric chamber. Resp Care Clin N Am. 1999;5:51–92. PMID: 10205813.

295 Hart GB, Strauss MB, Lennon PA. The treatment of decompression sickness and air embolism in a monoplace chamber. J Hyperb Med. 1986;1:1–7.

296 Kindwall EP. Decompression sickness. In: Davis JC, Hunt TK, editors. Hyperbaric oxygen therapy. Bethesda (MD): Undersea Medical Society; 1977. p. 125–40.

297 Elliott DH, Kindwall EP. Decompression sickness. In: Kindwall EP, Whelan HT, editors. Hyperbaric medicine practice. Flagstaff (AZ): Best Publishing; 1999. p. 433–87.

298 Banham N, Hawkings P, Gawthrope I. A prospective single-blind randomised clinical trial comparing two treatment tables for the initial management of mild decompression sickness. Diving Hyperb Med. 2022;52:85–91. doi: 10.28920/dhm52.2.85-91. PMID: 35732279. PMCID: PMC9522606.

299 Howard AE, Buzzacott P, Gawthrope IC, Banham ND. Effect of antiplatelet and/or anticoagulation medication on the risk of tympanic barotrauma in hyperbaric oxygen treatment patients, and development of a predictive model. Diving Hyperb Med. 2020;50:338–42. doi: 10.28920/dhm50.4.338-342. PMID: 33325013. PMCID: PMC8026222.

300 Banham NDG. Oxygen toxicity seizures: 20 years' experience from a single hyperbaric unit. Diving Hyperb Med. 2011;41:202–10. [cited 2024 Jan 12]. Available from: https://dhmjournal.com/images/IndividArticles/41Dec/Banham_dhm.41.4.202-210.pdf.

301 Lalieu RC, Bol Raap RD, Dubois EF, van Hulst RA. Sudden death after oxygen toxicity seizure during hyperbaric oxygen treatment: Case report. Diving Hyperb Med. 2020;50:185–8. doi: 10.28920/dhm50.2.185-188. PMID: 32557424. PMCID: PMC7481105.

302 Tsushima R, Mori K, Imaki S. Secondary deterioration in a patient with cerebral and coronary arterial gas embolism after brief symptom resolution: a case report. Diving Hyperb Med. 2024;54:61–4. doi: 10.28920/dhm54.1.61-64. PMID: 38507911.

303 Naval Sea Systems Command. US Navy diving manual, Revision 7, SS521-AG-PRO-010. Washington (DC): Naval Sea Systems Command; 2016.

304 Costa DA, Ganilha JS, Barata PC, Guerreiro FG. Seizure frequency in more than 180,000 treatment sessions with hyperbaric oxygen therapy – a single centre 20-year analysis. Diving Hyperb Med. 2019;49:167–74. doi: 10.28920/dhm49.3.167-174. PMID: 31523791. PMCID: PMC6884101.

305 Du L, Zhang R, Luo T, Nie M, Bi J. Effects of helium preconditioning on intestinal ischemia and reperfusion injury in rats. Shock. 2015;44:365–70. doi: 10.1097/SHK.0000000000000418. PMID: 26052960.

306 Yin H, Chen Z, Zhao H, Huang H, Liu W. Noble gas and neuroprotection: From bench to bedside. Front Pharmacol. 2022;13:1028688. doi: 10.3389/fphar.2022.1028688. PMID: 36532733. PMCID: PMC9750501.

307 Rocco M, Maggi L, Loffredo C, Pelli M, Di Benedetto P, Fiorelli S, et al. The impact of different gas mixtures on inflammatory responses in advanced recreational divers. Diving Hyperb Med. 2021;51:140–6. doi: 10.28920/dhm51.2.140-146. PMID: 34157728. PMCID: PMC8426122.

308 Hyldegaard O, Madsen J. Influence of heliox, oxygen, and N_2O-O_2 breathing on N_2 bubbles in adipose tissue. Undersea Biomed Res. 1989;16:185–93. PMID: 2741253.

309 Hyldegaard O, Madsen J. Effect of air, heliox and oxygen breathing on air bubbles in aqueous tissues in the rat. Undersea Hyperb Med. 1994;21:413–24. PMID: 8000281.

310 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;54:305–11. doi: 10.1001/archneur.1997.00550150061017. PMID: 9074400.

311 Imbert J-P, Matity L, Massimelli J-Y, Bryson P. Review of saturation decompression procedures used in commercial diving. Diving Hyperb Med. 2024;54:23–38. doi: 10.28920/dhm54.1.23-38. PMID: 38507907.

312 Edmonds C. Pearls from the deep. A study of Australian pearl diving 1988-1991. SPUMS Journal. 1996;26(Suppl):26–30.

313 Wong RM. Pearl diving from Broome. SPUMS Journal. 1996;26(Suppl):15–25.

314 Blatteau JE, Pontier JM, Buzzacott P, Lambrechts K, Nguyen VM, Cavenel P, et al. Prevention and treatment of decompression sickness using training and in-water recompression among fisherman divers in Vietnam. Inj Prev. 2016;22:25–32. doi: 10.1136/injuryprev-2014-041464. PMID: 25991710.

315 Pyle RL, Youngblood D. In-water recompression as an emergency field treatment of decompression illness. The Universal Diver. [cited 2024 Jan 31]. Available from: https://www.tecvault.t101.ro/In-water%20recompression.pdf.

316 Gempp E, Louge P, Blatteau J-E, Hugon M. Descriptive epidemiology 153 diving injuries with rebreathers among French military divers from 1979–2009. Mil Med. 2011;176;446–50. doi: 10.7205/milmed-d-10-00420. PMID: 21539168.

317 van Waart H, Harris RJ, Gant N, Vrijdag XCE, Challen CJ, Lawthaweesawat C, Mitchell SJ. Deep anaesthesia: The Thailand cave rescue and its implications for management of the unconscious diver underwater. Diving Hyperb Med. 2020;50:121–9. doi: 10.28920/dhm50.2.121-129. PMID: 32557413. PMCID: PMC7481118.

318 Harris RJ, Challen CJ, Mitchell SJ. The first deep rebreather dive using hydrogen: case report. Diving Hyperb Med. 2024;54:69–72. doi: 10.28920/dhm54.1.69-72. PMID: 38507913.

319 Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D, et al. CHEST Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med. 2012;367(20):1901–11. doi: 10.1056/NEJMoa1209759. PMID: 23075127.

320 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;30:195–206. PMID: 14620099.

321 Moon RE, editor. Adjunctive therapy for decompression illness. Kensington (MD): Undersea and Hyperbaric Medical Society; 2003.

322 Mitchell SJ. Lidocaine in the treatment of decompression illness: a review of the literature. Undersea Hyperbaric Med. 2001;28:165–74. PMID: 12067153.

323 Habibi MR, Habibi V, Habibi A, Soleimani A. Lidocaine dose-response effect on postoperative cognitive deficit; meta-analysis and meta-regression. Exp Rev Clin Pharmacol. 2018;11:361–71. doi: 10.1080/17512433.2018.1425614. PMID: 29310468.

324 Lambrechts K, Pontier J-M, Mazur A, Theron M, Buzzacott P, Wang Q, et al. Mechanism of action of antiplatelet drugs on decompression sickness in rats: a protective effect of anti-GPIIbIIIa therapy. J Appl Physiol (1985). 2015;118:1234–9. doi: 10.1152/japplphysiol.00125.2015. PMID: 25792711.

325 Pontier J-M, Vallée, Ignatescu M, Bourdon L. Pharmacological intervention against bubble-induced platelet aggregation in a rat model of decompression sickness. J Appl Physiol (1985). 2011;110:724–9. doi: 10.1152/japplphysiol.00230.2010. PMID: 21212250. PMCID: PMC3069627.

326 Bao X-C, Chen H, Fang YQ, Yuan HR, You P, Ma J, et al. Clopidogrel reduces the inflammatory response of lung in a rat model of decompression sickness. Respir Physiol Neurobiol. 2015;211:9–16. doi: 10.1016/j.resp.2015.02.003. PMID: 25784626.

327 Dutka AJ, Mink RB, Pearson RR, Hallenbeck JM. Effects of treatment with dexamethasone on recovery from experimental cerebral arterial gas embolism. Undersea Biomed Res. 1992;19:131–41. PMID: 1561719.

328 Dromsky DM, Weathersby PK, Fahlman A. Prophylactic high dose methylprednisolone fails to treat severe decompression sickness in swine. Aviat Space Environ Med. 2003;74:21–8. PMID: 12546295.

329 Francis TJ, Dutka AJ. Methyl prednisolone in the treatment of acute spinal cord decompression sickness. Undersea Biomed Res. 1989;16:165–74. PMID: 2734967.

330 Mayer D, Guerrero F, Goanvec C, Hetzel L, Linders J, Ljubkovic M, et al. Prevention of decompression sickness

by novel artificial oxygen carriers. Med Sci Sports Exerc. 2020;52:2127–35. doi: 10.1249/MSS.0000000000002354. PMID: 32251255.

331 Dromsky DM, Spiess BD, Fahlman A. Treatment of decompression sickness in swine with intravenous perfluorocarbon emulsion. Aviat Space Environ Med. 2004;75:301–5. PMID: 15086118.

332 Mahon RT, Watanabe TT, Wilson MC, Auker CR. Intravenous perfluorocarbon after onset of decompression sickness decreases mortality in 20-kg swine. Aviat Space Environ Med. 2010;81:555–9. doi: 10.3357/asem.2745.2010. PMID: 20540446.

333 Sheppard RL, Regis DP, Mahon RT. Dodecafluoropentane (DDFPe) and decompression sickness-related mortality in rats. Aerosp Med Hum Perform. 2015;86:21–6. doi: 10.3357/AMHP.4068.2015. PMID: 25565529.

334 Cronin WA, Hall AA, Auker CR, Mahon RT. Perfluorocarbon in delayed recompression with a mixed gender swine model of decompression sickness. Aerosp Med Hum Perform. 2018;89:14–8. PMID: 29233239.

335 Meng WT, Qing L, Li CZ, Zhang K, Yi HJ, Zhao XP, et al. Ulinastatin: a potential alternative to glucocorticoid in the treatment of severe decompression sickness. Front Physiol. 2020;11:273. doi: 10.3389/fphys.2020.00273. PMID: 32273851. PMCID: PMC7113395.

336 Meng WT, Qing L, Zhou Q, Xu WG. Xuebijing attenuates decompression-induced lung injuries. Diving Hyperb Med. 2020;50:343–9. doi: 10.28920/dhm50.4.343-349. PMID: 33325014. PMCID: PMC8026227.

337 Zhang K, Jiang Z, Ning X, Yu X, Xu J, Buzzacott P, et al. Endothelia-targeting protection by escin in decompression sickness rats. Sci Rep. 2017;7:41288. doi: 10.1038/srep41288. PMID: 28112272. PMCID: PMC5256092.

338 Mazur A, Guernec A, Lautridou J, Dupas J, Dugrenot E, Belhomme M, et al. Angiotensin converting enzyme inhibitor has a protective effect on decompression sickness in rats. Front Physiol. 2018;9:64. doi: 10.3389/fphys.2018.00064. PMID: 29545754. PMCID: PMC5838564.

339 Blatteau JE, Barre S, Pascual A, Castagna O, Abraini JH, Risso JJ, et al. Protective effect of fluoxetine on decompression sickness in mice. PLoS One. 2012;7(11):e49069. doi: 10.1371/journal.pone.0049069. PMID: 23145072. PMCID: PMC3493517.

340 Blatteau JE, de Maistre S, Lambrechts K, Abraini J, Risso JJ, Vallée N. Fluoxetine stimulates anti-inflammatory IL-10 cytokine production and attenuates sensory deficits in a rat model of decompression sickness. J Appl Physiol (1985). 2015;119:1393–9. doi: 10.1152/japplphysiol.00602.2015. PMID: 26494447.

341 Møllerløkken A, Berge VJ, Jørgensen A, Wisløff U, Brubakk AO. Effect of a short-acting NO donor on bubble formation from a saturation dive in pigs. J Appl Physiol (1985). 2006;101:1541–5. doi: 10.1152/japplphysiol.01191.2005. PMID: 16857861.

342 Randsoe T, Meehan CF, Broholm H, Hyldegaard O. Effect of nitric oxide on spinal evoked potentials and survival rate in rats with decompression sickness. J Appl Physiol (1985). 2015;118:20–8. doi: 10.1152/japplphysiol.00260.2014. PMID: 25377881.

343 Zhang K, Zhang H, Yi H, Huang G, Zhao X, Yu S, et al. The protective effects of 1,3-butanediol acetoacetate diester on decompression sickness in rats. J Appl Physiol (1985). 2021;131:435–41. doi: 10.1152/japplphysiol.00035.2021. PMID: 34166120.

344 Mitchell SJ, Merry AF. Perspective on cerebral microemboli in cardiac surgery: significant problem or much ado about nothing? J Extra Corpor Technol. 2015;47:10–5. PMID: 26390674. PMCID: PMC4566815.

345 Vann RD, Freiberger JJ, Denoble PJ, Dovenbarger J, Nord D, Winkler P, Marroni A. Flying after recompression therapy. Undersea Hyperb Med. 2004;31:304.

346 Uguccioni DM, Dovenbarger JA, Hobgood JA, Moon RE. Commercial airflight after recompression therapy for decompression illness. Undersea Hyperb Med. 1998;25(supp):36.

Submitted: 15 January 2024
Accepted: 31 January 2024

DIVER EMERGENCY SERVICES PHONE NUMBERS

AUSTRALIA – DAN
1800-088200 (in Australia toll free)
+61-8-8212-9242 User pays
(outside Australia)

NEW ZEALAND – DAN Emergency Service
0800-4DES-111 (in New Zealand toll free)
+64-9-445-8454 (International)

ASIA, PACIFIC ISLANDS – DAN World
+618-8212-9242

EUROPE – DAN
+39-06-4211-8685 (24-hour hotline)

SOUTHERN AFRICA – DAN
+27-10-209-8112 (International call collect)

USA – DAN
+1-919-684-9111

JAPAN – DAN
+81-3-3812-4999 (Japan)

ADSF
AUSTRALASIAN DIVING SAFETY FOUNDATION

Scholarships for Diving Medical Training for Doctors

The Australasian Diving Safety Foundation is proud to offer a series of annual Diving Medical Training scholarships. We are offering these scholarships to qualified medical doctors to increase their knowledge of diving medicine by participating in an approved diving medicine training programme. These scholarships are mainly available to doctors who reside in Australia. However, exceptions may be considered for regional overseas residents, especially in places frequented by Australian divers. The awarding of such a scholarship will be at the sole discretion of the ADSF. It will be based on a variety of criteria such as the location of the applicant, their working environment, financial need and the perception of where and how the training would likely be utilised to reduce diving morbidity and mortality. Each scholarship is to the value of AUD5,000.00.

There are two categories of scholarships:

1. ADSF scholarships for any approved diving medical training program such as the annual ANZHMG course at Fiona Stanley Hospital in Perth, Western Australia.
2. The Carl Edmonds Memorial Diving Medicine Scholarship specifically for training at the Royal Australian Navy Medical Officers' Underwater Medicine Course, HMAS Penguin, Sydney, Australia.

Interested persons should first enrol in the chosen course, then complete the relevant ADSF Scholarship application form available at: https://www.adsf.org.au/r/diving-medical-training-scholarships and send it by email to John Lippmann at johnl@adsf.org.au.
