Preconditioning and DCI

It is generally accepted that the most important risk factors for decompression illness (DCI) are dive time and depth. Divers are also very interested in how other factors such as exercise and hydration status may affect DCI risk. Preconditioning describes the use of physiological or pharmacological stimuli to increase resistance to particular injuries or illnesses. In this article, we seek to understand whether there are particular preconditioning practices divers can employ that may reduce their risk of DCI. We ask the experts.

The prevailing recommendation with regard to exercise and diving is that divers avoid strenuous physical activity around diving, but it has been suggested that certain exercise may reduce DCI risk. How might exercise increase or decrease the risk of DCI, and what advice would you give divers about exercise and diving?

Constantino Balestra: More and more researchers are demonstrating benefits of predive exercise. The mechanisms have not been definitively identified, but “movement” seems to be a clue. The benefit seems to lie in the concomitant actions of the heart, vascular system and lymphatic system.

Michael Bennett: The relationship between exercise and diving has become very interesting over the past few years. The traditional view is that predive exercise is a risk factor for DCI; this is based on the potential for increased tissue-nitrogen uptake with hyperdynamic circulation. However, recent evidence indicates this view may be too simplistic. Both animal and human studies suggest a single bout of moderate or strenuous exercise two to 24 hours before a simulated dive can reduce bubble formation (and presumably the risk of DCI). It is not yet clear why this should be so, but it seems likely the generation of nitric oxide (NO) during exercise may either favor the elimination of the nuclei where bubbles tend to form or otherwise alter the cells that line blood vessels (the endothelium). There are a number of alternative hypotheses, however, and this is a very active area of research. Jean-Eric Blatteau and colleagues postulated, for example, that the protective effect is due to moderate hypovolemia. Currently I advise divers there is no evidence that exercise before diving is harmful up to about two hours before immersion, but I do not actively advise divers to undertake exercise.

There is less controversy around the effects of exercise at other times with regard to DCI risk. Exercise during a dive increases nitrogen uptake and distribution to the tissues and is thought to increase the risk, while gentle exercise during decompression has been advocated to assist offgassing and reduce the risk. Vigorous exercise after completing a dive is discouraged because of the potential to promote bubble formation by mechanical stimulation

Alf Brubakk: Regular exercise is recommended for divers. Aerobic exercise prior to diving will reduce vascular bubble formation. Exercise after diving may increase or decrease bubble formation; the effects may be dependent upon general fitness levels. This is an area where information from which to make firm recommendations is lacking.

Most experts agree severe dehydration might increase DCI risk, but it has been suggested that mild to moderate dehydration may reduce the risk. What do you think about this, and what would you recommend divers do?

Balestra: There are points of view that assert a “normal” volume of blood plasma or even a moderately reduced plasma volume could possibly reduce the nitrogen saturation of the tissues during a dive. The actual take-home message is not to increase plasma volume too rapidly or too much as this will increase

urine production and not really hydrate the tissues. My advice is to drink a glass of water every 15 or 20 minutes to allow the tissues to be hydrated without increasing plasma volume.

Bennett: Some work investigating the effect of both exercise and exposure to heat on the risk of subsequent DCI may be interpreted as suggesting, somewhat paradoxically, that mild dehydration is protective. The suggestion is a consequence of one possible mechanism by which these challenges provide protection against bubble formation. Blatteau and colleagues suggested the moderate dehydration and decreased blood volume (hypovolemia) induced by predive exercise or heat exposure in a sauna might decrease cardiac output and reduce the delivery of nitrogen to the tissues. There are a number of competing theories, however, and I am not aware of any data that support this particular assertion.

The suggestion is actually rather surprising. Although the risks associated with dehydration have yet to be well defined, everything we know suggests predive fluids are a good thing rather than harmful. For example, in 2008 Gempp and colleagues published a crossover study that concluded: "Predive oral hydration decreases circulatory bubbles, thus offering a relatively easy means of reducing decompression sickness risk." In this study, prehydration with 1.3 liters of a saline/glucose mixture attenuated the dehydration and prevented the hypovolemia induced by diving but did not change plasma surface tension. My recommendation is divers should try to ensure adequate hydration before diving and actively avoid diving when dehydrated.

Brubakk: I do not know of any data that support this, and I do not think theory would suggest this. I recommend divers be well hydrated.

Some researchers have proposed predive administration of antioxidants such as vitamin C, other nutrients, or drugs such as nitroglycerin to reduce the risk of DCI. How might such agents reduce risk?

Balestra: Experience shows this approach does not really interfere with bubble production but with endothelial function. After a dive, when endothelial function is transiently impaired, antioxidants can prevent such impairment, but there is no clear demonstration that bubble production can be reduced with such agents. Research on this subject is ongoing.

Bennett: We have recently seen a growing interest in the modification of endothelial function by pharmacological means. In general, most interest is generated by agents that increase NO availability and the subsequent effect on sites (presumed to be on the endothelium) where gas bubbles form. Such bubble formation is likely to cause endothelial injury and promote both microvascular obstruction and activation of coagulation cascades — changes that might be directly responsible for the clinical picture of DCI. Indeed, although it is early, there is some experimental evidence from both animals and humans that administration of compounds such as those listed could significantly reduce the risk of DCI. Essentially, both NO donors (such as nitroglycerin) and antioxidants (such as Vitamin C) counteract the oxidative stress that is the cause of the endothelial damage that may be the reason bubble-induced injury produces such widespread effects in divers.

This is a fascinating area of research and may soon produce some definite recommendations for divers. At this time, however, we should exercise caution. Many of these agents have wide-ranging effects — some of which may result in considerably more harm than good — and as yet we have no practical evidence that clinical DCI can be prevented by these agents.

Brubakk: Antioxidants seem to reduce bubble formation. It may also be that antioxidants will reduce inflammatory responses that may play a role in DCI. This is an area that needs further study, but it is a

promising approach. At present, we know too little about the effects of antioxidants on healthy people.

Rune Djurhuus: NO is a small signalling molecule that causes relaxation and dilatation of the blood vessels. Animal studies have indicated administration of a pharmacological agent (e.g., nitroglycerin) that releases NO in the blood stream may reduce gas-bubble formation and increase survival after decompression. Conversely, inhibiting the enzyme nitric oxide synthase (NOS) that generates NO in the endothelial layer lining the inside of blood vessels markedly aggravated the symptoms of DCI. Moreover, physical exercise is also known to stimulate the generation of NO in the endothelium. A prevailing hypothesis has therefore been that NO generation plays a role in protecting the vascular system against adverse effects of gas bubbles during decompression.

Diving usually implies an elevated partial pressure of oxygen. We recently showed that such hyperoxic conditions had no effect on NOS's capability for generation of NO in isolated human endothelial cells. However, to function normally, the enzyme is dependent on several cofactors, in particular tetrahydrobiopterin (BH4). This compound is easily oxidized, and the oxidized form does not support NO synthesis. Exposing human endothelial cells to hyperoxic conditions (approximately three times the partial pressure of oxygen at sea level) caused the BH4 concentration to drop approximately 50 percent. The consequence of exposure to hyperoxic conditions while diving may therefore be a decreased level of BH4, which in turn limits NO generation by NOS and potentially increases the risk of DCI. It should be emphasized these results were obtained in an experimental model, but if the detailed mechanism can be elucidated and verified in animals (preferably humans), remedial actions seem possible. These might include counteraction of hyperoxic effects by additional supplies of BH4 or by administration of antioxidants that stabilize the cofactor in the reduced, active form. A simple antioxidant such as vitamin C has been shown to help sustain the level of BH4 in experimental models. As research progresses other factors may turn out to be more crucial.

Several other factors such as whole-body vibration before diving, oxygen prebreathing, work-up dives and predive sauna have also been proposed for preconditioning against DCI. Have any practical applications emerged from these proposals?

Balestra: These preconditioning techniques are directly related to moderate cardiac activity (sauna) or increasing lymphatic activity (whole body vibration, oxygen prebreathing). In some cases the oxygen prebreathing was performed too long before the dive for any denitrogenation effect to be considered. All the techniques listed are thought to be more related to moderate demicronucleation than denitrogenation.

Bennett: All these proposed measures constitute attempts to reduce the chance of DCI through preconditioning against bubble formation. The only one commonly applied to divers is work-up dives, whereby divers aiming at a challenging dive (usually deep) will perform a series of dives of increasing depth as they approach the date of the planned deepest dive. While there is little evidence for or against true preconditioning with this approach, there are a number of good reasons why work-up dives may be useful, including familiarization with equipment and sea conditions, equipment checking in a nonchallenging environment and refamiliarization with good diving practices.

There are ongoing efforts, particularly in Europe, to assess the role of a number of preconditioning strategies, including those mentioned above. Blatteau and colleagues, for example, reported a predive sauna exposure to reduce bubble counts following a simulated dive in human volunteers. At this time they all remain theoretical, and I am not aware of any practical applications that have come from this work to date.

Brubakk: No practical applications have emerged, but data suggest these techniques may reduce bubble

formation.

Meet the Experts

Costantino Balestra, Ph.D., is vice president of research and education at DAN Europe, DAN Europe's area director for Benelux and France and vice president of the European Underwater and Baromedical Society (EUBS). He also directs the Environmental, Aging and Occupational Physiology Lab at Haute Ecole Paul-Henri Spaak in Brussels, Belgium. His primary research interests are in the physiology of extreme environments and sports science.

Michael Bennett, M.D., FANZCA, ANZCA Cert DHM, is a senior staff specialist at the Prince of Wales Hospital and tenured associate professor of hyperbaric medicine at the University of New South Wales in Sydney, Australia. He has 17 years of experience with the management of remote diving injuries in the South Pacific and received his doctorate for work on the evidence basis of diving and hyperbaric medicine.

Alf O. Brubakk, M.D., is professor of environmental physiology at the Norwegian University of Science and Technology in Trondheim, Norway. He has a background in cardiology and anesthesiology, and he has studied decompression sickness for more than 20 years. He also studies other areas of environmental physiology, including the effects of cold and outer space.

Rune Djurhuus, Ph.D., is a principal scientist in biochemistry and toxicology at Norwegian Underwater Intervention in Bergen, Norway. His research focuses on chemical contamination of divers' breathing gas (hyperbaric toxicology) and cellular defense mechanisms related to endothelial damage due to decompression stress.