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REVIEW ARTICLE

Preconditioning Methods and Mechanisms for Preventing the Risk of Decompression Sickness in Scuba Divers: A Review

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Scuba divers are at risk of decompression sickness due to the excessive formation of gas bubbles in blood and tissues following ascent, with potentially subsequent neurological injuries. Since nonprovocative dive profiles are no guarantor of protection against this disease, novel means are required for its prevention including predive procedures that could induce more resistance to decompression stress. In this article, we review the recent studies describing the promising preconditioning methods that might operate on the attenuation of bubble formation believed to reduce the occurrence of decompression sickness. The main practical applications are simple and feasible predive measures such as endurance exercise in a warm environment, oral hydration, and normobaric oxygen breathing. Rheological changes affecting tissue perfusion, endothelial adaptation with nitric oxide pathway, up-regulation of cytoprotective proteins, and reduction of preexisting gas nuclei from which bubbles grow could be involved in this protective effect.

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INTRODUCTION

Scuba diving results in the production of venous gas emboli (VGE) due to the release of inert gas originally held in solution into the form of a free gas phase from peripheral tissues during decompression. When bubbles are excessively generated in blood and super-saturated tissues, signs and symptoms referred to as decompression sickness (DCS) may occur, potentially causing severe neurological damage. It is generally accepted that gas bubbles grow from preexisting nuclei attached to the vessel walls or by hydrodynamic cavitation resulting mainly from musculoskeletal activity (Blatteau et al. 2006b).

Doppler ultrasonic methods are able to quantify circulating bubbles by using established grading systems to evaluate the decompression stress and to distinguish between safe and unsafe profiles (Nishi et al. 2003). The general conclusions from extensive data gathered during previous experiments are that the presence of venous gas bubbles in the circulation indicates a higher statistical risk of DCS with increasing bubble grades (Sawatzky 1991). A number of reports have shown, however, that the presence of high VGE levels had a weak positive predictive value for DCS, while some divers who exhibited clinical signs of DCS were not carriers of detectable bubbles, specifically in saturation diving (Bayne et al. 1985, Powell et al. 1983). It is noteworthy that the absence of vascular bubbles is associated with an incidence of DCS below 1% in a study of 1,726 air dives and 1,508 heliox dives (Sawatzky 1991). These findings provide evidence that conservative dives that produce few or no bubbles could be considered safe and that the monitoring of Doppler-detectable VGE is a more useful method to improve decompression procedures than a predictive tool for DCS. Because the greatest strength of the bubble data is to predict negatively the occurrence of DCS when bubbles score is low, it appears relevant to use bubble measurement for testing procedures that might be beneficial to minimize DCS risk.

Currently, preventive measures for reducing the risk of DCS are based on the limitation of diver-specific risk factors and the influence of determining factors during and after the dive such as dive duration and depth, ascent protocol, ambient temperature, or exercising. Unfortunately, clinical data to support the importance and the definite role of each factor on DCS development are lacking due in part to the great inter/intravariability between individuals regarding susceptibility to DCS (Francis and Mitchell 2003).

Based on our clinical experience (Blatteau et al. 2005) and Divers Alert Network (DAN) statistics (2003), it is important to note currently that

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most injured divers presenting neurological DCS (75%–90%) followed their dive profile with a computer or a dive table without performing an inadequate decompression schedule (i.e., fast ascent or omitted decompression stops). This result puts forward the notion that conservative profiles are no guarantor of protection against DCS and that novel means are required for DCS prevention.

Preconditioning in SCUBA diving is a promising way involving several predive procedures for reducing vascular bubble formation during decompression. This term refers initially to numerous experimental studies demonstrating that brief episodes of ischemia could enhance the tolerance of the myocardium to further ischemic injury (Yellon and Downey 2003). Since, it has been described in various forms of stressful stimuli (hypoxia, heat exposure, hyperbaric oxygen) to protect a wide variety of organs such as the brain (Dirnagl et al. 2009).

The chain of events that induces preventive protection in divers and makes the organism more resistant to decompression stress is still elusive. Rheological changes affecting tissue perfusion, endothelial remodelling, upregulation of cytoprotective proteins, or reduction of preformed gas nuclei before diving might explain the beneficial effects of this strategy.

In this review, we focus on the clinical issues relating to practical application of several forms of preconditioning methods: specifically, we discuss the mechanisms that might operate on the attenuation of DCS risk.

Predive Endurance Exercise

Exercise has been long considered an additional risk factor for DCS, but recent evidence indicates that this notion needs updating.

Experimental studies in rats have shown that a single bout of high-intensity exercise 20 hrs before a simulated dive reduced bubble formation and prevented death (Wisløff and Brubakk 2001). A human study supported these animal data in which 12 divers reduced venous gas bubbles after performing a single bout of submaximal aerobic exercise 24 hrs before a simulated dive (Dujić et al. 2004). In two reports including 32 divers (Blatteau et al. 2006a), we have shown that a submaximal running session performed 2 hrs before a simulated dive (30 msw for 30 min followed by a 9 min stop at 3 msw) also could be protective in bubble depletion using the Kissman Integrated Severity Score (KISS; Nishi et al. 2003). In an additional work, we tested two intensities of cycling exercise in 31 divers 2 hrs before scuba diving in open water (Pontier et al. 2007). Our results confirm the data obtained in a hyperbaric chamber and suggest a protective effect of both moderate and strenuous exercise on bubble formation.

The mechanisms underlying this protective effect of exercise remain to be elucidated. Wisløff and Brubakk (2001) initially have suggested a nitric oxide (No)-mediated change in surface properties of vascular endothelium, a

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potential site of gas micronuclei. On the other hand, since NO is a vasodilator and has antiatherogenic properties, it is possible that its induction favours the elimination of gaseous nuclei. This could explain the temporary protection against bubble formation observed before the delayed regeneration of micronuclei population lasting 10–100 hrs (Yount and Strauss 1982). This proposed mechanism is not completely convincing, however, particularly in light of the experimental findings that bubble production is increased by NO blockade in sedentary but not in exercised rats (Wisløff et al. 2003). This indicates that the exercise effect may be mediated by factors others than NO, involving biochemical pathways such as heat shock proteins (HSP), antioxidants defences, or physical processes (Blatteau et al. 2006a). In this way, we postulated that predive exercise also could induce rheological changes that modify tissue perfusion. Indeed, the uptake or release of inert gas by a particular tissue depends on both the rate of blood flow to the tissue and the rate of gas diffusion into the tissue from blood. We observed that a moderate hypovolemia induced by a predive exercise might decrease stroke volume (Blatteau et al. 2007), reducing blood flow distribution to various tissues. This could reduce inert gas uptake during the dive and consequently attenuate postdive bubble formation (Figure 1).

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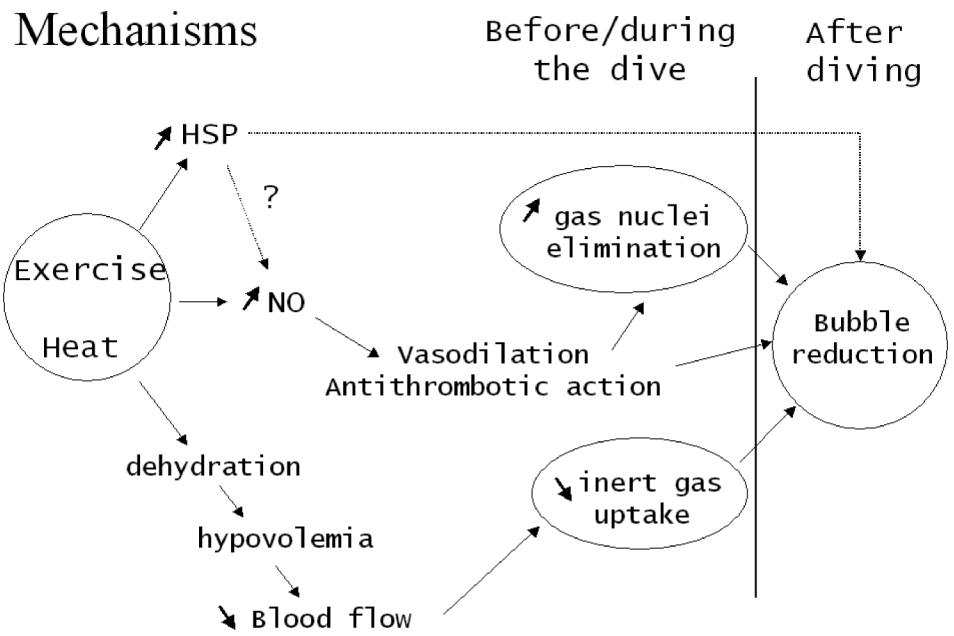

FIGURE 1 Proposed mechanisms for bubble reduction after predive exercise or heat exposure.

Heat Exposure Before Diving

Heat stress represents a nonpharmacological preconditioning strategy, which can lead to protection against various types of subsequent insults such as ischemia, hypoxia, inflammation, drugs (Kregel 2002), and even bubble-induced injury from decompression (Huang et al. 2003; Medby et al. 2008). It has been suggested that the protective effect of heat exposure against DCS observed in rats could be related to biochemical processes involving HSP of the 70 kDa range (Huang et al. 2003; Medby et al. 2008), and such HSP70 induction could be also involved in the mechanisms responsible for diving acclimatization after repeated compression–decompression cycles (Su et al. 2004). Furthermore, it has been demonstrated that HSPs also are able to interact with the endothelial NO pathway (Harris et al. 2003), which may influence the degree of bubble formation in hyperbaric conditions (Wisløff et al. 2003). Otherwise, it is well recognized that high environmental temperatures led to sweat response resulting in dehydration and, as mentioned above, we have shown that a moderate dehydration induced by a predive exercise could influence venous bubble formation (Blatteau et al. 2007).

We performed a study with the aim to determine the effectiveness of sauna-induced heat exposure prior to a simulated dive on bubble formation and to examine the adjustments in HSP70 concentrations and haemodynamic parameters (Blatteau et al. 2008). Sixteen divers underwent a simulated dive in a dry hyperbaric chamber to 400 kPa for 25 min, according to the MN90 table. The experimental dive was preceded by a far infrared-ray dry sauna session for 30 min at 65°C, ending 1 hour prior to the dive. Brachial artery flow mediated dilation (FMD), blood pressure, and bodyweight measurements were taken before and after the sauna session along with blood samples for analysis of rheological changes and plasma HSP70. Our results showed that a single predive sauna session significantly decreased circulating bubbles at rest and after knee flexing. Plasma HSP70 significantly increased 2 hrs after sauna completion. The sauna session led to an extracellular dehydration, resulting in hypovolemia (−2.7% plasma volume) and bodyweight loss (−0.6%), while a significant rise in FMD and a reduction in systolic blood pressure and pulse pressure also were observed.

From these findings, we speculated that heat exposure induced-dehydration and a NO pathway could be involved in this protective effect. It is unclear, however, whether HSPs act directly on the bubble formation process or influence the attenuation of tissue reaction to vascular bubbles (Huang et al. 2003). Further investigations are required to elucidate the preponderant mechanism underlying this heat exposure induced reduction in bubble formation (Figure 1). It is of interest to point out that a predive

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aerobic exercise performed within 2 hrs, including sweat dehydration, a potential increase in body temperature and HSP, and a rise in endothelial NO may provide some of the observed benefits as identified with heat exposure.

Predive Hydration

The possibility that fluid balance significantly affects DCS risk is not established in humans, and animal data are limited and conflicting (Broome et al. 1995; Fahlman and Dromski 2006). Anecdotal reports speculated that predive dehydration and hemoconcentration could be predisposing factors for DCS by increasing blood viscosity and by altering microcirculatory perfusion when bubble formation occurs (Aharon-Peretz et al. 1993; Plafki et al. 1997). Experimental studies suggested that during immersion, divers experience central fluid shifts that lead to a marked diuresis, with dehydration and reduction of plasma volume on surfacing (Jeanningros et al. 1999). Recently, a significant decrease in cardiac preload 1 hour after an open-sea scuba dive also has been observed using Doppler echocardiography, and this change could be attributed to a reduction in plasma volume secondary to immersion (Boussuges et al. 2006). These investigations put forward the idea that oral hydration should be particularly important after surfacing, notably in the case of repeated dives (Jeanningros et al. 1999). Additionally, it was suggested that a low plasma surface tension favours bubble formation (Hjelde et al. 2000), whereas the ingestion of normal saline solution prior to hypobaric exposure might afford protection against altitude DCS by temporarily raising surface tension (Walder 1948).

In eight military divers, we observed that oral hydration using a saline-glucose beverage (1300 ml during 50–60 min) prior to an open-sea field air dive at 30 msw depth for 30 min significantly decreases circulatory VGE (Gempp et al. 2009). The prehydration condition allowed attenuate dehydration induced by the diving session and prevented postdive hypovolemia. We hypothesized that the large-volume oral hydration might result in more rapid elimination of excess inert gas dissolved in body tissues during decompression, thus reducing bubble formation. An alternate explanation could be based on the activation of sympathetic vasomotor discharge to skeletal muscles consecutive to fluid ingestion (Scott et al. 2001) and gastrointestinal distension, leading to peripheral vasoconstriction, and consequently reduction in inert gas load during the dive. In this study, we did not observe changes in plasma surface tension after drinking or diving, indicating a lower influence of hydration status on this parameter than previously was thought and, finally, a lower impact on the course of bubble formation (Figure 2).

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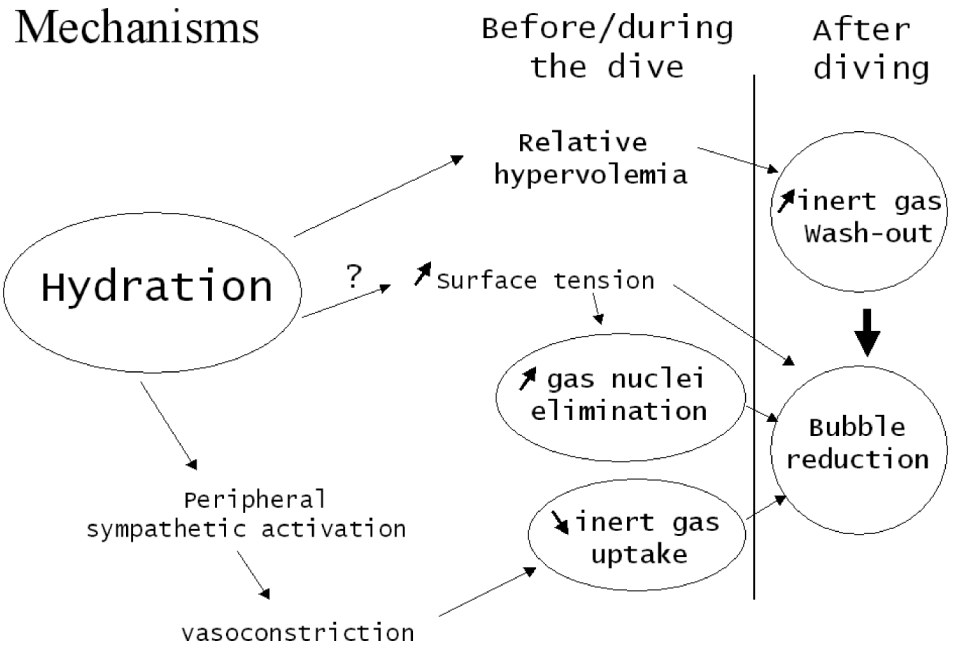

FIGURE 2 Proposed mechanisms for bubble reduction after predive oral hydration.

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Preoxygenation

The role of oxygen (O_2) breathing in the reduction of DCS risk has been extensively investigated before altitude decompression (Bateman 1951; Webb and Pilmanis 1999) or before extravehicular activity in space (Webb and Pilmanis 1998). This method also routinely is employed during decompression for deep air operational diving to accelerate the washout of nitrogen loaded in tissues, thus shortening the decompression time and lowering the incidence of DCS (Hamilton and Thalmann 2003). In the same way, using oxygen in a saturated condition for developing safe escape procedures may be of relevance to submarine rescue operations (Gennser and Blogg 2008, Soutiere et al. 2005). Several studies have shown that a single hyperbaric oxygen exposure before diving also appeared to be beneficial for preventing the occurrence of DCS in animals (Arieli et al. 2002; Butler et al. 2006; Katsenelson et al. 2007) and reducing bubble generation in humans (Landolfi et al. 2006). The mechanisms underlying these protective effects might be related directly to the physical effects of denitrogenation and indirectly to the antioxidant and anti-inflammatory properties of hyperbaric oxygen (HBO). Indeed, prophylactic HBO might impede vascular leukocyte sequestration caused by decompression stress (Martin and Thom 2002), decrease platelet activation (Landolfi et al. 2006), and enhance NO formation

(Thom et al. 2002). This approach did not seem as effective, however, when normobaric oxygen was used as pretreatment before a simulated dive in rats (Butler et al. 2006) or in pigs (Broome and Buttolph 1996). Recently, we performed a field study on 21 volunteer divers to evaluate the effect of 30 min normobaric O_2 breathing before diving upon bubble formation (Castagna et al. 2009). The participants carried out random repetitive open-sea dives under four experimental conditions: "air–air" (control), "O_2–O_2," "O_2–air," and "air–O_2," where "O_2" corresponds to a dive with oxygen prebreathing and "air" to a dive without oxygen administration. We found that O_2 prebreathing provides a significant reduction in decompression-induced bubble formation regardless of the experimental conditions. The beneficial effect of predive oxygen was observed after the first dive and was maintained after the second dive even when the latter was not preceded by preoxygenation. The "O_2–O_2" condition resulted in the highest reduction in bubble scores measured after the second dive. These results tend to indicate that oxygen has had a prolonged protective effect over time and that the cumulative effect of oxygen upon bubble reduction following repetitive dives also could be related with the additional role provided by supplemental oxygen upon remaining gas bubble population. Our data suggest that denitrogenation per se is not preponderant in the effectiveness of oxygen prebreathing in the removal of VGE. The proposed mechanism is based on the ability of oxygen to replace nitrogen in the gas nuclei by diffusion. Reduction of tissue oxygen pressure after switching from oxygen to air could enhance the consumption of oxygen from the nucleus, thus eliminating it completely (Arieli et al. 2002). Another possibility is that oxygen administration induced prolonged haemodynamic effects such as decrease in heart rate, cardiac output, and increase in systemic vascular resistance (Thomson et al. 2006, Waring et al. 2003), leading to a reduction in inert gas load in peripheral tissues during diving and subsequent postdive bubble formation.

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Predive Vibration

Vibration preconditioning been has recently investigated as another possible approach for reducing postdive bubble formation (Balestra et al. 2008). In that preliminary report, 14 healthy male military divers performed two identical dives one week apart, to 30 msw for 30 min, following French Navy standard dive procedures. One of the dives randomly was preceded by a 30 min whole-body vibration session (frequencies 40–80 Hz) with a commercially available vibration mattress, 1 hour prior diving. Before and after the vibration session, a measurement of the FMD response in the brachial artery also was performed. Doppler-detected bubbles analysis showed a reduction in KISS score after the vibration dive with knee flexing, but this condition did not result in a significant modification of the endothelial reactivity, as indicated by the FMD measurements. From these findings, the authors suggested

that external vibration could create shear forces that mechanically release the gas nuclei from endothelial wall or modify the vessel hydrophobic properties in a biochemical way, other than the NO pathway. If liberated into the venous blood stream before the dive, gas nuclei would be eliminated rapidly by the combined effects of surface tension and oxygen window (Blatteau et al. 2006b).

Medication Pretreatment: Futures Perspectives

Several studies have shown that environmental stress in relation to hyperbaric exposure results in endothelial dysfunction, both in animal (Nossum and Brubakk 1999) and in human subjects (Brubakk et al. 2005). Endothelial dysfunction is characterised by an impairment of NO bioavailability, which normally plays a key role in the regulation of vascular tone and maintenance of antiadhesive properties to the normal functioning endothelium. This condition is also associated with increased oxidative stress and increased synthesis of proinflammatory factors therefore, making, a favourable environment for a prothrombotic state.

A number of experiments in both animals and humans demonstrated that administration of a direct-acting NO donor could reduce decompression-induced vascular bubbles after a simulated saturation dive (Møllerlokken et al. 2006) or after short air dives (Dujić et al. 2006), while NO blockade has an opposite effect (Wisløff et al. 2003). The main hypothesis explaining these findings may be conferred on the ability of NO to preserve vascular integrity as a mediator of the hydrophilic/hydrophobic properties of the endothelial wall, on which gas bubbles or nuclei are presumed to be forming. It is strongly suggested that vascular bubble formation may contribute mainly to deleterious endothelial injury, leading to vascular obstruction, microcirculatory alterations, and activation of coagulation cascades, which could form the basis for the development of DCS and possible long-term asymptomatic neurological damages (Brubakk et al. 2005).

Recently, it has been shown that pharmacological intervention with acute or long-term oral antioxidants prior to diving could reduce the negative effects of a dive on endothelial function assessed according to the FMD method (Obad et al. 2007a, 2007b).

Some authors have postulated that endothelial dysfunction may be the consequence of oxidative stress resulting from hyperoxia during diving (Madden and Laden 2009). In that way, vascular preconditioning with vitamin C could attenuate the inflammatory response induced by endothelial activation at depth, thus limiting any possible systemic effect of subsequent gas bubble formation upon decompression (Madden and Laden 2009).

Statin medications are known to have a beneficial effect on the primary and secondary prevention of coronary heart disease events as well as in stroke prevention through the reduction in atherosclerosis progression.

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These therapeutic agents exert numerous pleiotropic effects that occur beyond the lipid lowering effect and contribute also to the antiatherogenic properties of this drug class. The action mechanisms are complex, including up-regulation of endothelial NO synthase, inhibition of vascular inflammation, immune modulation, activation of angiogenesis, and a possible effect on thrombogenicity (Blum and Shamburek 2009). Some authors argued that the potential role of statins in preservation of endothelial integrity could have an interest for mitigating the propensity to bubble formation via alterations in plasma rheology and surface tension (Duplessis and Fothergill 2008). A recent study, however, failed to demonstrate a reduction of precordial echocardiography-detected intravascular bubbles after prophylactic 80 mg atorvastatin administration for 4 days prior to a simulated dive at 2,8 ATA for 80 min (Duplessis et al. 2007).

Some experimental data support the use of intravenous perfluorocarbon (PFC) emulsion in cerebral arterial gas embolism prevention by increasing the volume of distribution of dissolved gas in the body, thereby facilitating tissular perfusion (i.e., O_2 delivery) and nitrogen washout (Spiess et al. 1986). It is speculated that administration of degassed liquids (ingestion or infusion) also could be involved in prevention of mild DCS (Watenpaugh 2003). In combination with oxygen breathing, PFC might reduce the morbidity and mortality of DCS swine if administered immediately after a saturation dive (Dainer et al. 2007, Dromsky et al. 2004). More research should be conducted, however, to learn about the potential deleterious effects of these therapeutic agents (e.g., pulmonary hypertension, increased seizure activity under HBO conditions; Dainer et al. 2007, Mahon et al. 2006) before generalizing them as an alternative nonrecompression DCS treatment.

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CONCLUSION

The recent findings mentioned in this article give new insights into the protective role of certain methods applied prior to diving for attenuating decompression stress. Preconditioning may be a simple, safe, and feasible preventive technique that could be added to the general recommendations for reducing the development of DCS. Evidence suggests that, for a population of trained and military divers, endurance exercise (even in a warm environment) associated with oral hydration prior to the dive is beneficial in vascular bubble reduction. Additional research will be helpful in the understanding of the biochemical and biophysical mechanisms influencing bubble formation, specifically the role of endothelium in the pathophysiology of DCS. In the future, drugs that modify bubble generation by improving endothelial function or reducing gas nuclei population could be used as possible candidates for preventing the occurrence of DCS, particularly in risky operational dives or in emergency situations such as submarine escape.

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