Diving and Hyperbaric Medicine

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SPUMS

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EUBS

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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

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DIVING AND HYPERBARIC MEDICINE

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Editor
Simon Mitchell editor@dhmjournal.com

European (Deputy) Editor
Lesley Blogg euroeditor@dhmjournal.com

Editorial Assistant
Nicky Telles editorialassist@dhmjournal.com

Submissions: https://www.manuscriptmanager.net/dhm

Subscriptions and print copies of back issues to 2017
Steve Goble admin@spums.org.au

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The Editor's offering

Welcome to the second issue of DHM in 2021, the second year of the COVID-19 global pandemic. In 2020 the South Pacific Underwater Medicine Society (SPUMS), the European Underwater and Baromedical Society (EUBS), and the Undersea and Hyperbaric Medicine Society (UHMS) all cancelled their annual scientific meetings as travel restrictions and concerns about delegate safety made holding them essentially impossible. The hope was that things would improve in 2021.

Well, 2021 is here and things have improved, but sadly not enough for large 'face-to-face' meetings to become viable. There are still constraints on travelling; some are 'hard limitations' imposed by closed borders, and some arise from individuals' anxiety about the potential hazards of travel and mingling with large groups. Fortunately, through use of virtual meeting technology we didn't have to endure a second consecutive year with no collegial academic activity, with two successful virtual meetings being recently held.

For SPUMS, the meeting (21–23 May) was a hybrid event facilitated by the 'travel bubble' established between Australia and New Zealand in April after both countries had eliminated community transmission of the COVID-19 virus. This allowed SPUMS to offer a virtual meeting using the Zoom platform, but with the option to attend the meeting hub at the Royal Australian Navy School of Underwater Medicine, Sydney in person for those who wished to do so. The hub was variably attended by 20–35 members, and there were up to another 70 from around the world online at different times. It was a fantastic meeting with the highlight being a captivating presentation by Richard Harris on his role as an anaesthetist and diver in the Thailand cave rescue; something previously described in DHM.[1] We congratulate Dr Doug Falconer and his helpers for running such a rewarding and useful event and thanks also to our widely distributed international members for attending and in many cases presenting.

The UHMS held an entirely virtual meeting over 10–12 June using the Webex platform. This too was an extremely successful undertaking with a remarkably good discussion component given the constraints of the medium. A highlight of substantial contemporary relevance was a session on diving after COVID-19 infection hosted by Prof Peter Lindholm and Dr Charlotte Sadler. They presented their algorithm for choosing appropriate investigations in a diving candidate or diver returning to diving after COVID-19 (which was recently published in DHM).[2] This was followed by some interesting perspectives from the US Navy and others on how to interpret the findings in making decisions on suitability for diving. Once again, congratulations to the UHMS team for providing this meeting after the disappointment of having to cancel the face-to-face in New Orleans.

Sadly, the EUBS 2021 annual scientific meeting scheduled for Prague has had to be postponed again, and will now be held in 2022. This EUBS meeting, along with the SPUMS (Tutukaka, New Zealand) and UHMS (Reno, Nevada) meetings will be highly anticipated and likely very well attended. The proliferation of on-line events over the last year has shown us that virtual meetings work, but there is no replacing the informal conversations, exchange of ideas and formation of linkages that occur at face-to-face meetings.

Finally, it gives me immense pleasure to note the Australian Government's recognition of Professor Michael Bennett as a Member of the Order of Australia (AM). Mike is a former president of SPUMS, on the editorial board of DHM and a prolific researcher/author, but it is his contribution to representing our field as respectful of proper science that will be his legacy. If the diving and hyperbaric discipline has a 'father' of evidence-based medicine then Mike is surely it. His efforts, particularly the publication of more than 30 systematic reviews and making his database of randomised controlled trials in diving and hyperbaric medicine freely available on line, have brought our field a legitimacy in the wider medical world that it might not have otherwise enjoyed. This was evidenced in 2011 with his invited publication of the first chapter on hyperbaric and diving medicine in the iconic general medical textbook Harrison's Principles of Internal Medicine. He has updated this chapter in every edition since. Congratulations Mike. Well deserved.

Simon Mitchell
Editor

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Cover photo caption: The COVID-era SPUMS hybrid-virtual annual scientific meeting in Sydney showing in-person attendees from Australia and New Zealand. Among our international attendees who can be seen on the Zoom screen behind are Jurg Wendling (Switzerland), Martin Sayer (UK), Mark Turner (UK), Tony Lee (Malaysia) and Vincenzo Zanon (Italy).

Original articles

Necrostatin-1 prolongs latency to convulsion in mice exposed to high oxygen partial pressure

Zhen-Biao Guan[1],* Yan-Yan Zhou[2],* Yi Cen[3], Han-De Feng[3], Wen-Wu Liu[4], Hong-Jie Yi[5], Hui Chen[3]

[1] *Department of Respiratory and Critical Illness, Changhai Hospital, the Naval Military Medical University, People's Liberation Army, Shanghai, 200433, China*
[2] *Department of Orthopedic Surgery, Changzheng Hospital, the Naval Military Medical University, People's Liberation Army, Shanghai, 200003, China*
[3] *Department of Anesthesiology and Perioperative Medicine, Shanghai Fourth People's Hospital, Tongji University School of Medicine, Shanghai, China*
[4] *Department of Diving and Hyperbaric Medicine, the Naval Military Medical University, People's Liberation Army, Shanghai, 200433, China*
[5] *Department of Hyperbaric Oxygen, Changhai Hospital, the Naval Military Medical University, People's Liberation Army, Shanghai, 200433, China*
* *Both Zhen-Biao Guan and Yan-Yan Zhou contributed to this article equally*

Corresponding author: *Dr Hui Chen, Department of Anesthesiology and Perioperative Medicine, Shanghai Fourth People's Hospital, Tongji University School of Medicine, No 1279, Sanmen Road, 200434, Shanghai, China*
chenhui_md@163.com

Key words
Animal model; Central nervous system; Inflammation; Necroptosis; Oxidative stress; Oxygen toxicity

Abstract
(Guan ZB, Zhou YY, Cen Y, Feng HD, Liu WW, Yi HJ, Chen H. Necrostatin-1 prolongs latency to convulsion in mice exposed to high oxygen partial pressure. Diving and Hyperbaric Medicine. 2021 June 30;51(2):134–139. doi: 10.28920/dhm51.2.134-139. PMID: 34157727.)
Introduction: Exposure to very high oxygen partial pressure may cause central nervous system oxygen toxicity (CNS-OT). The role of necroptosis in the pathogenesis of CNS-OT is still unclear.
Methods: In experiment one, male C57BL/6 mice in the oxygen toxicity (OT) group (n = 5) and necrostatin-1 (Nec-1; a necroptosis inhibitor) (1.5 mg·kg^{-1}, intraperitoneal) group (n = 5) were exposed to pure oxygen at 600 kPa, and the latency to tonic-clonic seizure was recorded. In experiment two, mice were divided into three groups: control group (n = 11), OT group (n = 12) and Nec-1 group (n = 12). Nec-1 was intraperitoneally administered 30 min before oxygen exposure. Mice in the OT group and Nec-1 group were exposed to pure oxygen at 400 kPa for 30 min, and then sacrificed; the brain was harvested for the assessment of inflammation, oxidative stress and necroptosis.
Results: Experiment one. Nec-1 pre-treatment significantly prolonged the latency to seizure (245 [SD 18] seconds in the OT group versus 336 (34) seconds in the Nec-1 group). Experiment two. Nec-1 pre-treatment markedly reduced inflammatory cytokines and inhibited cerebral necroptosis, but failed to significantly suppress cerebral oxidative stress.
Conclusions: These findings indicate necroptosis is involved in the pathogenesis of CNS-OT, and inhibition of necroptosis may prolong seizure latency, but the specific mechanisms should be investigated further.

Introduction

It has been confirmed that exposure to oxygen at a high partial pressure and/or for a long period may cause damage to the central nervous system (CNS) and pulmonary system. Generally, exposure to a pressure of oxygen (PO_2) above 140 kPa may lead to nausea, numbness, dizziness, twitching, hearing, visual disturbances, and even convulsions and unconsciousness, known as CNS oxygen toxicity (CNS-OT).[1] In diving and clinical practice, the PO_2 and duration of oxygen exposure are strictly controlled to avoid oxygen toxicity and thus the actual incidence of oxygen toxicity is relatively low. Currently, the pathogenesis of CNS oxygen toxicity is still poorly understood. Proposed mechanisms include: excess production of reactive oxygen species (ROS);abrupt increase of cerebral blood flow following vascular constriction, imbalance between excitatory and inhibitory neurotransmitters and others.[2]

Programmed cell death is the deliberate suicide of an unwanted cell in a multicellular organism. To date, several types of programmed cell death have been identified, including apoptosis, necroptosis, ferroptosis, autophagy and others.[3] It has been revealed that oxygen toxicity may

induce apoptosis of neuronal cells,[4,5] and inhibition of intrinsic apoptosis is helpful for the prevention of neonatal oxygen induced brain damage.[6] A previous study indicated that necroptosis was involved in the pathogenesis of acute hyperoxia-induced lung injury and anti-oxidative treatment inhibited the necroptosis and thereafter improved the lung injury.[7] However, whether CNS-OT may also induce necroptosis in the brain and whether inhibition of necroptosis protects from CNS-OT *in vivo* have never been investigated. This study aimed to investigate the role of necroptosis in CNS-OT in a mouse model.

Methods

The study protocol was approved by the Institutional Animal Care and Use Committee of the Naval Medical University (NMU 2020-0239), and efforts were made to minimise suffering to the animals used in this study.

ANIMALS AND GROUPS

Male C57BL/6 mice weighing 20 (SD 2) g were purchased from Shanghai SLAC Experimental Animal Centre and housed at 24 (1)°C, humidity of 54 (2)% and a 12/12 h light/dark cycle. All the animals were given *ad libitum* access to food and water. In experiment one, mice were divided into two groups: CNS-OT group (n = 5) and necrostatin-1 (Nec-1; an inhibitor of necroptosis) group (n = 5). In the Nec-1 group, mice were intraperitoneally injected with Nec-1 (Selleck, TX, USA; S8641) at 1.5 mg·kg^{-1} 30 min before oxygen exposure (see below), and the latency to convulsion was recorded and analysed. Nec-1 was dissolved in 1% dimethylsulfoxide in sterile saline, and Nec-1 solution was prepared immediately before administration. In experiment two, mice were randomly divided into 3 groups: control group (n = 11), CNS-OT group (n = 12), and Nec-1 group (n = 12). In the control group, mice were exposed to normobaric air in a chamber. In the CNS-OT and Nec-1 groups mice were exposed to hyperbaric oxygen (HBO). In the Nec-1 group, mice were intraperitoneally injected with Nec-1 at 1.5 mg·kg^{-1} 30 min before oxygen exposure; mice in the CNS-OT group were intraperitoneally injected with 1% dimethylsulfoxide in sterile saline of the same volume 30 min before oxygen exposure.

HBO EXPOSURE

Animals were placed singly in an animal compression chamber (RDC150-300-6, Naval Medical University, Shanghai, China). In experiment one, the chamber was flushed with pure oxygen (> 99%) for 5 min and then pressurised to 600 kPa at a rate of 100 kPa·min^{-1}. The latency to convulsion was recorded, and then animals were de-pressurised at a rate of 50 kPa·min^{-1}. The pressure of HBO was 600 kPa because the latency to convulsion was longer when the pressure was at a low level. In experiment two, animals were exposed to pure oxygen at 400 kPa for 30 min (avoiding onset of a convulsion), and then de-pressurised at a rate of 50 kPa·min^{-1}. Animals were subsequently anaesthetised with intraperitoneal 1% pentobarbital sodium (50 mg·kg^{-1}) and then sacrificed for sample collection. During HBO exposure the chamber was continuously ventilated with 100% oxygen at 0.5 L·min^{-1}. The whole brain was harvested for further examination. In the control group, seven mice were sacrificed for biochemical examinations and four mice for immunohistochemistry. In the CNS-OT group and Nec-1 group, seven mice were sacrificed for biochemical examinations and five mice for immunohistochemistry.

LATENCY TO CONVULSION

When the chamber pressure reached 600 kPa, the latency was recorded. The latency to convulsion was defined as the time from the arrival of chamber pressure at 600 kPa to the onset of tetanic contraction of the whole body and persistent spasm.[8]

BIOCHEMICAL EXAMINATION

In experiment two, brain tissues were homogenized in phosphate buffer solution (PBS), followed by centrifugation at 3,000 rpm for 15 min. The supernatant was harvested for the detection of protein concentration with BCA assay (Beyotime, Jiangsu, China). Then, the malonaldehyde (MDA) content, superoxide dismutase (SOD) activity and reduced glutathione (GSH) content were detected with commercially available kits (Beyotime, Jiangsu, China) according to manufacturer's instructions.[7] Similarly, the contents of interleukin-1β (IL-1β), interleukin-10 (IL-10) and tumour necrosis factor-α (TNF-α) were detected with enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's instructions.[7]

The receptor interaction protein 1 (RIP1), receptor interaction protein 3 (RIP3) and phosphorylated mixed lineage kinase domain-like protein (p-MLKL) are three crucial proteins involved in necroptosis. During necroptosis, RIP1 kinase activates RIP3, which then gains the ability to phosphorylate and activate MLKL.[9] The expression of RIP1, RIP3 and p-MLKL was detected in the brain tissues. In brief, the brain was collected and lysed in lysis buffer (20 mmol·L^{-1} Tris-HCl, pH 7.5, 150 mmol·L^{-1} NaCl, 1% Triton X-100; 1 mmol·L^{-1} ethylenediaminetetraacetic acid, 1 mmol·L^{-1} ethyleneglycol-tetraacetic acid, 2.5 mmol·L^{-1} pyrophosphate, 1 mmol·L^{-1} β-glycerophosphate) containing protease inhibitor mixture (Roche Applied Science, USA) on ice, followed by centrifugation at 3,000 rpm at 4°C for 15 min. After determination of protein concentration, equal amounts of protein were separated with 10% SDS-PAGE gels and polyvinylidene fluoride membranes (Bio-Rad, Hercules, CA, USA). After blocking with 5% milk, membranes were incubated with primary antibodies to RIP1 (1:1000), RIP3 (1:1000), p-MLKL (1:500), and β-actin (1:2000) (Abcam; Danvers, MA, USA) at 4°C overnight. Blots were washed with tris-buffered saline with Tween 20 thrice (6 min for each). After washing, blots were incubated with secondary

antibodies (1:2000) for 2 h at room temperature. Finally, bands were visualised with an Electro-Chemi-Luminescence (ECL) Substrate Kit (Amersham, Rahn AG, Zurich, Switzerland) and quantified with Bio-Rad Quantity One software (Bio-Rad, Hercules CA, USA).

IMMUNOPRECIPITATION OF RIP1/RIP3

The protein concentration was determined in the brain as mentioned above. Immunoprecipitation was used for determining the interaction of proteins and performed as manufacturer's instructions with the Pierce Co-Immunoprecipitation (Co-IP) Kit (Pierce Biotechnology; Rockford, IL, USA). One ml of lysates was mixed with 2 mg of rabbit anti-RIP1 antibody (Abcam, USA) followed by incubation at 4°C overnight. Subsequently, the lysates were mixed with 40 ml of re-suspended Protein A + G Agarose, followed by incubation at 4°C for 3 h with constant shaking. After washing five times in lysis buffer, proteins were boiled with 1× loading buffer for 10 min. The specimens were evaluated by Western blotting.

IMMUNOHISTOCHEMISTRY

Mice were anaesthetised and transcardially perfused with 4% paraformaldehyde and then with normal saline. The brain tissues were harvested and immediately fixed in 4% paraformaldehyde at 4°C. After treatment with 30% sucrose in 0.1 M PBS at 4°C overnight, the brain tissues were embedded in paraffin. 4-µm sections were obtained, deparaffinized and rehydrated in gradient alcohol. After antigen retrieval in citrate buffer (10 mM sodium citrate, 0.05% Tween 20, pH 6.0), brain sections were blocked in 2.5% normal serum and then treated with anti-RIP1/anti-RIP3 antibody at 4°C, overnight. After rinsing in PBS, sections were treated with secondary antibody, and counterstaining was done with hematoxylin. In negative controls, sections were incubated with PBS instead of primary antibody. Five randomly selected fields at a magnification of 400× (Nikon TE300; Nikon, Japan) were captured, and the immunopositive cells were counted by an investigator who was blinded to the experiment.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS version 21.0 (Statistical Product and Service Solutions Inc., Chicago, IL, USA). All data are expressed as mean and standard deviation (SD). Student's *t*-test was used to examine the difference in the latency between the two groups after using the Shapiro-Wilk test for normality. Comparisons were performed with one-way ANOVA among groups, followed by Tukey's post hoc test. A value of $P < 0.05$ was considered to indicate statistical significance.

Results

LATENCY TO CONVULSION

The latency to convulsion was 245 (SD 18) s in the control group. In the Nec-1 group, the latency to convulsion was prolonged to 336 (34) s. The first generalised, tonic-clonic

Figure 1

Oxidative stress and inflammation-related cytokines in the brain of different groups. A. IL-1β concentration; B. TNF-α concentration; C. IL-10 concentration; D. MDA concentration; E. 8-OHdG concentration; F. GSH concentration; G. SOD activity. ** $P < 0.01$ versus control group; # $P < 0.05$, ## $P < 0.01$ versus CNS-OT group. CNS-OT – central nervous system oxygen toxicity; GSH – glutathione; IL-1β – interleukin-1β; IL-10 – interleukin-10; MDA – malonaldehyde; Nec-1 – Necrostatin-1; TNF-α – tumor necrosis factor-α; SOD – superoxide dismutase; 8-OHdG – 8-hydroxydeoxyguanosine

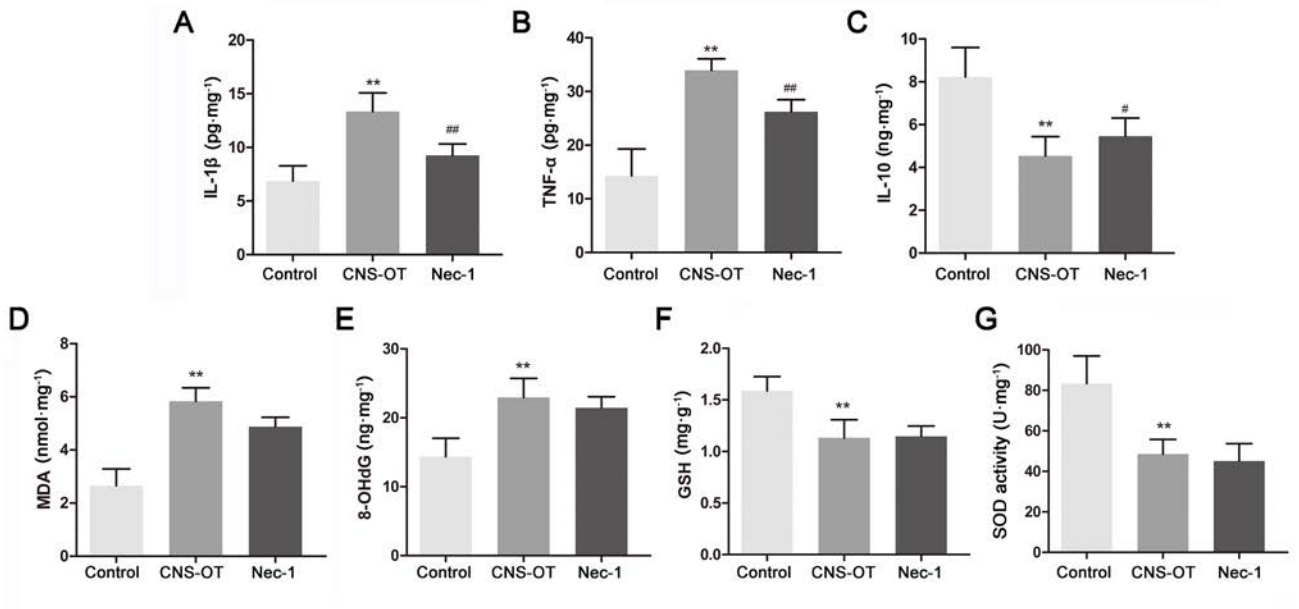


Figure 2

Detection of RIP1, RIP3 and MLKL protein expression in the brain (Western blotting). * $P < 0.05$ versus Control group; # $P < 0.05$ versus CNS-OT group. CNS-OT – central nervous system oxygen toxicity; Nec-1 – Necrostatin-1; RIP1 – receptor interaction protein 1; RIP3 – receptor interaction protein 3; p-MLKL– phosphorylated mixed lineage kinase domain-like protein

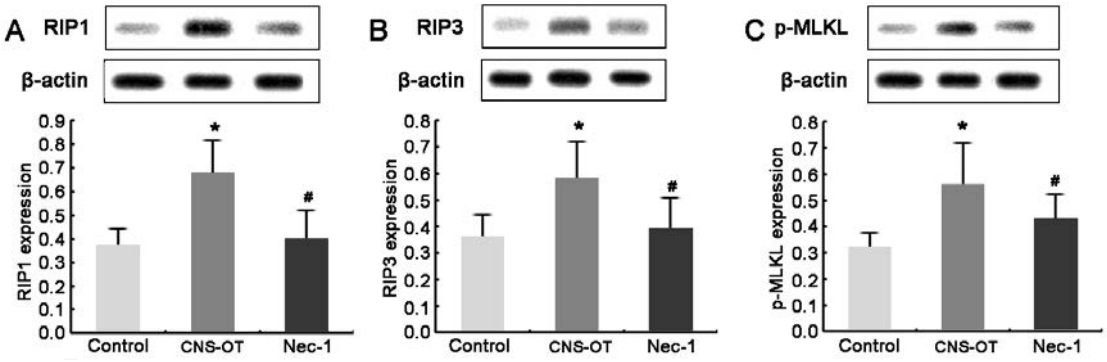
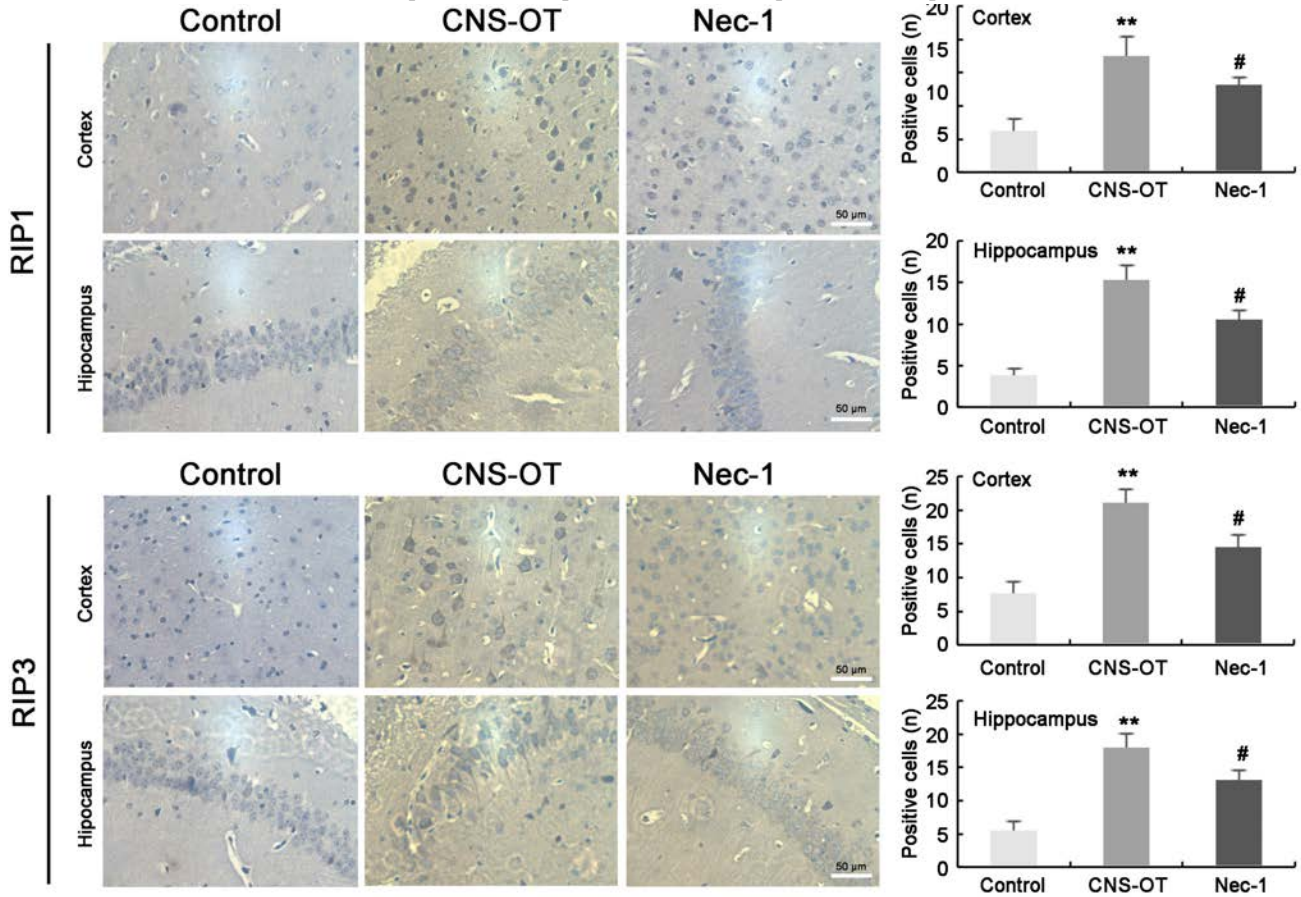


Figure 3

Immunohistochemistry for RIP1 and RIP3 in the cortex and hippocampus (× 400). Positive cells had brown granules. ** $P < 0.01$ versus Control group; # $P < 0.05$ versus CNS-OT group. CNS-OT – central nervous system oxygen toxicity; Nec-1 – Necrostatin-1; RIP1 – receptor interaction protein 1; RIP3 – receptor interaction protein 3



(grand mal) seizure was found at about 4 min after reaching 600 kPa, and thereafter these animals remained calm with significantly reduced activity in the chamber.

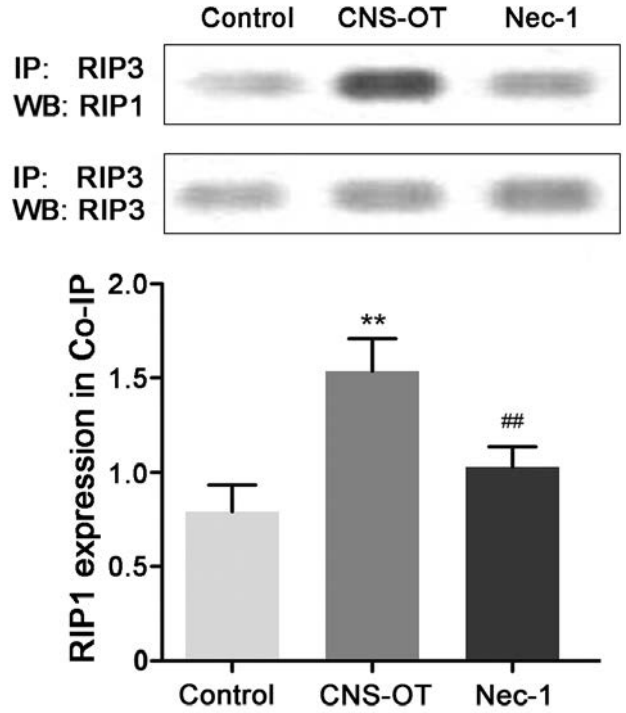
INFLAMMATION

HBO exposure increased cerebral contents of IL-1β and TNF-α ($P < 0.01$), but reduced the IL-10 content. Moreover, Nec-1 pre-treatment markedly reduced the contents of IL-1β and TNF-α ($P < 0.01$) and increased IL-10 ($P < 0.05$) as compared to the CNS-OT group (Figure 1 A, B, C).

OXIDATIVE STRESS

HBO exposure significantly increased cerebral MDA content, but markedly reduced the SOD activity and GSH

Figure 4
Co-Immunoprecipitation of RIP1 and RIP3 in the brain. ** $P < 0.01$ versus Control group; ## $P < 0.01$ versus CNS-OT group. CNS-OT – central nervous system oxygen toxicity; Nec-1 – Necrostatin-1; RIP1 – receptor interaction protein 1; RIP3 – receptor interaction protein 3; Co-IP – co-immunoprecipitation



content, but Nec-1 pre-treatment failed to significantly alter the MDA content, SOD activity and GSH content (Figure 1 D, E, F, G).

RIP1, RIP3 AND p-MLKL EXPRESSION

HBO exposure significantly increased the expression of RIP1, RIP3 and p-MLKL ($P < 0.05$ versus control group), and this increase was markedly inhibited by the pre-treatment with Nec-1 ($P < 0.05$ versus CNS-OT group) (Figure 2).

Numbers of RIP1-positive cells and RIP3-positive cells increased significantly in the hippocampus and cortex ($P < 0.05$ versus control group). However, in the presence of Nec-1 pre-treatment, the numbers of RIP1 positive cells and RIP3 positive cells reduced markedly in both hippocampus and cortex ($P < 0.05$ versus CNS-OT group) (Figure 3).

INTERACTION BETWEEN RIP1 AND RIP3

An interaction between RIP1 and RIP3 was significantly reinforced after HBO exposure, but pre-treatment with Nec-1 significantly inhibited the RIP1-RIP3 complex formation after HBO exposure ($P < 0.05$) (Figure 4).

Discussion

These results showed that high PO_2 exposure significantly increased oxidative stress and inflammation in the brain, which was accompanied by the elevation of cerebral necroptosis. However, inhibition of necroptosis before HBO exposure was able to prolong the latency to convulsion of mice, which was not related to the oxidative stress.

Although the pathogenesis of CNS-OT is still poorly understood, some mechanisms have been proposed: excess production of ROS, abrupt increase of cerebral blood flow following vascular constriction, imbalance between excitatory and inhibitory neurotransmitters and others.[2] Thus, some strategies targeting these potential mechanisms are also developed for the prevention of CNS-OT.

There is evidence that oxygen toxicity may induce the apoptosis of neuronal cells[4,5] and inhibition of intrinsic apoptosis is helpful for the prevention of neonatal oxygen induced brain damage.[6] Necroptosis is another type of programmed cell death. Necroptosis was initially recognised as a caspase-independent cell death mechanism induced by TNF in the presence of a pan-caspase inhibitor. Thereafter, numerous studies have revealed that necroptosis can also be activated by some other factors (such as ROS, calcium, Toll-like receptor agonists and interferon). During necroptosis, RIP3 is activated by RIP1 kinase and then gains the ability to phosphorylate and activate MLKL.[9] In our previous study, necroptosis was found to be involved in the pathogenesis of acute hyperoxia-induced lung injury and anti-oxidative treatment was able to inhibit the necroptosis and thereafter improve the hyperoxia induced lung injury.[7] The present study investigated whether necroptosis was involved in the pathogenesis of CNS-OT.

Experiment one showed that pre-treatment with Nec-1 (a RIP1 inhibitor) 30 min before HBO exposure significantly prolonged the latency to convulsion. This indicates that necroptosis is involved in the pathogenesis of CNS-OT. Thereafter, in experiment two, the key molecules (RIP1, RIP3, p-MLKL) in the necroptosis-related pathway and the interaction between RIP1 and RIP3 were examined. HBO exposure at 400 kPa for 30 min markedly increased the expression of RIP1, RIP3 and p-MLKL as well as the interaction between RIP1 and RIP3. There is evidence that necroptosis is closely related to inflammation and may act as a trigger of inflammation,[10] oxidative stress can induce necroptosis[11] and inhibition of oxidative stress suppresses necroptosis.[12] In a pulmonary oxygen toxicity model, edaravone, a known free radical scavenger, was able to inhibit necroptosis in the lung.[7] Thus, we speculate that excessive production of ROS induced by HBO exposure is, at least partially, responsible for the activation of necroptosis in the brain. In the present study, inflammatory cytokines and oxidative stress-related molecules were also detected in the

brain. Our results showed HBO exposure at 400 kPa for 30 min could increase both inflammation and oxidative stress. Nec-1 pre-treatment significantly reduced the expression of RIP1, RIP3 and p-MLKL and inhibited the production of inflammatory cytokines in the brain, but it failed to markedly inhibit the oxidative stress in the brain following HBO exposure. This may be explained by oxidative stress being an 'upstream' event in necroptosis.

There is evidence that HBO-induced seizures may cause a transient impairment of cognitive function in mice.[13] The hippocampus is involved in learning and memory. In the present study, RIP1 and RIP3 expression was measured in the hippocampus by immunohistochemistry. There was increased expression of both RIP1 and RIP3 in the hippocampus after HBO exposure at 400 kPa for 30 min. Whether necroptosis in the hippocampus is involved in the transient impairment of cognitive function is still unclear.

There were limitations in the present study. Nec-1 was administered at only one dose, and a dose-response effect on CNS-OT was not delineated. Although Nec-1 is protective in some types of brain injury,[14] the blood-brain-barrier (BBB) permeability increases following brain injury and Nec-1 may enter the brain under this condition. In our model, there was no evidence of increased BBB permeability. Of note, Nec-1 was also found to exert neuroprotective effects on prediabetic rats,[15] which might reflect that Nec-1 can enter the brain or is BBB-permeable. More studies are needed to confirm this issue. In addition, the toxicity of Nec-1 and the safety of Nec-1 used before HBO exposure should be further evaluated in more basic and clinical studies.

Conclusions

This study indicates that necroptosis is activated in the brain of mice following exposure to a high PO_2 with risk of CNS-OT, and that inhibition of necroptosis with Nec-1 delays the onset of convulsions following oxygen exposure. These findings suggest necroptosis plays a role in the pathogenesis of CNS-OT, and provide a potential strategy for the prevention of CNS-OT. More studies are needed to confirm these findings and investigate the possibility of Nec-1 being used in the prevention of CNS-OT.

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The impact of different gas mixtures on inflammatory responses in advanced recreational divers

Monica Rocco[1], Luigi Maggi[2], Chiara Loffredo[1], Massimiliano Pelli[1], Pia Di Benedetto[2], Silvia Fiorelli[1], Maurizio Simmaco[3], Roberto Alberto De Blasi[1]

[1] *Department of Surgical and Medical Science and Translation Medicine, Sapienza University, Rome, Italy*
[2] *Department of Anesthesia, Sant'Andrea Hospital, Rome, Italy*
[3] *Department of Neuroscience, Mental Health and Sensory Organs, Sapienza University, Rome, Italy*

Corresponding author: *Dr Luigi Maggi, Department of Anesthesia, Sant'Andrea Hospital, Rome, Italy*
maggi.medicina@libero.it

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Abstract
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Introduction: Decompression sickness (DCS) is considered a 'bubble disease'. Intravascular bubbles activate inflammatory responses associated with endothelial dysfunction. Breathing gas has been proposed as a potential risk factor but this is inadequately studied. Different gases are used in scuba diving. Helium-containing 'trimix' could theoretically mitigate inflammation and therefore reduce DCS risk. This study determined the effect of air and trimix on the inflammatory response following dives to 50 metres of sea water, and evaluated the differences between them in advanced recreational divers.
Methods: Thirty-three divers were enrolled in this observational study and were divided in two groups: 17 subjects were included in the air group, and 16 different subjects were included in the trimix (21% oxygen, 35% helium, 44% nitrogen) group. Each subject conducted a single dive, and both groups used a similar diving profile of identical duration. A venous blood sample was taken 30 min before diving and 2 h after surfacing to evaluate changes in interleukins (IL) IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, tumour necrosis factor α (TNFα), vascular endothelial growth factor (VEGF), Interferon γ (IFN-γ), monocyte chemoattractant protein 1 (MCP-1) and epithelial growth factor (EGF) after diving.
Results: No differences were observed between groups in demographic data or diving experience. Following the dive, IL-6 values showed a slight increase, while IL-8 and EGF decreased in both groups, without significant variation between the groups.
Conclusions: In physically fit divers, trimix and air gas mixture during deep diving did not cause relevant changes in the inflammatory markers tested.

Introduction

Decompression illness is a condition that includes decompression sickness (DCS) and arterial gas embolism (AGE). DCS is a 'bubble disease', where bubbles form due to gas supersaturation in tissues during ascent.[1] A correlation between the degree of bubbling and the risk of DCS has been identified, even if the presence of circulating bubbles cannot be used to predict DCS in individuals.[2]

Intravascular bubbles may trigger an inflammatory response associated with endothelial dysfunction.[3] Using a rat model of DCS some authors have suggested that bubbles may be the cause of decompression-induced endothelial damage, which results in the release of various inflammatory mediators.[4] Moreover, intravascular inert gas bubbles have been linked to the elevation of circulating microparticles observed both in humans and in animal models of diving and these microparticles are associated with inflammation and neutrophil activation.[5] In addition, acute changes of inflammatory factors have recently been used as biomarkers to predict decompression quality, even in the absence of DCS events.[6]

Different types of breathing gas are used in scuba diving: air and non-air mixtures. The latter contain mainly oxygen, nitrogen and helium that form nitrox (nitrogen + oxygen), heliox (helium + oxygen), and trimix (oxygen, helium and nitrogen) with different advantages and features.[7] Nitrox is mainly used for shallow recreational dives, heliox for deep diving, and trimix for deep but short dives, in order to avoid neurological side effects.[7] The use of trimix in scuba diving has recently become more widespread in order to reduce nitrogen narcosis compared to air diving.[8]

The aim of the present study was to assess the effect of two breathing gas mixtures on the inflammatory mediators in deep seawater dives, and to investigate the differences between trimix and air in physically fit divers.

Methods

All experimental procedures were performed in accordance with the Declaration of Helsinki. The Institutional Review Board of Sapienza University, Rome, Italy approved all protocols (CE 2035/2015). Written informed consent was obtained from all subjects.

STUDY POPULATION

This observational study enrolled 33 experienced, certified divers. Each diver was randomly allocated into one of two groups: air or trimix. The air group (A) was composed of 17 subjects, 16 men and one woman, while the trimix group (T) was composed of 16 subjects, 15 men and one woman. All subjects were physically fit to dive according to the International Diving Medicine Expert Board fitness to dive criteria (http://www.edtc.org/EDTC-Fitnesstodivestandard-2003.pdf): They were non-smokers and performed regular cardiac aerobic and muscle strengthening activity such as brisk walking, running, jogging and swimming during their week and deep dives 4–5 times a month. Body mass index (BMI) was calculated for all divers. All divers were instructed not to consume alcohol for 72 h or coffee for 6 h before the experimental dive.

DIVE EXPOSURE

Each diver performed an open water dive (east coast of Giannutri Island, Italy) during summer wearing a dry suit, to a depth of 50metres of sea water (msw) with a square profile and 20-min bottom time. The water temperature was 15°C at the bottom. The entire dive time was within 1 h. V-planner decompression software was used to calculate the decompression profile for both air and trimix groups (the 'V-planner' is freely available at: https://v-planner.soft.com). Different conservatism settings were used for the air and trimix profiles to result in decompression schedules with identical total decompression time (Figure 1).

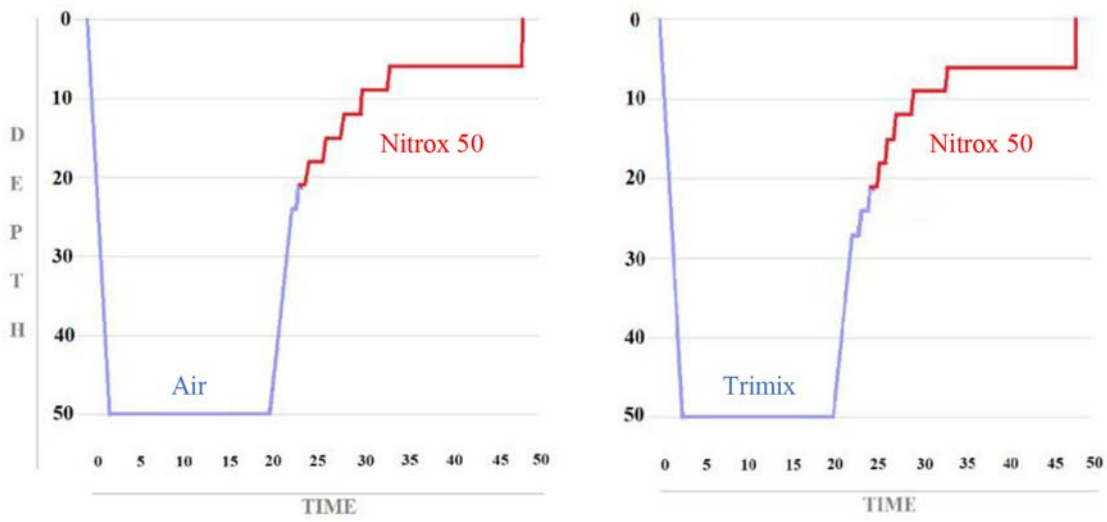
The divers in group A breathed compressed air (21% oxygen, 79% nitrogen) using open-circuit scuba equipment. The divers in group T breathed trimix 21/35 (21% oxygen, 35% helium, 44% nitrogen) also using open-circuit scuba. Both groups used a nitrox mixture (50% oxygen and 50% nitrogen) for decompression starting at 21 msw during the ascent until surfacing (Figure 1). Divers were requested to swim slowly and avoid effort as much as possible. We attempted to wait for constant environmental variables, such as water temperature (15 ± 2°C), same dive path using previously positioned markers on the seabed, and weather variables. The subjects were accompanied on the dive by safety divers who set the swimming pace.

LABORATORY ANALYSIS

A venous blood sample was taken from each diver 30 min before the dive and 2 h after surfacing, to evaluate pro-inflammatory interleukins (IL-1α, IL-1β, IL-6, IL-8), anti-inflammatory cytokines (IL-2, IL-4, IL-10), tumour necrosis factor alpha (TNFα), vascular endothelial growth factor (VEGF), interferon-γ (IFNγ), monocyte chemoattractant protein 1 (MCP-1) and epidermal growth factor (EGF) variations induced by diving.

The concentrations of these factors were simultaneously assessed using cytokine and growth factor arrays (Evidence Investigator Biochip Array technology®, Randox Laboratories, Crumlin, UK) in accordance with the

Figure 1
Air and trimix dive profile. Red lines signify Nitrox 50% used by both groups. Depth in metres of seawater and time in minutes



manufacturer's instructions. The sensitivities of the test kits were as follows: IL-1α – 0.8 pg·mL^{-1}; IL-1β – 1.6 pg·mL^{-1}; IL-6 – 1.2 pg·mL^{-1}; IL-8 – 4.9 pg·mL^{-1}; IL-2 – 4.8 pg·mL^{-1}; IL-4 – 6.6 pg·mL^{-1}; IL-10 – 1.8 pg·mL^{-1}; IFNγ – 3.5 pg·mL^{-1}; TNFα – 4.4 pg·mL^{-1}; VEGF – 14.6 pg·mL^{-1}; EGF – 2.9 pg·mL^{-1}; and MCP-1 – 13.2 pg·mL^{-1}.

The reference ranges for healthy adults for these molecules reported with the test kits are duplicated in Table 1.

The primary endpoint was to determine differences in blood cytokines before and after diving in volunteers breathing either air or trimix.

STATISTICAL ANALYSIS

Statistical analysis was performed using Sigmaplot (Systat Software, San Jose, CA, USA). Data normality was assessed using the Kolmogorov-Smirnov test. Data were expressed as means with standard deviation (SD) when normally distributed and as medians and 95% confidence intervals when non-normally distributed. Descriptive analysis was performed using percentages for binary variables. The Wilcoxon matched pair test was used to assess statistical significance before and after diving for non-parametric variables and repeated measures ANOVA was used for parametric variables. Variables that showed differences before and after diving were compared between air and trimix groups. Data were evaluated using *t*-test for independent data with alpha values of 0.05 and Welch's correction.

Results

All subjects completed the study. None of the divers developed DCS or pathological symptoms and signs. All divers performed their dives at the same sites with the same environmental conditions in terms of water temperature and visibility. There were no differences between the two groups in terms of demographic data or diving experience. There were no between group differences in mean age 46.1 (SD 4.9) years versus 47.6 (5.2), $P = 0.40$; BMI 22.6 (2.1) kg·m^{-2} versus 23.5 (2.4), $P = 0.26$; and the median number of yearly dives 50 (95% CI 29–80) versus 75 (49–101), $P = 0.65$. Pre-dive and post-dive results are shown in Table 2. The levels of IL-2, IL-4, IL-10, VEGF, IFNγ, TNFα, IL-1α, IL-1β, and MCP-1 did not significantly change after diving in both groups. IL-8 (Figure 2) and EGF (Figure 3) levels decreased after diving in both groups and IL6 increased (Figure 4). The increase in IL6 was smaller in the trimix dives than in the air dives, but this was not significant ($P = 0.67$). The decreases in IL8 and EGF were not different ($P = 0.47$ and $P = 0.72$, respectively). All molecules were within the normal ranges given in Table 1 both pre- and post-dive. No normal range was defined for MCP-1 and EGF.

Table 1
Reference ranges in healthy adults for inflammation markers assayed. EGF – epidermal growth factor; IFNγ – interferon gamma; IL – interleukin; MCP-1 – monocyte chemoattractant protein 1; TNFα – tumour necrosis factor alpha; VEGF – vascular endothelial growth factor

Inflammation marker	Reference (pg·ml^{-1})
IL-1α	0–3.9
IL-1ß	< 5.0
IL-6	< 7.0
IL-8	0–50.0
IL-2	< 50.0
IL-4	< 38.7
IL-10	< 5.7
VEGF	62.0–707.0
IFNγ	0–15.6
TNFα	< 8.1
MCP-1	undefined
EGF	undefined

Discussion

In the present study we observed a significant increase of IL6 and a decrease of IL8 and EGF levels in both groups which nevertheless remained within the respective normal ranges after a 50 msw dive. The gas mixture (air or trimix) did not influence the inflammatory response of the subjects studied. In the last decades, trimix has been introduced in scuba diving as an alternative to air to reduce gas density and the risk of nitrogen narcosis[7,8] and to explore deeper depths for longer durations using different decompression algorithms, which are still the subject of debate.[9]

Scuba diving triggers pro-inflammatory reactions in blood, with increased expression of adhesion molecules, activation of coagulation, and elevated circulating microparticles.[10–14] Such responses are triggered by oxidative stress and play important roles in maintaining physiological homeostasis. Bubbles, microparticles and circulating agents are, at least in part, responsible for inciting the so-called 'endothelial dysfunction' that, in turn, causes activation of the inflammatory response;[14] thus, monitoring post-dive circulating inflammatory molecules could provide biomarkers of decompression and DCS risk.

These data showed post-dive alterations in only IL-6, IL-8, and EGF levels. Specifically, IL-6 showed an increase, while IL-8 and EGF decreased, in both groups. Although they were

Table 2

Air and trimix groups pre- and post-50 msw dives, showing evaluation of: pro-inflammatory interleukins (IL-1α, IL-1β, IL-6, IL-8); anti-inflammatory cytokines (IL-2, IL-4, IL-10); and other factors, tumour necrosis factor alpha (TNFα), vascular endothelial growth factor (VEGF), interferon-γ (IFNγ), monocyte chemoattractant protein 1 (MCP-1) and endothelial growth factor (EGF). NA* – not applicable, the values for pre- and post-dive assays are too close to zero to produce a *P*-value

Marker	Pre-air pg·ml^{-1}	Post-air pg·ml^{-1}	*P*-value	Pre-trimix pg·ml^{-1}	Post-trimix pg·ml^{-1}	*P*-value
Inflammatory factors						
IL-1α median (95% CI)	0 (0, 0)	0 (0, 0)	1	0 (0, 0)	0 (0, 3.34)	0.125
IL-1ß median (95% CI)	0 (0, 0)	0 (0, 0)	0.812	0 (0, 0)	0 (0, 0.33)	0.125
IL-6 median (95% CI)	0.98 (0.85, 1.76)	1.90 (1.27, 3.90)	0.015	0.83 (0.71, 1.19)	1.17 (0.85, 2.71)	0.0002
IL-8 mean (SD)	20.08 (11.23)	11.88 (6.88)	0.0235	22.94 (11.59)	12.68 (7.52)	0.005
Anti-inflammatory factors						
IL-2 median (95% CI)	0 (0, 0)	0 (0, 4.27)	0.187	0 (0, 0)	0 (0, 0)	NA*
IL-4 median (95% CI)	0 (0, 4.42)	1.25 (0, 1.37)	0.105	0 (0, 1.27)	0 (0, 1.25)	0.812
IL-10 median (95% CI)	0.00 (0.00, 1.05)	0 (0, 0.96)	1	0 (0, 0)	0 (0, 0)	NA*
Other factors						
VEGF mean (SD)	203.62 (16.38)	224.39 (23.08)	0.336	189.90 (18.63)	188.40 (18.84)	0.912
INFγ median (95% CI)	0 (0, 0)	0 (0, 0)	NA*	0 (0, 0.25)	0 (0, 0.24)	0.875
TNFα median (95% CI)	2.00 (1.62, 2.18)	1.78 (1.58, 2.01)	0.427	1.81 (1.47, 2.44)	1.72 (1.47, 2.13)	0.135
MCP-1 mean (SD)	337.53 (23.33)	383.75 (28.25)	0.076	361.41 (32.59)	361.52 (42.84)	0.997
EGF mean (SD)	170.57 (60.82)	81.11 (71.84)	0.0005	144.68 (45.41)	58.48 (59.31)	0.0001

statistically significant changes, the values remained within the reference values suggesting dubious clinical relevance and lack of support for any difference between air and trimix. We could argue that the dives were not long enough to manifest a difference in nitrogen and helium gas uptake and washout, or that the dive profile was not 'strenuous' enough to observe significant differences in inflammation. Endothelial physiology, besides on individual genetics, is certainly linked to the inflammatory response but the severity of these reactions increases with increasingly stressful decompression.[13,15]

The increase in IL6 observed after diving was not of a magnitude associated with inflammatory disease, but more in line with increases associated with physical exercise.[16] Several studies have reported that physical activity can induce an acute phase response characterised mostly by an increase in IL6.[17,18] A cytokine cascade induced by exercise markedly differs from that induced by infections in lacking the classical surge in proinflammatory cytokines as TNFα and IL-1β. It is plausible, besides, that the post-exercise EGF reduction, is finalised to facilitate defence mechanisms against oxidative stress and may be linked to the role of EGF in reactive oxygen species (ROS) production.[19] The alterations of IL and EGF in our study, although significant, however, were negligible, and most probably the result of an average physical effort.

The properties of helium (one of the trimix gases) have also been studied extensively outside of diving medicine, arousing much interest in the field of ventilation and organ protection[20] as well on the human or animal immune response.[21–23] There have been conflicting results. One human study of cardiac preconditioning by inhaled helium suggested a mild anti-inflammatory effect.[21] Another study of acute lung injury in newborn pigs breathing heliox or

Figure 2
IL-8 levels before and after dives using air or trimix. Box and whisker plots show median, interquartial range, and highest and lowest values

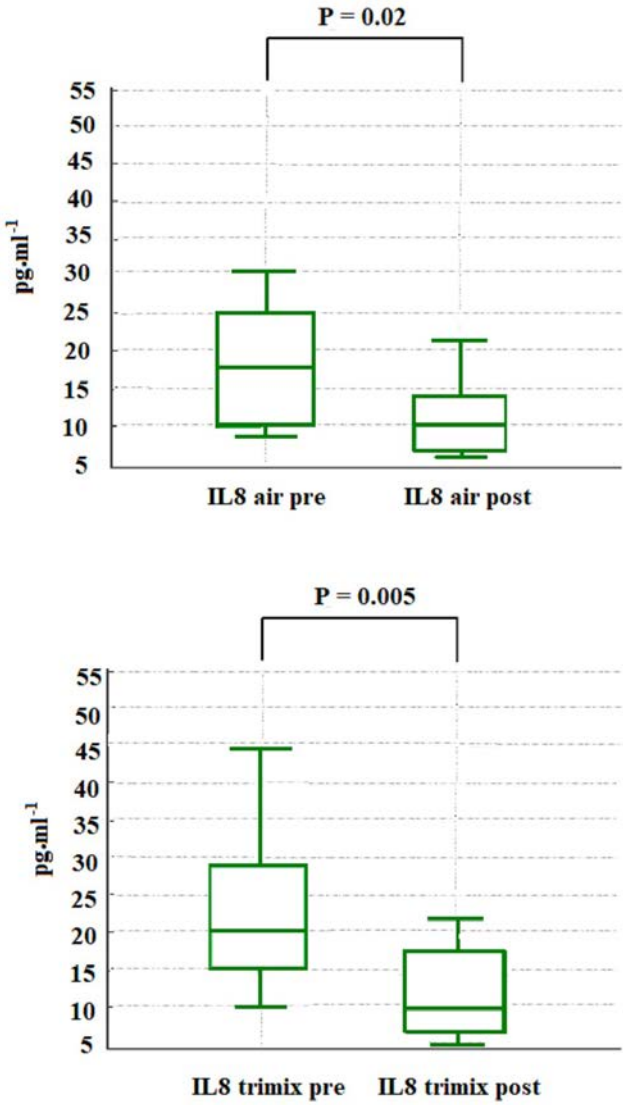
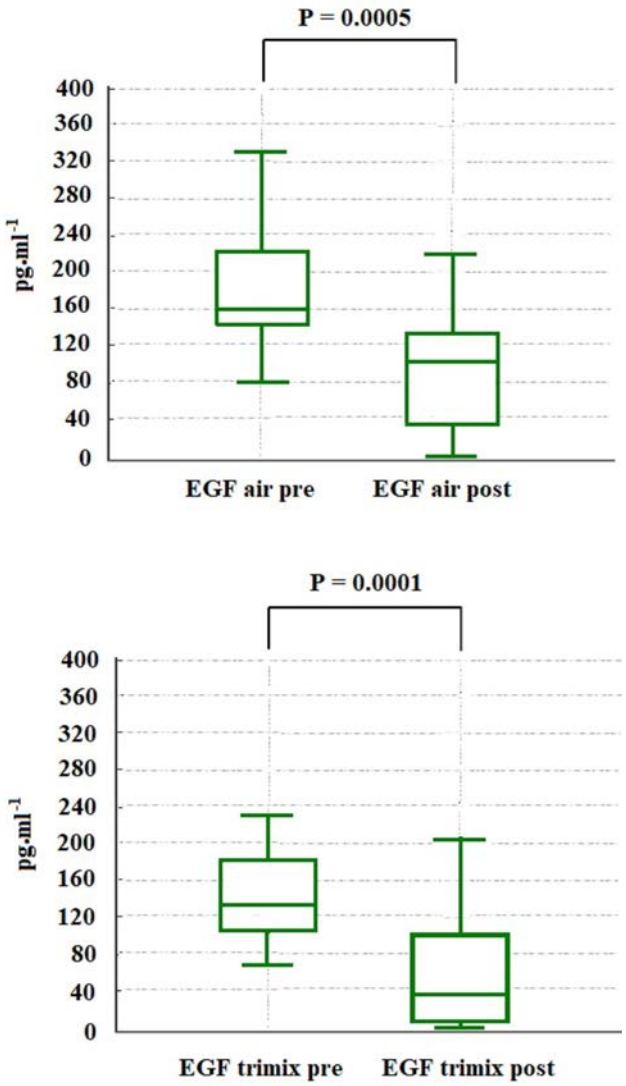


Figure 3
EGF level changes before and after dives using air or trimix. Box and whisker plots show median, interquartial range, and highest and lowest values

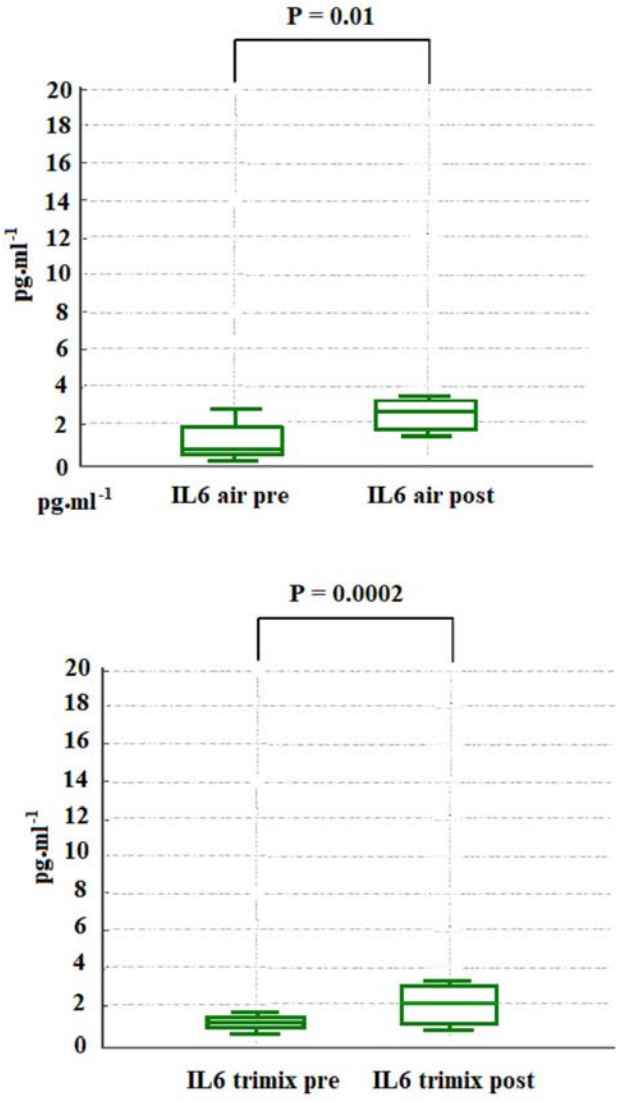


nitrox showed less lung inflammation reflected by lower tissue IL-6 and IL 8 in the heliox group.

Another study using human divers[6] compared a 30 msw no-stop air dive and 50 msw trimix dives using either a ratio decompression profile (RDP) or a compartment decompression model (CDM) decompression. The shorter no-stop air dive to 30 msw and the 50 msw RDP dive were more pro-inflammatory (in terms of chemokines – C-C motif chemokine ligand 2 [CCL2] and C-C motif chemokine ligand 5 [CCL5]) than the 50 msw CDM dive. The authors proposed a protective effect of helium on the endothelium to explain the apparently paradoxical worse outcome for the shallower air profile compared to one of the deeper trimix decompression profiles. There was no difference in CCL2 or CCL5 after a comparable level of surface swimming exercise, suggesting that in their experimental setting decompression and not physical exercise induced the changes in these inflammatory markers. It was hypothesised that divers who performed CDM were exposed to helium for a longer period of time than the other trimix group. It seemed likely that this gas was able to increase nitrous oxide (NO) and to induce the activation of nuclear factor erythroid 2-related factor 2 and the consequent reduction of systemic inflammation and oxidative stress.[23]

These experimental studies, although conflicting, invoke a possible anti-inflammatory role of helium. Our study found no difference in most of the inflammatory factors (including MCP-1) measured between the trimix and air groups casting doubt on a protective effect of helium unless, as noted above, our dives were not 'strenuous' enough during decompression to observe a significant anti-inflammatory role of helium.

Figure 4
IL-6 level changes before and after dives using air or trimix. Box and whisker plots show median, interquartial range, and highest and lowest values



LIMITATIONS OF THE STUDY

There are some limitations in our study. The presence of VGE in these divers was not evaluated and their possible correlation with inflammatory factors studied in order to identify a further indicator of decompression stress. Furthermore, systemic inflammatory markers were evaluated only at 2 h after diving and measures were not subsequently repeated; therefore, we can only suggest the activation-deactivation mechanism of the inflammatory cascade, as described above.

In addition, the study had a small but selected sample size and only included divers certified to perform technical dives at 50 msw, with a similar age and BMI. We attempted to minimise bias due to environmental parameters (same temperature and same dive path, previously decided) and procedural conditions (low physical exertion controlled by an external team of scuba divers). The two study groups did not perform both dives (crossover study); thus, it remains possible that an unknown factor was different in the two groups.

Lastly, the dive profile was not 'strenuous' enough to observe significant inflammatory changes. Further studies should select a dive profile known to induce inflammatory responses, at least using air or nitrox breathing gas.

Conclusions

In physically fit divers, no differences in inflammatory factors were found after deep diving using trimix versus air as the breathing gas. However, the dive profiles induced only small changes in inflammatory markers. The changes observed were within the normal range and were consistent with exercise induced changes.

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Mortality rate during professionally guided scuba diving experiences for uncertified divers, 1992–2019

Peter Buzzacott[1], Al Hornsby[2], Karl Shreeves[2]

[1] *Prehospital, Resuscitation and Emergency Care Research Unit, School of Nursing, Curtin University, Western Australia*
[2] *Professional Association of Diving Instructors (PADI Worldwide Corp), Rancho Santa Margarita, CA, USA*

Corresponding author: *Dr Peter Buzzacott, Prehospital, Resuscitation and Emergency Care Research Unit, School of Nursing, Curtin University, Western Australia*
peter.buzzacott@curtin.edu.au

Key words
Diving deaths; Diving industry; Epidemiology; PADI; Recreational diving; Risk; Training

Abstract
(Buzzacott P, Hornsby A, Shreeves K. Mortality rate during professionally guided scuba diving experiences for uncertified divers, 1992–2019. Diving and Hyperbaric Medicine. 2021 June 30;51(2):147–151. doi: 10.28920/dhm51.2.147-151. PMID: 34157729.)
Introduction: The aim of this study was to re-examine the mortality rate among participants in the Professional Association of Diving Instructors' (PADI)'s Discover Scuba Diving (DSD) programme.
Methods: Fatalities reported to PADI as having occurred during DSD scuba dives were counted for each year between 1992 and 2019. DSD participant registrations were also counted for each year. The data were conveniently divided into two equal 14-year periods, 1992–2005 ('early') and 2006–2019 ('late'). To smooth out the year-to-year variation in raw rates, Monte Carlo simulations were performed on the mean rate per 100,000 participants per year during each period.
Results: There were a total of 7,118,731 DSD participant registrations and 79 fatalities during the study period. The estimated overall mean mortality rate in the early period was 2.55 per 100,000 DSD registrations whereas the estimated rate of 0.87 per 100,000 DSD registrations was significantly lower in the late period ($P < 0.0001$).
Conclusions: PADI's contemporary Discover Scuba Diving introductory scuba experiences, at 0.87 fatalities per 100,000 participants, have a calculated mortality rate that is less than half that calculated for 1992–2008. The late period's rate improvement appears due either to significant under-registration in the early period, or to significant safety-performance improvement in the late period or, more likely, some combination of the two.

Introduction

Introductory scuba diving programmes allow individuals who are not certified divers to experience scuba diving under the direct supervision of a professional instructor, and are among recreational scuba diving's most frequent scuba programs worldwide. The Professional Association of Diving Instructors (PADI)'s Discover Scuba Diving (DSD) program is likely the most popular such program by a large margin.[1] PADI requires their professional members to use prescribed DSD program participant materials and requires participant registration to allow quality management follow-up by PADI. Every participant with an e-mail address receives a course evaluation questionnaire, PADI's standard quality-management instrument. This process also gives PADI a unique data set: the number of participants in its formal introductory scuba program.

Although there have been incremental revisions over time, which is typical of scuba programs, the DSD introductory program was launched in largely its current format in 1992.[1] Before approximately 2002, instructors would photocopy participant registration forms and, after completion of the diving experience, these forms needed enveloping, addressing and stamping, then mailing in to the local PADI regional office for PADI to then mail out a course evaluation questionnaire.[2]

The early 2000's were a time of significant changes in the recreational scuba industry. A new medical assessment form, widely adopted by recreational diving instructors globally, was launched in 2000 to assess whether would-be divers should undertake further assessment by a physician before being taken into the water. Internet use became widely adopted and was used to advertise the DSD program online increasingly frequently, as more and more travellers planned holidays using the internet. Very large dive centres commenced using the program in a number of diving hotspots, for example in Cairns, Australia and the Caribbean.

Based on anecdotal reports that not all DSD participants were registered, in 2001 and 2002 PADI engaged an independent market research company to conduct an online survey of PADI members, to estimate the 'true' number of DSD experiences being conducted each year.[3] Both individual DSD instructors and dive centres responded. Almost half

(47%) of surveyed dive centres that conducted DSD in 2002 also reported not registering any DSD participants. Moreover, just 21% of dive centres reported registering all their 2002 DSD participants.[3] The study suggested that the number of registered DSD participants underestimated the true number of DSD divers.

At about the same time, PADI required instructors to use a new, full-colour, glossy participant registration form. It had a tear-off card for the customers and was pre-addressed to return participant registrations to PADI. This method was followed by the introduction of an online registration system, making the process even more convenient and efficient. The annual number of DSD registrations doubled in two years, then doubled again, going from almost 200,000 registered DSD participants in 2002/03 to nearly 800,000 in 2007/08. This level of introductory scuba participation had never before been documented.

At the 2010 Divers Alert Network Recreational Diving Fatalities Workshop the President/CEO of PADI presented a seminal diver mortality study, which showed the raw number of fatalities per 100,000 participants for a range of diver training programmes, 1989–2008.[1] Of high interest was the DSD mortality rate, since this program is typically taken by participants who have not previously been certified as trained recreational divers. The programme is designed to enable a complete novice to try scuba for the first time in the open water, always directly supervised by a PADI Instructor.[2]

Although it was made clear that, while the fatality counts were likely accurate (because all, or nearly all, fatalities were likely known and counted), the numbers of DSD participants' figures were suspected to have been artificially-low due to a proportion of participants not having had their participant registration forms submitted to PADI (even though participant registration was contractually required of members).[1,3] Factors affecting participant registration may have included the cost of hiring staff to envelope and address photocopied forms, especially in areas where there was an intense dive season.[3] Because DSD registrations were suspected to have been lower than actual participation, the published DSD mortality rate per 100,000 participants was considered artificially high in the 2010 paper.

The aim of this study was to re-examine the mortality rate among DSD participants using today's much larger (and likely more accurate) annual denominators, and to compare the current mortality rate with that of an earlier period. The null hypothesis is that the calculated mortality rate per 100,000 DSD participants per year has not significantly changed.

Methods

Ethics approval was granted by the Human Research Ethics Committee of Curtin University, approval HRE2020-0444 dated 11 August 2020. Fatalities reported to PADI as having occurred during DSD scuba dives, which are contractually required to be reported to PADI by its members, were counted for each year between 1992 and 2019. DSD participant registrations were also counted for each year. The data, stored in Excel and analysed using SAS ver 9.4 (SAS, Cary, NC), were conveniently divided into two equal 14-year periods, 1992–2005 ('early') and 2006–2019 ('late'). Individual raw mortality rates per 100,000 registrations were calculated for each year. Potential linear trends in increasing or decreasing raw rates were tested for significance in each period by univariate regression. To smooth out the year-to-year variation in raw rates, Monte Carlo simulations were performed on the mean rate per 100,000 participants per year during each period, with 10,000 iterations and resampling. The resultant 10,000 14-year mean mortality rates were normally distributed for each period, in accordance with Central Limit Theorem. Standard deviations around the estimated means for each period were too disparate to pool the variance (Table 1); therefore, a Student's *t*-test with un-pooled (Satterthwaite) variances was used to assess the magnitude of the difference in estimated mean mortality rate during each period (early versus late).[4] Significance was accepted at $P < 0.05$.

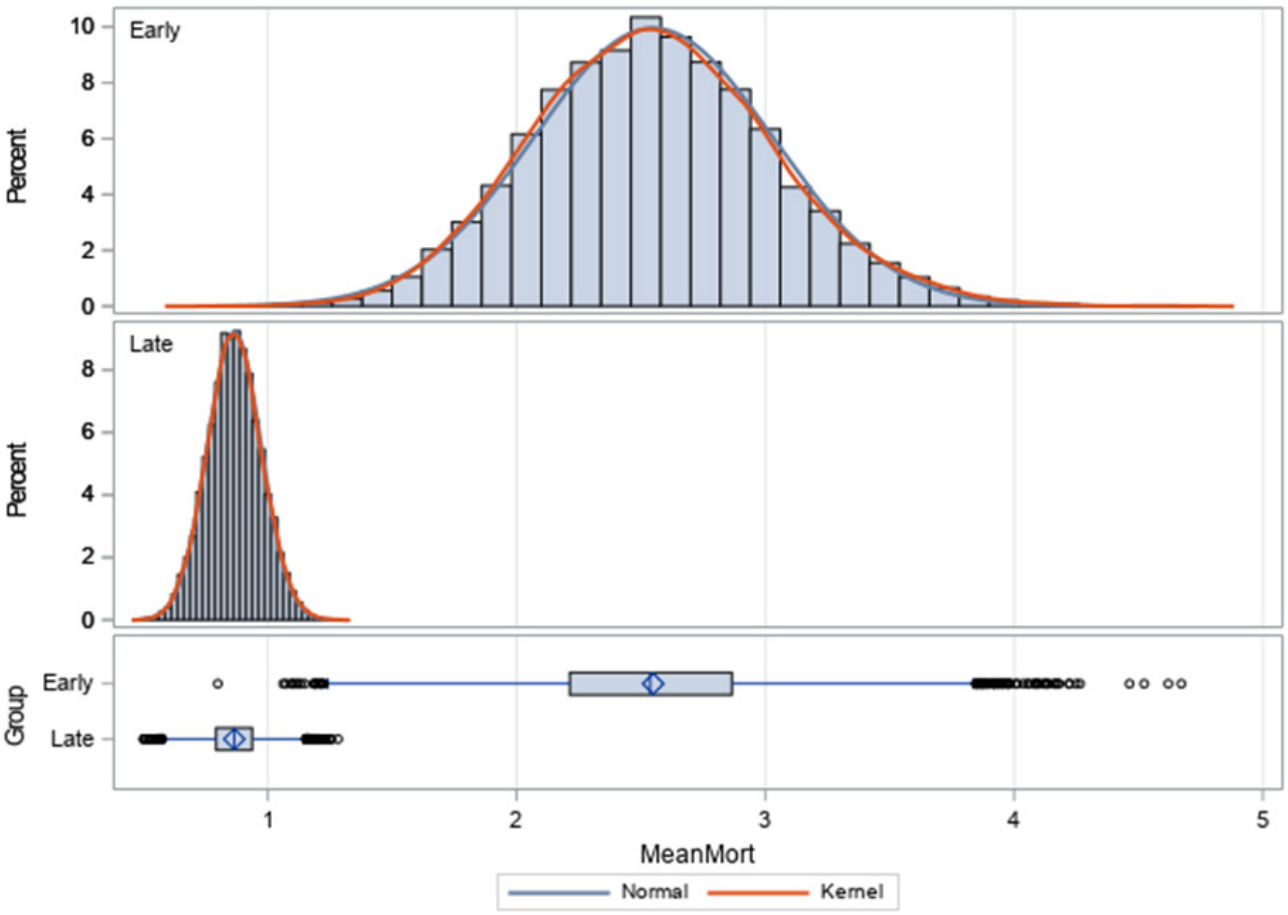
Results

There were a total of 7,118,731 DSD participant registrations and 79 fatalities during the study period. There was no linear trend in increasing or decreasing raw rate per 100,000 registrations associated with calendar year during either the early period (t = -1.45, $P = 0.17$) or the late period (t = 1.06, $P = 0.30$). The results of the Monte Carlo simulation are presented in Table 1. The distributions of the estimated means (n = 10,000 per period) are shown in Figure 1. The estimated mean mortality rate per 100,000 DSD registrations was significantly lower (t = 341, $P < 0.0001$) in the later period.

Table 1
Descriptive characteristics of the raw and estimated mean mortality rates per group (early or late) generated by Monte Carlo simulation

Group	Registrations	Fatalities	Raw rate per 100,000	Estimated mean (SD)	Estimated 95% CI	Estimated means (*n*)
Early	1,355,987	28	2.06	2.55 (0.48)	2.54, 2.56	10,000
Late	5,762,744	51	0.88	0.87 (0.11)	0.86, 0.87	10,000

Figure 1
Histogram with box-and-whisker plots for 10,000 estimated mean mortality per 100,000 participants, by group (early or late)



Discussion

The annual mean number of fatalities per 100,000 DSD participants during a recent 14-year period was significantly lower than in the 2010 analysis.[1] Presently, calculated overall mortality during DSD experiences is less than half that described just a decade ago, both in raw numbers and in the Monte Carlo simulation. We infer that this is likely in part due to increased accuracy of participant registration numbers, and that prior mortality rate estimates were artificially high due to relatively less-consistent participant registration. However, additional measures aimed at reducing participant risk during the conduct of DSDs were added over the years, including the evolution of required training materials, a reduction in the instructor-to-participant supervision ratio, increased quality-management control made possible through increased registrations, and increased DSD-instructor training during PADI Instructor Development Courses, any or all of which may have contributed to the reduction as well, but by what scale remains unquantifiable. Whether the significantly lower rate in the later period is due to greater DSD registration compliance, or improved safety, or some combination of both, we posit the mortality rate of 0.87 per 100,000 participants reported herein for the latter period represents the most accurate estimate to date.

While a variety of methods have been utilised to estimate mortality rates in recreational scuba diving, using them for making direct comparisons between locations, types of diving or diving groups is problematic. This is due to a lack of commonality and consistency of research methodologies, missing data, different levels of diver experience and/or training and, typically, differences in important influences upon diver behaviour, such as the presence of professional supervision, dive site selection, the total number of dives involved, etc. Furthermore, the DSD programme is a single dive experience, making comparisons with groups undertaking a series of multiple dives, or comparisons with annual mortality rates, invalid. That being said, comparisons between studies using similar dive-count methodologies may provide some indications of comparative risk. Unfortunately, studies with reliable denominators are rare and mortality rates based on retrospectively recalled survey estimates differ substantially from rates calculated using actual dive counts, such as in the present study.

In 2000/01 in British Columbia, dive cylinder air fills were counted and mortality over 14 months was estimated at 2.05 per 100,000 dives.[5]

A similar method was employed at a US Military base at Okinawa 1989–95, where there were few (if any) opportunities to obtain air-fills elsewhere, generating an estimated mortality rate of 1.3 deaths per 100,000 dives.[6]

In 1993/94 a count was made of scuba cylinder air-fills in Victoria, Australia,[7] where mortality was estimated at 2.5 per 100,000 dives.[8]

Scuba cylinder air-fills were also counted in Japan, at popular dive sites where access to diving was limited to registered diving companies. Mortality was calculated in 2000 at 1.75 per 100,000 dives, (with 95% confidence interval 1.06, 2.44).[9]

Direct comparisons of scuba diving's mortality rate with that of other activities are difficult. In the various annual mortality rate comparisons that have been made, scuba diving consistently has a low mortality compared with many other types of adventure recreation,[10] especially considering the potential risks. It should be noted that rigorous training and implementation standards are used to address and manage the risks and severity of incidents inherent in scuba and any underwater excursion. While any death is viewed as one too many, DSD discloses this risk in an informed consent process, and its standards manage the risk with the aim of making morbidity as low as possible.

A relatively recent separate analysis identified that, among certified divers being supervised by a PADI diving professional in North America and the Caribbean, such as when diving from commercial dive operator boats, 57% ($n = 70$) of the 122 recreational diver fatalities had a medical cause of death, as opposed to other causes directly associated with diving *per sé,* such as running out of air.[11] In the present study, however, while medical causes have been reported in some DSD fatalities the proportion of all DSD fatalities that were attributed to medical causes could not be reliably determined as the fatalities were distributed globally and in many cases medical examiner reports and/or autopsies were not included in the reports filed with PADI.

Never before have diving fatalities with an exposure denominator of > 7,000,000 introductory scuba experiences over 28 years been reported. Nonetheless, the limitations of this study include that the number of participants who are not registered remains unknown, but if this bias is in fact considerable, (as suspected), and its scale were known, then it would lower the estimated mortality rate even further. Especially given today's online interconnectedness, we consider the likelihood of there being a substantial discrepancy between the number of annual fatalities and the number reported to PADI to be slim, at best. Another limitation is that these data and conclusions apply only to the PADI DSD introductory scuba experience. Other training organisations have their own such programmes, but do not use the same instructional system and therefore, may have differing mortality rates. That said, because PADI has an estimated 70% global market share in recreational diving, the DSD numbers likely represent two thirds to three quarters of global introductory scuba experiences.

Conclusions

PADI's DSD introductory scuba experience presently, at 0.87 fatalities per 100,000 participants, has a calculated mortality rate per 100,000 participants that is less than half that calculated in 2008 for the 1992–2008 period. The more recent period's rate improvement may be due either to significant under-registration in the early period, or to significant safety-performance improvement in the later period or, possibly, some combination of the two. Regardless, the data suggest the DSD mortality rate compares favourably with mortality in recreational scuba diving overall.

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Conflicts of interest and funding

Within the previous three years PB was employed by Divers Alert Network in North Carolina, which provides insurance to scuba diving instructors, and both AH and KS are currently employed by the Professional Association of Diving Instructors. All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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Retrospective review of enquiries to the Québec diving medicine call centre: 2004 through 2018

David PM Monnot[1,2], Jocelyn Boisvert[2], Dominique Buteau[2,3], Neal W Pollock[1,2]

[1] *Department of Kinesiology, Université Laval, Québec, QC, Canada*
[2] *CISSS Chaudière-Appalaches (CHAU-Hôtel-Dieu de Lévis), Hyperbaric Medicine Unit, Emergency Department, Lévis, QC, Canada*
[3] *Family Medicine and Emergency Medicine Department, Université Laval, Québec, QC, Canada*

Corresponding author: *Dr David Monnot, Service de médecine hyperbare, Centre de médecine de plongée du Québec, Hôtel-Dieu de Lévis, 143 rue Wolfe, Lévis, QC, G6V 3Z1, Canada*
david.monnot@fmed.ulaval.ca

Key words
Diver emergency service; Diving incidents; Epidemiology; Hyperbaric facilities; Medical database; Telemedicine

Abstract
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Introduction: The Centre de Médecine de Plongée du Québec (CMPQ) established a bilingual 24-hour dive emergency call line and diving medicine information service in 2004. The toll-free number (888-835-7121) works throughout Canada. Calls and emails (cmpq.cisssca@ssss.gouv.qc.ca) are answered by a CMPQ coordinator or on-call hyperbaric physicians and other consultants as needed. We reviewed 15 years of activity.
Methods: Details of phone calls and email enquiries to the centre were reviewed individually and compiled into a database. Data were analysed to characterise contact volume and issues addressed. Contacts were categorised into five groups: information only (INF); medical opinion required (MOP); medical issue after the critical period of urgency had passed (PUR); current urgent but not immediate life-threatening issue (NLT); and immediate life- or health-threatening issue (ILT). Data presented as mean (standard deviation) or percentage.
Results: A total of 3,232 contacts were made from May 2004 through December 2018: 19 (SD 8) per month [215 (70) per year]. Primary issues of concern were: emergency planning (20%); technical (not medical/physiology) questions (16%); otorhinolaryngological (12%); and decompression sickness-related (7%). Categorisation was 52% INF, 28% MOP, 13% PUR, 7% NLT, and 0.1% ILT, with 0.2% lacking sufficient detail to categorise. The nature of the diving activity of interest was determined in 67% of cases: 48% (n = 1,039) professional; 46% (n = 1,008) recreational; and 1% (n = 11) breath-hold.
Conclusions: The call centre serves as a resource to the community, providing information on health and safety for diving in addition to being available to assist with emergent needs.

Introduction

Compressed gas diving is used worldwide for a range of recreational and professional activities. The former includes casual diving through to exploration activities, and the latter instruction, scientific, aquaculture, inspection, construction, demolition and a host of military and police work. While exposures can vary in intensity, for example, in depth, time, and ambient temperature, fundamental physiological hazards are shared, and in many ways distinct from those experienced in other non-diving activities. A number of services have been established to help address the health and safety needs of divers. The most well-known of these are the medical call services provided by Divers Alert Network (DAN) through DAN America,[1] DAN Suisse through DAN Europe,[2] and the Divers Emergency Service (DES) through DAN Asia Pacific.[3]

The Commission de la santé et de la sécurité du travail (CSST; renamed in 2014 Commission des normes, de l'équité, de la santé et de la sécurité du travail [CNESST]) reviewed practices following a concerning number of diving-related accidents in Québec, Canada. One of the recommendations made was to put in place a consultation service to ensure optimal care for victims of diving accidents.[4] The Centre de médecine de plongée du Québec (CMPQ) programme, located in Lévis, Province of Québec, Canada, was instituted in 2004 with a bilingual (French and English) 24-hour dive emergency call line and diving medicine information service. The goal was to meet the needs of professional and recreational divers, including emergency management and diving health information. The toll-free number (888-835-7121) works throughout Canada. Calls and emails (cmpq.cisssca@ssss.gouv.qc.ca) are answered by a CMPQ coordinator or on-call hyperbaric

physicians and other consultants as needed. Our goal was to review 15 years of call centre activity.

Methods

Approval for this retrospective review of data was obtained from the research ethics board of CISSS de Chaudière-Appalaches (number 2019-604). Data from May 2004 through December 2018 were reviewed.

DATA COLLECTION AND PROCESSING

CMPQ documentation of contacts was analysed and tabulated. The details of all incoming phone calls and email inquiries to the CMPQ were reviewed individually and compiled into a database. Individual contacts were assessed to characterise contact volume and issues addressed, separating them into categories according to issues of concern. If a contact involved multiple purposes, it was categorised based on the chief concern. Contacts with insufficient information to classify were put in the 'other' category.

Contacts were treated as independent and were distributed into five classes relating to the degree of urgency: information only (INF); medical opinion required (MOP); medical issue arising after a critical period of urgency had passed (PUR); currently urgent but not immediately life-threatening issue (NLT); and immediately life- or health-threatening issue (ILT). INF included requests for meetings, reports, current knowledge, and technical questions on diving or hyperbaric chamber operations. MOP included queries regarding medical contraindications relating to diving or hyperbaric activity, requests for expertise on cases encountered from doctors outside the CMPQ and questions relating to fitness to dive. Neither INF nor MOP contacts included a notion of medical urgency. PUR included requests for medical consultation, requiring intervention or not, with the point of contact being more than 48 hours after the reference event occurred. NLT included requests for intervention, aid, or medical consultation initiated within 48 hours of the reference event, but with no threat to life indicated. ILT included contacts referring to medical emergencies in which an imminent life threat was deemed possible.

Contacts were assessed for temporal patterns (daily, weekly, and seasonal presentation), the form of the contact (phone or email), point of origin (within or outside Canadian territory), and status (individuals involved or medical professionals providing care).

Descriptive data are presented as means and standard deviations (SD) with range, or percentages, as appropriate. Transformation operations were carried out for the main health issues of concern to evaluate contact patterns evolving over time. Averages for main health issues of concern were calculated based on the total number of annual requests. This yielded the observable share for each main health issue of concern per year, without the influence of the total number of requests. A weighted mean by year was then computed. The mean was then subtracted for each of the proportional averages (central operation). This allowed main health issues of concern to be observed on a comparable scale. Relative standard deviation (RSD) was computed to compare the degree of dispersion of centre contacts. RSD depicts the percentage of variation around the average to facilitate comparison of multiple averages with potentially different natures. Pearson χ^2 was used to assess the fluctuation of contacts over time. The probability of observing events at specific times or periods was predicted using Poisson's law. The lambda parameter was calculated as the average number of expected events for the period concerned. Statistical significance was accepted in all cases with $P < 0.05$.

Results

A total of 3,232 contacts were captured from May 2004 through December 2018 (Figure 1). There was insufficient detail to categorise in only 0.2% of the contacts. The frequency of contacts was 19 (SD 8) (range 2–42) per month, or 215 (70) (38–329) per year. Seasonal patterns were evident with 22 (5) (2–42) in the warmer months (May through October) and 15 (4) (4–29) contacts per month documented in the colder months (November through April). Over half of all contacts were for information only.

The form of contact was 73% (n = 2,353) telephone, 26% (n = 847) email, and one from mail, with < 1% (n = 31) with insufficient data to classify (Figure 1, Table 1). The mean annual telephone call volume was 2.8 times greater than the email volume, with a difference of 9% between the two RSDs (calls 35% and emails 44%). The fluctuation of calls and emails varied both year-to-year ($\chi^2 = 87.6$, df = 14, $P < 0.0001$) and monthly ($\chi^2 = 54.2$, df = 11, $P < 0.0001$).

Figure 1
Distribution of call centre contacts by year (2004 represents a partial first year of operation). The mean (standard deviation) (range) is presented in the legend for each form

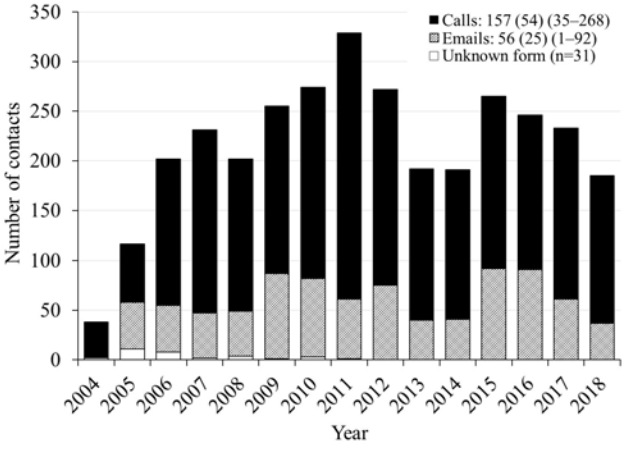

Table 1

Classification by form of contact. ILT – immediate life-threatening issue; INF – information only; MOP – medical opinion required; NLT – current urgent but not immediate life threatening issue; PUR – medical issues arising after the critical period of urgency had passed. The dash (–) means not applicable. * Seven calls did not have enough information to be classified

Form of contact	*n*	%	Classification of contacts									
			ILT		NLT		PUR		MOP		INF	
			n	%	*n*	%	n	%	n	%	n	%
Calls*	2,353	73	4	< 1	208	9	405	17	743	32	986	42
Emails	847	26	–	–	–	–	16	2	167	20	664	78
Mail	1	< 1	–	–	–	–	–	–	–	–	1	100
Unknown	31	1	–	–	4	13	4	13	8	26	15	48
Total	3,232	100	4	< 1	212	7	425	13	918	28	1,666	52

The dispersion of calls was evenly distributed among four classes of contacts (excluding ILT), while emails favoured information requests.

The distribution of contact concerns is summarised in Table 2. The five leading topics of concern for all contacts were: emergency planning (20%); technical questions not related to medicine or physiology (16%); otorhinolaryngologically-related (12%); decompression sickness-related (7%); and medical exam-related (7%). The emergency planning category included requests regarding dive emergency plans, reports of end-of-dive activity, and questions relating to the feasibility of emergency plans in a particular situation. Emergency planning captured both professional and recreational diving activities. The nature of technical questions varied dramatically. Examples include requests for a type of O-ring compatible with oxygen for a hyperbaric chamber, and how to make the type of gas mixture appropriate for a specific dive. Comparing the form of contact, the largest proportion of phone calls involved otorhinolaryngological issues (15%), and the largest proportion of emails concerned emergency planning (38%).

The classification of contacts is summarised in Table 3. It should be noted that multiple contacts related to individual events were sometimes received by the call centre in the days following the event. Repeated contacts were recorded as INF and then classified according to the subject.

A modest annual variation in the classification of contacts was observed, with an average variation difference of 5% between the RSDs (INF 37%, MOP 44%, PUR 32%, and NLT 43%; Figure 2). Seasonal patterns in contact classification varied considerably, as did the inter-class variability (Figure 3). INF contacts showed relatively little variation by month (RSD INF = 22%). MOP and PUR contacts showed greater variability (RSDs MOP = 31%, PUR = 43%). The share relating to emergencies had a very strong seasonal variation (RSD NLT = 78%). The warmer months, reflecting higher activity levels, showed the greatest variation within classes.

The first part of the week tended to be busiest for all telephone calls (all calls had available data). Monday–Tuesday contributed 43% of the call volume, and Monday–Wednesday 61% (data not shown). Weekends provided 9% of the call volume. Emails were distributed more uniformly between working days with a ratio of 18% per day, with a drop to 8% on weekend days. The proportions observed by weekday remained similar regardless of the month of the year. The pattern differed for emergency calls, with weekend calls representing 36% of the total. Seasonal patterns of emergency calls also emerged, with the number of calls per month doubling in the warmer months. Urgent calls (ILT and NLT) were split with 80% in the warmer months and 20% in the colder months. The numbers indicate a probability of receiving more than one emergency call as 0.1% during the week and 0.4% during the weekend in the warmer months; and 0.02% during the week and < 0.01% during the weekend in the colder months.

The pattern of call times differed between weekdays and weekends (66% of calls had available data). The contact time was 12:30 (0:40) on weekdays and 15:28 (2:37) on weekends. Approximately 10% of all calls were made between 18:00 and 08:00. Focusing on emergency calls with call time available (n = 159; 75% of emergency calls), 28% were made between 18:00 and 08:00. Weekday emergency calls came in at 13:57 (3:09), and weekend emergency calls at 15:09 (3:42).

The background of divers or divers-in-training making contact was determined in 67% of cases (n = 2,175). The distribution was 48% professional (n = 1,039); 46% recreational (n = 1,008); and 1% freediver (n = 11). Recreational divers tended to make telephone contact with CMPQ (90%; n = 906 in the known cases). Professional divers used telephones in 61% (n = 638) of their contacts. The majority of contacts from professional divers involved requests for information (86%). Contacts from recreational divers most commonly related to requirements for medical opinion and past urgent conditions (Table 4). Contacts related to an emergency condition made at least 48 hours after the situation developed were 8.5 times more

Table 2

Distribution and frequency of categories among the forms of contact. CMPQ – Centre de médicine de plongée du Québec. The dash (–) means not applicable. * One emergency planning contact was by post mail (not shown on table). # The seven cases with missing data were all phone calls

Category of contacts	*n*	%	Form of contact					
			Calls		Emails		Missing data	
			n	%	*n*	%	*n*	%
Emergency planning*	656	20	329	14	326	38	–	–
Technical questions	512	16	286	12	217	26	9	29
Otorhinolaryngology	385	12	355	15	25	3	5	16
Decompression sickness	230	7	206	9	19	2	5	16
Medical exam	212	7	161	7	50	6	1	3
Medication	165	5	142	6	22	3	1	3
Musculoskeletal	120	4	108	5	11	1	1	3
Information about CMPQ	88	3	59	3	28	3	1	3
Pulmonary	72	2	61	3	11	1	–	–
Search for diving physician	67	2	53	2	11	1	3	10
Cardiovascular	60	2	49	2	11	1	–	–
Asthma	47	1	36	2	11	1	–	–
Vertigo	36	1	34	1	2	< 1	–	–
Thoracic pain	30	1	29	1	1	< 1	–	–
Headache	25	1	25	1	–	–	–	–
Contamination	24	1	22	1	2	< 1	–	–
Skin	24	1	22	1	2	< 1	–	–
Head trauma	21	1	19	1	2	< 1	–	–
Eye	20	1	17	1	3	< 1	–	–
Pregnancy	19	1	17	1	2	< 1	–	–
Teeth	16	< 1	12	1	3	< 1	1	3
Abdominal region	15	< 1	14	1	1	< 1	–	–
Panic	11	< 1	10	< 1	1	< 1	–	–
Marine life-induced injuries	10	< 1	9	< 1	1	< 1	–	–
Nausea	9	< 1	7	< 1	2	< 1	–	–
Cold	5	< 1	4	< 1	1	< 1	–	–
Pollution	4	< 1	1	< 1	3	< 1	–	–
Drowning	4	< 1	4	< 1	–	–	–	–
Other	338	10	255	11	79	9	4	13
Missing data#	7	< 1	7	< 1	–	–	–	–
Total	3,232	100	2,353	73	847	26	31	1

frequent for recreational divers than for professional divers (Table 4). For example, recreational divers made contact more than eight days after an event in 29 cases, with the longest delay involving an individual who waited eight months to consult for chronic pain in the abdomen that appeared post-dive. In contrast, only two cases of contact after eight days were identified for professional divers. It should be noted that a substantial portion of contacts were made by 'divers prior to beginning training', both professional and recreational, inquiring about medical conditions or skills necessary to start the practice of diving. These contacts were classified as having an undetermined background (recreational or professional).

The breakdown of class of contacts associated with the most commonly raised health problems is summarised in Figure 4. The frequency of contacts regarding specific issues was fairly stable, with annual fluctuations around 2% (Figure 5).

Table 3

Distribution and frequency of categories among classes for all contacts. CMPQ – Centre de médecine de plongée du Québec; DCS – decompression sickness; ILT – immediate life- or health-threatening issue; INF – information only; MOP – medical opinion required; NLT – current urgent but not immediate life threatening issue; PUR – medical issues arising after the critical period of urgency had passed. The dash (–) means not applicable. * Six of the seven missing data cases did not have enough information to be classified

Category of contacts	*n*	%	Classification of contacts									
			ILT		NLT		PUR		MOP		INF	
			n	%	*n*	%	*n*	%	*n*	%	*n*	%
Emergency planning	656	20	–	–	–	–	–	–	–	–	656	39
Technical questions	512	16	–	–	–	–	–	–	–	–	512	31
Otorhinolaryngology	385	12	–	–	30	14	174	41	148	16	33	2
DCS	230	7	–	–	83	39	77	18	37	4	33	2
Medical exam	212	7	–	–	–	–	–	–	87	9	125	8
Medication	165	5	–	–	–	–	2	< 1	163	18	–	–
Musculoskeletal	120	4	–	–	10	5	39	9	66	7	5	< 1
Information about CMPQ	88	3	–	–	–	–	–	–	–	–	88	5
Pulmonary (excluding asthma)	72	2	–	–	12	6	12	3	40	4	7	< 1
Search for diving physician	67	2	–	–	–	–	–	–	–	–	67	4
Cardiovascular	60	2	1	25	1	< 1	1	< 1	52	6	5	< 1
Asthma	47	1	–	–	–	–	–	–	42	5	5	< 1
Vertigo	36	1	–	–	3	1	24	6	7	1	2	< 1
Thoracic pain	30	1	1	25	10	5	11	3	3	< 1	5	< 1
Headache	25	1	–	–	10	5	9	2	6	1	–	–
Contamination	24	1	1	25	6	3	7	2	1	< 1	9	1
Skin	24	1	–	–	6	3	15	4	2	< 1	1	< 1
Head trauma	21	1	–	–	–	–	–	–	21	2	–	–
Eye	20	1	–	–	7	3	3	1	9	1	1	< 1
Pregnancy	19	1	–	–	–	–	1	< 1	16	2	2	< 1
Teeth	16	< 1	–	–	1	< 1	6	1	7	1	2	< 1
Abdominal region	15	< 1	–	–	3	1	3	1	9	1	–	–
Panic	11	< 1	–	–	8	4	–	–	3	< 1	–	–
Marine life-induced injuries	10	< 1	–	–	–	–	8	2	1	< 1	1	< 1
Nausea	9	< 1	–	–	2	1	3	1	4	< 1	–	–
Cold	5	< 1	–	–	1	< 1	2	< 1	1	< 1	1	< 1
Pollution	4	< 1	–	–	1	< 1	–	–	–	–	3	< 1
Drowning	4	< 1	1	25	1	< 1	–	–	–	–	2	< 1
Other	338	10	–		17	8	28	7	193	21	100	6
Missing data*	7	< 1	–	–	–	–	–	–	–	–	1	< 1
Total	3,232	100	4	< 1	212	7	425	13	918	28	1,666	52

The four ILT contacts represented cases requiring immediate medical care. The first case involved loss of consciousness due to equipment failure during the dive (drysuit and mask leak then water aspiration through the regulator). The second case involved gas poisoning during the dive which was believed to lead to toxic pneumonitis. The third case concerned a professional diver developing a pneumomediastinum during a dive. The fourth case involved loss of consciousness developing during a dive, believed to be secondary to a cardiac problem. The coordination of intervention and treatment was quickly implemented for the first three cases and the patients were treated without any declared sequelae. The subject in the fourth case died nine hours later while under medical care.

Evaluating the INF calls (n = 986), only 27 (3%) required a physician response, with the majority being addressed by a technically knowledgeable non-physician.

Figure 2

Distribution of class over all years. Each bar represents the total number of contacts per year. The mean (standard deviation) (range) is presented in the legend for each class. ILT – immediate life-threatening issue; INF – information only; MOP – medical opinion required; NLT – current urgent but not immediate life threatening issue; PUR – medical issues arising after the critical period of urgency had passed

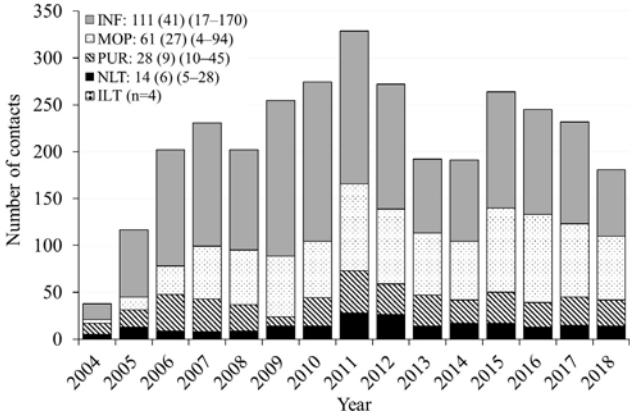

Figure 3

Seasonal distribution (n = 3,232; contacts distributed by month). The mean (standard deviation) (range) is presented in the legend for each class. ILT – immediate life-threatening issue; INF – information only; MOP – medical opinion required; NLT – current urgent but not immediate life threatening issue; PUR – medical issues arising after the critical period of urgency had passed

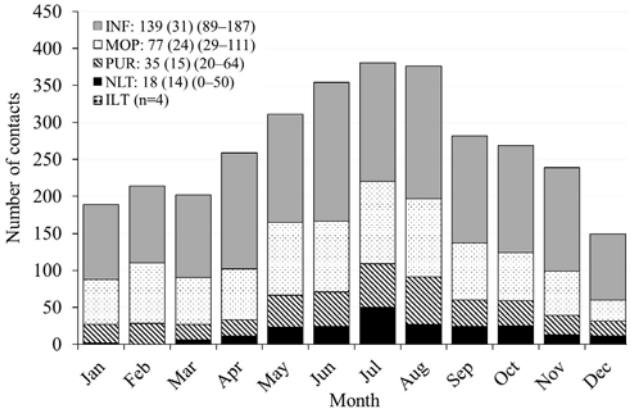

Table 4

Classification by type of diver. ILT – immediate life-threatening issue; INF – information only; MOP – medical opinion required; NLT – current urgent but not immediate life threatening issue; PUR – medical issues arising after the critical period of urgency had passed The dash (–) means non-applicable. * Five cases among recreational divers did not have enough information to be sorted into the five classes of contacts. #The unknown types are those which are declared divers but without specifying if they were recreational, professional or freedivers

Type of diver	*n*	%	Classification of contacts									
			ILT		NLT		PUR		MOP		INF	
			n	%	*n*	%	*n*	%	*n*	%	*n*	%
Recreational*	1,008	46	3	< 1	150	15	280	28	372	37	198	20
Professional	1,039	48	1	< 1	36	3	33	3	80	8	889	86
Free diver	11	1	–	–	3	27	4	36	1	9	3	27
Unknown#	117	5	–	–	11	9	48	41	32	27	26	22
Total[1]	2,175	100	4	< 1	200	9	365	17	485	22	1,116	51

The origin of contacts was established in 54% of cases (n = 1,733) (Table 5). Almost all of the contacts came from within Canada (98%; n = 1,702).

Discussion

The degree of urgency is an important metric in evaluating the activity of an emergency call centre. In the case of the CMPQ, 20% of the contacts were related to an urgent state (ILT, NLT, or PUR) from 2004 through 2018. This rate was similar to those reported for the Swiss DAN call centre for 2008 and 2009.[2] It was lower than the 31% reported for the DAN America call centre for 2010 through 2015;[1] and far lower than the > 90% reported for the DES Australia call centre for 1991 through 2007.[3] Variations are expected, with some services perceived as more appropriate for strict emergent events and others serving as a broader resource. Although the proportional share relating to emergencies and information remains comparable, the contact volume varies greatly depending on the centre. Determining call centre support needs must reflect regional, and possibly evolving, demands.

The marked paucity of contacts regarding events with the highest level of urgency (ILT) almost certainly indicates that such cases are generally entered into the medical system through traditional emergency medical services or possibly by direct arrival at the hyperbaric centre. The predominance of calls related to past urgent conditions and medical opinions likely reflects a desire for what is likely to be perceived as reliable specialist information.

The preponderance of emergency calls coming in on the weekend and non-emergency contacts made in the early part

Figure 4

Main health issues distributed by classification. CVD – cardiovascular; DCS – decompression sickness; ENT – ear nose and throat (otorhinolaryngology); MED – medications; MSK – musculoskeletal; PUL – pulmonary (excluding asthma). Only one immediate life-threatening case was captured in these six categories; it is not visible but it is included under CVD

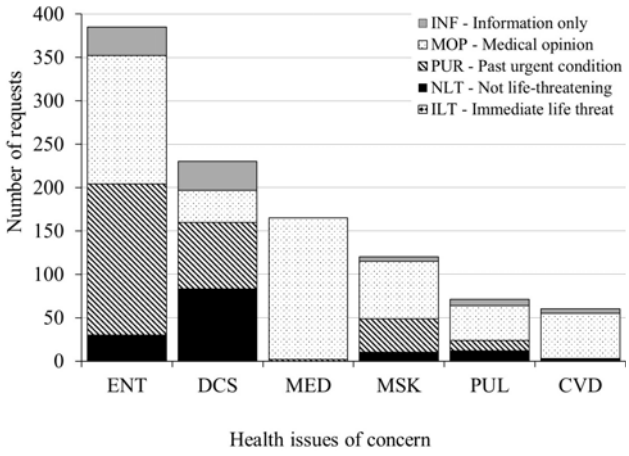

Figure 5

The figure represents the variation around its centred average, a weighted mean by year. The percent described in the legend represents the annual average variation for the six most common health issues. CVD – cardiovascular; DCS – decompression sickness; ENT – ear nose and throat; MED – medications; MSK – musculoskeletal; PUL – pulmonary (excluding asthma)

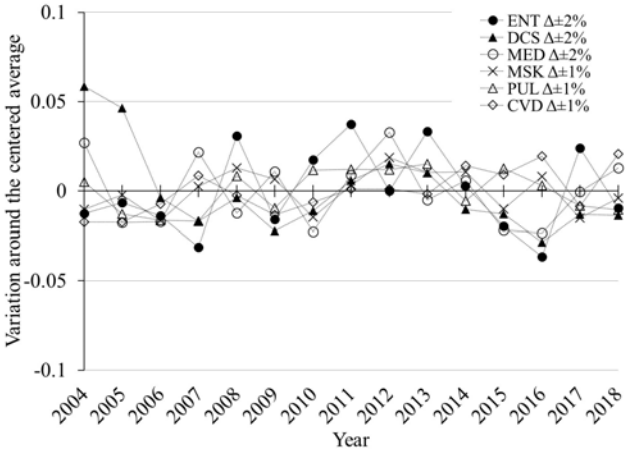

Table 5

Origin of contacts by location. The dash (–) means non-applicable

Form of contact	*n*	Distribution by location									
		Within Québec (km)						Canada-elsewhere		International	
		0 to 100		101 to 1,000		> 1,001					
		n	%	*n*	%	*n*	%	*n*	%	*n*	%
Calls	1,453	490	34	896	62	8	< 1	45	3	14	1
Emails	267	51	19	163	61	2	< 1	34	13	17	6
Mail	1	–	–	1		–	–	–	–	–	–
Unknown form	12	1	8	10	83	–	–	1	8	–	–
Total	1,733	542	31	1,070	62	10	1	80	5	31	2

of the week, particularly within the warmer months, reflects patterns observed by others.[3,5] Given that the majority of emergency calls were for recreational divers, it is expected that a higher volume would come in on weekends. It is noteworthy that the probability of receiving an emergency call in the warmer season was four times greater on weekends (data not shown).

Seasonal variations in contact volumes are expected given environmental conditions and accessibility issues in the colder months. Call times followed unsurprising trends according to both days of the week and season. The finding that almost one-third of emergency calls were made outside of normal business hours is similar to that reported by others,[3] and it speaks to the value of maintaining 24-hour services.

The contact volume and diversity indicated that both professional and recreational subgroups of the diving community utilise the CMPQ services in Québec. Recognition within the province appears to be substantial given the considerable portion of applicant diver contacts. Recreational divers appear to use it as more of a primary service, while professional diver may use it to augment other resources. The high frequency of contacts for emergency plans is consistent with a trusting relationship between divers and the CMPQ. Further expanding both awareness and trust could reduce the delay to solicit advice that is noteworthy in the recreational community. This could improve health and safety and reduce unaddressed concerns in an active population.

Call centre records can be helpful in identifying both issues in which community education could be improved

and emerging patterns of concern. The current data indicate substantial ongoing interest in questions or issues related to otorhinolaryngology and decompression sickness (Figure 5). Others have noted similar high frequency interest.[6–8] Moreover, the overall patterns only showed minimal variation over the reported years (Figure 5), suggesting that health issues of concern were not substantially changing in the community. It would be prudent for educators to expand general education to bolster understanding of topics frequently raised. The CMPQ, along with other bodies, could serve as a resource to develop relevant educational materials.

The most frequently addressed health issues of concern identified in this dataset, in rank order, involved otorhinolaryngology, decompression sickness, medications, musculoskeletal, pulmonary (excluding asthma, which was considered separately), and cardiovascular concerns (Figure 4). This could provide a reasonable priority list for developing educational initiatives. Otorhinolaryngological and decompression sickness issues might most effectively be addressed through expansion of existing training materials. High quality data regarding utility, impact, interactions, and hazards of medications in association with diving are lacking. This is an area in which additional research and ongoing consultation on a case-by-case basis will be needed. Call centre data could be useful to identify specific medications or interactions to be prioritised for study. Questions related to musculoskeletal issues are diverse, but patterns could also emerge to help focus research efforts. Pulmonary issues represent topics requiring ongoing consultation, research, and education. For example, the hazard of and risk factors for immersion pulmonary oedema require better education and case-by-case consultation. As a special case tabulated separately, there is both an idiosyncratic and evolving picture regarding the hazards of asthma and diving that warrants case-by-case consultation.

Questions regarding cardiovascular issues and diving are important due to frequent participation in diving by older individuals and growing complexities of care and/or treatment options. Patent foramen ovale (PFO) represents a common subtopic. Questions frequently arise regarding the importance of PFO and the merits, hazards, and need for surgical correction. It is likely that additional effort to educate the diving public across all levels of participation could benefit the community.

The observation that an important portion of information-related calls with the call centre did not require physician assistance is meaningful. While it is important to have clinicians on call, many inquiries can be addressed by persons with broad knowledge of the diving and hyperbaric field.

The scope of service is possibly one of the most interesting elements of the CMPQ to consider. The vast majority of contacts came from the province of Québec, but this is almost certainly a function of lack of awareness across the country. The fact that the service is bilingual may not be well known, but it is important. Practically, it is possible that the centre could be expanded into a national service with relatively modest effort. Many issues faced by divers are common to all environments, and cold water is a consideration in most Canadian diving. Future possibilities will be discussed separately.

The relatively small number of hyperbaric facilities and specialists across the country make it relatively easy to maintain effective lines of communication. A centralised service could provide an effective clearinghouse. On-call staffing could be increased with technical and medical resources drawn from across the nation. Expanding national collaboration could reduce the burden on local resources and provide opportunities to enhance training and preparedness for medical professionals who may normally see relatively few diving-related cases locally. An enhanced service could include additional efforts in data collection, educational content development, and timely dissemination of relevant information to both medical and diving communities. Expanding the resources available to the diving community could improve operational safety and readiness without legislative changes that have in some cases been promoted, but not established, outside of Québec.

LIMITATIONS

There were several limitations in this study. Most importantly, call centre interactions can rarely confirm diagnosis in the cases of health concerns, and follow up data were frequently not available. Insufficient information could produce errors in the classification of contacts. Consequently, this work is best interpreted as providing a broad description of patterns in call centre interactions.

Treating each contact as independent fails to capture situations in which multiple contacts address a single event or situation. The mitigation is that only the first contact in a medical emergency was defined as such, with follow up contacts counted as information only requests and the contact categories according to the primary subject.

The process of collecting data from all types of requests also evolved over time as prioritisation was given to the most efficient way to route each request to the appropriate destination. The methods used to record information changed over the years reviewed. Phone calls from May 2004 to December 2005 were first manually transcribed and then reported in a written monthly summary. The complete conversations sent by email were also deposited in this report. From August 2007, the monthly was accompanied by a call summary sheet, which included details for each call received and annual summaries. In August 2010 a monthly summary table was added. The monthly summary table was composed of seven columns which provided date, hours and time duration of call, identification, contact form and

a brief sentence on the topic. Gathering information based on the words used by callers or writers several years is easier with multiple sources. Details provided had evolved through the years. The monthly summary was suspended in January 2013 which caused the loss of the details of email conversations. The availability of the call summary sheet gradually decreased in 2015, leaving the monthly summary as the most robust source of contact data.

Many cases do not provide enough information to fit clearly into the designed configuration, and on several occasions it was difficult to be able to categorise the contacts. Some involved multiple topics, and the effort to determine the main reason was imperfect. Although the information available was not uniform, patterns were established confidently.

The origin of contacts by location must not to be confused with location of the cases for which the call (or email) was made. For example a call regarding a dive emergency planning might be done from the company location while the place of diving activity concerns a dam located 1,000 km away.

Conclusions

This review describes 15 years of activity in telemedicine and an emergency diving call centre based in Lévis, Québec, Canada. The service is utilised by professional and recreational divers and persons involved in the care of divers. Although the vast majority of contacts involve requests for information, there is a large proportion seeking medical opinions or remote medical consultation. Not surprisingly, greater activity is found during the warmer months. The call centre has provided a resource to the community, primarily providing information on health and safety for diving in addition to being available to assist with emergent needs. The insights gained here could help to organise, refine, and/or expand capabilities and enhance the training of divers and those responsible for the health and safety of divers. The service has the potential to expand across Canada as a national resource.

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Oxygen toxicity seizure mimics

Kevin Foley[1], Neil Banham[1], Samantha Bonnington[1], Ian Gawthrope[1]

[1] *Department of Hyperbaric Medicine, Fiona Stanley Hospital, Perth, Australia*

Corresponding author: *Dr Neil Banham, Department of Hyperbaric Medicine, Fiona Stanley Hospital, 11 Robin Warren Drive, Murdoch WA 6150, Australia*
neil.banham@health.wa.gov.au

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Hyperbaric oxygen treatment; Recompression; Neurology; Brain; Risk factors; Hyperbaric research; Clinical audit

Abstract
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Introduction: Oxygen toxicity seizures (OTS) are a well-recognised complication of hyperbaric oxygen treatment (HBOT). As such, seizure-like activity during HBOT is usually presumed to be a result of central nervous system oxygen toxicity (CNS-OT). Four cases are reported here where causes other than CNS-OT were determined as being the likely cause of the seizure; causes we have labelled 'OTS mimics'. Through review of the current literature, and our hyperbaric medicine unit's experience to date, we aimed to highlight the relevance of these OTS mimics, as the potential for significant morbidity and mortality exists with incorrect diagnoses.
Methods: A retrospective review of the medical records of all patients treated at the Fiona Stanley Hospital and Fremantle Hospital hyperbaric medicine units who had a seizure during HBOT between November 1989 and June 2020. These events were reviewed to determine whether causes for seizures other than oxygen toxicity were evident.
Results: Four OTS mimics were identified: posterior reversible encephalopathy syndrome, pethidine toxicity, previous subarachnoid haemorrhage with resultant epilepsy, and severe hypoglycaemia.
Conclusions: This case series highlights the need for caution when diagnosing an apparent OTS. Multiple conditions may mimic the signs and symptoms of oxygen toxicity. This creates scope for misdiagnosis, with potential for consequent morbidity and mortality. A pragmatic approach is necessary to any patient exhibiting seizure-like activity during HBOT, with suspicion for other underlying pathologies.

Introduction

Oxygen toxicity seizures (OTS) are a rare but well-recognised and feared complication of hyperbaric oxygen treatment (HBOT), with a reported incidence of between 0.01% and 0.06% for 'routine' treatments.[1,2] Although certain prodromal signs and symptoms of oxygen toxicity are now well recognised, there remains a large variation in presentation and onset, often indistinguishable from other diagnoses.[3] There is potential for seizures occurring due to other causes being attributed to central nervous system oxygen toxicity (CNS-OT) if they occur in or around HBOT.

Methods

Approval was obtained for data review and extraction (GEKO Quality Activity 35539).

A retrospective review was undertaken of the medical records of all patients treated at the Fiona Stanley Hospital and Fremantle Hospital hyperbaric medicine units who had a seizure during HBOT between November 1989 and June 2020. These records were reviewed by the author group to determine whether causes for seizures other than oxygen toxicity were evident.

Results

There were 25 OTS in 64,491 patient treatments over the past 30 years; the first 25 years at Fremantle Hospital and the last five years after relocation to Fiona Stanley Hospital. Four cases were found in which patients initially perceived to experience an OTS were, on further assessment, deemed to have suffered a seizure for other reasons. All other seizures that occurred were considered to be OTS. Each case (presented below) highlights the ease of misdiagnosis of oxygen toxicity, while emphasising the need to consider other potentially more sinister pathologies.

CASE REPORTS

Case 1: Posterior reversible encephalopathy syndrome (PRES)

A 22-year-old female was referred for treatment of purpura fulminans, secondary to *Escherichia coli* sepsis,

on a background of systemic lupus erythematosus and immunosuppression. She had developed multiple areas of acral ischaemia of all limbs secondary to sepsis, and was referred for HBOT to maximise limb viability prior to amputation.

HBOT was performed at 203 kPa (two atmospheres absolute [atm abs]) in a monoplace chamber as the patient was unable to hold a mask (required to deliver an air-break if higher treatment pressures were used), and was unable to tolerate a head hood.

During her sixth HBOT session, she suffered a seizure, occurring after 52 minutes of breathing oxygen (O_2) at 203 kPa. Generalised tonic-clonic activity for approximately one minute preceded signs in keeping with an absence seizure lasting a further two minutes. Oxygen delivery to the chamber was replaced with air immediately after seizure onset, and treatment was aborted. The chamber was decompressed over six minutes when seizure activity had ceased and spontaneous respirations had recommenced, during which time the patient was not responding appropriately to questions. On removal from the chamber the patient appeared coherent, but with no recollection of the event. She denied any prodromal symptoms or headache. Her blood pressure was recorded as normal post seizure and other vital signs were within normal limits, with a finger-prick blood glucose level (BSL) of 6.7 $mmol \cdot L^{-1}$ (120.7 $mg \cdot dL^{-1}$). No focal neurological signs were evident on examination.

No previous history of seizures had been documented. On collateral history, the patient's family reported recent episodes of abnormal shaking, while unresponsive to voice. This would occur for two to three minutes at a time before self-resolving. These had not been reported to staff prior to the time that this seizure had occurred. One such episode of abnormal movements had been witnessed by HMU staff following a HBOT session, but was not considered to be a seizure as these movements stopped on demand and there was no post-event confusion. A functional cause/pseudo-seizure was postulated as the aetiology. The patient specifically denied any headache at that time.

Following recovery from her seizure, the treating team was advised to consider the possibility of an organic cause such as encephalitis. A magnetic resonance imaging (MRI) brain scan was performed, showing multiple old infarcts and new areas of hyper-attenuation in the posterior occipital lobes. This finding was in keeping with PRES; a condition characterised by seizures, headaches and altered levels of consciousness. Oral nifedipine was commenced for management of PRES. HBOT was discontinued due to increased risk of seizures during future treatments. The patient had no further seizures during her hospital admission, and was followed up on an outpatient basis by the neurology team.

Case 2: Pre-existing seizure disorder

A 47-year-old male, ex-Navy diver, was referred for emergency HBOT for treatment of presumed cerebral arterial gas embolism (CAGE) with United States Navy Treatment Table 6 (USN TT6). This followed an episode of loss of consciousness following a dive. Initial history was received from the attending ambulance crew, who had received history from a participating dive instructor. The patient was completing a refresher open water dive course at the time of the episode. He had descended to approximately 3 metres depth without issue. He then began staring vacantly and was unresponsive to commands, before floating to the surface. A generalised seizure was witnessed at the surface before the patient was removed from the water and transferred to hospital. Uncertainty regarding speed of ascent or if breath was held prompted a diagnosis of CAGE as the most likely cause for his symptoms.

No focal neurology was noted on arrival to the Emergency Department (ED). Bloods performed were unremarkable. Non-contrast cranial computerised tomography (CT) scanning was performed showing a previously coiled basilar tip aneurysm but no new intracranial pathology.

During the final hour of treatment at a pressure of 190 kPa (1.9 atm abs) on O_2 being delivered by head hood, the patient had a generalised tonic-clonic seizure that lasted approximately two minutes. Blood was noted inside the patient's mouth, and there was loss of urinary continence. He was unresponsive, and making snoring sounds. The BSL was recorded as 6.5 $mmol \cdot L^{-1}$ (117.1 $mg \cdot dL^{-1}$). O_2 was removed immediately upon seizure onset, and the attending doctor entered the chamber to accompany the patient during decompression.

Later a collateral history from the patient's dive instructor was obtained. The patient had slowly risen to the surface, away from the dive group. He was breathing but unresponsive to command. The instructor brought the patient to shore where he proceeded to have a generalised seizure.

The patient was found to have a history of seizures on a background of previous subarachnoid haemorrhage (SAH), with multiple known aneurysms. This evolving history made the diagnosis of CAGE less likely, and more likely to represent a seizure episode underwater. With a further seizure in the hyperbaric chamber at 190 kPa, this was considered not to be a manifestation of oxygen toxicity, but more likely a pre-existing seizure disorder.

The patient was admitted under the neurology team. An electroencephalogram (EEG) was performed showing findings in keeping with disturbance of structure or function over the left hemisphere with epileptogenic potential. MRI brain showed no infarct or acute intracranial findings. He was

commenced on regular leviteracetam. No further HBOT was performed, and the patient was advised to cease scuba diving.

Case 3: Pethidine toxicity

A 28-year-old female underwent emergency HBOT for traumatic compartment syndrome of her right arm. Referral for HBOT was made post emergency fasciotomy.

Treatment at 284 kPa (2.8 atm abs) was initially planned, until the patient was found to be 22 weeks pregnant. The decision was changed at this point to treat at 203 kPa (2.0 atm abs). The rationale for this choice of treatment pressure was not documented.

The patient was initially quite anxious, with some difficulty equalising her ears during compression. Intravenous (IV) pethidine titrated to 130 mg was administered for severe pain in the affected limb. Seventeen minutes into the first O_2 period the patient suffered a generalised tonic-clonic seizure, lasting approximately five minutes before self-resolving. O_2 via head hood was removed immediately after onset and the attending doctor entered the chamber. Diazepam 2.5 mg IV was administered in the post-ictal phase and the hyperbaric treatment was aborted. Observations were within normal limits. The patient was rousable but irritable and no focal neurological deficits were demonstrated. Subsequently it was noted the patient had received 1,300 mg of pethidine in the preceding 28 hours. Pethidine's major metabolite (norpethidine) has well documented epileptogenic effects, and a relatively long half-life of 14–21 hours. HBOT was discontinued after this. It is possible that oxygen toxicity may have contributed to the onset of this seizure, although seizures may occur spontaneously with pethidine toxicity, and 'pure' oxygen toxicity seizures are uncommon at 203 kPa (2.0 atm abs).[2] Had the information regarding the patient's recent extremely high dosing of pethidine been known, it may have been that the risk benefit decision would have been not to proceed with HBOT.

Case 4: Hypoglycaemia

A 38-year-old female was referred for HBOT for a non-healing wound on her right forefoot, secondary to poor diabetic control. Thirty HBOT sessions were originally planned at a pressure of 243 kPa (2.4 atm abs) in a multiplace chamber, with O_2 delivered by head hood. During her fifth treatment, she became confused towards the end of the second O_2 period. She was noted to be staring vacantly, and unresponsive to voice at which point her head hood was removed. She then began twitching, and briefly lost consciousness, presumed secondary to oxygen toxicity. At this point the attending doctor entered the chamber and the hyperbaric treatment was aborted. BSL was checked, and had decreased to 1.4 mmol·L^{-1} (25.2 mg·dL^{-1}). This was successfully treated with oral glucose. Fifteen minutely BSLs were performed, with slow recovery. After monitoring in the HMU and after provision of a meal, the patient was discharged home, with alterations made to her insulin regime.

That day the patient had reported a BSL of 3.1 mmol·L^{-1} (55.9 mg·dL^{-1}) on waking, prior to breakfast and administration of 6 units of Novorapid® insulin. Her next BSL was 10.1 mmol·L^{-1} (182.0 mg·dL^{-1}) immediately prior to commencing HBOT, at approximately 0900 hours. For subsequent treatments, her BSLs were checked half hourly while in the chamber, with no further issues noted. Nineteen treatments were completed in total, discontinuing due to lack of clinical response.

Discussion

The symptoms and signs of CNS-OT, as described by Donald in 1947, have been observed in many patients since his original research.[2–5] Certain predisposing factors to CNS-OT have since been identified, with higher OTS rates documented with higher pressure treatment tables and for emergency indications.[2,6–9] When treating dysbarism, the rates of OTS have been reported from 0.28–1.11% of treatments.[2,6,10,11] An increased rate of OTS occurrence has also been reported with the first HBOT for carbon monoxide poisoning.[2,7,9]

The signs and symptoms of OTS have been described as notoriously "*unpredictable*", with "*large variation*".[3] Patients receiving elective HBOT will often be elderly, suffer from chronic pain, and have multiple comorbidities including diabetes mellitus, cardiac disease, or an active infection. These factors may lead to diagnostic uncertainty in the event of loss of consciousness, or a seizure during HBOT.

UNDERLYING SEIZURE DISORDERS

To date, patients with epilepsy have not been found to be at an increased risk of OTS.[4,7]

The recommended management of epileptic patients undergoing HBOT includes confirmation of therapeutic levels of any anti-epileptic medication. However, seizures during treatment due to underlying disorders can still occur, and pose a diagnostic dilemma. The question remains as to whether such seizures would have occurred regardless of HBOT, or were provoked by a synergistic effect from hyperoxia.

Case 1 involved a female with PRES; characterised by white matter vasogenic oedema of the posterior occipital and parietal lobes of the brain, leading to headaches, seizures, altered mental status and visual loss. It is often associated with acute hypertension, which if treated, will usually resolve the syndrome within a week.[12] There seem to be many

possible triggers, including abrupt arterial hypertension, impaired renal function, pregnancy, immunosuppressive therapies and various inflammatory conditions. It is becoming an increasingly recognised disorder with the advent of neuroimaging.[13] In this instance, suspicion of alternate diagnoses prompted an MRI brain, revealing pathognomonic findings of PRES. While approximately 75 percent of patients have moderate to severe hypertension at presentation, PRES may occur in normotensive patients, and is more common in patients with systemic lupus erythematosus; both seen in the patient presented. Treatment with an antihypertensive is still recommended and was given in this case. A combination of seizures, visual disturbance and / or headache, should lead to an early MRI brain.

Case 2 involved a male with previously documented seizures with a known cause that had not been divulged. Although previously working as a Navy diver, to the best of our knowledge no dive medical had been performed since suffering a SAH in 2014. Collateral history for this patient revealed likely seizure activity soon before treatment, initially presumed to be the result of CAGE. This was followed by a further seizure in the chamber, mistakenly attributed to oxygen toxicity. The identification of the underlying pathology facilitated improved patient disposition, with further unnecessary HBOT avoided. This highlights the importance of repeat dive medicals following significant morbidity, and the need to closely investigate anyone with a history of intracranial pathology.

EPILEPTOGENIC MEDICATIONS

Emergency HBOT indications such as necrotising infections, severe decompression illness (DCI) or crush injury may warrant large doses of analgesics such as pethidine, fentanyl, or tramadol. Those with coinciding acute or chronic infections may be receiving high doses of penicillins, cephalosporins or antifungals. Each of these medications has the potential to lower the seizure threshold in a susceptible individual, or in some cases, directly induce a seizure through neurotoxic effects.[14]

Case 3, originally reported in 1998, involves the effects of pethidine toxicity, which through its active metabolite, norpethidine, has the direct potential to induce seizures.[14–16] Currently many patients will receive HBOT despite co-administration of such medications. Difficulty may arise in distinguishing between the provocation of an OTS, and the unmasking of an underlying seizure disorder. A retrospective analysis from 2004 examined the rate of OTS from 107,264 HBOT sessions performed in 30 hyperbaric centres in Germany.[17] Two cases were excluded from this series, with seizures in the chamber instead being deemed due to high dose cefazolin treatment. To date, minimal literature exists surrounding seizure-provoking medications during HBOT, focussing more on cases of true oxygen toxicity. A case series from several hyperbaric units in Milwaukee, Wisconsin, USA reviewed seven seizures among five patients undergoing HBOT.[18] Each case highlighted other potential causes for seizures, including high doses of ceftriaxone, tramadol, selective serotonin reuptake inhibitors, and tricyclic antidepressants concurrently used among these patients. Other relevant drugs include high dose penicillins and cephalosporins, narcotics, pethidine, corticosteroids, and acetazolamide. Other factors referenced included narcotic withdrawal, alcohol withdrawal, and carbon dioxide retention in patients undergoing HBOT.

Additional medication choices during HBOT remain an important factor before and during treatment. If possible, seizure-provoking medications are best avoided, but each case requires a consideration of risk versus benefit.

HYPOGLYCAEMIA

A large cohort of patients receiving HBOT suffer from diabetes mellitus, notably those with consequent peripheral vascular disease and non-healing lower limb wounds. Some evidence suggests that HBOT does not cause a clinically significant decrease in BSL among diabetics.[19] However a study from 2013 demonstrated that finger-prick capillary sampling may not be an accurate reflection of venous glucose during HBOT.[20] Wilkinson et al reported increased peripheral insulin sensitivity following HBOT, maintained for at least 30 minutes after exiting the hyperbaric chamber. This was initially demonstrated in healthy individuals, and later in obese males, both with and without type 2 diabetes mellitus.[21–23] Irrespective of potential direct effects of hyperbaric oxygen, these patients will undergo periods of fasting in the chamber, while isolated if treated in a monoplace environment. With this comes the potential for adverse events, particularly in those with labile BSLs, and those who remain asymptomatic until severe hypoglycaemia occurs.

Common symptoms of hypoglycaemia such as twitching, agitation, confusion, nausea, visual changes, peri-oral paraesthesia and eventually seizures, all overlap with those of CNS-OT. Case 4 demonstrates their homogeneous presentation, as symptoms began with twitching and confusion, followed by loss of consciousness. The BSL just prior to commencement of that day's HBOT was 10.1 $mmol \cdot L^{-1}$ (182.0 $mg \cdot dL^{-1}$), resulting in the attending medical staff initially identifying the episode as a result of oxygen toxicity. As per the unit's emergency procedures for OTS, BSL was checked immediately as standard, and the patient was promptly treated for severe hypoglycaemia. Failure to identify the true cause of symptoms in this case could have led to significant deleterious effects for this patient.

It has become routine in our unit since 2003 to document finger-prick glucose in diabetic patients immediately before

and after each HBOT. This is also performed during HBOT if the patient develops symptoms of hypoglycaemia or oxygen toxicity. Diabetic patients treated in the monoplace chambers are supplied with a prophylactic syringe of oral glucose, to be consumed if symptoms of hypoglycaemia develop.

Many additional seizure mimics are now well recognised within the emergency setting. A clinical review published in 2016 lists these seizure differentials, along with salient signs and symptoms to aid in differentiation.[24] That study reported 20% of presumed epileptic patients were misdiagnosed in emergency departments, being later identified as suffering most commonly from syncope or psychogenic non-epileptic seizures. Patients receiving HBOT not uncommonly suffer from some form of cardiac disease. A forceful Valsalva manoeuvre combined with a degree of autonomic failure and the 'dive reflex' may be enough to induce a syncopal episode.[25] Other causes include stroke, hyponatraemia, sleep disorders such as narcolepsy with catoplexy, movement disorders, and migraine.[26] From this we can extrapolate the possibility of confusion between seizures and seizure-like presentations.

OTS, in general, occur at higher pressures, with a significantly lower incidence at treatment pressures of 203 kPa (2 atm abs) or less.[2] A review of 62,614 HBOT sessions from a single unit in Israel reported no OTS from 12,303 treatments performed at pressures below 203 kPa.[27] However most (> 51%) treatments included in this cohort were at a maximum pressure of 151 kPa (1.5 atm abs). This is below the minimum therapeutic pressure used across Australasia. Reports of three OTS occurring at 190 kPa (1.9 atm abs) have been documented.[2] The seizure in each of these cases occurred during decompression from earlier treatment pressure exposure to 243 or 284 kPa. This highlights the difficulty in diagnosing or excluding OTS based solely on treatment pressure.

Conclusion

This case series highlights the need for caution when labelling an OTS. Multiple conditions may mimic the signs and symptoms of oxygen toxicity. This creates scope for misdiagnosis, with potential for morbidity and mortality. A pragmatic approach is necessary to any patient exhibiting seizure-like activity in the hyperbaric chamber, with suspicion for other underlying pathologies.

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Oxygen toxicity seizures during United States Navy Treatment Table 6: An acceptable risk in monoplace chambers?

Samantha Bonnington[1], Neil Banham[1], Kevin Foley[1], Ian Gawthrope[1]

[1] *Department of Hyperbaric Medicine, Fiona Stanley Hospital, Murdoch, Western Australia*

Corresponding author: *Dr Neil Banham, Department of Hyperbaric Medicine, Fiona Stanley Hospital, 11 Robin Warren Drive, Murdoch, WA 6150, Australia*
neil.banham@health.wa.gov.au

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Abstract
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Introduction: Hyperbaric oxygen treatment (HBOT) may be complicated by oxygen toxicity seizures, which typically occur with hyperbaric partial pressures of oxygen exceeding 203 kPa (2 atmospheres absolute). All other hyperbaric units in Australia exclusively use a multiplace chamber when treating with United States Navy Treatment Table 6 (USN TT6) due to this perceived risk. The purpose of this study was to determine the safety of a monoplace chamber when treating decompression illness (DCI) with USN TT6.
Methods: A retrospective review of the medical records of all patients treated at Fiona Stanley Hospital Hyperbaric Medicine Unit with USN TT6 between November 2014 and June 2020 was undertaken. These data were combined with previous results from studies performed at our hyperbaric unit at Fremantle Hospital from 1989 to 2014, creating a data set covering a 30-year period.
Results: One thousand treatments with USN TT6 were performed between 1989 and 2020; 331 in a monoplace chamber and 669 in a multiplace chamber. Four seizures occurred: a rate of 0.59% (1/167) in a multiplace chamber; and none in a monoplace chamber, indicating no statistically significant difference between seizures in a monoplace versus multiplace chamber ($P = 0.31$).
Conclusions: The rate of oxygen toxicity seizures in a monoplace chamber is not significantly higher than for treatment in the multiplace chamber. We conclude that using the monoplace chamber for USN TT6 in selected patients poses an acceptably low seizure risk.

Introduction

Recompression using oxygen is the standard treatment for cases of decompression illness (DCI); a collective term for the dysbaric injuries cerebral arterial gas embolism (CAGE) and decompression sickness (DCS). Initial treatment usually involves recompression with United States Navy Treatment Table 6 (USN TT6).[1]

Oxygen toxicity seizures are a rare, but well-recognised and feared complication of hyperbaric oxygen treatment (HBOT), with a reported incidence in the region of 0.06%.[2] Evidence suggests that incidence is related to increased inhaled partial pressure of oxygen and duration of treatment.[2–7]

Hyperoxia creates free radicals that interact with membranes of neurological cells causing lipid peroxidation and alteration of electrical activity.[8,9] Added to this, increased levels of nitric oxide cause cerebral vasodilatation which counteracts the normal physiological vasoconstriction response to hyperoxia.[10]

The rate of seizures in the treatment of DCI is demonstrated to be higher at 0.28% to 1.11% likely reflecting the increased pressure and duration used in the treatment.[2,11–13] However, more seizures have been documented during initial USN TT6 treatments than with follow-up treatments to similar pressures (which are typically of shorter duration at 284 kPa and overall).[2] The role of monoplace chambers for the treatment of DCI has recently been reviewed by Clarke, who concluded that "*today's monoplace chamber can successfully support a majority of DCI cases, when overseen by a knowledgeable physician*".[14]

Monoplace chambers have been used to treat stable patients with DCI requiring USN TT6 in Western Australia since their introduction at Fremantle Hospital (FH) in 2001. More serious forms of DCI requiring inside attendant care and management continue to be treated in the multiplace

chamber. The Hyperbaric Medicine Unit (HMU) at Fiona Stanley Hospital (FSH) has continued this practice since its transition from FH in November 2014. This is in contrast to all other HMUs in Australia with access to monoplace chambers, who view the risk of seizures during treatment with a USN TT6 as unacceptably high (personal communications, 2020).

The aim of this study was to determine if the treatment of DCI with USN TT6 in a monoplace chamber presents an unacceptable risk of seizures.

Methods

Written approval was obtained for data review and extraction (Governance, Evidence, Knowledge, Outcomes [GEKO] Quality Activity 35028).

A database of all treatments and complications for both units has been maintained since the opening of FH HMU in November 1989. We reviewed the records of all patients treated for DCI with USN TT6 between November 2014 and June 2020 at FSH. This involved review of patients' electronic medical records using the hospital records system Bossnet®, and accessing the HMU database to review the treatment profile and chamber used for each session. We determined the number of patients who received a USN TT6 and whether the treatment took place in a monoplace or multiplace chamber. We reviewed the notes for each session to determine if there were any complications with treatment, primarily central nervous system toxicity (CNS-OT). In addition, the log book containing comprehensive details of all seizure episodes since 1989 was cross referenced.

All patients who underwent recompression for suspected DCI using USN TT6 in a monoplace chamber were included in the study. Monoplace treatments were performed in either a Sechrist 3200 or Sechrist 3600 (Sechrist Industries, Anaheim, CA, USA) chamber.

Previous studies had been conducted at FH HMU covering two separate periods, totalling 25 years in the following periods: November 1989–November 2009;[2] and November 2009–November 2014 (previously unpublished audit). The results of these studies at FH were combined with the results from those at FSH to create a data set spanning 30 years. Statistical analysis was performed using a Fisher's exact test; a P-value of < 0.05 was considered to be statistically significant.

A USN TT6 in our unit consists of the tables shown in Figures 1 and 2.

The monoplace TT6 utilised was developed by Dr Robert Wong, a previous Medical Director of FH HMU, being modified from the multiplace and standard US Navy version by the addition of an extra 20 minute oxygen (O_2) breathing period at 284 kPa (2.8 atmospheres absolute [ATA]) and then decompression to 190 kPa (1.9 ATA) over 10 minutes to compensate for the limitation of the Sechrist 3200 chamber which has a slowest decompression rate for this pressure differential of 10 minutes, and to allow the change of the in-chamber atmosphere from air to 100% O_2. The advantage of this is that it avoids the use of a mask to breathe O_2 for the 2 hours at 190 kPa and the further 30 minutes for decompression to sea level pressure.

When using the monoplace chamber for a USN TT6 treatment the patient initially uses a built-in breathing system (BIBS) oro-nasal mask secured with head straps to breathe 100% O_2, with the surrounding chamber environment containing air. The air source is the hospital medical air supply which meets the Australian/New Zealand Standard 2568 for purity and absence of contamination. The exhaled breaths are into the surrounding chamber air, which is continually flushed at approximately 300 $L \cdot min^{-1}$, preventing O_2 and carbon dioxide (CO_2) accumulation. Scheduled air breaks are achieved by removal of the mask for 5 minutes. During decompression to 190 kPa the chamber air is replaced by 100% O_2 while the patient continues to breathe O_2 via the BIBS. At 190 kPa the BIBS is utilised to provide the required air break.

In the event of features of oxygen toxicity developing whilst breathing 100% O_2 via the BIBS, the gas supply to the mask can be switched immediately to air. If prodromal features of CNS-OT develop while the chamber is filled with O_2, the patient is instructed to breathe air via the BIBS and the chamber can also be purged with air at 400 $L \cdot min^{-1}$, although this will take many minutes to achieve an air atmosphere.

Results

There were 1,000 treatments with USN TT6 performed between 1989 and 2020, 331 in a monoplace chamber and 669 in a multiplace chamber. There were four recorded oxygen toxicity seizures within this 30-year study period. All seizures occurred in the multiplace chamber; a rate of 0.59% (1/167 treatments), and none occurred in a monoplace chamber. These data are summarised in Table 1. There was no statistically significant difference between seizure rate in a monoplace versus multiplace chamber ($P = 0.31$).

One seizure occurred in the first O_2 period, two in the third and two during the 190 kPa (1.9 ATA) phase of TT6. Details of individual cases experiencing seizures are summarised in Table 2.

One seizure that occurred during the study period was in a complex patient with previous subarachnoid haemorrhage (SAH) following basilar artery tip rupture which had been coiled twice. His SAH previously presented with seizures and he was known to have three other aneurysms under surveillance. His history revealed a head strike before diving, and a moment of decreased consciousness in the water followed by a tonic-clonic seizure during descent at

Figure 1

USN TT6 modified for use in the monoplace chamber. The pressure shown is gauge pressure. Total length of treatment is 4 h 35 min. BIBS – Built-in breathing system; FSH – Fiona Stanley Hospital; kPa – kilopascals; O_2 – oxygen; Pt – patient; min – minutes; USN TT6 – United States Navy Treatment Table 6

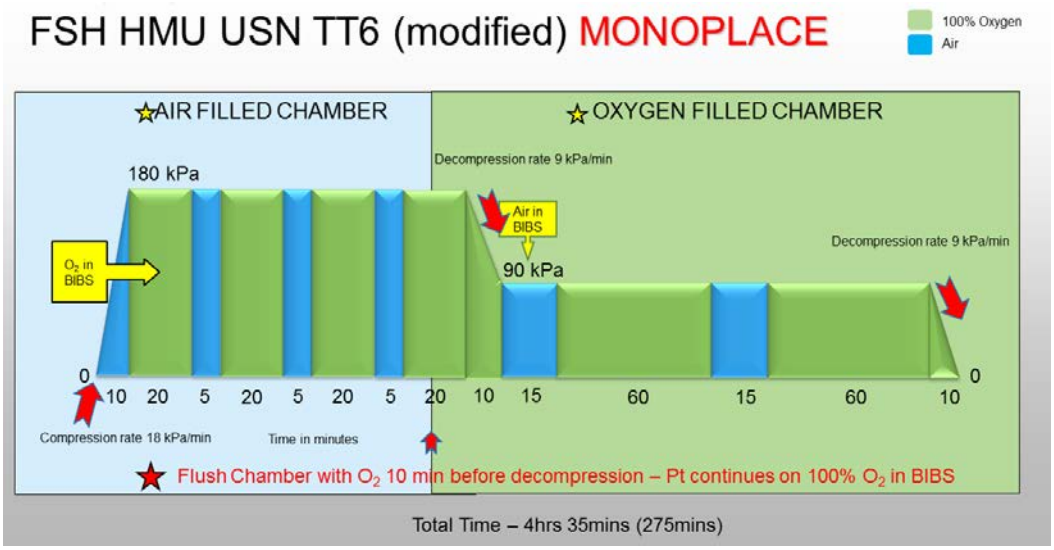
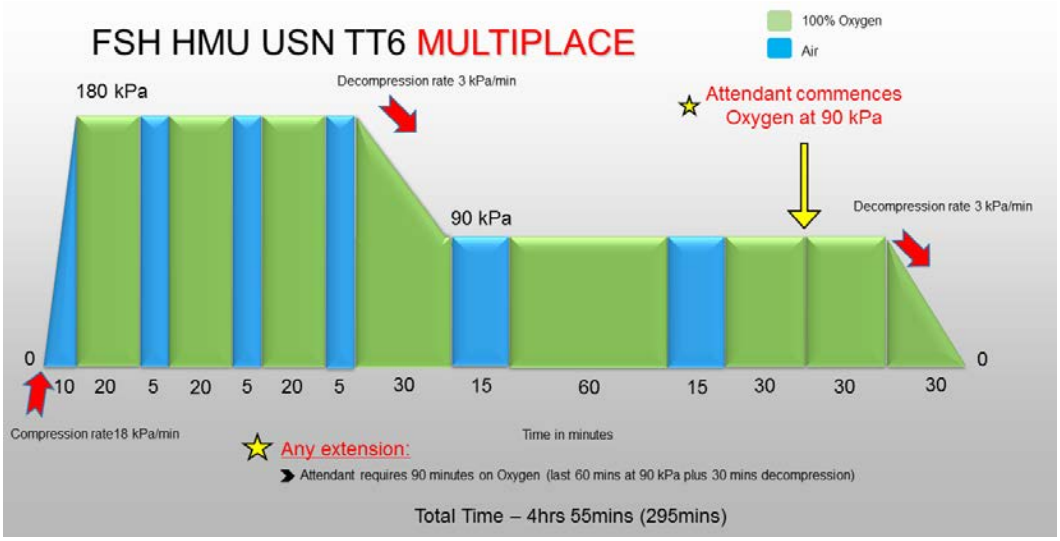


Figure 2

USN TT6 for use in the multiplace chamber. The pressure shown is gauge pressure. Total length of treatment is 4 h 55 min. FSH – Fiona Stanley Hospital; kPa – kilopascals; min – minutes; USN TT6 – United States Navy Treatment Table 6



3 metres depth. His brain computerised tomography scan (CT) was difficult to interpret due to previous coiling, but did not reveal any bleeding nor intravascular gas. He was treated for presumed CAGE given a normal brain CT, and suffered a further two-minute seizure at 190 kPa in the final hour of USN TT6 in the multiplace chamber. The subsequent collateral history revealed a likely seizure disorder rather than oxygen toxicity. For this reason the episode was excluded from analysis but is reported elsewhere.[15]

Discussion

This study presents a data set spanning 30 years, including 20 years of using monoplace chambers to treat selected patients for DCI with USN TT6. During the period studied there were four seizures presumed secondary to CNS-OT recorded, all of which occurred in the multiplace chamber. This study showed no significant difference between seizure occurrence in a multiplace versus monoplace chamber (P = 0.31), however, it is likely that it was underpowered to demonstrate such a difference.

Although CNS-OT is a rare occurrence, the treatment of DCI presents a higher risk of seizure when compared to treatment of other conditions. The reasons behind this are likely multifactorial relating to the pressure and duration of treatment, inter-individual variability and the physiology behind the injury itself.[13]

Table 1

Oxygen toxicity seizure rate during 1,000 USN TT6 (United States Navy Treatment Table 6) treatments. USN TT6 used for decompression illness (DCI) including iatrogenic embolism. FH – Fremantle Hospital; FSH – Fiona Stanley Hospital; Mono – monoplace chamber; Multi – multiplace chamber

Time Period	Chamber	USN TT6 numbers	Seizure number	Seizure %	Seizure rate
2014–2020 FSH data	Mono	90	0	0	0
	Multi	33	0	0	0
2009–2014 FH data Unpublished	Mono	120	0	0	0
	Multi	43	0	0	0
1989–2009 FH data Published[2]	Mono	121	0	0	0
	Multi	593	4	0.67	1/148
Totals	Mono	331	0	0	0
	Multi	669	4	0.59	1/167
	Both	1000	4	0.40	1/250

Table 2

Details of four patients experiencing oxygen toxicity seizures during USN TT6 treatments for decompression sickness (DCS) or cerebral arterial gas embolism (CAGE). All seizures occurred between 1989 and 2009 at Fremantle Hospital. CT – computerised tomography; EEG – electroencephalogram; F – female; M – male

Case	Age (y)	Sex	Indication	Risk factor	HBOT sessions	O_2 period	Pre-seizure time on O_2 (min)	Comments
1	31	M	CAGE	Salt water aspiration	11	5th (at 193 kPa)	125	P_aCO_2 48 mmHg prior
2	24	M	CAGE	Nil	2	End of 3rd	59	Nil
3	36	F	DCS	Nil	2	End of 1st	16	CT brain normal EEG epileptiform
4	36	F	DCS	Nil	2	End of 3rd	55	Same patient as 3

It is for this reason that all other Australian HMUs with monoplace chamber capability in addition to a multiplace chamber, use a multiplace chamber for USN TT6 treatment, as it allows an inside attendant to be available in the event of a seizure.

PRESSURE

Treatment with USN TT6 involves pressurisation to 284 kPa. Since Donald made the association between increased oxygen pressure and duration of exposure with seizure risk,[3] research has been aimed at quantifying this relationship. Multiple studies have shown this association, with any treatment above 203 kPa showing significantly increased risk.[2,4] Although one study reported a threefold increase in seizure incidence with increased chamber pressure to 284 kPa, this did not reach statistical significance.[4] Other research, however, demonstrated a significant relationship between increasing pressures above 203 kPa and seizure risk.[2]

Early data reported a significant increase in CNS symptoms at 340 kPa when compared to treatment at 284 kPa for the same duration.[16] Although this does not delineate seizures from other CNS symptoms, logic would suggest that increasing pressure would increase seizure risk.

DURATION

Whether the duration of hyperbaric oxygen exposure infers an increased seizure risk is contentious. Donald described the association between duration of exposure to hyperbaric oxygen and risk of seizures.[3] However, later research found no relationship between length of treatment and seizure occurrence when treating carbon monoxide poisoning at 284 kPa.[17] This could be due to the addition of regular air breaks which is postulated to reduce the risk[18] although the addition of air breaks was not demonstrated to influence seizure rate in a review of CNS-OT at 243 kPa in Australian HMUs.[19] A previous study reported that receiving air breaks was actually a risk factor for having a seizure.[4]

As the risk of oxygen toxicity seizure increases with pressure and duration of O_2 exposure,[2–7] it would follow that USN TT6 infers increased risk for CNS toxicity given the initial pressure of 284 kPa and total treatment duration of more than four hours. This being said, a large study showed no significant increased risk of seizure when treating with USN TT6 compared to subsequent treatments with USN TT5, citing the small patient numbers as a possibility for this result.[2] These two treatment tables have identical initial treatment profiles for the first two 20-minute oxygen breathing periods at 284 kPa, but the USN TT5 is shorter

overall because of one less 20-minute oxygen period at 284 kPa and a reduced treatment time at 190 kPa. The study reported no seizures during 731 USN TT5 vs. four reported cases in 721 USN TT6. Despite the absolute numbers, this did not reach statistical significance.[2] We were unable to find any reported cases in the literature of seizure during USN TT5.

PATHOLOGY OF DCI

The higher reported rate of seizures when treating DCI indicates a risk specifically related to the injury process. The 'first treatment effect' was described by Wilkinson after reporting that the incidence of seizures in the first treatment for DCS was higher than subsequent treatments at 1.8%.[13] This could be due to the postulated neurological injury and that the first treatment is the longest and most provocative exposure. This has also been reported with HBOT for treatment of carbon monoxide poisoning.[2,17,20] Our study findings were consistent with this result, as all seizures reported were during the first treatment for DCI.

Wilkinson reported an incidence of seizures of 0.5% when treating DCS at 284 kPa compared to medical indications (including carbon monoxide poisoning and treatment of acute infections),[13] and although this did not achieve statistical significance, it is a trend reported by others.[2,12] Interestingly, he reported that the occurrence of seizures when treating diving-related CAGE was not elevated similarly to DCS, but it was for iatrogenic CAGE (2/53). He commented that the small numbers complicate interpretation. This higher rate of oxygen toxicity has also been reported when treating DCI at pressures between 240 kPa and 290 kPa, with an incidence of 0.6% recorded.[12] One hypothesis behind this increased risk with DCI is that nitrogen bubbles create a neurological injury which increases the susceptibility to CNS-OT.[13]

INDIVIDUAL RESPONSE

As Donald observed, despite knowing possible risk factors, the susceptibility to oxygen toxicity varies between individuals and within the same person on different days.[3,21] This has been substantiated by reports that some people appear resistant to the side effects of hyperoxia.

The use of monoplace chambers presents an opportunity to treat patients without the need for an inside attendant. This eliminates the risk of DCI to the attendant staff member,[21] and reduces costs involved by limiting the number of staff required to be present during treatment. It also allows rapid removal of a patient in the case of an emergency, something that is more difficult to achieve in a multiplace chamber given the potential risk of DCI to the attendant – an outside attendant may have to pressurise to remove the patient and then allow safe decompression of the inside attendant. Another benefit of monoplace chambers is availability. At least in the USA, there are many more monoplace than multiplace chambers. Utilisation of the monoplace chamber for treatment of DCI could avoid potentially long transport times to a suitable multiplace facility.

OTHER RISK FACTORS

Hypercapnia is a recognised risk factor for increased seizure rate, as are numerous medications which are recognised to lower the seizure threshold. One of the patients who seized during a TT6 treatment of CAGE had aspirated and had a mildly elevated $PaCO_2$ of 48 mmHg (normal 35–45) documented in the emergency department prior to commencing HBOT. He was otherwise treated conservatively and did not require intubation.

During treatment in a monoplace chamber, an outside attendant can closely monitor the patient for prodromal symptoms of CNS-OT and the BIBS rapidly switched to deliver air when appropriate, although it has been reported that not all oxygen toxicity seizures have prodromal symptoms, and signs are notoriously *"unpredictable"* with *"large variation"*.[2]

The incidence of DCI in hyperbaric attendants ranges from 0 to 37 per 100,000 sessions (0.037%) and, although this presents a small risk, it is a risk that can be reduced by using a monoplace chamber where appropriate.[22]

Monoplace chambers have been used safely to treat with USN TT6 in centres without access to a multiplace chamber.[11] The use of monoplace chambers in the treatment of DCI was first advocated in 1974.[23] However, shorter treatment tables using no air breaks were used (unlike a USN TT6) as was the case in a 2006 report.[24] Results from the present study concur with those of these previous studies despite the different treatment tables used.

It should be noted that patients in this unit are screened for appropriateness for USN TT6 treatment in a monoplace chamber. Unstable patients requiring one-to-one nursing care or medical intervention, analgesia, repeated neurological examination or ongoing haemodynamic support would be treated in a multiplace chamber. Information on managing intensive care-level patients in monoplace chambers can be found elsewhere.[25] Neither benzodiazepines nor other anticonvulsant medications were administered prophylactically to patients undergoing HBOT.

Conclusion

Treatment of appropriately selected DCI cases using USN TT6 in a monoplace chamber appears to be an acceptable, safe and cost-effective option.

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The usefulness of the RSTC medical questionnaire in pre-participation health risk assessment of recreational scuba divers in Hong Kong

Tsz-Ki Cheung[1,2], Willem AJ Meintjes[1]

[1] *Department of Global Health, Stellenbosch University, Cape Town, South Africa*
[2] *Family Medicine and Primary Healthcare Division, The Chinese University of Hong Kong, Hong Kong*

Corresponding author: *Dr Cheung Tsz Ki, Family Medicine and Primary Health Care Division, JC School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong*
jackietkcheung@gmail.com

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Abstract
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Introduction: The current practice in Hong Kong is to have potential recreational divers complete a Recreational Scuba Training Council self-declared medical statement (RSTC form) prior to participation in diving. There are no reports in the literature on the usefulness of the Chinese version of the form.
Methods: The Professional Association of Diving Instructors (PADI) RSTC form (Chinese version) was completed by 117 research participants who were then individually interviewed (without examination) to establish whether relevant information was not captured by the form. Any discrepancies or problems identified were recorded for further analysis.
Results: Among participants, 15.4% expressed difficulty in completing the RSTC form. Less than one-third (28.2%) replied 'all negative' to the questions. Some health conditions that could impose diving risks were not elicited by the questionnaire alone. Nevertheless, there was good sensitivity, specificity, positive predictive value and negative predictive value with the exception of a few questions. However, significant discrepancies were identified when comparing the English and Chinese versions. There was also uncertainty with aspects of implementation, including attitudes of the user and provider, reliability of self-declaration answers and the handling of completed questionnaires.
Conclusions: Health screening with a questionnaire for recreational divers remains practical and acceptable. Full revision of the RSTC form in Chinese is recommended in view of problems with the construct validity and translation. People should be informed about the non-prescriptive approach of health assessment for recreational divers. Further research on the implementation of the form may help to improve the screening strategy in the future.

Introduction

Scuba diving has unique health risks. These are dynamic, multi-factorial and dependent on different modes of diving.[1,2] For simplicity and regulatory reasons, participants are grouped into recreational and non-recreational (for example commercial and military) divers. All scuba divers that decide to dive for enjoyment and not for financial gain are regarded as recreational scuba divers.

In order to manage diving-related health risks in recreational divers, the current practice in most parts of the world is to have potential participants sign a self-declaration medical statement prior to allowing participation. Many dive certification agencies adopted the Recreational Scuba Training Council medical statement (RSTC form).[3] The form consists of a self-declaration section, including a medical questionnaire that needs to be completed by the participant. The participant is assumed to have no need for medical consultation or examination if all questions are answered negatively. Positive responses will direct the person to medical consultation prior to possible engagement in dive activities.[4,5]

While the RSTC form has undergone update and review over time, there is no study on the usefulness of the Chinese version of the form. This study aimed to assess the usefulness of the most widely adopted Chinese version of the form among potential Hong Kong Chinese divers and to identify any potential pitfalls with the medical questionnaire component of the form. It will be a useful basis for assessment of the upcoming new diving medical screening questionnaire.

Methods

Ethical approval for the study was obtained from the Stellenbosch University Health Research Ethics Committee (ethic reference number U19/09/042).

Participants were recruited during the primary investigator's on-duty sessions at three private primary care clinics in

October and November 2019. All primary care clinic attendants were invited to join the research if they met the inclusion criteria for participation in the study. These included being 18 years or older, and being willing and able to complete the questionnaire and the informed consent document. Patients who were acutely ill or unable to read the Chinese questionnaire were excluded. The RSTC form [10063C(Rev 09/01)Ver. 2.0] was distributed to research participants.[6] They were asked to complete the form and the researcher would go through the same questionnaire with the research participant immediately afterwards. The researcher would ask the questions as though conducting a consultation in the sequence of the questionnaire. Clarifications were made by the researcher on the identified ambiguous wordings and translation. The participants would also be encouraged to discuss and express their ideas in filling the form. No clinical examination or screening tools apart from the history taking were performed for the research. All discrepancies or issues identified were recorded for analysis.

In order to have a 90% power to detect at least one occurrence of a problem with the questionnaire when the assumed prevalence of the condition is 2% in the population, a sample size of 114 individuals was required.[7]

In the analysis, the clinical consultation and interview was considered the gold standard to determine the sensitivity, specificity, positive and negative predictive values of the questions.

The IBM SPSS statistics package version 26 (IBM, Armonk (NY), USA) was used for data analysis.

Results

A total of 496 clinic visitors were encountered, of whom approximately 25% met the inclusion criteria of the study. Most excluded cases were due to age being under 18 years. The overall response rate among eligible visitors was 94.4%. A total of 117 questionnaires and successful interviews were completed. The demographics of the study participants are shown in Table 1, while their question responses and comparison with the medical interview are displayed in Table 2. Problems identified during the interviews are shown in Table 3.

Table 1
Demographics of study participants ((*n* = 117)

Characteristic	*n* (%)
Diving experience	
No experience	83 (70.9)
Discovery dive	25 (21.4)
Open water	3 (2.6)
Advanced open water	1 (0.9)
Rescue diver	0 (0)
Divemaster	5 (4.3)
Diving Instructor	0 (0)
Education level	
Primary	6 (5.1)
Secondary	58 (49.6)
Tertiary	53 (45.3)
Age Group	
18–29	44 (37.6)
30–39	40 (34.2)
40–49	14 (12)
50–59	12 (10.3)
60 or above	7 (6)
Gender	
Male	69 (59)
Female	48 (41)

Discussion

GENERAL OVERVIEW OF DATA ANALYSIS

Most questions had high positive and negative predictive values (at least 80% and 98% respectively) (Table 2). Question 5 ("*Frequent or severe attacks of hay fever or allergy?*"), question 7 ("*Any form of lung disease?*") and question 18 ("*Inability to perform moderate exercise....*") were the only exceptions. All questions were high in specificity (> 95%), but the sensitivity had a wide range. Questions 5, 7, 11 ("*Epilepsy, seizures...*"), 22 ("*Back, arm or leg problems following surgery, injury or fracture?*"), 32 ("*Hernia?*") and 33 ("*Ulcers or ulcer surgery*?") were questions that had lower sensitivity (< 70%), indicating that these questions were not good at identifying respondents who actually had these conditions.

The relatively low negative predictive values of questions on hay fever, allergy and lung diseases (questions 5 and 7) may relate to the wording of the questions. Both questions also had low sensitivity in this study cohort. Some replied "*no*" to question 5, despite the presence of intermittent allergic rhinitis. For question 7, those with asthma or hyperactive airway problems did not reply "*yes*". Some said that they were not aware that the airway problem was also a form of lung disease.

For question 32 ("*Hernia*"), the low sensitivity may relate to use of a medical term in the Chinese translation, instead of a more commonly used term in society for the condition. The same occurred with the inquiry regarding skin ulcer or ulcer surgery (question 33), where the Chinese version adopted a rather technical term.

The study reported a low positive predictive value to the inquiry regarding physical fitness (question 18). People expressed difficulty in understanding the given example (walk 1.6 km/one mile within 12 minutes).

Some health conditions that could impose diving risks on individuals were not directly elicited by the questionnaire alone (Table 3).

Table 2

Participant responses to the questionnaire and the sensitivity, specificity, positive and negative predictive values of each question. FP – false positive; FN – false negative; NPV – negative predictive value; PPV – positive predictive value; TN – true negative; TP – true positive; Sens – sensitivity; Spec – specificity. ** – denotes values that could not be calculated. For discussion purposes, questions were assigned numbers from top to bottom, left to right of the Chinese RSTC form [10063C(Rev 09/01)Ver2.0]

	Statement in the questionnaire	TP	FP	FN	TN	Sens	Spec	PPV	NPV
1	Could you be pregnant, or are you attempting to become pregnant?	3			114	100%	100%	100%	100%
2	Are you presently taking prescription medications? (with the exception of birth control or anti-malarial)	11		1	105	92%	100%	100%	99%
3	Are you over 45 years of age and can answer YES to one or more of the following? - currently smoke a pipe, cigars or cigarettes - have a high cholesterol level - have a family history of heart attack or stroke - are currently receiving medical care - high blood pressure - diabetes mellitus, even if controlled by diet alone	17	4	1	95	94%	96%	81%	99%
4	Asthma, or wheezing with breathing, or wheezing with exercise?	27		1	89	96%	100%	100%	99%
5	Frequent or severe attacks of hay fever or allergy?	9		16	92	36%	100%	100%	85%
6	Frequent colds, sinusitis or bronchitis?	25	3		89	100%	97%	89%	100%
7	Any form of lung disease?	5		18	94	5%	100%	100%	84%
8	Pneumothorax (collapsed lung)?	1			116	100%	100%	100%	100%
9	Other chest disease or chest surgery?	1			116	100%	100%	100%	100%
10	Behavioural health, mental or psychological problems (panic attack, fear of closed or open spaces)?	3		1	113	75%	100%	100%	99%
11	Epilepsy, seizures, convulsions or take medications to prevent them?	1		1	115	50%	100%	100%	99%
12	Recurring complicated migraine headaches or take medications to prevent them?	4	1		112	100%	99%	80%	100%
13	Blackouts or fainting (full/partial loss of consciousness)?	7		2	108	78%	100%	100%	98%
14	Frequent or severe suffering from motion sickness (seasick, carsick, etc.)?	22		1	94	96%	100%	100%	99%
15	Dysentery or dehydration requiring medical intervention?	5			112	100%	100%	100%	100%
16	Any dive accidents or decompression sickness		1		116	**	99%	0%	100%
17	History of recurrent back/spine disease?	5		2	110	71%	100%	100%	98%
18	Inability to perform moderate exercise (example: walk 1.6 km/one mile within 12 minutes)?	2	1		114	100%	99%	67%	100%
19	Head injury with loss of consciousness in the past five years?				117	**	100%	**	100%
20	Recurrent back problems?	5		1	111	83%	100%	100%	99%
21	Diabetes?	2			115	100%	100%	100%	100%
22	Back, arm or leg problems following surgery, injury or fracture?	2		1	114	67%	100%	100%	99%

Table 2 continued.

	Statement in the questionnaire	TP	FP	FN	TN	Sens	Spec	PPV	NPV
23	High blood pressure or take medicine to control blood pressure?	9			108	100%	100%	100%	100%
24	Heart disease?	2			115	100%	100%	100%	100%
25	Heart attack?	2			115	100%	100%	100%	100%
26	Angina, heart surgery or blood vessel surgery?	2			115	100%	100%	100%	100%
27	Sinus surgery?				117	**	100%	**	100%
28	Ear disease or surgery, hearing loss or problems with balance?	1			116	100%	100%	100%	100%
29	Ear equalisation problem during air travel?	13		2	102	87%	100%	100%	98%
30	Recurrent ear problems?	1			116	100%	100%	100%	100%
31	Bleeding or other blood disorders?				117	**	100%	**	100%
32	Hernia?	2		2	113	50%	100%	100%	98%
33	Ulcers or ulcer surgery?			1	116	0%	100%	**	99%
34	A colostomy or ileostomy?				117	**	100%	**	100%
35	Recreational drug use or treatment for, or alcoholism in the past five years?	3			114	100%	100%	100%	100%

Table 3
Problems identified during the interviews with 117 participants

Find difficulty in filling the questionnaire	
Yes *n* (%)	18 (15.4%)
No *n* (%)	99 (84.6%)
Problematic question (number of respondents); details of the problem encountered	
Question 6 (2); uncertainty about the definition of "*frequent attack*"	
Question 7 (1); is allergic airway a kind of lung disease?	
Question 8 (1); do not know the meaning of collapsed lung/pneumothorax	
Question 9 (1); should breast surgery be declared as chest surgery?	
Question 15 (5); should the use of medication be classified as medical intervention?	
Question 18 (1); cannot appreciate the example (walk one mile within 12 minutes)	
Question 32 (3); do not know the translated medical term "*hernia*"	
Question 33(1); do not know the translated term "*ulcers*"	
Conditions of respondents that were not detected by the questionnaire (number of respondents)	
Hyperlipidaemia in respondent < 45 years old (1)	
Hepatitis B carrier that needed regular follow-up (1)	
History of appendicectomy done (1)	
History of breast lump with lumpectomy done (1)	
History of hypothyroidism that previously needed thyroxine replacement (1)	
History of hyperthyroidism (? Grave's disease) (1)	
History of lymphoma with full remission > 10 years (1)	
Eye condition (Retinitis pigmentosa) with deterioration of visual acuity (1)	
Chronic renal failure on continuous ambulatory peritoneal dialysis (1)	

NEEDS OF MEDICAL SCREENING FOR RECREATIONAL DIVERS

Only 33 out of 117 (28.2%) of the research participants replied negatively to all questions, and 25 (75.8%) of these were truly "*all negative*" upon interview. While the research cohort might be different from actual potential scuba diving participants, it supported the need for pre-dive medical assessment. Standardised diving medical evaluation can also help different stakeholders to gauge the potential risks and draw a line of acceptance. In modern times, this is relevant to the liability of individuals and the involved parties. Until further research deems otherwise, use of a self-declaration questionnaire for screening is still the most widely accepted strategy.[8–10]

A highly prescriptive set of rules in the determination of medical clearance is usually adopted for commercial or military divers.[11–14] For recreational divers, the medical evaluation is more intended for health risk identification. Thereafter, the risks should be mitigated and/ or accepted or evaluated as being unacceptable ('high risk'). High risk individuals are subsequently advised against participation.[11,15,16]

One major drawback in using only a self-declaration questionnaire for screening is the definition of threshold of risk acceptance that is presumably defined by the diving medical expert panel involved in the design of the questionnaire. Use of screening questionnaires will unavoidably lead to excessive medical referral in the current logistics if every detail and extent of conditions are included. On the other hand, overly selective questions could be challenged for the risk of missing other important conditions.

LOCAL USE OF RSTC FORM

As in most parts of the world, in Hong Kong there is no legal restriction in relation to individuals participating in recreational scuba diving.[17] A self-regulatory system is adopted among diving organisations. With the Professional Association of Diving Instructors (PADI) being the dominant diving training agency in the territory, the PADI RSTC form is hence the most commonly used medical statement in the local diving community.[18] Unless specifically indicated otherwise, traditional Chinese/Cantonese is the language used for written documents, instruction and teaching among the local Chinese population.

The PADI RSTC form has had regular updating and revision with time. The 2001 Chinese translation version [10063C(Rev.09/01)Ver. 2.0] was derived from the 1998 English version.[6] The updated Chinese version [10038TC(Rev. 6/12)Ver. 1.0] was not launched until 2012.[3,19] For many years, the 2001 Chinese version has been the most commonly available form.

In brief, the 2012 Chinese version adopted the changes in the 2001 English version, where the question on ear equalisation problems during air travel (question 29 in the 2001 Chinese version) was removed. The question on past history of recurrent back and spine disease (question 17 in the 2001 Chinese version) was replaced by the inquiry of any back/ spine surgery (question 20 in the 2007 English version). Other questions in the 2012 Chinese version were the same as the 2001 Chinese version (grossly the same sequence and exactly the same wordings), except for the new question on back/spine surgery as mentioned above.

ASSUMPTIONS WHEN USING QUESTIONNAIRE FOR SCREENING

The meaningful implementation of the questionnaire relies on a number of assumptions, including: 1) the validity of the questionnaire (original design); 2) the validity of the applied form (for example: Translation version); 3) appropriate implementation of the screening (time, place, person); 4) users' understanding and co-operation; 5) people completing the questionnaire correctly and honestly; and 6) appropriate handling of the completed questionnaire (referral, inquiry, feedback system). These assumptions are further discussed below.

Validity of the original questionnaire design

Some health conditions of the respondents were not detected by the questionnaire (Table 3). While not all conditions would result in unacceptable diving-related health risk, it is unreasonable for participants and diving agencies to assume liability without prior warning. For example, a participant with retinitis pigmentosa was not detected by the questionnaire alone. Another respondent with a lipid disorder was younger than 45 years old. According to the questionnaire, he was not expected to indicate this cardiovascular risk factor.

In an analysis of recreational diving fatalities, cardiac events were considered the disabling injury in 26% of cases.[20] In other studies trauma resulted in 5% of disabling injuries.[20–25] According to a report that reviewed the coroner's records of reported diving-related fatalities (2006–2009) in Hong Kong, two out of eight cases were trauma-related (impact with boat or boat propeller). One case was definitely related to a cardiac incident and another case was suspected to be cardiac related.[25] It seems reasonable to assume the mortality and morbidity pattern among Hong Kong divers is similar to other nationalities, although it would be preferable to have more evidence to support this observation. Moreover, diving incidents among Hong Kong residents during their diving trips outside Hong Kong were not explored. Re-examining the scope and design of the questionnaire will improve its validity since evidence has grown in recent years.[26]

Table 4
Discrepancies in translation. Q – question (with numbers corresponding to those in Table 2)

Question number in Chinese version (2001/2012)	Original question / words in the 2007 English version	Identified problem(s) in the Chinese version of the corresponding question
Q2 / Q2	Are you presently taking prescription medications? (with the exception of birth control or anti-malarial)	The exception of anti-malarial is not mentioned
Q3 / Q3	...diabetes mellitus, even if controlled by diet alone	Incorrect translation. Meaning becomes "*diabetes mellitus, even with diet control*" instead of the original idea of identifying diabetics with or without use of medications
Q4 / Q4	Asthma, or wheezing with breathing...	Incorrect translation. Not exact translation of "*asthma*" in Chinese. Uses a term with the meaning of "*shortness of breath*"
Q6 / Q6	Frequent colds, sinusitis or bronchitis?	Use of an ambiguous Chinese term that means "*flu*" instead of "*colds*"
Q10 / Q10	...psychological problems (Panic attack, fear of closed...)	Misleading translation of "*panic attack*" into words that imply physical attack ("*assault*")
Q14 / Q14	Frequent or severe suffering from motion sickness...	Mistranslation of "*or severely suffering from*". Only asks whether or not the respondent has "*frequent suffering*"
Q18 / Q17	Inability to perform moderate exercise (example: walk 1.6 km/ one mile within 12 mins)?	Misleading translation of "moderate exercise" as "*gentle exercise*" There is no mention that the example is just a reference.
Q19 / Q18	Head injury with loss of consciousness in the past five years?	Incorrect translation. Meaning becomes "*Any head injury after loss of consciousness, in the past five years?*"
Q27 / Q27	Sinus surgery?	Incorrect translation. The term becomes "*venous sinus surgery*" instead of original enquiry of "*nasal sinus surgery*"
Q28 / Q28	Ear disease or surgery, hearing loss....	Failure to include "*ear surgery*" in the translation

Concerning the same organ system, there are questions of a general nature, and also enquiries on specific conditions. For example, comparing the answers to question 4 ("*Asthma, or wheezing...*") and question 7 ("*Any form of lung disease*"), a significant number of respondents who replied positively to question 4 did not think they had lung disease. The isolated specific disease entities inquiry seemed useful.

Validity of the translation version

Comparison of the 2007 RSTC English version with the 2001 and 2012 RSTC Chinese version shows that some questions in the Chinese and English version are significantly different in terms of the meaning and question details. Discrepancies identified are presented in Table 4.

It would be preferable to have a translated version with the same meaning yet in simple, understandable and legally acceptable expressions and presentation. The use of illustrations in addition to a 'word for word' translation may be useful. This is done for one question (question 34) in the Chinese version. The term colostomy is followed by the explanatory note: "*artificial anus*". The inconsistencies with the original intended questionnaire design will impact negatively on the construct validity of the translated version of the questionnaire. The sub-optimal and incorrect translations could result in potentially high-risk divers being missed.

Implementation of the questionnaire screening

Details of the local implementation of the RSTC form need future research.

All trainee divers are required to submit a medical screening questionnaire. According to the recreational diving safety manual (page 73) promulgated by the Hong Kong Underwater Association, all entry level scuba divers are recommended to pass a pre-dive diving medical examination by a licensed physician.[17] This is not a mandatory step and is therefore unlikely to be implemented in practice.

It is assumed that participants receive questionnaires with adequate time to grasp questions and respond appropriately before the practical sessions. Individuals are expected to complete the documents on their own without input from medical professionals. In this study, 15.4% of respondents found difficulties in understanding some expressions in the questionnaire (Table 3).

Participants are supposed to answer "*yes*" if they are not sure about a question. However, we cannot assume this

occurs. For example, with question 27 ("*Sinus surgery*"), 100% of respondents gave a negative answer to the unknown condition (incorrect Chinese translation). People reacted simply by ignoring the unfamiliar conditions being asked and giving "*no*" as the answer.

There is currently no requirement for recreational divers to undergo regular medical screening in order to keep diving certification validated. The diver will be required to complete the health screening questionnaire again only upon enrollment in another new certification course. Medical clearance is mandatory, according to PADI, if the participant has any significant medical problem during the dive course. The lack of longitudinal surveillance of the divers' health status is alarming. Cardiovascular risk of individuals increases with age. People may not be aware of these potential problems when they are allowed to dive with the diving certification card they obtained when they were younger.[26]

User attitude

New scuba divers may have problems in completing the questionnaire on their own as discussed above. People are told to review any questions regarding the medical statement or the medical questionnaire section with their instructor before signing. Yet, it is stressed that the scuba instructor is not a medical expert.[4,5] It may be useful to explore the attitude of the questionnaire providers (for example dive shops and diving instructors) in future studies. This may help to improve the way the RSTC form is used.

Reliability of self-declaration answers

The false positive and false negative answers were minimal except for questions 5 and 7. Most admitted to carelessness, or uncertainty about the wording of the questions. Yet the study also suggested that respondents were willing to reply honestly to the questions. Further research may help to elicit whether or not pre-participation divers are inclined to conceal their medical history in order to pass the screening. The questionnaire should not be perceived as a barrier to participating in recreational diving. Honesty may be promoted if people understand that the questionnaire screening is not used to disqualify people from participation. It is used to identify someone that may benefit from having a formal medical assessment. People with significantly high risk will be advised against scuba diving for the safety of themselves and others.

Handling of completed questionnaires

This study did not examine the follow-up proceedings with the completed questionnaires. Diving instructors are expected to check the medical screening form and suggest physician consultation for potential medical clearance when it is indicated.[4,5]

The uniqueness of diving medicine and the lack of training opportunities in Hong Kong means that the number of well-trained medical professionals will remain inadequate for the foreseeable future. This barrier in having an appropriate fitness-to-dive assessment should not be underestimated. The RSTC form provides guidance to physicians (Guidelines for recreational scuba diver's physical examination).[3,6] The majority of doctors in Hong Kong are trained with English as the language in their professional career. It is uncertain whether someone who completes the Chinese version of the questionnaire will go to a doctor with the English version guideline as reference for the doctor.

It is also known that opinions of diving doctors (with postgraduate training on diving medicine) and general practitioners may not be consistent regarding fitness-to-dive.[27]

LOCAL CIRCUMSTANCES WITH THE USE OF RSTC FORM

The diving mortality of Hong Kong divers was not reported to be higher compared to other places despite the use of the Chinese RSTC form with its intrinsic problems.[25] This may be explained by the high standard of the local recreational diving operations. Most local scuba diving operations are non-decompression stop seawater dives with maximum depth of 10 meters or less in environments with no overhead hazards. This mode of recreational diving might change with time, subsequently leading to an alteration in health risks of participants.

Nonetheless, some individuals are happy to take high risks and some people continue to participate in scuba diving despite medical contraindications.[28] Risk appreciation by these individuals should only be assumed if adequate understanding and guidance is secured beforehand. The screening questionnaire by default should be one cornerstone to help all stakeholders to gauge and communicate about the acceptance of risk.

BIAS OF THE STUDY

There is selection bias by involving only clinic attendants. The age criteria excluded all youngsters who could be potential scuba divers. Further research that focuses on junior divers is needed. The collected data relied heavily on the recall of the study participants and history taking skill of the researcher. Although the researcher tried to explore relevant medical history, observational bias was unavoidably introduced without objective investigations or tools used.

IMPLICATIONS FOR THE 2020 NEW FORM

The recreational diving medical screening questionnaire has been substantially revised and a new version has been published since June 2020.[29] The new version retains most

of the enquires of the previous versions but the presentation and the questionnaire format are markedly modified. It is expected that the local diving community will move to use the new form in coming time especially after the COVID-19 pandemic. Based on the identified problems in this study, the authors plan to have ongoing reassessment of the updated version in a similar manner. Investigations of different non-English versions may help to clarify the situation.

Conclusions

Pre-participation health screening of recreational scuba divers is considered a useful risk management tool. Screening with questionnaires is still a practical and acceptable method. However, it should be noted that the assumptions leading to meaningful screening by self-declaration questionnaire may not be met. There are problems with the construction validity and translation of the RSTC form's Chinese version. Further updating of the RSTC form will likely improve its credibility. However, problems related to language translation of the form need special attention. The new 2020 version will likely face similar challenges. At the same time, the recreational diving community should be informed about the non-prescriptive approach of health assessment for recreational divers. Further research on the attitude of related parties towards the medical questionnaire can help to improve the implementation of the screening strategy in the future.

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Sinus barotrauma in diving

Oskari H Lindfors[1], Anne K Räisänen-Sokolowski[2,3], Jari Suvilehto[4], Saku T Sinkkonen[1]

[1] *Department of Otorhinolaryngology – Head and Neck Surgery, Head and Neck Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland*
[2] *Department of Pathology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland*
[3] *Centre for Military Medicine, Finnish Defence Forces, Helsinki, Finland*
[4] *Mehiläinen Oy, Helsinki, Finland*

Corresponding author: *Dr Oskari H Lindfors, Department of Otorhinolaryngology – Head and Neck Surgery, Head and Neck Center, Helsinki University Hospital, P.O.Box 263, FI-00029 HUH, Helsinki, Finland*
oskari.lindfors@helsinki.fi

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Abstract
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Introduction: Sinus barotrauma is a common occurrence in diving and subaquatic medicine, potentially compromising dive safety. To gain a more thorough understanding of the condition, an in-depth investigation is justified.
Methods: This was a survey study. An anonymous, electronic questionnaire was distributed to 7,060 recipients: professional divers of the Finnish Border Guard, the Finnish Rescue Services, and the Finnish Heritage agency, as well as recreational divers registered as members of the Finnish Divers' Association reachable by email (roughly two-thirds of all members and recreational divers in Finland). Primary outcomes were self-reported prevalence, clinical characteristics, and health effects of sinus barotrauma while diving. Secondary outcomes were adjusted odds ratios (OR) for frequency of sinus barotrauma with respect to possible risk factors.
Results: In total, 1,881 respondents participated in the study (response rate 27%). A total of 49% of the respondents had experienced sinus barotrauma while diving and of those affected, 32% had used medications to alleviate their symptoms. The factors associated with sinus barotrauma were pollen allergies (OR 1.59; 95% CI 1.10–2.29), regular smoking (OR 2.04; 95% CI 1.07–3.91) and a high number of upper respiratory tract infections per year (≥ 3 vs. < 3 infections per year: OR 2.76; 95% CI 1.79–4.24).
Conclusions: Sinus barotrauma is the second most common condition encountered in diving medicine, having affected 49% of the respondents. Possible risk factors include allergies to pollen, regular smoking, and a high number of URTIs per year.

Introduction

Sinus barotrauma while diving is considered to be the consequence of insufficient paranasal sinus ventilation during ambient pressure changes, when either ascending or descending on a dive, or when diving in a multilevel environment. The sinuses most often affected are considered to be the frontal and maxillary sinuses, while involvement of the sphenoid and ethmoid sinuses is thought to be less common.[1–4] Symptoms include pain and pressure sensations in the corresponding facial regions, headache in the corresponding cranial regions, and sometimes epistaxis.[1,3–8] Rare complications include vision loss,[9–12] orbital wall fractures with subcutaneous/periorbital emphysema,[13–16] and pneumocephalus.[17,18]

Prevalence estimations vary. Numbers as low as < 0.1% have been reported in hyperbaric pressure chamber tests of Taiwanese navy recruits,[19] while up to 7% of Swiss professional divers and caisson workers have reported sinus barotrauma symptoms in their respective working environments.[20] Conversely, in the case of less experienced, recreational divers, larger numbers between 17–26% have been reported.[21,22] Sinus barotrauma is widely considered the second most common condition in all diving and subaquatic medicine, second only to barotrauma of the ears.[1,23]

Considering the large amount of recreational diving, the relative commonness of sinus barotraumas and the potential hazards they pose in a subaquatic environment, an in-depth look at the issue is definitely warranted. To this end, the primary objective of this study was to determine the frequency, clinical characteristics, and the short-term health effects of sinus barotrauma while diving. The secondary goal was to elucidate possible risk factors, the tertiary goal to find out whether repeated exposure to barometric stress might lead to an increase in sinus barotrauma during one's diving career. The study in question was carried out in conjunction with a similar study on middle ear barotrauma in diving, published previously.[24]

Methods

ETHICAL CONSIDERATIONS

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa (§6164/HUS/2508/2018).

STUDY DESIGN

Previous literature describing questionnaires on sinus barotrauma while diving was reviewed. None of the published questionnaires were directly applicable to the objectives of the study, so a new questionnaire was developed by the research group, utilising previous literature.

The questionnaire consisted of 20–52 questions (depending on answers) designed to examine the respondents' diving and medical histories and frequency of sinus barotrauma while diving. Furthermore, the respondents were asked about possible pressure-chamber testing, clinical characteristics and their need for medications and otorhinolaryngology-related (ORL-related) surgical procedures due to sinus barotrauma. The English translation of the questionnaire is presented in Appendix 1*.

The questionnaire was electronically sent via email to 7,060 recipients: professional divers of the Finnish Border Guard, the Finnish Rescue Services, and the Finnish Heritage Agency, as well as recreational divers registered as members of the Finnish Divers' Association reachable by email (roughly two-thirds of all members and all recreational divers in Finland). Data acquisition was carried out between November 2018 and September 2019, consisting of the primary email and repeated reminder emails at approximately 1–2 month intervals. Full details of data acquisition are presented in Appendix 2*.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS Statistics for Windows, version 25.0, released 2017 (IBM Corp, Armonk, NY, USA). A two-tailed *P*-value of < 0.05 was interpreted to indicate statistical significance.

Descriptive statistics are presented as numbers and percentages for categorical variables and as medians and interquartile ranges (IQR) for continuous variables. Categorical data were analysed using Fisher's exact test (two-tailed) or where appropriate, the Chi-Square test. Continuous variables were analysed using the Mann-Whitney U test or the Kruskal-Wallis test as appropriate. The Bonferroni correction was applied to account for multiple comparisons.

Multivariable binary logistic regression analyses were performed to identify factors associated with sinus barotrauma while diving. Variables included in the models were sex, number of diving years, age, body mass index (BMI), pollen allergies, smoking and the number of upper respiratory tract infections (URTI) per year. The results are presented as adjusted odds ratios (OR) with 95% confidence intervals (CI). The frequency of sinus barotrauma was dichotomized at two different cut-off points: between "*never*" and at least "*sporadically*" suffering from sinus barotrauma during one's life; and between suffering from sinus barotrauma only "*sporadically*" and at least "*occasionally*". These two separate cut-off points were chosen to gain a better overall understanding of factors associated with the condition.

Results

OVERVIEW OF THE STUDY SAMPLE AND SINUS BAROTRAUMA WHILE DIVING

The survey achieved a final response rate of 26.6% (1,881 responses from 7,060 invitations). Details of the study sample and the frequency of sinus barotrauma while diving is presented in Table 1.

In total, males made up a majority of the study sample, comprising 79.8% of the respondents. A quarter (23.2%) of the respondents were professional divers, the other three quarters (76.8%) being recreational. Most respondents reported being scuba divers (91.9%), some reporting technical diving (18.3%) and some free diving (15.6%) as their respective diving types. Median (IQR) age was 43 (35–52) years, 44 (36–53) in males and 41 (33–50) in females. Further characteristics of the study sample are presented in Table 1.

Previous ORL-related surgical procedures had been carried out to 37.0% of the respondents, the most common being adenoidectomy (26.2%), myringotomy (10.5%), tympanostomy (4.9%) and functional endoscopic sinus surgery (4.5%). Septoplasties, which were reported by 3.2% of the respondents, were more common in males than females (3.9% vs. 0.5%, respectively). Of the respondents, 16.6% reported zero URTIs per year, another 50.9% one URTI per year, a further 22.5% two URTIs per year, the final 9.9% three or more URTIs per year.

Sinus barotrauma while diving had been experienced by 48.9% of the respondents. While 41.0% had experienced symptoms "*sporadically*", smaller proportions had experienced them "*occasionally*" (7.4%), "*almost always*" (0.4%) or "*always*" (0.1%) when diving.

Footnote: * Appendices 1–3 are available on DHM Journal's website: https://www.dhmjournal.com/index.php/journals?id=147

Table 1

Overview of the study sample. Categorical data presented as n (%) and continuous data presented as median (IQR). * Data missing in two cases. BET – balloon eustachian tuboplasty; BMI – body mass index; FESS – functional endoscopic sinus surgery; ORL – otorhinolaryngology; RFA – radiofrequency ablation; URTI – upper respiratory tract infection

Variable	All (*n* = 1,881)	Female (*n* = 380)	Male (*n* = 1,501)
Age (years)	43 (35–52)	41 (33–50)	44 (36–53)
Height (cm)	178 (172–183)	167 (163–171)	180 (175–184)
Weight (kg)	83 (74–91)	68 (62–75)	85 (78–94)
BMI ($kg \cdot m^{-2}$)	26 (24–28)	24 (22–27)	26 (25–28)
Diving (years)	10 (4–17)	6 (3–11)	10 (4–20)
Number of dives*	200 (80–550)	150 (50–400)	200 (100–600)
Diving type			
Professional	436 (23.2%)	30 (7.9%)	406 (27.0%)
Recreational	1,445 (76.8%)	350 (92.1%)	1,095 (73.0%)
Diving mode			
Free diving	293 (15.6%)	53 (13.9%)	240 (16.0%)
Scuba diving	1,728 (91.9%)	359 (94.5%)	1,369 (91.2%)
Technical diving	344 (18.3%)	46 (12.1%)	298 (19.9%)
Smoking			
Never	1,542 (82.0%)	318 (83.7%)	1,224 (81.5%)
Occasionally	242 (12.9%)	37 (9.7%)	205 (13.7%)
Regularly	97 (5.2%)	25 (6.6%)	72 (4.8%)
Allergies			
Any allergy	629 (33.4%)	157 (41.3%)	472 (31.4%)
Pollen	451 (24.0%)	96 (25.3%)	355 (23.7%)
Animal	226 (12.0%)	64 (16.8%)	162 (10.8%)
Food	151 (8.0%)	54 (14.2%)	97 (6.5%)
Other	99 (5.3%)	42 (11.1%)	57 (3.8%)
Surgical procedures (ORL-related)			
Any procedure	696 (37.0%)	127 (33.4%)	569 (37.9%)
Adenoidectomy	492 (26.2%)	93 (24.5%)	399 (26.6%)
Myringotomy	198 (10.5%)	43 (11.3%)	155 (10.3%)
Tympanostomy	93 (4.9%)	19 (5.0%)	74 (4.9%)
BET	14 (0.7%)	4 (1.1%)	10 (0.7%)
Myringoplasty	22 (1.2%)	2 (0.5%)	20 (1.3%)
FESS	84 (4.5%)	12 (3.2%)	72 (4.8%)
Septoplasty	60 (3.2%)	2 (0.5%)	58 (3.9%)
RFA (inf. turbinates)	16 (0.9%)	4 (1.1%)	12 (0.8%)
Cleft palate	2 (0.1%)	0 (0.0%)	2 (0.1%)
URTI per year			
0	313 (16.6%)	52 (13.7%)	261 (17.4%)
1	958 (50.9%)	193 (50.8%)	765 (51.0%)
2	424 (22.5%)	96 (25.3%)	328 (21.9%)
≥ 3	186 (9.9%)	39 (10.3%)	147 (9.8%)
Sinus barotrauma in diving			
Never	961 (51.1%)	205 (53.9%)	756 (50.4%)
Sporadically	772 (41.0%)	152 (40.0%)	620 (41.3%)
Occasionally	139 (7.4%)	22 (5.8%)	117 (7.8%)
Almost always	7 (0.4%)	1 (0.3%)	6 (0.4%)
Always	2 (0.1%)	0 (0.0%)	2 (0.1%)

Table 2
Multivariable logistic regression analyses of factors associated with sinus barotrauma while diving. An adjusted OR over 1 indicates an increase in the odds of experiencing sinus barotraumas while diving. BMI – body mass index; CI – confidence interval; OR – odds ratio; URTI – upper respiratory tract infection

Variable	Frequency of sinus barotrauma in diving	
	Never (n = 961) versus Sporadically, Occasionally Almost always, Always (n = 920)	Never, Sporadically (n = 1,733) versus Occasionally, Almost always, Always (n = 148)
	OR (95% CI)	**OR (95% CI)**
Age	0.97 (0.96–0.98)	0.98 (0.96–1.00)
Diving years	1.05 (1.04–1.07)	1.02 (1.00–1.05)
BMI	1.03 (1.00–1.05)	0.99 (0.95–1.04)
Sex		
Male	1.00	1.00
Female	1.02 (0.80–1.30)	0.68 (0.42–1.10)
Allergies (pollen)		
No	1.00	1.00
Yes	1.49 (1.19–1.86)	1.59 (1.10–2.29)
Smoking		
Never	1.00	1.00
Occasionally	1.07 (0.80–1.41)	1.04 (0.61–1.76)
Regularly	0.86 (0.56–1.32)	2.04 (1.07–3.91)
URTI per year		
< 3	1.00	1.00
≥ 3	1.70 (1.24–2.34)	2.76 (1.79–4.24)

FACTORS ASSOCIATED WITH THE FREQUENCY OF SINUS BAROTRAUMA

Factors associated with the frequency of sinus barotrauma while diving are presented in Table 2. The frequency of the symptoms was best explained by pollen allergies and the number of URTIs per year, smoking having a more moderate association to the symptoms. No correlation to age, number of diving years, body mass index (BMI) or sex was detected in the analysis.

Those with pollen allergies had an adjusted OR of 1.49 (95% CI 1.19–1.86) for experiencing sinus barotraumas at least "*sporadically*" and an OR of 1.59 (95% CI 1.10–2.29) for experiencing them at least "*occasionally*", compared with those without such allergies. Moreover, those with ≥ 3 URTIs per year had an adjusted OR of 1.70 (95% CI 1.24–2.34) for experiencing symptoms at least "*sporadically*" and an OR of 2.76 (95% CI 1.79–4.24) for experiencing them at least "*occasionally*", compared with those who reported having < 3 URTIs per year.

While no association between smoking habits and symptoms at least "*sporadically*" was detected, regular smokers did have an OR of 2.04 (95% CI 1.07–3.91) for experiencing symptoms at least "*occasionally*", compared with non-smokers.

CHARACTERISTICS OF SINUS BAROTRAUMA

Characteristics of sinus barotrauma and its circumstances are presented in Table 3. The table consists of questionnaire results from respondents affected by sinus barotrauma (n = 920) and is divided into two categories (n < 3 and n ≥ 3) based on the respondents' reported number of URTIs per year (as it was shown to be highly associated with the condition in Table 2).

Most respondents, 77.8%, had experienced sinus barotrauma symptoms 1–9 times, a further 13.6% 10–19 times and the final 8.6% 20 or more times while diving. The number of sinus barotrauma episodes increased as the number of URTIs per year increased (P = 0.042) and notably, a total of 72.0% of the respondents reported an URTI 100% of the times they had experienced sinus barotrauma while diving.

Sinus barotrauma symptoms were reported mainly when descending by 83.2% and mainly when ascending by 29.6% of the respondents. Symptoms predominantly manifested in relatively shallow depths, where relative volume changes in response to increasing pressure are the largest: in 41.0% of cases, the symptoms appeared at 0–4 metres of seawater (msw) and in another 40.1% at 5–9 msw. The final 18.9% reported symptoms at a depth of ≥ 10 msw.

Table 3

Characteristics of sinus barotrauma while diving and the effect of number of URTIs per year. * Data missing in 256 cases. Categorical data presented as n (%) and analysed using Fisher's exact (two-tailed). Subscripts $_a$ and $_b$ denote a subset of categories whose column proportions do not differ significantly from each other at the .05 level. msw – metres of sea water; URTI – upper respiratory tract infection

Variable	All (*n* = 920)	URTIs per year		*P*-value
		< 3 (*n* = 807)	≥ 3 (*n* = 113)	
Symptoms				
1–9 times	716 (77.8%)	633 (78.4%)	83 (73.5%)	0.042
10–19 times	125 (13.6%)	112 (13.9%)	13 (11.5%)	
≥ 20 times	79 (8.6%)	62 (7.7%)$_a$	17 (15.0%)$_b$	
% of symptomatic times related to URTI*				
100%	478 (72.0%)	409 (71.6%)	69 (74.2%)	0.657
51–99%	64 (9.6%)	54 (9.5%)	10 (10.8%)	
≤ 50%	122 (18.4%)	108 (18.9%)	14 (15.1%)	
Symptoms during dive				
Mainly ascending	272 (29.6%)	233 (28.9%)	39 (34.5%)	0.227
Mainly descending	765 (83.2%)	669 (82.9%)	96 (85.0%)	0.687
Symptoms manifested at:				
0–4 msw	377 (41.0%)	330 (40.9%)	47 (41.6%)	0.991
5–9 msw	369 (40.1%)	324 (40.1%)	45 (39.8%)	
≥ 10 msw	174 (18.9%)	153 (19.0%)	21 (18.6%)	
Symptoms manifested as:				
Pain (cheek area)	488 (53.0%)	428 (53.0%)	60 (53.1%)	1.000
Pain (forehead area)	667 (72.5%)	585 (72.5%)	82 (72.6%)	1.000
Epistaxis	177 (19.2%)	155 (19.2%)	22 (19.5%)	1.000
Other	36 (3.9%)	28 (3.5%)	8 (7.1%)	0.071
Symptoms lasted for:				
≤ 2 min	515 (56.0%)	457 (56.6%)	58 (51.3%)	0.415
≤ 2 hours	313 (34.0%)	273 (33.8%)	40 (35.4%)	
≤ 2 days	72 (7.8%)	59 (7.3%)	13 (11.5%)	
> 2 days	20 (2.2%)	18 (2.2%)	2 (1.8%)	
Symptoms before dive				
Yes	313 (34.0%)	259 (32.1%)	54 (47.8%)	0.001
No	607 (66.0%)	548 (67.9%)	59 (52.2%)	
Changing vulnerability over the years				
Less	359 (39.0%)	320 (39.7%)	39 (34.5%)	0.495
Same	523 (56.8%)	455 (56.4%)	68 (60.2%)	
More	38 (4.1%)	32 (4.0%)	6 (5.3%)	

Symptoms of sinus barotrauma were mainly pain in the frontal (72.5%) and maxillary (53.0%) sinus regions, epistaxis being less prevalent but still reported by 19.2% of the respondents, and more often reported by those with symptoms on ascent (31.0% vs. 15.3%, $P < 0.001$). Other symptoms (3.9%) mainly included pressure sensations of the frontal and maxillary regions, nasal discharge from the nasal cavity, and pain and sensory disturbances of the teeth.

The symptoms dissipated in ≤ 2 min in 56.0% of cases, in 2–120 min in 34.0% of cases and in 2 h–2 d in 7.8% of cases. The final 2.2% reported the symptoms lasting for > 2 d. Notably, symptoms lasting for > 2 h were more often reported by those with symptoms on ascent. A third (34.0%) reported symptoms of poor pressure equalisation preceding the incident dive.

Symptom development over the years was also examined. While more than half (56.8%) reported no change in the frequency of the symptoms in any direction, roughly a third (39.0%) reported currently experiencing less symptoms than previously during their diving careers. A marginal proportion, 4.1%, reported currently experiencing symptoms more often than previously.

Table 4

Health effects of sinus barotraumas while diving and the effect of number of URTIs per year. Categorical data presented as n (%) and analysed using Fisher's exact (two-tailed). FESS – functional endoscopic sinus surgery; RFA – radiofrequency ablation

Variable	All (n = 920)	URTI per year		P-value
		< 3 (n = 807)	≥ 3 (n = 113)	
All medication				
All	298 (32.4%)	255 (31.6%)	43 (38.1%)	0.197
All, last 12 months	157 (17.1%)	125 (15.5%)	32 (28.3%)	0.001
All, earlier	171 (18.6%)	156 (19.3%)	15 (13.3%)	0.155
Prescribed				
All	228 (24.8%)	190 (23.5%)	38 (33.6%)	0.027
Last 12 months	118 (12.8%)	91 (11.3%)	27 (23.9%)	< 0.001
Earlier	125 (13.6%)	112 (13.9%)	13 (11.5%)	0.560
Non-prescribed				
All	176 (19.1%)	152 (18.8%)	24 (21.2%)	0.525
Last 12 months	90 (9.8%)	71 (8.8%)	19 (16.8%)	0.011
Earlier	93 (10.1%)	86 (10.7%)	7 (6.2%)	0.181
Surgical procedures due to symptoms				
All	107 (11.6%)	85 (10.5%)	22 (19.5%)	0.011
Adenoidectomy	53 (5.8%)	43 (5.3%)	10 (8.8%)	0.133
FESS	47 (5.1%)	34 (4.2%)	13 (11.5%)	0.004
Septoplasty	20 (2.2%)	15 (1.9%)	5 (4.4%)	0.087
RFA (inferior turbinates)	10 (1.1%)	7 (0.9%)	3 (2.7%)	0.114

HEALTH EFFECTS OF SINUS BAROTRAUMAS

Health effects of sinus barotraumas are presented in Table 4. The table consists of questionnaire results from respondents affected by sinus barotrauma (n = 920) and is divided into two categories (n < 3 and n ≥ 3) based on the respondents' reported number of URTIs per year.

Medication due to sinus barotrauma had been used by 32.4% of the affected divers, 24.8% reporting the use of prescribed medications and 19.1% the use of non-prescribed ones. The use of medications was more frequent among those who reported having ≥ 3 URTIs per year, this applying to both non-prescribed (P = 0.011) and prescribed (P = 0.001) medications, as well as all medications together (P = 0.001). The medications used were mainly decongestants.

Surgical procedures due to sinus barotrauma had been undertaken by 11.6% of affected divers. Adenoidectomies had been performed on 5.8%, while 5.1% had undergone functional endoscopic sinus surgery (FESS), 2.2% had septoplasties, and 1.1% had radiofrequency ablation of inferior turbinates. Notably, those with ≥ 3 URTIs per year had undergone FESS significantly more often than those with < 3 URTIs per year (11.5% vs. 4.2%, P = 0.004).

Discussion

COMPARISON WITH PREVIOUS RESEARCH

In this study, the number of URTIs and pollen allergies were both associated with sinus barotrauma while diving. Although several case reports of recent URTIs leading to sinus barotrauma exist,[13,15] no publications with large sample sizes have documented the connection (as subjects with active URTIs are naturally excluded from studies). Despite this, URTIs are still widely considered to be a risk factor for sinus barotrauma while diving,[2–5,7,23] and the analogous connection between chronic rhinosinusitis and sinus barotrauma has been documented.[12,25] The connection to pollen allergies is not entirely new either. In one study, a history of sinusitis and/or allergic rhinitis was shown to be associated with sinus barotraumas while diving.[22] As patients with any active rhinologic pathology were (naturally) excluded from the study, no connection to active disease states could be detected.

Sinus barotrauma while diving had affected 48.9% of the respondents. While incidences of < 0.1% have been reported in Taiwanese navy recruits in pressure chamber measurements,[19] up to 7% of Swiss professional scuba divers reported having experienced such symptoms.[20] In

less experienced, recreational divers, 26% of diving course participants experienced one or more sinus barotrauma episodes during their training.[22] Considering that the present study examined the lifetime (to date) prevalence of sinus barotrauma, the numbers naturally surpass those reported above.

Symptoms most often appeared when descending rather than ascending (83.2% vs. 29.6%, respectively), in agreement with previous reports.[20,22] The symptoms that appeared when ascending tended to be more severe and sustained compared to those that appeared when descending; this might be partly explained by the fact that a dive can be discontinued if symptoms appear on descent, but not if they appear on ascent.

Moreover, symptoms appeared in relatively shallow waters (81.1% reported symptoms at < 10 msw) where the relative volume change in response to increasing pressure is the largest. To the best of our knowledge, no previous studies have reported on the depth at which the symptoms occurred, although general mentions of this do appear in the previous literature.

The symptoms most often manifested in the frontal regions as described previously,[1] with maxillary pain and epistaxis being less frequently reported. Although we failed to include simply "*headache*" as a symptom and could therefore risk overlooking the prevalence of sphenoid sinus barotraumas, only 3.9% reported having had "*other*" symptoms, and none of these were further specified as being headache-related. To the best of our knowledge, the duration of sinus barotrauma symptoms has not been previously reported in any large cohorts.

Finally, a total of 11.6% of symptomatic respondents reported undergoing ORL-related surgical procedures due to sinus barotrauma while diving. Whereas the other procedures could plausibly have been undertaken in response to sinus barotrauma, the reports of adenoidectomies most likely represent a misunderstanding by the respondents (as adenoidectomy is a paediatric procedure completely unrelated to sinus ventilation), and therefore, should be interpreted with caution.

STRENGTHS AND LIMITATIONS

The external validity of the results is certainly the study's largest limitation. As our study population did not consist of the entire target population (i.e., all recreational and professional divers in Finland) and our study sample was comprised of only 26.6% of the potential population, the results cannot be considered representative of all Finnish divers. However, as our study is (by far) the largest survey on sinus barotrauma to date, the results are, nevertheless, a valuable contribution to research on sinus disorders in diving.

Regarding internal validity, the data describing the frequency, characteristics and health effects of sinus barotrauma can be considered reliable. However, the results identifying possible risk factors are vulnerable to several biases, and multivariable logistic regression analyses were utilised to best minimise this effect. In our analysis, both a large number of URTIs and pollen allergies were associated with sinus barotraumas while diving; both of these hypotheses being further supported by applying the Bradford-Hill guidelines for observational data (see Appendix 3*).

The main strength of the study is its large size. In addition, another strength is the level of detail elicited by the questions: no previous studies have examined sinus barotrauma while diving in such an elaborate manner. Also, the anonymity of the questionnaire further strengthens the findings; with no possibility of identification, any motivation for dishonesty disappears when submitting one's response.

Other limitations include the use of patient-reported and hence completely subjective estimations of all collected data. This limitation could not be avoided as many of the outcomes investigated were in themselves subjective. Nevertheless, there is a possibility that some of the symptoms attributed to sinus barotrauma here were the result of other pathologies, such as barodontalgia, for example. Finally, given the 27% response rate, the possibility of a reporting bias among respondents cannot be excluded.

As sinus barotrauma while diving seems to be relatively common with no means to control the pressure equalisation to one's paranasal sinuses, the best preventive measure seems to be to abstain from diving when suffering from an URTI, or symptoms of active allergies. Future research should focus on further examining these possible risk factors, recognising others, and on developing the best possible treatment modalities to combat the issue.

Conclusion

Sinus barotrauma seems common in both recreational and professional divers, having affected, at some time or another, 48.9% of the 1,881 divers who responded. Symptoms most often involved the frontal and maxillary regions and appeared at relatively shallow depths. Sinus barotrauma was strongly associated with a high annual number of URTIs, allergies to pollen and possibly smoking. Future research should focus on verifying these findings and on recognising other factors potentially involved. Abstaining from diving seems essential when suffering from an URTI.

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Appendix 1. English translation of the questionnaire
Appendix 2. Details of data acquisition
Appendix 3. Application of the Bradford-Hill guidelines for observational data: sinus barotraumas while diving and the condition's possible risk factors

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Incidence of cardiac arrhythmias and left ventricular hypertrophy in recreational scuba divers

Peter Buzzacott[1,2], George Anderson[1,3], Frauke Tillmans[1], James W Grier[4], Petar J Denoble[1]

[1] *Divers Alert Network, Durham, North Carolina, USA*
[2] *Prehospital, Resuscitation and Emergency Care Research Unit, School of Nursing Curtin University, Western Australia*
[3] *Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA*
[4] *Department of Biological Sciences, North Dakota State University, Fargo, North Dakota, USA*

Corresponding author: *Dr Peter Buzzacott, Prehospital, Resuscitation and Emergency Care Research Unit, School of Nursing, Curtin University, Western Australia*
peter.buzzacott@curtin.edu.au

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Cardiovascular; Diving research; Echocardiography; Health status; Risk factors; Scuba; Sudden cardiac death

Abstract
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Introduction: The aims of this study were to investigate the potential impact of age, sex and body mass index (BMI) upon the incidence of arrhythmias pre- and post- diving, and to identify the prevalence of left ventricular hypertrophy (LVH) in older recreational divers.
Methods: Divers aged ≥ 40 years participating in group dive trips had ECG rhythm and echocardiograph recordings before and after diving. Arrhythmias were confirmed by an experienced human reader. LVH was identified by two-dimensional echocardiography. Weighted (0.5 fractional) values were used to account for participation by seven divers in 14 trips.
Results: Seventy-seven divers undertook 84 dive trips and recorded 677 dives. Among divers with no pre-trip arrhythmias (n = 55), we observed that 6.5 (12%) recorded post-trip arrhythmias and the median increase was 1.0 arrhythmia. In divers with pre-trip arrhythmias, 14.5 had a median of 1.0 fewer post-trip arrhythmias, 2.0 had no change and 5.5 had a median of 16.0 greater. Age, but neither sex nor BMI, was associated with change in the number of arrhythmias before and after dive trips (P = 0.02). The relative risk for experiencing a change in the frequency of arrhythmias after a diver trip, was 2.1 for each additional 10 years of age (95% CI 1.1, 4.0). Of the 60 divers with imaging of their heart, five had left ventricular hypertrophy.
Conclusions: We observed a higher than expected prevalence of arrhythmias. Divers with pre-trip arrhythmias tended to be older than divers without pre-trip arrhythmias (P = 0.02). The prevalence of LVH in our cohort was one quarter of that found post-mortem in scuba fatalities.

Introduction

Sudden cardiac death (SCD) is one of the most common causes of scuba fatalities, accounting for 20–30% of all cases.[1–3] SCD is an unexpected natural death from a cardiac cause within one hour of the onset of acute symptoms in a person with no prior acute condition that would appear fatal.[3] The most common suspected mechanism of SCD is acute arrhythmia triggering cardiac arrest, and the incidence of SCD increases with age, both in the general population and in scuba divers.[1,4] SCD is now more commonly suspected in recreational diving fatalities than even just two decades ago, and recreational diving fatalities also appear to be increasing with both age and body mass index (BMI).[5]

SCD is poorly understood, and there may be contributing factors associated with scuba diving. Known risk factors for SCD in the general population include a history of coronary heart disease, male sex, cigarette smoking, hypertension, diabetes mellitus, hypercholesterolaemia, obesity and left ventricular hypertrophy (LVH).[4,6–8] LVH is strongly associated with age, high systolic blood pressure and obesity.[6,9] Prevalence of LVH varies between populations. In Norway, for example, among 126 control subjects with no history of either inflammatory joint disease or cardiovascular disease, seven (6%) had LVH and 27 (21%) concentric left ventricular geometry (concentric LVH or concentric remodelling).[10] In 100 consecutive North American scuba diver autopsy reports, LVH was identified in 31% of the divers, whereas in a similar age-sex control group of autopsies from traffic fatalities in San Diego County that occurred over the same period (2007–11), prevalence of LVH was 20% (P = 0.042).[11]

Compared with movement on land, movement underwater exacts additional demand for oxygen and, consequently, both

stroke volume and heart rate increase.[12,13] This occurs while immersion itself causes blood shift from the cardiovascular periphery to the thoracic cavity, placing further stress on the cardiovascular system.[14] These stresses may alter the incidence of arrhythmias in divers and could subsequently be provoking factors for SCD. An earlier study showed arrhythmias in young scuba divers.[15]

The aims of this study were to investigate the potential impact of age, sex and BMI on the incidence of arrhythmias pre- and post-diving, and identify the prevalence of LVH in older recreational divers.

Methods

Prior to the study commencing, human research ethics approval was obtained from the Divers Alert Network Institutional Review Board. Divers aged ≥ 40 years participating in group dive trips were recruited and signed informed consent was obtained. A medical history questionnaire was completed and divers with medical contraindications for diving were excluded from further participation. The study involved six dive trips over seven years (2013–2019).

Prior to dive trips, each subject's blood pressure was recorded in both arms using either a mechanical manometer and stethoscope or an electronic blood pressure monitor (model BP761N, Omron Healthcare Co. Ltd, Muko, Kyoto, Japan) and averaged. Before and after dive trips, a 12-lead electrocardiogram (ECG) and rhythm recordings for either 300 or 360 seconds, depending on the PC-based system used (PC ECG, Midmark IQecg or IMED Cardiax) and echocardiographic measurements were collected (General Electric Vingmed Ultrasound).

Divers rested in a supine position for a few minutes until heart rates stabilised. Then baseline conventional 10 second 12-lead ECGs plus the 5–6 minute rhythm recordings were conducted. Arrhythmias were identified by the various ECG systems' automated interpretation software and confirmed or corrected by an experienced human reader (JG), then categorised by type and frequencies of arrhythmias counted. Arrhythmias were classified as premature ventricular contraction (PVC), premature atrial contraction (PAC) or 'other' (other premature ectopic beats including the less-common premature junctional contraction (PJC) and some with ambiguous origins). They were scaled to a 300 second standard and summed to give a total number pre- and post-dive trip. The numbers of arrhythmias mentioned further in this article are the total numbers of PVC, PAC or 'other' per five minutes ECG recording time. Left ventricular hypertrophy (LVH) was identified by echocardiography.

The M-mode study was performed under two-dimensional control using commercially available Vivid Q-7 (GE Healthcare, Chicago, USA). End-diastolic and end systolic measurements were taken by an experienced technician with the patient in partial left lateral decubitus according to the American Society of Echocardiography recommendations.[16] Frames with optimal visualisation of interfaces and showing simultaneous visualisation of septum, left ventricular internal diameter (LVID) and posterior wall were used for reading. Measurements were made on the screen using callipers. A long-axis parasternal approach was first examined to check perpendicularity of the ultrasonic beam with respect to the septum. Then, the short-axis approach was used to take left ventricle (LV) diastolic and systolic measurements (the average of three consecutive cycles on the best single reading set was considered). The LV mass (LVM) was calculated using Equation 1.[17]

$$LVM\ (g) = 0.80 \times (1.04 \times [(\text{septal thickness} + \text{LVID diastolic} + \text{posterior wall thickness})^3 - (\text{LVID diastolic})^3]) + 0.6 \quad \text{(Eq. 1)}$$

Left ventricular mass index (LVMI) was calculated by dividing LVM by body surface area (BSA) which was calculated using equations 2 and 3 (where W = weight in kg and H = height in cm).[18]

$$\text{Women BSA} = 0.000975482 \times W^{0.46} \times H^{1.08} \quad \text{(Eq. 2)}$$

$$\text{Men BSA} = 0.000579479 \times W^{0.38} \times H^{1.24} \quad \text{(Eq. 3)}$$

The relative wall thickness (RWT) was calculated using equation 4.[19]

$$RWT = (2 \times \text{posterior wall thickness}) / \text{LVID diastolic} \quad \text{(Eq. 4)}$$

LVH was established based on published LVMI cut-off values.[20] Male subjects with LVMI ≥ 125g·m^{-2} were classified as LVH and female subjects with LVMI ≥ 110 g·m^{-2} were classified as LVH. Geometry of LVH was classified according to published threshold values.[21] Subjects with No LVH and an RWT < 0.43 were classified as normal (N). Subjects with no LVH and an RWT ≥ 0.43 were classified as exhibiting concentric remodelling (CR). Subjects with LVH and an RWT < 0.43 were classified as eccentric hypertrophy (EH). Subjects with LVH and an RWT ≥ 0.43 were classified as concentric hypertrophy (CH).
Table 1 displays these classifications.

Sensus Ultra dive loggers (Reefnet, Mississauga, Canada) were worn by most of the divers (n = 59 of 84 diver-trips, 70%) with a default sampling rate of one record per 10 seconds. These loggers recorded dive duration, water temperature and estimated depth based on recorded water pressure. Water temperature and dive depths were weighted by dive duration to calculate overall means. All dives were made with open-circuit equipment using compressed air or nitrox.

Table 1

Classification table showing left ventricular mass index (LVMI) cut off values used to establish left ventricular hypertrophy (LVH), and relative wall thickness (RWT) cut off values to define left ventricular geometry. CH – concentric hypertrophy; CR – concentric remodeling; EH – eccentric hypertrophy; LVH – left ventricular hypertrophy; LVMI – left ventricular mass index; N – normal

Parameter	Subject sex	Threshold $g \cdot m^{-2}$	Classification	RWT	
				< 0.43	≥ 0.43
LVMI	male	≥ 125	LVH	EH	CH
		< 125	No LVH	N	CR
	female	≥ 110	LVH	EH	CH
		< 110	No LVH	N	CR

Data were stored in MS® Excel and imported into SAS (SAS, Cary, NC) version 9.4 for analysis. Skewness and kurtosis were measured for quantitative variables (e.g., age and BMI), histograms were plotted and normality was tested using the Shapiro-Wilk test. Means and standard deviations are reported for quantitative variables with Gaussian distributions, and medians with interquartile ranges (IQR) for non-parametrically distributed data. Range is reported in place of IQR when $n < 4$.

Differences between the number of pre-dive and post-dive arrhythmias (dA) were classed as less, none, or more. For regression analysis, data from the 14 dive trips made by seven divers who attended two dive trips each were given a weighting of 0.5 and the other 70 single dive trip participants were given a weighting of 1.0. The weighted ternary outcomes (dA`) were tested for association with age, sex and BMI in a weighted multivariate logistic regression model, stratified by dive trip (Trip). The model was optimised by backwards elimination according to the hierarchical principle, with non-significant interactions removed first. Significance was accepted at $P < 0.05$. The initial model is shown in Equation 5.

$$\mathrm{Ln}[P(dA`_i)/[1 - P(dA`_i)]] = \alpha_j + \beta_1 Sex_i + \beta_2 Age_i + \beta_3 BMI_i + \beta_4 Sex_i * Age_i + \beta_5 BMI_i * Age_i + \beta_6 Sex_i * BMI_i + \beta_7 Sex_i * Age_i * BMI_i + \beta_8 Trip_i \quad \text{(Eq. 5)}$$

Where α_i = the intercept for outcome j, $\beta_{1\text{-}8}$ are the respective estimates for each independent variable for each participant i, Sex = male (0) or female (1), Age is in whole years, BMI is in $kg.m^{-2}$ and Trip is the individual group dive trip (1–6). Deviance and Pearson Goodness of Fit Tests were performed to assess if expected outcomes significantly differed from observed outcomes. $P \leq 0.05$ was accepted as significant when deciding whether to reject the null hypothesis that there was no association between an ordinal increase in the number of arrhythmias between pre- and post-dive trip ECG recordings and either age, sex or BMI.

To test if any change in arrhythmias was associated with divers who recorded pre-dive arrhythmias, a binary outcome variable (Change, 0 or 1) was fitted to the optimised model described above. A Wilcoxon signed-rank test was used to assess differences in number of post-trip arrhythmias, among divers who had recorded pre-trip arrhythmias.

Because the study design was a prospective cohort study, not a case-control design, adjusted odds ratios (OR) generated by the logistic regression were converted to adjusted relative risks (RR) using Equation 6 and contingency Table 2. The 95% confidence intervals for the RR were calculated by substituting the respective OR for the 95% confidence interval OR generated by the regression. P_c is the unadjusted risk in the control group (pre-trip, where arrhythmias = no).

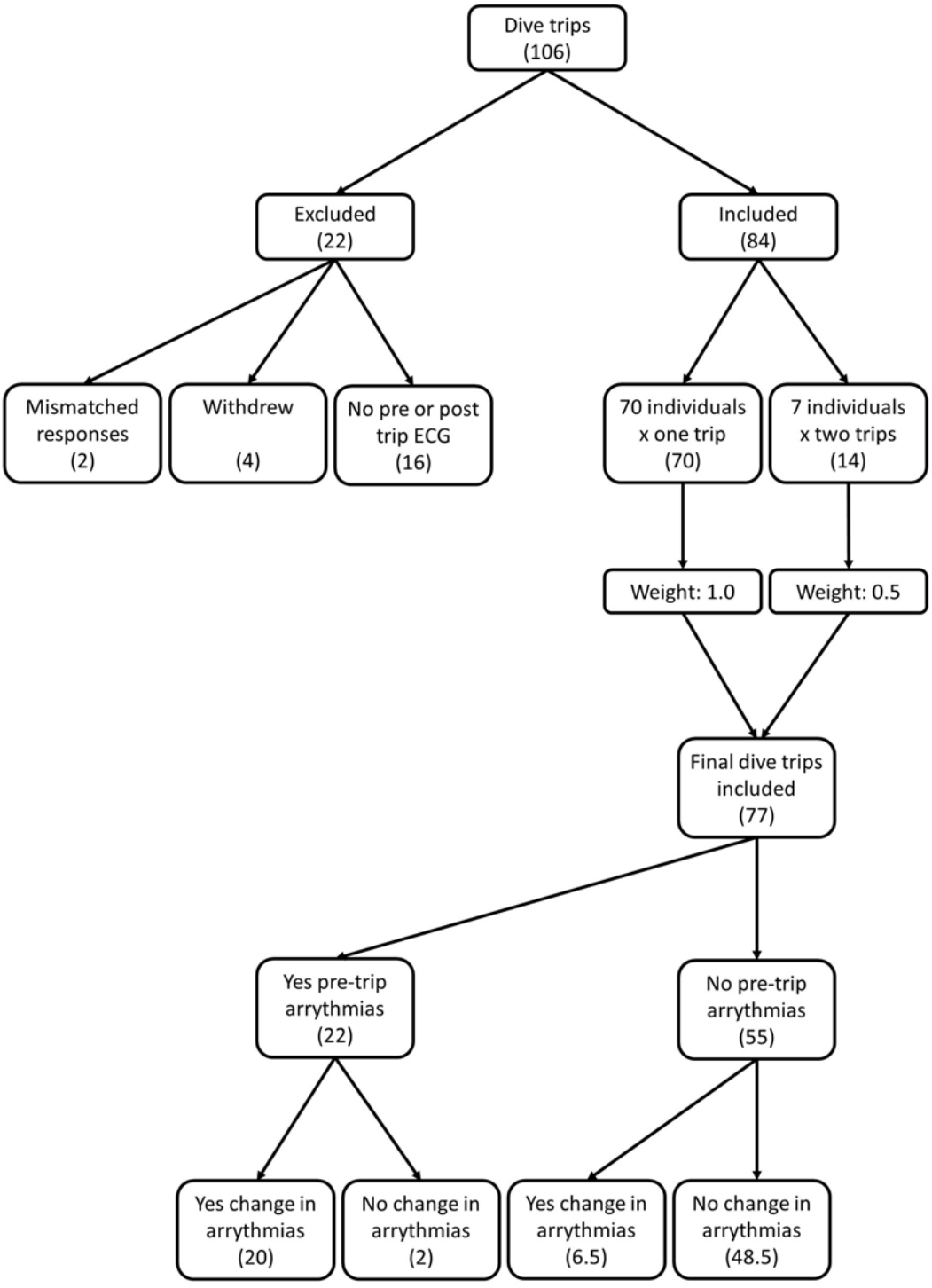
$$RR = \frac{OR}{(1-P_c)+(P_c.OR)} \quad \text{(Eq.6)}$$

Results

There were 106 diver trips recorded by eligible divers. Of those, 22 diver trips were excluded from the analysis, (after four withdrew, one diver gave mismatched responses on two separate trips and 16 had either pre-trip or post-trip ECG recorded, or neither, but not both). The final dataset for analysis consisted of 84 diver trips made by 77 individual divers (seven divers each made two trips). Dive loggers were worn during 59/84 diver trips (70%), recording a total of 677 dives (Figure 1), a mean of 11.5 dives per recorded diver trip (SD 9.2).

Mean age at the start of each trip was 53 (SD 9) years in females (n = 30, 36%) and 59 (9) years in males (n = 54, 64%). Mean body mass index (BMI) was 27 (4) $kg.m^{-2}$ in females and 29 (5) $kg.m^{-2}$ in males. Thirty divers (39%) reported being past smokers, having smoked for between 2–30 years, but only one diver reported being a current smoker. Sixty-seven (87%) self-reported consuming alcoholic drinks. Six divers (8%) reported a family history of heart disease, 26 (34%) had been diagnosed with high cholesterol of whom 16 (21%) were taking medication for it; 25 (32%) had been diagnosed with high blood pressure and 19 (25%) were prescribed blood pressure medication. Three subjects (4%) had a history of previous myocardial infarction and one of those subjects had undergone previous cardiac surgery. Two (3%) subjects reported a history of

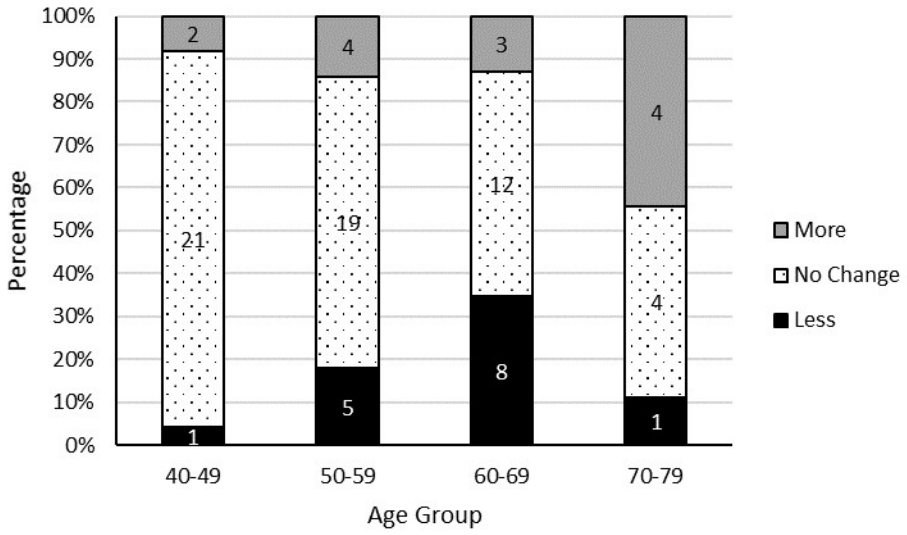
Figure 1
Selection process for inclusion of subjects and data



cardiomyopathy and two subjects (3%) reported exercise induced shortness of breath. A total of 39 (51%) reported currently taking any prescription medication. Mean blood pressure before diving trips was 129/82 mmHg. Mean heart rate prior to diving was 68 beats per minute (bpm) and post-diving it was 72 bpm.

With regards to diving experience, the divers reported a median lifetime experience of 300 dives (IQR 484), diving for a median of 20 years (IQR 29) and having made a median of 12 dives (IQR 27) during the previous six months. The median number of dives made during each trip was 11 (IQR 17), with a median total bottom time of 9 hours (IQR 17). Weighted mean depth was 8.6 metres of seawater

Figure 2
Changes in detected arrhythmias between pre- and post-dive trips, by age group, with *n* labelled



(msw) (SD 4.1), median maximum depth 23 msw (IQR 25) and weighted mean water temperature 21°C (SD 8, range 8–28°C). Median maximum ascent rate during each trip was 9.7 m.min^{-1} (IQR 4.0).

Conventional 10 s 12-lead ECGs from the divers showed similar arrhythmias to the longer rhythm recordings for those divers who presented arrhythmias. The conventional 10 s 12-lead ECGs were otherwise predominantly normal. Only one of the many 12-lead ECGs was automatically interpreted as LVH by machine algorithm, confirmed by the human reader (JG).

Fitting the data to the model shown in Equation 5, the initially optimised model following backwards elimination is shown in Equation 7, (without coefficients).

$$\mathrm{Ln}[P(dA`_i)/[1-P(dA`_i)]] = \alpha_j + \beta_2 Age_i + \beta_8 Trip_i \quad \text{(Eq. 7)}$$

After adjusting for stratification of the data by dive trip, age (but neither sex nor BMI) was associated with change in the number of arrhythmias recorded before and after dive trips (R^2 = 0.27, P = 0.021). Differences between pre- and post-dive trips in the number of arrhythmias detected over 5 min are shown by age group in Figure 2.

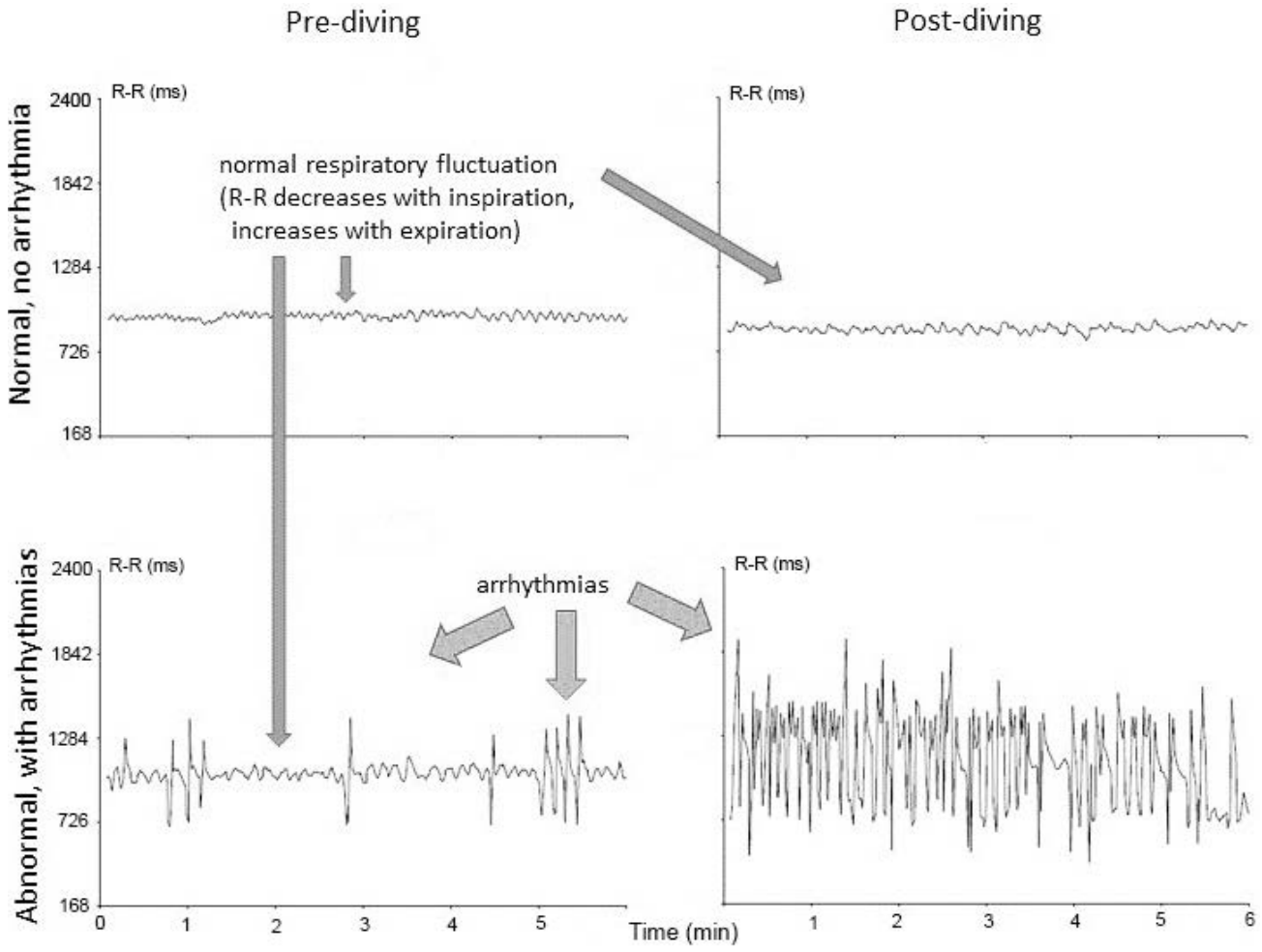
There were 23 diver trips made by 22 divers where the diver recorded arrhythmias before the diving commenced (Table 2). Of the 22 divers with pre-trip arrhythmias, 10 showed single PVCs (median 2, IQR 2) , eight showed single PACs (median 3, IQR 20.5), and nine showed "*other*" (unspecified) arrhythmias. These were the only divers who were able to record fewer arrhythmias after their dive trips, since the others each had no pre-trip arrhythmias, (and one cannot have fewer than zero arrhythmias).

The median decrease in number of arrhythmias (among n = 14.5 divers who recorded fewer post-trip arrhythmias) was 1.0 (IQR 3.0) while the median post-trip increase in arrhythmias among divers (n = 5.5) who had recorded pre-trip arrhythmias was 16.0 (IQR 17.0, P = 0.0003). Figure 3 illustrates exemplar pre- and post- diving beat-to-beat ECG recordings both for a diver without pre-trip arrhythmias and a diver with pre-trip arrhythmias. Among divers with no pre-trip arrhythmias (n = 55), we observed that 6.5 (12%) recorded post-trip arrhythmias and the median increase was 1.0 (IQR 7.0). Of the 55 divers without pre-dive arrhythmias, 6.5 showed arrhythmias post-dive, namely 3 PVCs (median 1, range 26), 2 PACs (median 3, range 4) and 3 'other' (unspecified). Of the 22 divers with arrhythmias pre-dive, 14.5 had less arrhythmias post-dive: 4 PVCs (median 1.5, IQR 9.5); 3 PACs (median 1, range 87); 2 "other" (unspecified); and 8.5 none. In contrast, 5.5 had

Table 2
Contingency table used to convert the adjusted OR into RR, (with weighting for number of trips), showing number of divers and number of dive trips

Divers		**Change in arrhythmias**		
		Yes	**No**	**Total**
Pre-Trip Arrhythmias	Yes	20	2	22
	No	6.5	48.5	55
	Total	26.5	50.5	77
Diver trips		**Change in arrhythmias**		
		Yes	**No**	**Total**
Pre-Trip Arrhythmias	Yes	21	2	23
	No	7	54	61
	Total	28	56	84

Figure 3
Examples of beat-to-beat (R-R) interval (milliseconds [ms]) trends of divers before versus after dive trips, 360 sec (6 min) recordings



more arrhythmias: 2 PVCs (median 29, range 56); 2 PACs (median 30.5, range 47); and 3 'other' (unspecified). In two divers, the number of arrhythmias pre- and post-dive was unchanged (both 'other' (unspecified)).

Of the 77 divers, $n = 14$ (18%) recorded PVCs and of those, six recorded a post-trip decrease in the number of PVCs, seven recorded an increase and one recorded the same number of post-trip PVC over 300 seconds as they did pre-trip. Using a prior diagnosis of high blood pressure as a simple proxy for cardiovascular risk, there was no significant difference in the prevalence of high blood pressure between those with increased arrhythmias (4/24) and those without (8/52).

In the penultimate analyses divers ($n = 48.5$) who had no arrhythmias either before or after dive trips ($n = 56$) were compared with divers ($n = 28.5$) in whom the number of arrhythmias either increased or decreased following dive trips, shown in Table 2. Hosmer and Lemeshow goodness of fit test Chi-square $P = 0.32$, $R^2 = 0.25$ and age was again associated with change in the number of arrhythmias recorded before and after dive trips ($P = 0.016$), (after adjusting for stratification by dive trip). Mean age among the 28.5 divers who recorded a change in the frequency of arrhythmias after their dive trips was 61.8 years (SD 8.2), a mean of 7.3 years older than the divers who experienced no arrhythmias either before or after diving. Compared with divers who recorded no arrhythmias either before or after dive trips, the OR for experiencing a change in the frequency of arrhythmias after a dive trip (either more, or less), was 2.7 for each additional 10 years of age (95% CI 1.2, 5.9), and 2.0 for each additional 7 years of age (95% CI 1.1, 3.5). Using Equation 2 and the values shown in Table 2, these ORs were converted to RR using Pc = (6.5/55). Compared with divers who recorded no arrhythmias either before or after dive trips, the RR for experiencing a change in the frequency of arrhythmias after a dive trip (either more, or less), was 2.1 for each additional 10 years of age (95% CI 1.1, 4.0), and 1.7 for each additional 7 years of age (95% CI 1.1, 2.7).

Finally, two-dimensional echocardiography imaging of the heart was available for 60 of the 77 (78%) divers. Of those, five divers (8%) had left ventricular hypertrophy identified and 36 (60%) had abnormal left ventricular geometry detected ($n = 33$, 55% with concentric remodelling and

n = 3, 5% with concentric hypertrophy). Of the 60 divers with heart imaging, 40 reported no history of high blood pressure and 20 reported a prior diagnosis of high blood pressure. Within those sub-groups, there were 2/40 (5%) and 3/20 (15%) with LVH respectively.

Discussion

In this prospective study, recreational divers who experienced a change in the frequency of recorded arrhythmias after a dive trip, compared with before the trip, were older by a mean of 7 years ($P = 0.021$). Furthermore, the RR for experiencing a change in the frequency of recorded arrhythmias associated with a mean of seven additional years of age was 1.7. The clinical significance of this observation is for now unclear, and warrants further investigation. Divers who recorded at least one pre-trip arrhythmia also appeared to record more freequent post-trip arrhythmias than divers who did not record a pre-trip arrhythmia (6/23 diver trips vs. 7/61 diver trips, median 16.0 more vs. 1.0 more respectively, $P = 0.0003$).

Arrhythmias were observed in 28.5 of 77 divers (37%). This likely represents a higher frequency than would be observed for the general public in this age group under comparable measurement conditions aside from diving. Lindberg et al.[22] found a much lower prevalence (13%) of arrhythmias in a large elderly population (mean age 74 y) in Sweden. A UK study of half a million community-dwelling middle-aged to elderly adults (mean age 58 y) found an even lower 2% prevalence of baseline abnormal rhythms.[23] Differences between study design and population samples may account, at least in part, for these lower prevalences than found in the present study.

The limitations of this study include that age is a confounder for arrhythmias, and the age of those with arrhythmias was older than the age of the divers without arrhythmias. Stratum-specific risk ratios for divers aged < 58 vs. ≥ 58 years might uncover the scale of any potential confounding by age but the sample size in this study is too small for that sub-analysis. Also, among the divers with pre-trip arrhythmias, it is not certain how much of an influence diving had on the observed changes, or if other factors played a greater role (exercise, alcohol consumption, etc). The sampled population was non-random (divers on pre-organised trips), almost entirely Caucasian from the USA, and may not represent recreational divers in this age group in general. There was wide variation among divers including age and other demographic characteristics, physical and medical conditions, diver histories, and recent diving activities. There was also wide variation among dive trips including depths of dives, water temperatures (and types of protective suit), lengths of trips (from one or two to seven days), and whether live-aboard or shore-based (all trips were in salt water). Furthermore, there was variation, evolution, and refinement over the seven-year period of this study in our methodology and protocols, including equipment used, technician experience, and such factors as elapsed time between the last dive of a trip and when post-diving recordings were made.

Some arrhythmias such as atrial fibrillation were suspected to have occurred in divers during these trips but, by chance, were not captured during our relatively brief periods of measurement. Longer (hours) and more frequent (including at night) periods of measurement, such as with Holter recorders or even long-recording heart rate monitors such as those commonly used by runners and cyclists, would greatly enhance the ability to detect arrhythmias which are highly variable and erratic in their occurrence. We recommend longer recordings in future studies.

Abnormal non-respiratory or non-phasic sinus arrhythmia (nrSA), as opposed to normal respiratory arrhythmia, occurred in several of the divers. Non-respiratory SA is an arrhythmia of interest and potential issue of concern for diving. However, it is quite variable; it is not well studied or understood; its frequency and measurable characteristics are affected by heart rate; and the definitive identification of nrSA is not well standardised and can be problematic in some cases. Furthermore, quantification of nrSA also is not standardised and is not compatible with counts of the other arrhythmias. Hence, we excluded nrSA from the present analyses.

A potential confounding factor in our study is exercise-induced arrhythmias, including structural differences of the heart in athletes vs. non-athletes who experience arrhythmias.[24] Our methods did not permit direct assessment of the exercise factor *per se*. However, swimming, breath-hold diving, scuba diving, and even simple face immersion have long been known associated with increased arrhythmias.[15,25,26]

Risks for mortality and morbidity from arrhythmias are highly variable and dependent on numerous factors including the kind of arrhythmia and an individual's associated heart conditions. Calculating the actual risks of PVCs leading to more serious problems including death have been problematic and appear to vary among populations.[27,28] The strengths of this study include the prospective cohort design, though further studies of a more controlled, less exploratory nature are warranted. In particular, the effect of diving upon the incidence of PVCs remains to be quantified. We have developed and refined protocols that could support such studies.

Of additional concern is the pre-hypertension mean blood pressure recorded before diving, that half the cohort were currently taking prescribed medication, and that most of the cohort (86%) reported regularly consuming alcohol. One third had been diagnosed with high blood pressure at some time and one quarter were currently taking medication for this. We also noted three times as many cases of LVH (15%) in the divers with high blood pressure, compared with 5%

LVH among divers with no history of high blood pressure, though the number of LVH overall (n = 5) was too small from which to draw firm inferences. Despite these concerns, these were apparently relatively active divers, having made a median of 12 dives during the previous six months.

Compared with a case-control study, the prevalence of LVH in the present study of active divers was 8%, similar to that observed in a Norwegian control group,[10] but far lower than the 31% detected in 100 consecutive recreational scuba diver autopsies.[11] This supports the concern that LVH may be an important contributor to diving fatalities. It may also prove important to clarify the relationship between LVH and changes in arrhythmias after dive trips. For the moment, the evidence for this potential association is limited and the role of this potential risk factor remains to be confirmed. It should be noted that our LVH data were derived from two-dimensional echocardiography imaging. Although we originally expected the conventional 12-lead ECGs to provide LVH data, that did not occur. Conventional 12-lead ECGs are, in fact, notoriously poor for interpreting LVH.[29,30] Advanced ECG and a new approach that considers left ventricular electrical remodelling have proven much better for detecting LVH and related conditions, and should be considered in future studies.[30]

Insights from this study and future research may help provide recommendations to divers and potential divers for participating in diving, particularly as they age, similar to recent recommendations for non-diving activities.[31]

Conclusions

Among this cohort of active, older recreational divers with pre-existing risk factors for SCD:
a) A higher than expected prevalence of arrhythmias was observed;
b) divers with pre-trip arrhythmias tended to be older than divers without pre-trip arrhythmias;
c) in the unweighted sample, one-in-nine divers (n = 7 out of 61) with no pre-trip arrhythmias recorded post-trip arrhythmias;
d) compared with pre-trip no-arrhythmia divers, divers with pre-trip arrhythmias showed increased post-trip arrhythmias, which was related to age, but not to BMI or sex;
e) compared with pre-trip no-arrhythmia divers, divers with pre-trip arrhythmias were at elevated risk for changes (up or down) in the frequency counts of arrhythmias over 300 seconds post-trip;
f) the prevalence of LVH in this cohort was one quarter of that found in 100 recreational scuba diving autopsies, suggesting the possibility LVH may be associated with increased risk of mortality while scuba diving; and
g) these results provide a step toward making recommendations to older and arrhythmia-prone persons for participating in scuba diving.

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Review article

Diving-related disorders in commercial breath-hold divers (Ama) of Japan

Kiyotaka Kohshi[1,2], Hideki Tamaki[2,3], Frédéric Lemaître[4,5], Yoshitaka Morimatsu[2], Petar J Denoble[6], Tatsuya Ishitake[2]

[1] *Division of Neurosurgery, Nishinihon Hospital, Kumamoto, Japan*
[2] *Department of Environmental Medicine, Kurume University School of Medicine, Kurume, Japan*
[3] *Division of Surgery and General Medicine, Tamaki Hospital, Yamaguchi, Japan*
[4] *Faculty of Sport Sciences, University of Rouen, Mont-Saint-Aignan, France*
[5] *CRIOBE USR 3278, CNRS-EPHE-UPVD, PSL, France*
[6] *Divers Alert Network, Durham NC, USA*

Corresponding author: *Dr Kiyotaka Kohshi, Division of Neurosurgery, Nishinihon Hospital, 3-20-1 Hattanda, Kumamoto-higashi, Kumamoto 861-8034, Japan*
kohshi33@gmail.com

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Breath-hold diving; Decompression illness; Diving profiles; Indigenous divers; Prevention; Stroke

Abstract

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Decompression illness (DCI) is well known in compressed-air diving but has been considered anecdotal in breath-hold divers. Nonetheless, reported cases and field studies of the Japanese Ama, commercial or professional breath-hold divers, support DCI as a clinical entity. Clinical characteristics of DCI in Ama divers mainly suggest neurological involvement, especially stroke-like cerebral events with sparing of the spinal cord. Female Ama divers achieving deep depths have rarely experienced a panic-like neurosis from anxiety disorders. Neuroradiological studies of Ama divers have shown symptomatic and/or asymptomatic ischaemic lesions situated in the basal ganglia, brainstem, and deep and superficial cerebral white matter, suggesting arterial insufficiency. The underlying mechanism(s) of brain damage in breath-hold diving remain to be elucidated; one of the plausible mechanisms is arterialization of venous nitrogen bubbles passing through right to left shunts in the heart or lungs. Although the treatment for DCI in Ama divers has not been specifically established, oxygen breathing should be given as soon as possible for injured divers. The strategy for prevention of diving-related disorders includes reducing extreme diving schedules, prolonging surface intervals and avoiding long periods of repetitive diving. This review discusses the clinical manifestations of diving-related disorders in Ama divers and the controversial mechanisms.

Introduction

Decompression illness (DCI), a collective term for the dysbaric diseases decompression sickness (DCS) (caused by bubbles formed from dissolved gas) and arterial gas embolism (AGE) (caused by bubbles introduced to the arterial circulation by pulmonary barotrauma), is well known in compressed-air divers or caisson workers; however, the existence of this condition among breath-hold divers has been disputed by scientists and medical professionals. Since the 1960s, when Cross published articles on 'taravana', a diving syndrome of breath-hold pearl divers of the French Polynesian archipelago of Tuamotu,[1] the occurrence of serious neurological disorders after repetitive breath-hold diving has been widely debated. Nonetheless, a few cases of Japanese commercial or professional breath-hold (Ama) divers afflicted with neurological diving accidents were seen in the 1990s.[2,3] Moreover, a survey conducted in a village of Japan showed that more than half of the Ama divers had experienced neurological events related to diving work.[4] Since Wong summarised the clinical symptoms associated with breath-hold diving,[5] this condition has become more widely recognised.[6,7] Reviews of the symptoms of DCI in breath-hold and compressed gas diving show many manifestations in common,[5,8,9] though some differences in typical presentations may be identified (see Diving-induced disorders). Our aim here is to provide a review of clinical characteristics of diving-related disorders in Ama divers based on our previous case series and field studies, discuss uncertainty about the mechanisms, and propose strategies that could help to treat and protect these divers.

Ama divers

The commercial or professional breath-hold divers of Japan and Korea have been in existence for more than 2,000 years. These divers are scientifically and collectively called Ama (sea women and men) since their diving work was first published by a Japanese scientist in 1932.[10] The origin of the Ama diving practice is not well known; one theory contends that this diving tradition originated from male Polynesian pearl divers. The breath-hold diving profession was essentially for men in warm areas and it was introduced to cold waters of Japan and Korea where the ocean floor is rich in shellfish.[11] Women in these areas may have started to engage diving activities because their physiques are better suited to overcome cold stress.[11] The number of male Ama divers increased because of the advent of wetsuits for thermal protection in 1960s.[12]

In Japan, Ama divers start their profession at the age of 15–16 years and continue working for more than 20 years.[11,12] Divers older than 60 years are not rare; most male divers are between 30 and 50 years, and females between 40 and 60 years old.[13] The Korean Ama divers included men as well as women up to the 17th century; however, nowadays all the divers are female.[11] About 11,000 Ama divers dwell in Japan according to a questionnaire survey compiled in 1986, and 80% of them were male.[13] These Ama divers harvest the ocean floor by gathering seaweed, abalone, and sea urchins daily.

There are two types of diving methods for Ama divers: Cachido divers dive unassisted without any aids; and Funado divers use weights for descending.[11] Funado divers are either pulled up by assistants (completely assisted) or swim up without assistance (partially assisted). Cachido divers generally dive to depths of 3–10 metres of seawater (msw), and the diving depths of Funado divers are deeper; occasionally over 30 msw. In general, Ama divers began to work as Cachido in shallow water, and then graduated to become Funado. One reason for this is a need to develop more rapid middle ear pressure equalisation during fast descending in Funado divers. Most Funado divers are male, while almost all female divers are Cachido.

Working practice

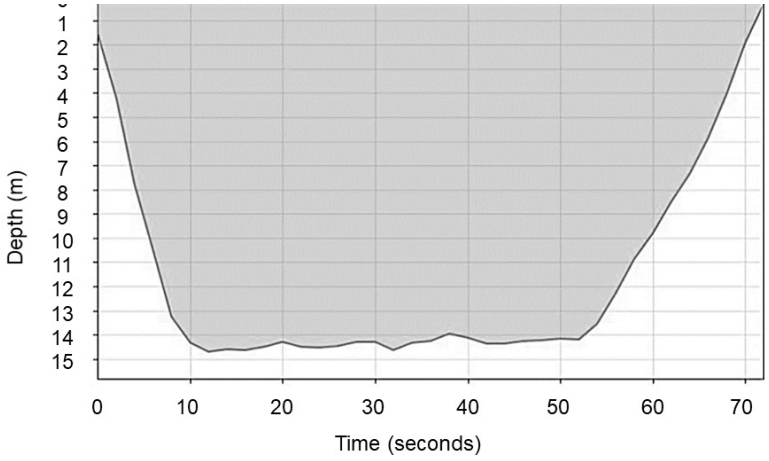
Traditionally, Ama divers were not equipped with any diving devices, except for their facemasks.[11] They wore traditional working clothing such as cotton bathing suits and loincloths. Ama divers make their dives using only light cotton suits mainly in the warm season, while Korean divers worked using only light cotton suits even in wintertime. Since wearing wetsuits has become popular among the fishery divers in Japan for more than half a century, longer-lasting and deep diving is possible even in winter. They wear wet suits and fins and carry weight belts to achieve neutral buoyancy (4–8 kg).

Cachido divers walk into the sea from the shore and swim to the diving grounds holding wooden tubs, and they swim unassisted up to 10 msw in depth from drifting tubs. In Cachido, swimming down and up requires significant energy. Funado dive from boats using iron weights (15–25 kg), and swim to the surface with or without assistance (Figure 1).

Figure 1

A male Funado dive photographed during breath-hold diving. His boat was equipped with a rolling machine to pull up his weight and a basket for seafoods (A). He descended to the floor using an iron weight (B), and swam to the surface without assistance (C)

Figure 2
Representative dive logger record showing the depth-time profiles of a single breath-hold dive



Their partners on the boats pull the weights and/or the Ama divers to the surface after each dive. Funado divers dive up to 30 msw and stay down longer owing to less exertion. Ama divers hyperventilate briefly during each surface interval and emit a pursed-lip whistle before descending. The divers take a couple of deep breaths, dive to the desired depth and stay 15–45 seconds at the bottom for harvesting (Figure 2). After the 30–120 second period of each dive, Ama make their next dive, typically after 30–60 seconds of surface rest, but occasionally up to 10 minutes or longer. Ama divers work 2–6 hours in the sea in one or two shifts per diving day; the duration of the morning shift is 2–4 hours and the afternoon shift is 1–2 hours, taking a lunch break of half an hour. Nowadays, diving depth is measured sonically using fish finders.

Ama divers use small cabins in their boats for frequent warming using propane stoves. After arriving at the diving locations, they stay in the cabin until they are warm enough to perspire. Another group of Ama divers who dive at shallow depths make fires to warm their bodies before and after each shift of dives, either on the beach or in cabins on the seashore.

There are marked differences in the harvesting time and days, and diving patterns and apparel in accordance with union rules. Local Japanese union rules in some areas do not allow the use of wetsuits in order to protect their natural resources from over-harvesting. Moreover, the divers are only allowed to work in specific harvesting seasons in all areas.

Diving-induced disorders

Our preliminary interview survey of 16 Funado divers showed that 13 of them had a history of diving accidents and that nine of them had experienced stroke-like neurological symptoms during or after more than 3 hours of repetitive dives.[4] In another study of Japanese Ama divers, 12 of 173 divers (11 of 29 Funado and only one of 144 Cachido, all male) had experienced stroke-like neurological events during or immediately after repetitive breath-hold diving (Table 1).[14] The most common symptoms were numbness in eight cases, dizziness in eight cases and motor weakness on one side (hemiplegia) in six cases. Other symptoms were speech disturbance, limb pain and visual disturbance. Dizziness was particularly common after continuous long-lasting dives in assisted Ama divers. Two of these 12 divers with neurological events also had severe musculoskeletal pain in the knee and limbs, but none of the divers had a skin rash. Many of the neurological disorders were transient and resolved completely in 10 divers. The other two had unresolved symptoms: one with a residual partial visual deficit and the other with sensory numbness of his hand. None of the divers experienced spinal cord disorders, which frequently occurs in compressed-air divers or workers.

Cross reported that out of 235 observed breath-hold pearl divers, 47 (20%) exhibited neurological symptoms known as 'taravana' diving syndrome at the end of 6 hours of diving per day during a three-week period in 1958 (Table 1).[1] The taravana syndrome included partial or complete paralysis in six divers, transient unconsciousness in three cases, mental disturbance and death in two cases, respectively. One of the divers undertaking 18 to 20 breath-hold dives to a depth of 40 msw in less than 2 hours, showed no life-threatening signs after diving work and during the return trip to the village. Another was pulled into the canoe in a semi-comatose state and died 2 hours later. Our case series have shown that Ama divers have experienced serious neurological manifestations which include unconsciousness, seizure, and/or brain stem involvement.[2,4,15,16] These serious neurological DCI events in Ama divers are consistent with the symptoms seen in taravana syndrome in Polynesian pearl divers.

Stroke-like brain involvement in DCI is common in Ama divers,[4,14] while spinal cord involvement, unlike in compressed-air divers and workers, is extremely rare. Typically, cerebral DCI manifests with unilateral sensory numbness or hemiplegia, disturbed speech, and/or visual deficit after repetitive dives exceeding 20 msw in depth executed over shifts longer than three hours.[2,3,15,16] Post-

Table 1
Diving events in Japanese Ama and Polynesian divers. Numbers in parentheses are numbers of cases

Diving group	Ama divers (11/29 assisted, 1/144 non-assisted) in 2009 [14]	Polynesian divers (47/235 assisted) in 1958 [1]
Symptoms (*n* cases)	Dizziness/vertigo/nausea (8) Sensory numbness (8) Hemiplegia (6) Speech disturbance (3) Limb pain (2) Visual disturbance (1)	Vertigo/nausea/mental anguish (34) Paralysis (6) Unconsciousness (3) Mentally affected (2) Death (2)
Dive profiles Mean (SD) or range	Dive depth (msw): 15.0 (3.3) Dive time (sec): 63.0 (16.4) Surface interval (sec): 26.0 (13.7) Length of diving shifts (hours): 5.5 (0.7) Rest time between shifts (min): 36.3 (15.5)	Dive depth (msw): 30–40 Dive time (sec): 90 Surface interval (min): 3–10 Length of diving shift (hours): 6

dive neurological events in Ama divers have often not been considered serious because symptoms resolved spontaneously within several hours or disappeared rapidly after hyperbaric therapy. However, in rare cases post-dive neurological events presented with altered level of consciousness or death.[1,4] One study has classified diving-related symptoms in breath-hold divers into two types; one is benign and quickly reversible, characterised by dizziness, vertigo, nausea, anxiety and fatigue, and the other is serious disease presenting with neurological and persistent disorders.[6] Ama divers experiencing neurological symptoms after repetitive dives require early diagnosis and treatment.

Another controversy is whether psychiatric disorders appear in breath-hold diving. Male Ama divers have reported no psychiatric disorders following diving work, although they may occasionally complain of anxiety during deep and long-lasting dives. In contrast, female Ama divers have suffered specific psychiatric disorders called 'Chiyamai'.[17] A survey of 44 female Ama divers noted that nine had mental disturbances related to anxiety attacks. On the particular island involved, the diving depths and durations were deeper and longer than in other areas,[18] and the diving patterns were similar to those of male Ama divers with diving accidents.[4,14] Although the clinical features of these diving related psychiatric episodes closely resemble those of some types of panic disorders, female divers did not have depersonalisation or de-realisation. The clinical symptoms included palpitation, dizziness or unsteady feelings, dyspnoea, nausea and/or hot flushes; palpitations being the most frequent among them. Several Ama divers who had experienced the illness could not dive and had to stop their diving work. Others who had recovered from the illness were unable to dive at great depths and always had to take anti-anxiety medicine prior to diving.

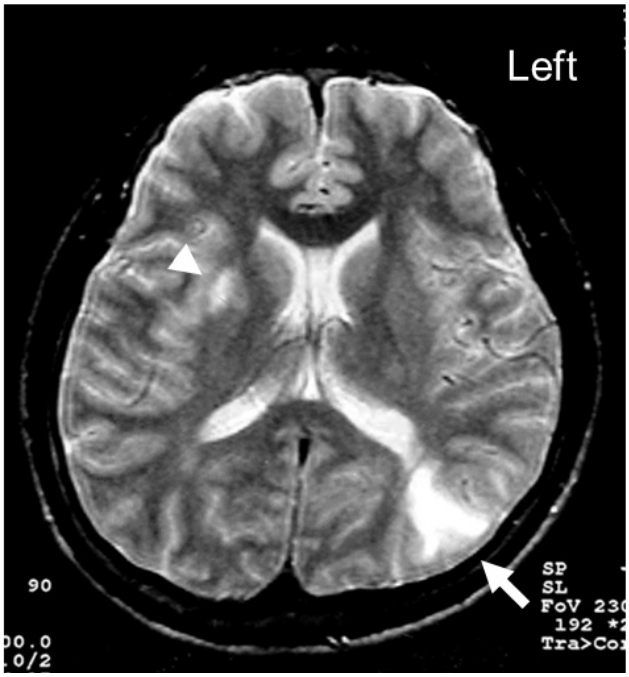
Except for the above specific cases, no diving-related psychiatric disturbances among female or male Ama divers have been reported where diving depths are shallower. However, Polynesian pearl divers frequently experienced mental anxiety as a form of taravana syndrome, and a few cases were affected with symptoms such as restlessness, irritability and altered comprehension.[1] Therefore, there is a possibility that deep and long-lasting repetitive breath-hold dives cause psychological conditions in Ama divers. Further studies are needed to investigate whether breath-hold diving affects psychological or mental functions.[19]

Brain imaging

There was no DCI reported among Ama divers until our group described two cases of cerebral infarction in 1998 occurring after repetitive dives to 15 to 25 msw.[2] There are now many reports of ischaemic brain lesions in breath-hold divers documented using magnetic resonance imaging (MRI). Brain MRIs in Ama divers with a history of DCI showed multiple cerebral infarcts in areas corresponding to the symptoms and elicited signs (Figure 3). The brain lesions are localised in the basal ganglia, internal capsule, and deep and superficial white matter.[20] In another study, we further investigated whether long-term breath-hold divers who exhibited cerebral symptoms and also those who did not would exhibit cerebral damage on MRI.[21] Twelve Japanese Funado divers with an average age of 54.9 (SD 5.1) years and diving experience of 29.8 (7.6) years were examined. Four had histories of transient diving-related neurological symptoms, and eleven demonstrated ischaemic cerebral lesions. These lesions were situated in the cortical and/or subcortical area (nine cases), deep white matter (four cases), the basal ganglia (four cases), and the thalamus (one case). Cerebral hyperintensities observed with T2-MRI are seen in healthy subjects, and the prevalence increases with older age, occurring in 10–20% of people aged around 60 years.[22,23] However, the higher prevalence of cerebral ischaemic lesions in Ama divers cannot be simply explained by aging.

The types of brain lesions in the Ama divers were identical to those seen in compressed-air divers or patients suffering iatrogenic AGE.[24–26] The ischaemic lesions in the basal ganglia were situated in the terminal zone, and the lesions involving deep or superficial white matter corresponded to border zone or watershed regions. They are so-called

Figure 3
Magnetic resonance imaging (MRI) of the brain in a male Ama diver with right homonymous hemianopsia. T2-weighted MRI obtained on the 5th day after the accident showed two increased signal intensities in the left occipital lobe (arrow) and the right basal ganglia (arrow head)



'low-flow' cerebral infarctions resulting from low perfusion pressure in the terminal supply areas, and may be due to cerebral AGE. The previously mentioned studies in Ama divers demonstrated that long-lasting breath-hold diving may cause damage to the brain, probably through accumulation of repeated transient cerebral arterial ischaemic injury. Moreover, another study suggests possible underestimation of the true damage to the brain.[27] In that study, five elite breath-hold divers with normal neurological examinations and brain MRIs all exhibited diffusely abnormal perfusion images of the brain using single photon emission tomography (SPECT) scans. In our series of 12 Ama divers, frontal lobe atrophy was found in two cases.[21] Recently, a possible impairment of cerebral autoregulation in elite competitive breath-hold divers has been reported.[28] Long-term repetitive breath-hold diving probably affects cerebral perfusion in a fashion that may increase susceptibility to local or diffuse ischaemia caused by AGE, and this is an important issue for future research.

Mechanisms of injury

The mechanisms of DCI incidents after repetitive breath-hold diving are poorly understood. A more recent study has demonstrated that deep repetitive breath-hold dives lead to endothelial dysfunction that may play a role in neurological DCI.[29] It was suggested that intravascular microparticles following breath-hold dives initiate a systemic inflammatory process including neutrophil activation.[30] It is possible that some forms of neurological DCI are a "*reversible cerebral vasoconstriction syndrome*" resulting from a transient segmental constriction of cerebral arteries.[31] However, some Ama divers with neurological DCI showed large multifocal ischaemic cerebral lesions on MRI studies.[20] These findings are more compatible with cerebral infarcts caused by a large gas or thrombotic emboli load.[26] Moreover, serious stroke-like neurological disorders were immediately relieved by recompression.[32] The dramatic and rapid response suggests the presence of bubbles in the cerebral arteries. Nitrogen accumulation in fat tissues increases throughout repetitive breath-hold diving despite quickly reaching a steady state in the brain, heart and viscera.[33]

Given high cerebral blood flow and consequently 'fast' nitrogen kinetics, the development of in situ bubbles in the brain is unlikely. The characteristics of diving accidents in Ama divers are that stroke-like brain involvement is common, and moreover their MRI findings suggest occlusion of cerebral arteries.[20] In one case of an Ama diver who suffered neurological symptom onset, computed tomography showed an air density area in the parietal lobe of the brain 3 hours later.[34] After repetitive breath-hold dives with short surface intervals, venous nitrogen bubbles may arise from the peripheral fatty tissues similar to the mechanisms seen in compressed-air diving. Some investigators have reported venous bubbles following repetitive breath-hold dives in Ama and spearfishing divers.[35–37] However, venous bubbles should be filtered by lung capillaries and would enter the cerebral arterial circulation unless they arterialize across a right-to-left shunt (RLS). Serious neurological events are usually induced in repetitive breath-hold diving, while the detection of venous bubbles is more difficult in breath-hold divers than in compressed-air divers.[29,35,36,38] Why lesions in breath-hold diving mainly involve the brain but not spinal cord is an unresolved question.[39]

Bubbles formed in the venous blood after long-lasting repetitive breath-hold dives, can cross from the venous side to the arterial side of the circulation (arterialization) in the presence of an intracardiac RLS and/or intrapulmonary arterio-venous shunt (AVS). While the proportion of cerebral ischaemic lesions were closely related to the presence of intracardiac RLS in compressed-air divers,[40,41] RLSs have not been detected in Ama and other breath-hold divers with brain involvement.[3,34,42,43] These reported cases suggest that neurological DCI in breath-hold divers cannot be explained only by intracardiac RLS, and alternative mechanisms have been suggested.[44] After repetitive deep breath-hold diving venous bubbles may be retained or trapped in the pulmonary arterioles. Then, when the divers continue with repetitive descents, the trapped bubbles may be compressed and therefore able pass through the pulmonary circulation. Arterialized bubbles might then expand during each ascent and accumulate in the terminal supply areas of the brain, border zones and watershed regions. It has

previously been suggested that this is the most likely hypothesis to explain cerebral involvement in Ama divers.[14]

Arieli has published a new theory of decompression bubbles developing from intravascular gas micronuclei on small distal arterial walls.[45] Elevation of nitrogen tension in the brain and blood results in enhanced nitrogen transfer to these nuclei which become bubbles. However, this hypothesis cannot explain why one or more large ischaemic lesions are not invariably accompanied by multiple small ones in the subcortical areas,[2,3,34] where arterial gas embolism typically involves the small arteries (average diameter, 30 to 60 microns).[46] Hypoxia following breath-holding may affect the opening of intrapulmonary AVSs which exist in normal humans.[47] We consider cerebral DCI in Ama divers is explained by arterialization of venous nitrogen bubbles and cerebral arterial gas embolism as the main mechanism. However, the pathophysiology is not clear and probably multifactorial.

Diffuse cerebral hypoperfusion or brain atrophy in breath-hold divers suggests that there is endothelial damage of cerebral arteries caused by micro-emboli-like microbubbles and microparticles. While microbubbles smaller than 22 microns in diameter can pass through cerebral capillaries,[48] it has been shown that this damages the blood-brain barrier.[49] In addition, others have suggested that microparticles play an important role in cerebral endothelial dysfunction after breath-hold diving.[29] There is a possibility that such micro-embolic particles induce cerebral hypoperfusion or brain atrophy.

Treatment

Hyperbaric oxygen treatment (HBOT) has a key role in treating bubble disease and appears to be effective for the hyperacute phase of iatrogenic arterial gas embolism,[50,51] although the beneficial effect has not been shown in acute ischaemic stroke not caused by bubbles.[52] Twenty two divers with cerebral symptoms of DCI who received HBOT within 6 hours all completely recovered.[53] In fact, the rate of spontaneous clinical recovery is high in patients with cerebral AGE following decompression although the improvement is not invariably sustained.[54] Another study described early normobaric oxygen breathing completely relieved or improved DCI symptoms in 65% of 1,045 cases.[55] In Ama divers, DCI symptoms typically reflect cerebral involvement (stroke-like symptoms). For the treatment of DCI in breath-hold divers, oxygen breathing should start as early as possible, followed by HBOT within 6 hours after the onset. Permanent brain injury may be prevented by early treatment so it must be emphasised in local diving villages that HBOT should start as soon as possible.

Prevention

Prevention of DCI is important for Ama divers. One somewhat radical preventative strategy previously proposed was to take a breath of oxygen immediately prior to the dive to minimise inert gas uptake.[56] However, this might risk oxygen toxicity, and many Japanese diving fishermen do not have access to oxygen for their diving work, even as a first aid strategy. A more practical approach is to take longer surface intervals. As shown in the study of taravana by Cross,[1] pearl divers in Mongareva Lagoon who spent at least 10 minutes at the surface between dives never developed this condition, whereas many divers in another lagoon using shorter surface intervals of three to five minutes experienced taravana. A short surface time would increase the risk of DCI, particularly when diving to deeper depths.[57]

Based on our surveys of Ama divers with neurological DCI,[4,14] multiple repetitive breath-hold dives to depths shallower than 20 msw for several hours with short recovery periods can lead to nitrogen accumulation in tissues analogous to the amounts found in compressed-air diving. A simulation of the diving pattern of Japanese Ama divers performing 30 dives to a depth of 20 msw over an hour found that nitrogen loading in the fat increased throughout repetitive breath-hold diving despite reaching a steady state value after five dives in the brain, heart and viscera.[33] Diving to 20 msw repeatedly for several hours would require an average surface-to-dive time (S/D) ratio of more than 0.8 to avoid development of DCI.[58] Our survey showed the S/D ratio in Ama divers with neurological disorders tended to be low in comparison to that of divers without events.[14] While dive depth, bottom time and duration of the diving pattern are well known as risk factors for DCI in breath-hold diving, short surface interval is a possible major cause in breath-hold dives to 10–20 msw. The risk of DCI in Ama divers can be decreased by taking a longer surface interval and a shorter diving shift of less than two hours. Twenty years ago, serious manifestations occasionally appeared in Ama divers in a district of Japan, but they became rare after educational meetings for Ama divers were introduced at the union.[59] However, neurological events happened in some divers whose shifts were longer than two hours,[15,16] and the union rule may need to include the time of single diving shift.

Conclusions

Repetitive breath-hold dives can cause decompression disorders characterised by stroke-like brain involvement. Brain MRIs of Ama divers showed symptomatic and/or asymptomatic ischaemic lesions typically situated in the terminal and border zones of cerebral arteries. The prevalent theory of brain involvement is that arterialised venous gas bubbles passing through right to left shunts may be a plausible mechanism. Although no therapeutic strategy has been established specifically for DCI in breath-hold divers, early oxygen breathing is recommended to help mitigate permanent brain ischaemic injuries. It is more important for Ama divers to protect themselves from the diving-related disorders by reducing hard diving schedules of long-lasting repetitive dives and short surface intervals.

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Case reports

Results of hyperbaric oxygen treatment in an at-risk nasal flap following trauma

Sinem Kara[1], Ender İnci[1], E Deniz Gözen[1,2], K Cenk Gülgün[3], H Murat Yener[1,2]

[1] *ENT Department, Istanbul University – Cerrahpasa, Istanbul, Turkey*
[2] *Istanbul University – Cerrahpasa, Istanbul, Turkey*
[3] *Oksimer Hyperbaric Oxygen Center, Istanbul, Turkey*

Corresponding author: *Dr Sinem Kara, Istanbul University – Cerrahpasa, Medical Faculty, ENT Department Cerrahpasa Mh. Kocamustafapasa Cd. No: 53, 34096 Fatih/Istanbul, Turkey*
sinemkara25@hotmail.com

Key words
Injuries; Hyperbaric medicine; Outcome; Skin; Surgery

Abstract

(Kara S, İnci1 E, Gözen ED, Gülgün KC, Yener HM. Results of hyperbaric oxygen treatment in an at-risk nasal flap following trauma. Diving and Hyperbaric Medicine. 2021 June 30;51(2):207–209. doi: 10.28920/dhm51.2.207-209. PMID: 34157737.) Hyperbaric oxygen treatment (HBOT) is widely used in otorhinolaryngology for various purposes. A 20-year-old male patient was admitted following a traumatic nasal wound which occurred several hours prior. He had a nasal glass cut from the radix to the supratip area which was primarily closed by non-absorbable suture. The following day, there was a haematoma and necrosis of the skin. The haematoma was drained under local anaesthesia. Blood supply to the nasal skin was severely compromised and only the columellar artery remaining intact, by definition designating this a difficult to heal wound with the risk of overall healing failure. Necrosis of the skin had developed within the first 24 hours. Accordingly, the patient underwent 30 HBOT sessions (two hours at 253.3 kPa) twice daily for four days and daily thereafter. Antibiotic cover and conservative wound management were also used. Complete healing was achieved without the need for additional surgical intervention. We conclude that timely use of HBOT may be a valuable adjunct to conservative wound management in a case of sharp nasal trauma.

Introduction

Hyperbaric oxygen treatment (HBOT) is widely used in otorhinolaryngology for various purposes. It is used in wounds that are difficult to heal.[1,2]

Blood supply to the nasal skin is derived from two separate branches. The first is the columellar artery branch of the superior labial artery and the angular artery which is a branch of facial artery. The second arises from the dorsal nasal branch of the ophthalmic artery. Therefore, this situation puts the blood supply of the tissue in a risky situation in nasal skin incisions and cuts. We present a case in whom the nasal skin had a large cut interrupting most of its blood supply; only the columellar artery was intact. There was progressive skin ischaemia and necrosis but complete recovery was achieved using a strategy that combined conservative wound management, antibiotics and early adjunctive HBOT.

Case report

The patient gave permission for this report and the photographs to be published. A 20-year-old male patient was admitted with a traumatic cut to the nose occurring a few hours earlier. The cut extended from from the radix to the supratip area (Figure 1a). The skin flap appeared to have lost most of its blood supply. Haemostasis was achieved by using electrocautery. The cut was closed by interrupted suture with 5.0 propylyne (Figure 1b). Oral antibiotics were prescribed (500 mg cefuroxime twice daily for two weeks and 500 mg ornidazole three times a day for one week).

At the first follow-up visit the following day, the patient had a haematoma and necrosis of the dorsal skin (Figure 1c). The hematoma was drained under cover of local anaesthesia (1 ml of 2% lignocaine + 0.0125 mg adrenaline diluted with 1 ml of isotonic solution). HBOT was immediately initiated with the intent of correcting immediate signs of ischaemia and ischaemic reperfusion injury, preventing progression of necrosis and facilitating healing and angiogenesis. Treatment was undertaken in a HYTECH multiplace hyperbaric oxygen chamber (HYTECH, Phoenix, USA). The treatment sessions were planned so that the patient was breathing pure oxygen (100% O_2) for two hours at 253.3 kPa (2.5 atmospheres absolute) pressure. HBOT was administered twice daily for the first four days, and once daily thereafter for a total of 20 sessions. As a result of significant improvement observed (with the contraction of the necrosis and the onset

Figure 1
A. Sharp trauma to the nasal skin at the first admission; B. After the primary closure (day 1); C. Haematoma and skin necrosis at the first visit (day 2)

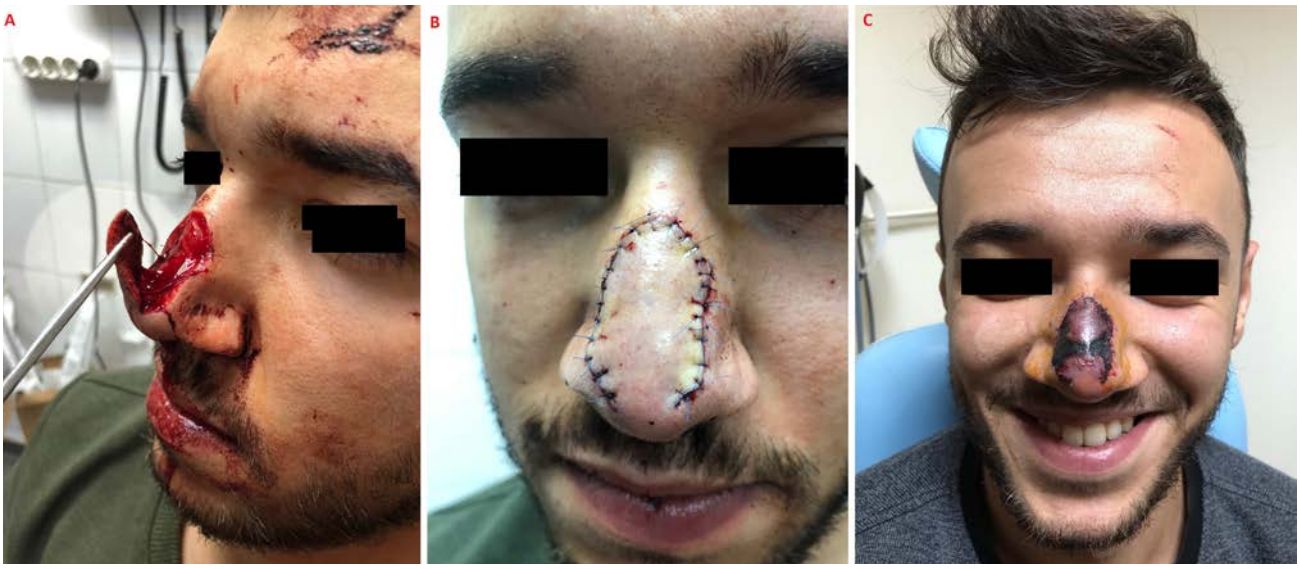
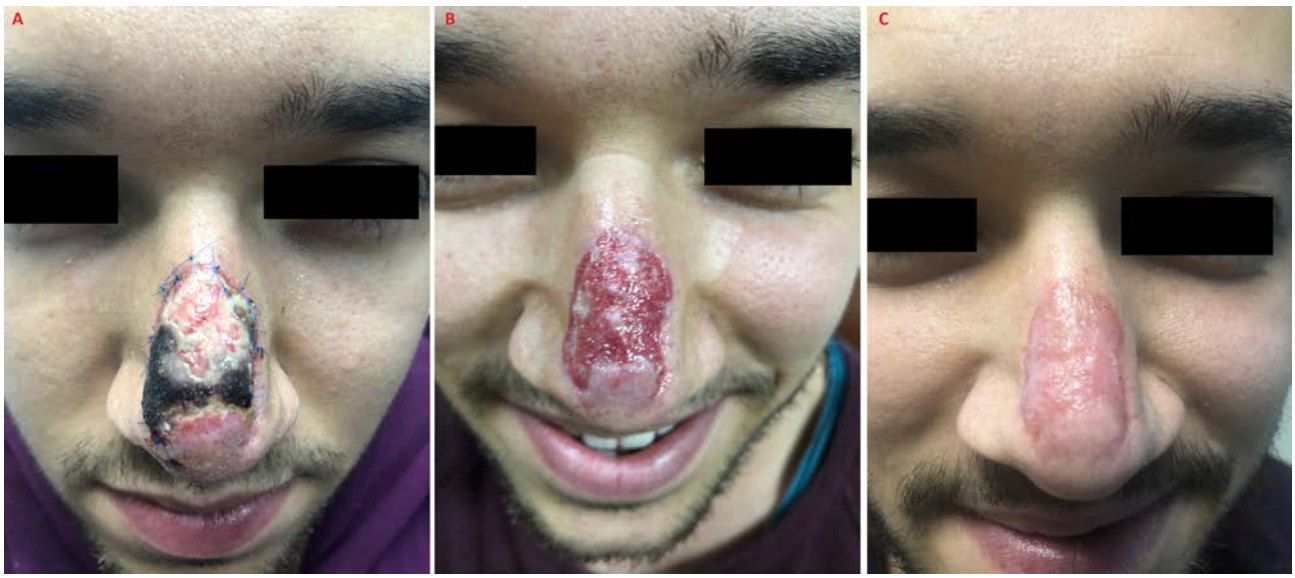


Figure 2
A. Appearance at the 15th HBOT session; B. Appearance at the 30th HBOT session; C. Full recovery, one month after the last HBOT session



of vigorous granulation), the treatment was extended for 10 sessions, and was completed in 30 sessions. Air-breaks were not used during the treatment. The patient had daily wound dressing in that period using povidone iodine as an antiseptic. The skin sutures were removed at one week and no further debridement was needed. Necrotic skin detected in the first visit sloughed off and epithelisation started following granulation (Figures 2a and b). One month after the 30 HBOT sessions, the patient had full recovery. (Figure 2c).

Discussion

This report presents a difficult case of sharp nasal trauma with depleted blood supply of the skin which was treated with adjunctive HBOT. This, together with haematoma drainage, electrocautery, sutures and daily wound dressing prevented further surgical intervention.

Two recent reviews suggest that adjunctive use of HBOT in some surgical patients is associated with improved

outcomes.[3,4] Another study highlighted the use of HBOT as an additional treatment in acute wounds.[5] Although it is already known that HBOT is beneficial in chronic non-healing wounds, it is emphasised here that HBOT may also be beneficial in compromised acute wounds.

The role of reactive oxygen species, microvascular vasoconstriction and endothelial cell-neutrophil adhesion in ischaemia-reperfusion injuries is well known, and early application of HBOT is crucial in acute ischaemic wounds.[6] In the present case, when acute ischaemic damage was observed, HBOT was started urgently, and was associated with early signs of healing.

Studies have shown that hyperbaric oxygen therapy improves tissue hypoxia, increases perfusion, decreases oedema, decreases inflammatory cytokines, increases fibroblasts, increases collagen production and increases angiogenesis.[5] Therefore, we advise that HBOT be considered as an additional treatment in cases where tissue blood supply is considered to be insufficient. As seen in the present case, some tissues are more prone to ischaemic hypoxia due to poor blood supply.

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Prolonged syncope with multifactorial pulmonary oedema related to dry apnoea training: Safety concerns in unsupervised dry static apnoea

Juan M Valdivia-Valdivia[1,2], Anne Räisänen-Sokolowski[3,4], Peter Lindholm[5]

[1] *Neurosurgery Department, St. Joseph's Hospital, Tampa FL, USA*
[2] *International Association for Development of Apnea (AIDA International) – Medical and Science Committee, Zurich, Switzerland*
[3] *Pathology, Helsinki University and Helsinki University Hospital, Helsinki, Finland*
[4] *The Centre for Military Medicine, The Finnish Defense Forces, Helsinki, Finland*
[5] *Department of Emergency Medicine, University of California San Diego, San Diego CA, USA*

Corresponding author: *Professor Peter Lindholm, Department of Emergency Medicine, University of California San Diego, San Diego CA, USA*
plindholm@health.ucsd.edu

Key words
Breath-hold diving; Case reports; Hypoxia; Imaging; Lung; Pulmonary oedema; Unconsciousness

Abstract

(Valdivia-Valdivia JM, Räisänen-Sokolowski A, Lindholm P. Prolonged syncope with multifactorial pulmonary oedema related to dry apnoea training: Safety concerns in unsupervised dry static apnoea. Diving and Hyperbaric Medicine. 2021 June 30;51(2):210–215. doi: 10.28920/dhm51.2.210-215. PMID: 34157738.)
Many competitive breath-hold divers use dry apnoea routines to improve their tolerance to hypoxia and hypercapnia, varying the amount of prior hyperventilation and lung volume. When hyperventilating and exhaling to residual volume prior to starting a breath-hold, hypoxia is reached quickly and without too much discomfort from respiratory drive. Cerebral hypoxia with loss of consciousness (LOC) can easily result. Here, we report on a case where an unsupervised diver used a nose clip that is thought to have interfered with his resumption of breathing after LOC. Consequently, he suffered an extended period of severe hypoxia, with poor ventilation and recovery. He also held his breath on empty lungs; thus, trying to inhale created an intrathoracic sub-atmospheric pressure. Upon imaging at the hospital, severe intralobular pulmonary oedema was noted, with similarities to images presented in divers suffering from pulmonary barotrauma of descent (squeeze, immersion pulmonary oedema). Describing the physiological phenomena observed in this case highlights the risks associated with unsupervised exhalatory breath-holding after hyperventilation as a training practice in competitive freediving.

Introduction

Freediving-related cerebral hypoxia is well documented.[1,2] In-water activities bear a risk of cerebral hypoxia manifesting as loss of motor control, and loss of consciousness (LOC).[2,3] Dry apnoea exercises (performed on land), which are commonly performed by competitive freedivers, also carry this risk albeit without risk of drowning. These apnoea exercises improve breath-hold ability; their benefits are attributed to increased tolerance to hypercapnia, hypoxia, and onset and strength of the diving response.[4–6] They also familiarise the diver to the uncomfortable sensation of dyspnoea/asphyxia. When performing dry training, hyperventilation can be used to prolong apnoea time with the absence of diaphragmatic contractions, creating a state whereby hypoxia may be achieved without hypercapnia-induced dyspnoea.

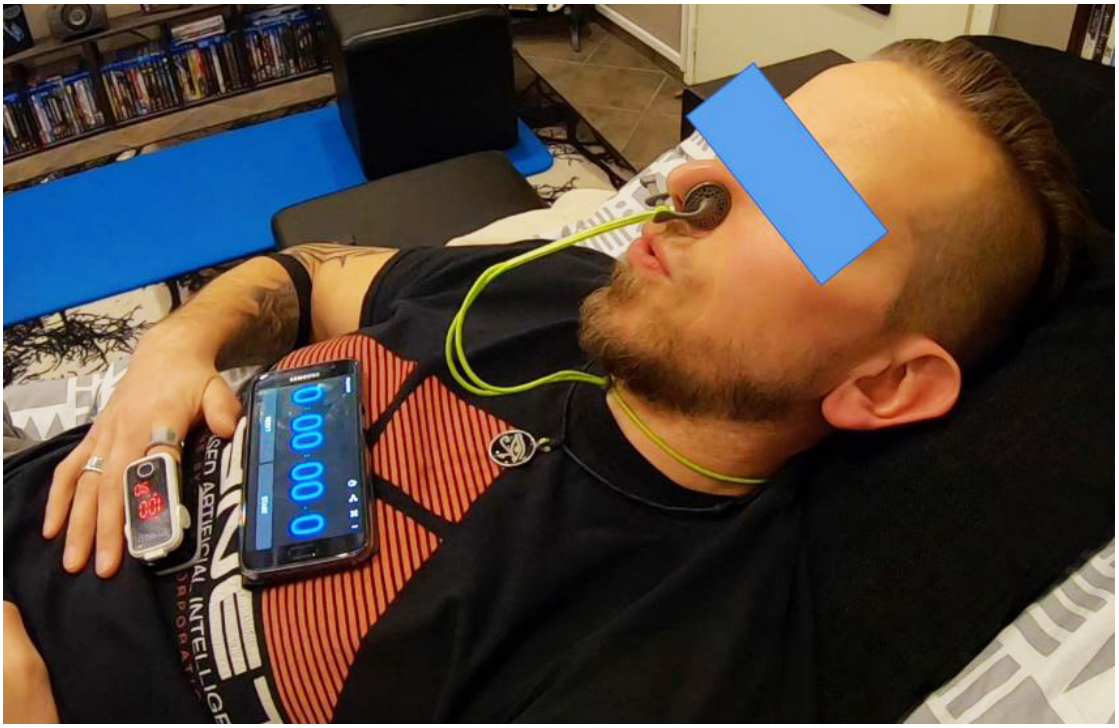
Residual volume (RV) apnoea is the performance of a breath-hold after a fully-controlled forced exhalation, creating inflexion of the diaphragm. In addition, some divers practice glossopharyngeal exsufflation to further reduce pulmonary lung volume to 200–300 ml below RV.[7] This manoeuvre is used to practice flexibility of the ribcage and diaphragm, as well as to increase the rate of induction of hypoxaemia when pulmonary oxygen stores are limited. Some breath-hold divers can hold their breath for 2–3 minutes on empty lungs without loss of consciousness. In addition, a decrease of the intra-alveolar gas pressure down to -90 cm H_2O has been reported.[7] This will decrease the gas diffusion gradient via reduction of P_AO_2 by 1–2 kPa, but will also create a sub-atmospheric intrathoracic pressure that will increase fluid transfer, shifting blood stores centrally and possibly creating pulmonary oedema.

A case is described which demonstrates these physiological phenomena and risk of this practice, hoping to raise awareness of the risks of unsupervised dry apnoea training at pulmonary RV.

Case report

The diver gave written informed consent for publication of this report. A male freediver, 181 cm, 43-years-old,

Figure 1
The diver in a in a semi-reclined (45 degree) position for dry apnoea training with nose clip and pulse oximeter. Picture is a screen shot from the diver's video recording



healthy, non-smoker, no medications, suffered an incident of prolonged unconsciousness and subsequent hospitalisation. He reports never having experienced collapse or syncope before this incident. He had videoed (GoPro Hero 7 Black, China) his training session and was wearing a pulse oximeter (Prego, model PM009, Shenzhen Aeon Technology, Shenzhen, China).

His dry apnoea routine consisted of vigorous hyperventilation (2 s inspiration, 2 s forced exhalation, for approximately 2 min), followed by forced exhalation to RV prior to breath-holding using a nose-clip (Figure 1). The video documented his prolonged unconsciousness (over 3 minutes) with an apneustic breathing pattern and prolonged episodes of recurrent apnoea.

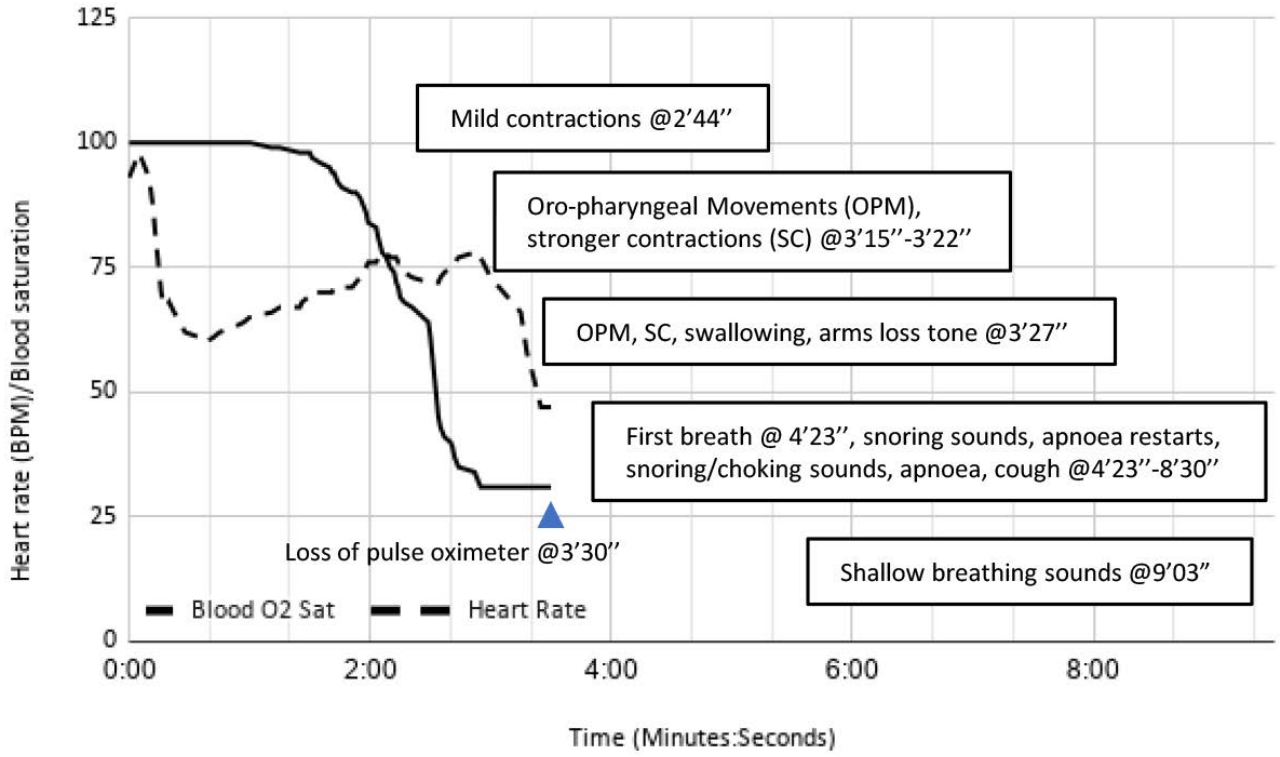
SYNCOPE EPISODE

The course of events is described in Figure 2. Pulse oximetry measurements made from the finger may not represent central hypoxia, and equipment is rarely calibrated below 50%.[8] The diver's saturation declined steadily to 35%, at which point his first mild diaphragmatic contractions were observed, at 2 min 44 s. Thereafter, saturation dropped to 31% and the diver displayed swallowing movements and stronger contractions. An evident change in mental status was seen at 3 min 30 s, with clinical presentation of a right-sided conjugate gaze to the horizon, a subtle loss of motor control of the arms, bilateral upper extremity extension, and right-hand thumb opposition. This caused the pulse oximeter to fall out of sight. At 3 min 43 s there was bilateral upper extremity decerebrate posture in extension, along with sustained head extension, and the gaze continued to be right sided only. At 4 min, the video tilted with only audio remaining; the audio track suggests that breathing was resumed at 4 min 23 s. Thereafter, snoring and choking sounds were evident (resembling possible upper airway obstruction or upper airway muscle discoordination). Coughing and apnoea restarted several times to 8 min 30 s. At 9 min 03 s, shallow breathing could be heard, at close to tidal volume breaths.

Heart rate was 98 beats per minute (bpm) when breath-holding started. It declined to 60 bpm within 30s and thereafter fluctuated between 60–78 bpm. When the contractions started at 3 min, there was a rapid decline to 47 bpm.

The diver estimated that he resumed consciousness 15 min after the episode. He was sweaty and nauseous with a strong headache. He then tried a breathing manoeuvre that creates breathing with positive end expiratory pressure (PEEP), however, oxygen saturation did not rise higher than 90%. After an hour, the diver called an ambulance and was taken to hospital. There he was imaged with a chest X-ray, followed by computed tomography (CT) of the chest, and blood tests. There were no saved reports regarding blood pressure or other abnormal findings on physical examination. He desaturated to 85% during the night. His inflammatory

Figure 2
Chart depicting the timeline for oxygen saturation (%) and heart rate (beats per minute) during the apnoea training. The appearance of various symptoms is shown at the time points noted



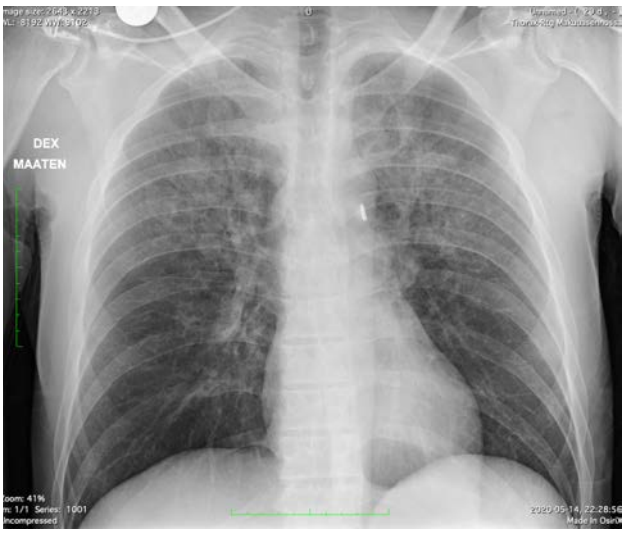
markers were normal, as well as troponin T (TnT), but pro-brain natriuretic peptide (NT pro-BNP) was slightly elevated (158 ng·L^{-1} versus normal value < 84 ng·L^{-1}). He was negative for COVID-19 and cardiac echocardiography was normal. The patient was hospitalised for three days (with supplemental O_2 the first evening and night), and had a checkup five weeks later (including chest CT), with no abnormal findings.

RADIOGRAPHIC FINDINGS

A chest X-ray was taken five hours after the incident (Figure 3). It showed bilateral opacities in the upper half of the lungs, with some subpleural sparing. The opacities had a nodular (or airspace) distribution with very minimal interstitial oedema. Below the hilar regions there were no findings.

The CT pulmonary angiography was performed the following day (Figures 4–6). It showed bilateral ground glass opacities in a pattern following the boundaries of the secondary lobule.[9] Opacities were mainly distributed in the upper lobes, with some in the upper parts of the lower lobes and intralobular gradient as evidence of settling of fluid in a gravity-dependent manner.[10] There were also some peribronchial opacities in the right lower lobes (upper medial part), (paraspinal) suggesting oedema or bleeding. The bronchi were patent, with no findings suggestive of aspiration.

Figure 3
Chest X-ray showing bilateral opacities as pulmonary oedema with a clear distribution in the upper parts of the lungs (the upper half of the lungs are whiter than the lower parts, which is an abnormal finding)



Discussion

To our knowledge this is the first report of dry apnoea training causing pulmonary oedema requiring hospitalisation. As this training method is used commonly among freedivers, raising awareness of its potential adverse effects would be of benefit.

Figure 4
Axial image of upper part of the lungs showing oedema in a distribution following the secondary lobule; Four white arrows point to examples of the 1–2 cm structure that is opacified by oedema

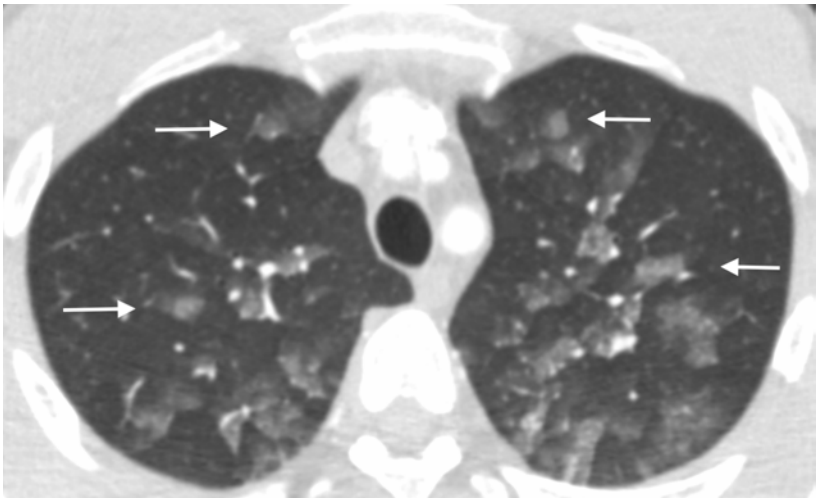
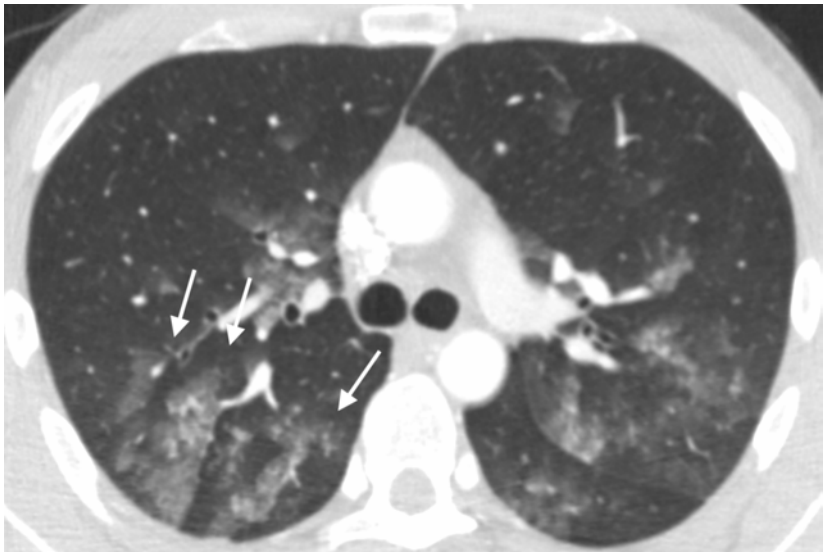


Figure 5
Axial image of middle part of the lungs with three white arrows pointing in the direction of the radial distribution or streak appearance of the edematous lung suggesting some parts where spared, possibly due to partial lung collapses

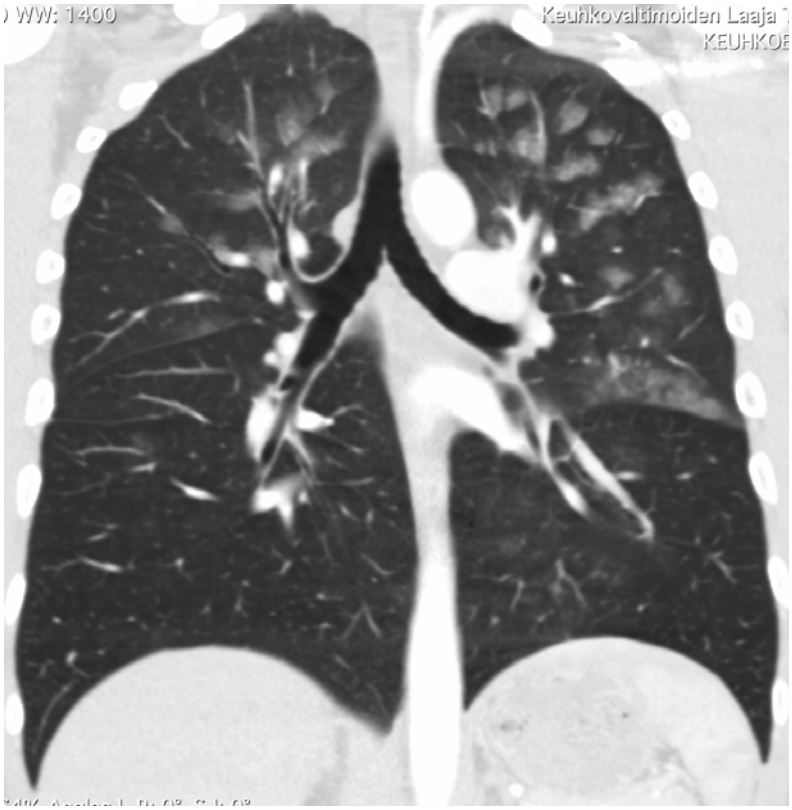


Several practices for apnoea training involve total lung capacity ('full lungs'), RV ('empty lungs or forced exhale'), or a degree in between (referred to as functional residual capacity or passive exhale). Some practices carry higher risk for cerebral hypoxia than others. As the lungs are the major oxygen store, it would be expected that the duration of breath-holding needed to reach hypoxia can be modulated by the amount of inspired air. Hyperventilation is used to delay dyspnoea caused by hypercapnia. This diver used a low lung volume to limit oxygen stores, decrease the alveolar-capillary pressure gradient (negative pressure), and the Bohr effect (hypocapnia) to attain hypoxia.

The practice of RV dry apnoea made during a stretching routine, familiarises the practitioner with the sensation of collapsed lungs and contractions when the diaphragm is introflexed, and simulates some of the sensations perceived at depth when lung volume is compressed. It is also practiced with the notion that it increases the flexibility of the diaphragm and thus the ability to 'collapse' the thoracic cage.

This diver presented with hypoxaemia, and imaging revealed alveolar pulmonary oedema, which could be multifactorial but sub-atmospheric alveolar pressure should be considered primarily. A residual volume breath-hold, with contractions of the diaphragm against a closed mouth (and/or glottis)

Figure 6
Coronal image of the middle part of the lungs showing gravity dependent consolidation within each opacity and the upper lung distribution



will create a relative negative pressure within the alveoli. Many humans also react to dry breath-holding with central hypertension (systemic vasoconstriction as part of the diving response), increasing pulmonary blood volume ('blood shift') and pressure gradient for capillary-alveolar transudation.[11] This would be analogous to the mechanism for a 'negative pressure oedema' observed, for example, in tracheal obstruction.[12]

The prolonged syncope also offers the possibility that severe hypoxia (for minutes) would limit the left ventricular cardiac output causing heart failure, and thus pulmonary venous stasis might cause high pulmonary capillary pressure. Pulmonary oedema is not uncommon in myocardial dysfunction. In this case, the diver made an attempt to breathe but may have been impeded by: upper airway dysfunction related to cerebral hypoxia; upper airway obstruction related to the use of nose clip; and the high muscle effort needed to ventilate from a starting point of RV with partial atelectasis. The prolonged state of cerebral hypoxia was also a consequence of his inefficient recovery breathing.

Prolonged hypoxia could also cause hypoxic pulmonary vasoconstriction in the lungs similar to high altitude pulmonary oedema, although this mechanism seems less likely given the specific distribution of the oedema.

The diver had a predominantly upper lung oedema distribution in comparison to the more common butterfly-wing shape in cardiogenic oedema. This was interpreted as an effect of the diver holding his breath at residual volume with the lower lobes collapsed in partial atelectasis,[13] thus protecting the tissue from transudation (less capillary-alveolar pressure difference if the alveoli are collapsed). It is noteworthy that the oedema showed streaks in the upper lobes, possibly due to radial or subsegmental atelectasis. It is highly likely that the nose clip worsened the diver's ability to resume breathing after syncope. Spasms are a common symptom and the muscles closing the mouth (e.g., masseter) would be stronger than the opposing ones.

In conclusion, we would advise against self-practice/unsupervised dry breath-holds for hypoxic conditioning with a nose clip. It cannot be said for certain that the diver would have resumed spontaneous breathing without the nose clip, so preferably all such dry exercises should be observed or supervised.

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Hyperbaric oxygen treatment for toxic epidermal necrolysis: A case report

Selin Gamze Sümen[1], Sezer Yakupoğlu[2], Tuna Gümüş[3], Nur Benzonana[4]

[1] *University of Health Sciences, Hamidiye Medical Faculty, Department of Underwater and Hyperbaric Medicine, Istanbul, Turkey*
[2] *University of Health Sciences, Kartal Dr Lütfi Kirdar City Hospital, Department of Anesthesiology and Reanimation, Istanbul, Turkey*
[3] *University of Health Sciences, Kartal Dr Lütfi Kirdar City Hospital, Department of Underwater and Hyperbaric Medicine, Istanbul, Turkey*
[4] *University of Health Sciences, Kartal Dr Lütfi Kirdar City Hospital, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey*

Corresponding author: *Dr Selin Gamze Sümen, Sağlık Bilimleri Üniversitesi, Hamidiye Tıp Fakültesi, Sultan 2. Abdulhamid Han Eğitim ve Araştırma Hastanesi, Selimiye Mh., Tıbbiye Cd., 34668, Üsküdar/Istanbul, Turkey*
sgsumen@gmail.com

Key words
Case reports; Drugs; Hyperbaric medicine; Outcome; Side effects; Skin; Toxicity

Abstract

Sümen SG, Yakupoğlu S, Gümüş T, Benzonana N. Hyperbaric oxygen treatment for toxic epidermal necrolysis: A case report. Diving and Hyperbaric Medicine. 2021 June 30;51(2):216–219. doi: 10.28920/dhm51.2.216-219. PMID: 34157739.) Toxic epidermal necrolysis (TEN) is a potentially life-threatening muco-cutaneous disease, largely caused by an idiosyncratic reaction to medication or infectious disease, and is characterised by acute necrosis of the epidermis. No definitive consensus regarding the treatment of TEN has been agreed. A 60-year-old woman, diagnosed with multiple myeloma three months prior, was admitted with signs of TEN to the intensive care burns unit. She had been given ciprofloxacin to treat a urinary tract infection. She complained of malaise and pain, with maculopapular and bullous eruptions over her whole body on the third day of ciprofloxacin administration. Her supportive cares included intravenous immunoglobulins, pain control with analgesics, wound care, nutrition, and fluid support. Hyperbaric oxygen treatment (HBOT) was added on the second day of admission. The patient underwent 5 sessions of HBOT at 243.1 kPa (2.4 atmospheres absolute). Desquamation was noted to stop after the first session of HBOT and re-epithelisation commenced rapidly. The patient was discharged from the burn unit after 14 days of hospital admission. Improvement in this case was temporally related to the initiation of HBOT.

Introduction

Toxic epidermal necrolysis (TEN) is a muco-cutaneous disease, typically caused by idiosyncratic adverse reactions to medication use or from infectious agents.[1] It is characterised by acute necrosis of the epidermis. Although rare (the incidence rate is 0.5–1.4 per million per year), the condition of the patient is usually characterised by a rapid deterioration in clinical state due to the systemic effects of the disease.[1] As a consequence of this rapid deterioration in clinical status, the mortality rate may be up to 40% despite the application of multiple treatments tailored for the disease.[1–3]

Patients typically present with symptoms of fever, sore throat, myalgia, coupled with the cutaneous findings, such as macular erythematous eruptions, bullae or necrosis of the skin.[4] The current treatment modalities consist of intravenous immunoglobulin, pain control with analgesics, wound care, nutrition and fluid support, and anti-infective therapy tailored in accordance with the signs and symptoms of the patient.[5,6] A patient is reported who had an acute skin eruption diagnosed as TEN and who underwent emergency hyperbaric oxygen treatment (HBOT) which was temporally associated with onset of improvement.

Case report

Written consent was obtained from the patient to publish this account of her case and photographs.

The patient was a 60-year-old woman with a medical history of chronic renal failure, hypertension and multiple myeloma, the latter diagnosed three months earlier. Due to difficulties in accessing the patient's medical records at another hospital, the details of treatment of the multiple myeloma could not be obtained. However, the patient had been administered vancomycin and gentamicin therapy after being diagnosed with acute bacterial endocarditis. Vancomycin was stopped on the 25th day of therapy because of a diffuse

Figure 1
Upper body skin appearance on admission, prior to HBOT

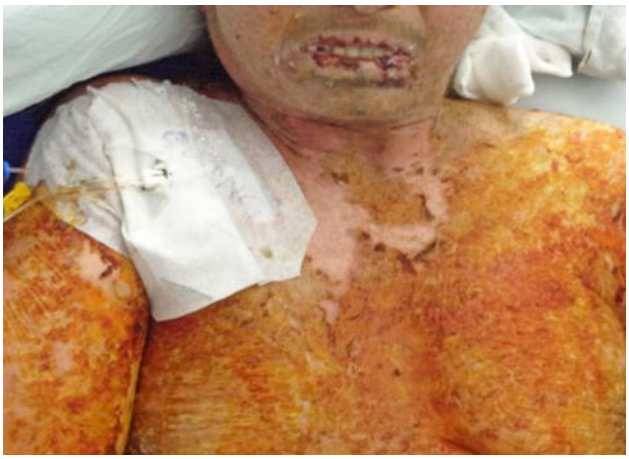
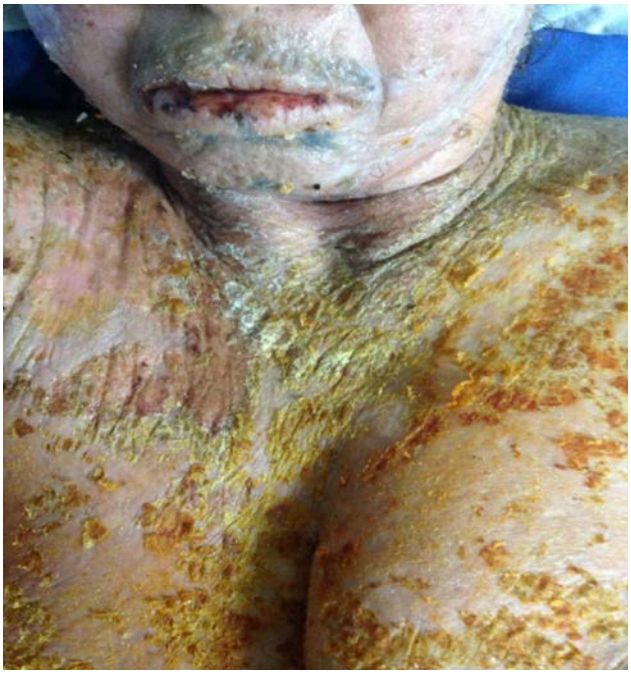


Figure 2
Upper body after completion of HBOT showing regression of skin eruptions



maculopapular rash attributed to vancomycin allergy. She was then transferred to a tertiary facility for autologous haematopoietic stem cell transplantation. Ciprofloxacin (400 mg orally once daily) was started because of urinary tract infection spotted by chance in addition to the acute bacterial endocarditis. The next day, cutaneous lesions together with erythematous maculopapular eruptions with desquamations were observed on her lips, face, head, neck, and arms. On the third day of the antimicrobial therapy, she experienced fever, malaise, and pain, with maculopapular eruption over the whole body. The administration of ciprofloxacin was halted due to the extensive skin eruption, facial swelling and oedema of upper and lower limbs. Purulent secretions and hyperaemia were observed in her conjunctivae, bullous lesions appeared, and desquamation started on the fifth day of admission. She was referred to a dermatology inpatient ward, where she was treated with intravenous immunoglobulin. Her general medical condition deteriorated, and the patient was transferred to the burns intensive care unit.

On her admission to the hospital, she was found to be afebrile with basal temperature of 36.2°C, a pulse rate of 90 beats per minute, and elevated systolic blood pressure at 164/79 mmHg. Her body, including her eyelids, was oedematous and there were bullous maculopapular eruptions (Figure 1). A gentle pressure on the skin caused detachment of epidermis from dermis (known as a positive Nikolsky sign).[4] Furthermore, her conjunctivae were hyperaemic, and her lips were covered with haemorrhagic and erosive lesions with crusts. Eighty percent of her body surface area was affected. The prognosis was evaluated via a severity-of-illness score specifically developed for TEN (SCORTEN). This validated assessment tool is typically used worldwide and based on seven clinical and laboratory findings. The mortality rate increases from 3.2 % with a score of 0–1 to 90% with a score of ≥ 5.[4] The SCORTEN score was calculated as 5 and predicted mortality risk was estimated to be 90%. Laboratory evaluation of her blood sample showed: leucopenia (white blood cell count 2.15 x $10^{9}\cdot L^{-1}$, reference range 4.5–10 x $10.0^{9}\cdot L^{-1}$); anaemia (red blood cell count 2.59 x $10^{12}\cdot L^{-1}$, reference range 3.5–5.5 x $10^{12}\cdot L^{-1}$); haemoglobin: 7.6 $g\cdot dL^{-1}$; haematocrit: 23.2%.

Moreover, *Klebsiella pneumoniae* and *Acinetobacter baumanii* were cultured from her blood taken on the first and fourth days of admission respectively. Based upon the sensitivities of the isolates from the blood cultures, the patient was treated with meropenem and colistin for fourteen days. Subsequent to this two-week intravenous antimicrobial treatment, repeat blood cultures of the patient were negative on the day of discharge from the burn care unit. Symptomatic treatment included pain control with opioid analgesics, wound management, prevention of stress ulcers, nutrition, and fluid support. As a consequence of widespread lesions on the skin and difficulty in wound healing, HBOT was also added to her medical treatment on the second day of admission. The patient underwent five sessions of HBOT applied at 243.1 kPa for 120 minutes per session in a multiplace chamber. Epidermal detachment was noted to stop within 24 hours of commencing HBOT and re-epithelisation started rapidly. The general condition of the patient improved daily and the rash subsided (Figure 2). The patient was transferred out of intensive care to a general ward after 14 days once her clinical status improved.

Discussion

TEN is most often a drug or infectious agent-mediated disease process that presents with signs ranging from erythema multiforme, bullous detachment to necrosis of the skin. It has been described with 220 medications, but only particular drugs are strongly associated with the occurrence of the disease.[3,4,7] The term toxic epidermal necrolysis was defined by scientist Alan Lyell in the 1950's.[8] The incidence rate in clinical studies is 0.5–1.4 cases per million per year. Men are less affected than women with a ratio of 1:1.5.[4] The development of TEN following administration of certain antimicrobial drugs, especially fluoroquinolones (ciprofloxacin, ofloxacin, levofloxacin, norfloxacin) is widely reported.[9–13] The patient reported here was also treated with a fluoroquinolone before admission. Although the skin rashes appeared after administration of ciprofloxacin, it is difficult be certain which drug precipitated the TEN reaction. Underlying malignancy such as multiple myeloma or other medications may be considered to contribute to the presentation of the disease.

Patients usually present with constitutional symptoms such as fever, sore throat, cough, myalgia, and malaise on the first three days of disease. In addition to systemic symptoms, the cutaneous findings initially present as erythematous eruptions, purpura or bullae and frequently disseminate all over the body.[4,7] These lesions exhibit Nikolsky's sign which is defined as separation of epidermis triggered by slight pressure on the skin surface.[14] The disease has a high morbidity and mortality rate associated with being susceptible to secondary super-infection.[15]

TEN patients are usually treated in either intensive care units or burns units at hospitals. The essential treatment of TEN necessitates prompt diagnosis and withdrawal of causative medications. Patients with TEN are provided with supportive care consisting of isolation, fluid and electrolyte replacement, regulation of acid-base imbalance, nutrition support, analgesia, prophylaxis of deep vein thrombosis, prevention of pressure ulcers and infection, and appropriate wound management.[16] HBOT has been widely used in the treatment of various wound types, and was applied here as an adjunct to supportive care. Potential contributions to benefit include antimicrobial effect, reversal of tissue hypoxia, reduction of tissue oedema, enhancement of immune function, and acceleration of epithelialisation.[17,18] After five HBOT sessions, re-epithelialisation was apparent. Our literature review revealed only one similar case report in which three patients with drug-induced TEN were treated with HBOT. It was concluded that patients were successfully treated by means of HBOT after applying approximately 10 treatments.[19]

The mortality rate of TEN is high, and although there are several supportive treatment options, HBOT as an early adjunct to standard supportive care may reduce both morbidity and mortality and enable shorter hospitalisation.

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Hyperbaric oxygen treatment for intrauterine limb ischaemia: A newborn in the chamber

Bengusu Mirasoglu[1], Hande Cetin[1], Sevgi Ozdemir Akgun[2], Samil Aktas[1]

[1] *Istanbul Faculty of Medicine, Underwater and Hyperbaric Medicine Department, Istanbul, Turkey*
[2] *Istanbul Faculty of Medicine, Pediatrics Department, Istanbul, Turkey*

Corresponding author: *Dr Bengusu Mirasoglu, Istanbul Tip Fakultesi, Sualti Hekimligi ve Hiperbarik Tip Anabilim Dali, 34093 Fatih, Istanbul, Turkey*
bengusu.mirasoglu@istanbul.edu.tr

Key words
Case reports; Limb salvage; Neonatal thromboembolism; Neonatal gangrene; Safety

Abstract

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Intrauterine limb ischaemia is a rare condition that may have devastating results. Various treatments are reported in the literature; however, results are not always promising and amputations may be required for some patients. Post-natal hyperbaric oxygen treatment (HBOT) may be a useful treatment option for the salvage of affected limbs. A patient who was born with total brachial artery occlusion and severe limb ischaemia was referred for HBOT. The patient underwent the first HBOT session at her 48th hour of life. A total of 47 HBOT sessions were completed (243.1 kPa [2.4 atmospheres absolute], duration 115 minutes being: 15 minutes of compression; three 25-minute oxygen periods separated by five-minute air breaks; and 15 minutes of decompression), four in the first 24 hours. Full recovery was achieved with this intense HBOT schedule combined with anticoagulation, fasciotomy and supportive care. The new-born tolerated HBOT well and no complications or side effects occurred. To the best of our knowledge, our patient is one of the youngest patients reported to undergo HBOT.

Introduction

Intrauterine limb ischaemia, also called neonatal gangrene, is a rare condition that may have devastating results. A definitive management algorithm has not yet been defined. Several treatments including thrombolysis, systemic anticoagulation and surgical or radiological thrombectomy have been reported, however amputation may be inevitable.[1] Hyperbaric oxygen treatment (HBOT) may be a useful option for the salvage of affected limbs. The case is presented of a neonate born with severe intrauterine limb ischaemia and successfully treated with HBOT combined with anticoagulation, fasciotomy and supportive care.

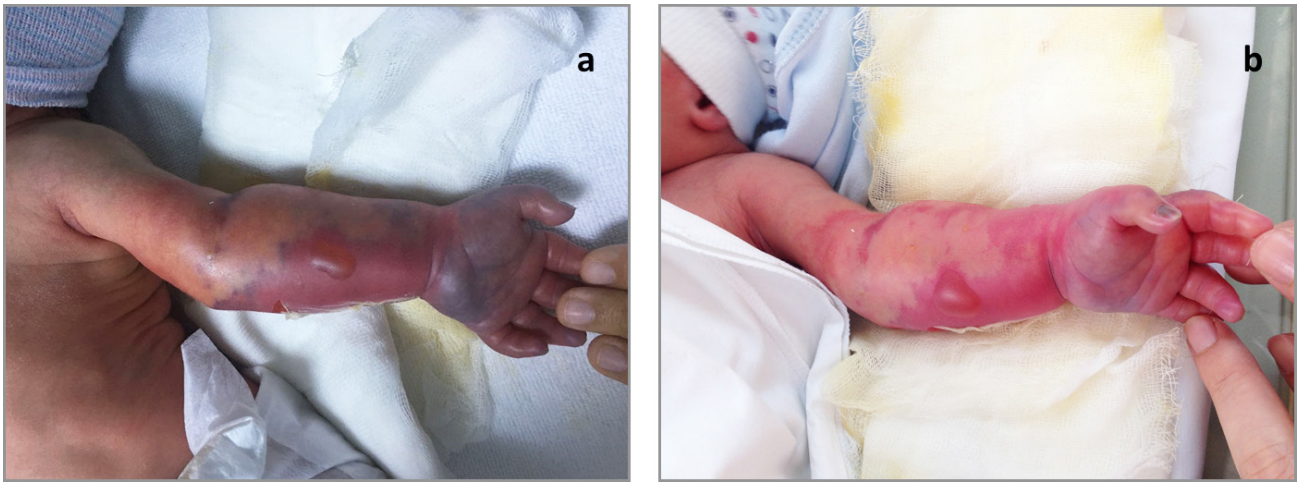
Case report

A 2,960 g female baby was born to a gravida two para one mother at 39 weeks of gestation via caesarean section due to breech presentation. The 23-year-old mother was an undocumented migrant unknown to medical services and had not received any antinatal care. She did not report any medical conditions and her physical examination was unremarkable. The baby's vitals were normal but a marked cyanosis of the left forearm was noted at delivery. Spontaneous movement and reflexes of this extremity were absent. Heparin infusion was started immediately but there were no improvements. Amputation was considered and the patient was transferred to our hospital at age 36 hours for the intervention. She was admitted to neonatal intensive care in order to monitor for possible heparin-related or further thromboembolic problems.

Upon arrival, cyanosis was evident from the midline between elbow and shoulder to the tip of the fingers (Figure 1a). The arm was cold up to the shoulder and flaccid. There were blisters some of which were sloughing on the arm and hand. Peripheral pulses were non-palpable. Colour Doppler revealed the absence of flow in brachial, radial and ulnar arteries, indicating a thrombus in the axillary artery. Computed tomography angiography confirmed the occlusion. Venous flow was normal. The patient was evaluated by the vascular surgeons and neither thrombectomy nor recombinant tissue plasminogen activator (rtPA) were found appropriate due to the risks involved and the delay. A shoulder disarticulation was proposed.

Meanwhile the patient was referred to the hyperbaric medicine department for HBOT. After careful evaluation she underwent her first treatment at her 48th postnatal hour. Significant improvement was not observed after the first session but since the baby was not ready for amputation yet, a second HBOT session was given six hours later. Warming

Figure 1
Patient's arm at presentation (a) and after the second HBOT session (b). Restoration of reperfusion can be observed clearly



and a pinkish colour change was observed in the ischaemic extremity during this session and persisted afterwards (Figure 1b). As evidence of tissue perfusion was noted, surgery was postponed and further HBOT was planned.

During the first day, she underwent two more HBOT sessions with six-hour intervals between. For the following eight days HBOT was given every eight hours. Ischaemia regressed gradually. Afterwards, the patient underwent HBOT twice a day for a week and then once daily for five more days. HBOT was administered at 243.1 kPa (2.4 atmospheres absolute) for a total of 115 minutes. Treatment involved 15 minutes of compression; three 25-minute oxygen periods separated by five-minute air breaks; and 15 minutes of decompression. On the ninth day, plastic surgeons performed fasciotomy on the forearm and hand on suspicion of compartment syndrome although there were no suggestive signs (Figure 2). Intravenous heparin infusion (20 $mg \cdot kg^{-1} \cdot hour^{-1}$) was changed to subcutaneous enoxaparin (1.8 $mg \cdot kg^{-1} \cdot day^{-1}$) at the end of one week. Petrolatum based gauze dressings were applied daily to all wounds. At the end of 47 sessions HBOT was stopped as tissue perfusion was restored and significant healing was observed in the fasciotomy wound. No side effects or complications related to HBOT were recorded. Physiotherapy was started in the second week. Antibiotic therapy and fluid replacement were provided during the course of treatment.

Etiological studies were performed after admission. Plasma protein C, protein S, antitrombin III, and homocysteine levels were within the normal ranges for neonates. Screening for Factor V Leiden, methylenetetrahydrofolate reductase and prothrombin 20210 gene mutations were negative. Antiphospholipid and anticardiolipin antibodies were also normal. Echocardiography did not show any pathological findings. All metabolic studies were within normal limits.

Eventually, the size of the volar fasciotomy wound and the wound on the dorsal forearm reduced more than 75%. The hand wounds closed totally (Figure 3). Skin grafting was not necessary. On her repeat Doppler studies, collateral circulation was visualised. The arm and hand gained motor function. Arm development was normal and shoulder to elbow and elbow to wrist length did not differ from the opposite extremity. Physical therapy was planned for slight ulnar deviation of the hand. The patient was discharged on the 48th day of life with daily enoxaparin to be given weekly. All wounds closed in the first month after discharge. No wound or ischaemia related problems occurred during six months follow up.

Discussion

HBOT is a non-invasive treatment modality where patients breathe 100% oxygen under pressure higher than 101.3 kPa (one atmosphere absolute). It increases the dissolved oxygen content in the blood plasma and so provides hyperoxygenation to tissues that have increased oxygen demand or reduced supply. This increase in blood oxygen content and partial pressure also compensates for arterial vasoconstriction caused by hyperoxia. HBOT has been shown to promote vascular proliferation by increasing vascular endothelial growth factor elaboration and stem cell mobilisation as well as enhancing host defense against infections and regulating the anti-inflammatory response.[2,3] It has also been shown to have a role in ameliorating ischaemia-reperfusion injury which can be a major concern in the acute setting.[4]

HBOT has been used successfully for acute peripheral ischaemia like crush injuries, frostbites or other insults to circulation like thrombembolism.[5,6] By providing oxygenation until flow is restored or adequate collateral circulation is established, it increases viability and survival

Figure 2
Arm during fasciotomy operation. Tissues are well perfused

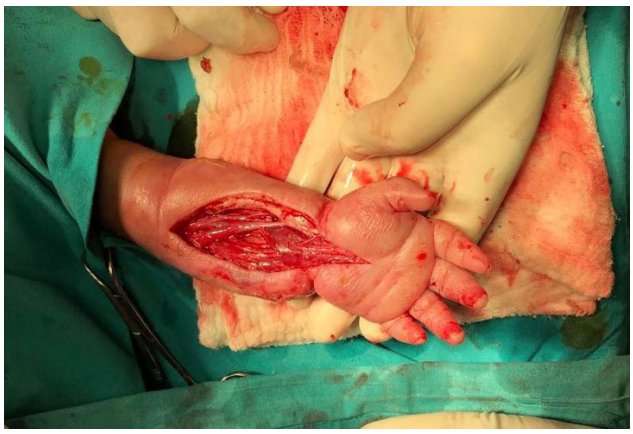
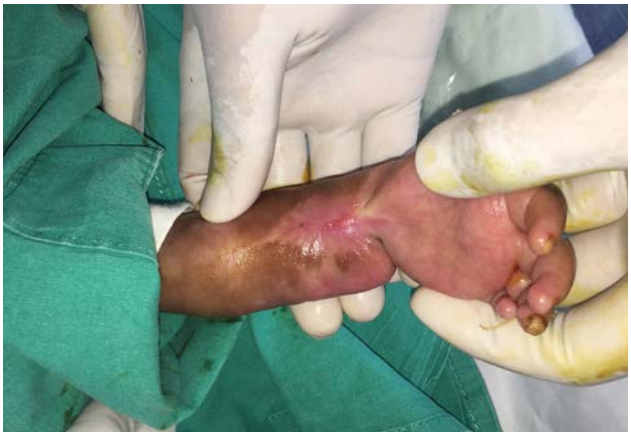


Figure 3
Arm just before discharge. Ischaemia regressed totally and fasciotomy wound almost closed



of poorly perfused tissues besides supporting collateral development. Infants are known to have a higher potential for early collateralisation compared to adults.[7] In this regard, it can be speculated that these effects of HBOT will be augmented and the chance of limb survival will be greater in infants even when total arterial occlusion is present. Indeed, there are a number of reports showing favourable results with HBOT in childhood acute ischaemic conditions, especially thromboembolic incidents.[8-10]

Current data on neonatal extremity ischaemia mostly comes from postnatal incidents which are typically iatrogenic.[1,11] Intrauterine ischaemia which comprises only a small proportion of all neonatal incidents is generally associated with foetal thromboembolism. Promising results have been reported with current treatment options; however, some patients remain unresponsive and require amputations.[12,13] Despite potential benefit, use of HBOT for intrauterine incidents is limited. In the only report available, an infant avoided a below-the-hip amputation but required below the knee amputation. In that case, daily HBOT was started on the seventh day, when leg ischaemia was unresponsive to thrombolysis.[14] The present case, on the other hand, underwent HBOT much earlier and with a considerably more aggressive schedule. Amputation was avoided without thrombolytic treatment.

Prompt initiation and frequent application of HBOT in the early period are of critical importance for the management of acute ischaemia. Skeletal muscle and nerves can tolerate interruption of blood flow for about 4–6 hours before necrosis and irreversible injury occur.[15] Therefore, it is crucial to oxygenate the compromised tissues within these intervals. A full recovery as achieved in our case may be achieved with an intense treatment schedule. Also, patients should be closely monitored for signs of reperfusion such as color change, warming and regaining movement. However, absence of these signs in the first sessions should not lead to early quitting of HBOT as clinically apparent change may be delayed.

Safety of HBOT in the paediatric patient population is considered a concern by some authors.[11] Its use for carbon monoxide intoxication, haemorrhagic cystitis, crush injuries or other peripheral ischaemic conditions like purpura fulminans in paediatric patients has been increasing lately and no serious side effects have been reported. Our patient, despite her young age and intense schedule, also tolerated the treatment well.

In this case, limb loss was avoided by applying HBOT early and with an intense schedule. We suggest that adjunctive HBOT may be useful for management of intrauterine arterial occlusions and should be considered for limb salvage.

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Pulmonary barotrauma with cerebral arterial gas embolism from a depth of 0.75−1.2 metres of fresh water or less: A case report

Ulrika Lindblom[1], Carl Tosterud[1,2]

[1] *Swedish Armed Forces, Diving And Naval Medicine Centre, Karlskrona, Sweden*
[2] *Capio Saint Goran Hospital, Stockholm, Sweden*

Corresponding author: *Dr Ulrika Lindblom, SSS FM DNC, Box 527, SE-371 23 Karlskrona, Sweden*
ulrika.x.lindblom@mil.se

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Abstract

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During underwater vehicle escape training with compressed air, a fit 26-year-old soldier suffered pulmonary barotrauma with cerebral arterial gas embolism after surfacing from a depth of 0.75–1.2 metres of freshwater or less. She presented with an altered level of consciousness. Rapid neurological examination noted slurred speech, a sensory deficit and right hemiparesis. Eleven hours after the accident, hyperbaric oxygen treatment was initiated using US Navy Treatment Table 6. The soldier almost completely recovered after repeated hyperbaric oxygen treatment. Given the very shallow depth this is an unusual case with only two similar case reports published previously.

Introduction

Cerebral arterial gas embolism (CAGE) is a serious medical condition where air enters the central circulation and reaches the brain, disrupting circulation, initiating inflammation and causing stroke-like symptoms. CAGE secondary to pulmonary barotrauma was originally described during free ascent training for submarine rescue[1] and diving with compressed air,[2] but it has also been described after breath-hold diving[3,4] and as a complication of various invasive medical procedures.[5] Hyperbaric oxygen treatment (HBOT) is the preferred treatment for CAGE[6] and should be initiated as soon as possible, but can have significant positive effect even if the treatment is delayed.[7] The minimum depth from which surfacing can provoke pulmonary barotrauma and CAGE has not previously been defined. A case is presented which occurred after ascent from a very shallow depth, between 0.75–1.20 metres of freshwater (mfw), or less.

Case description

In September 2017, a fit 26-year-old female Combat Vehicle 90 (CV90) crew member was undertaking submerged vehicle escape training with a short term air supply system (STASS) in a swimming pool. STASS is a breathing device consisting of a small cylinder with 70 L of compressed air at 200 kPa (Figure 1) and has been used by helicopter crews for many years. During the training, a shallow water egress trainer (SWET) (Figure 2) is submerged, from which the trainees escape, breathing compressed gas from the STASS. Due to some serious accidents where a CV90 was accidentally submerged, the Swedish Army introduced this training for CV90 crews in 2017.

The SWET is first positioned upside down and then tilted slightly sideways in the water (Figure 2). The soldier, becoming submerged while strapped to the chair gradually learns to grab the STASS and escape through the 'roof', which symbolises the hatch of the CV90, during five exercises with increasing levels of difficulty. In the present case the soldier was uncomfortable breathing from the STASS underwater and had to repeat two of the five exercises, making the total number of exercises seven. After the sixth exercise, the soldier complained about a sharp headache focused on a point to the left in the back of her head, but continued. After escaping from the SWET the seventh and final time, the soldier stood up in the water without the mouthpiece, then fell towards the instructors. She was placed in a supine position beside the pool with 100% oxygen administered immediately. The officers present performed a rapid medical assessment, finding bilaterally dilated pupils, loss of sensation in the right part of the face and a reduced motor function in the right arm and foot. The soldier was responsive and could follow instructions, but talked slowly, incoherently, with slurred speech. Afterwards the soldier could remember the last exit from the SWET and how she felt her shoulder hitting the bottom of the pool. After that she had partial amnesia for 20 minutes.

An ambulance and the on-call military diving physician arrived in 10 minutes, and the neurological findings were confirmed. The soldier was helped to a sitting position

Figure 1
Short-term air supply system (STASS) (reproduced with the permission of the Swedish Armed Forces)

Figure 2
The shallow water egress trainer (SWET) used during the accident (reproduced with the permission of the Swedish Armed Forces)

twice within the first 20 minutes to remove wet clothing and lost consciousness both times. She was taken to the emergency department at the local hospital and was initially managed as a drowning accident. At the emergency department a computed tomography (CT) scan of head and thorax was performed approximately 90 minutes after the accident. It showed no cerebral hemorrhage, no evidence of intracerebral gas, no air trapped in the mediastinum and no pneumothorax. The physician at the emergency department intended to admit the patient with a diagnosis of stroke, but after discussion with the military diving physician the soldier was transported in a fixed wing aircraft with normal-pressure cabin 1,400 km (870 miles) to the nearest available recompression chamber.

US Navy Treatment Table 6 was initiated 11 hours after the accident. One hour into the treatment, the soldier had almost completely recovered. The treatment table was not extended, and after its completion the only recidual symptom was a minimal reduction of motor function in the right arm and thigh, and minor sensory loss in the upper right extremity. During the following two days she was re-treated three times for 90 minutes at 243 kPa (2.4 atmospheres absolute). Two magnetic resonance imaging (MRI) scans of the brain were performed two and four days after the accident, without any pathological findings. The soldier was released from hospital four days after the accident in good condition with only a negligible sensory loss in the upper right extremity. After the accident, additional medical examination of the soldier, including spirometry, coagulation markers, vasculitis markers, transthoracic echocardiogram for persistent foramen ovale (PFO) and a CT-angiogram of the carotid arteries all showed no pathology.

The technical investigation showed no malfunction of the STASS equipment used. Measurements after the accident revealed that the distance from the water surface to the soldier's mouth was 0.75 mfw if she was turned completely upside down. The maximum depth of the pool was 1.2 mfw.

Discussion

CAGE following a pulmonary barotrauma is a well described complication in compressed air diving. Air in a distensible space will expand as the surrounding pressure decreases. This means that divers holding their breath during ascent are at risk for barotrauma of the lung. If alveoli and adjacent blood vessels are simultaneously damaged air may enter the pulmonary vessels, pass to the left atrium, and distribute in the systemic circulation. Given the brain receives 20–25% of the cardiac output, some of the bubbles will inevitably enter the cerebral circluation. Large bubbles may become trapped in cerebral arteries and cause ischaemia. Bubbles that redistribute through the cerebral circulation can initiate a secondary inflammatory response. Manifestations of CAGE include loss of consciousness, confusion, focal neurological deficits and ischaemia.[5]

In the present case the soldier is thought to have experienced pulmonary barotrauma when surfacing from a depth of 1.2 mfw or less. Such an event at such shallow depth has, to our knowledge, been described only twice before.[8,9]

Nevertheless, it has been shown that a transpulmonary pressure between 73–90 mmHg can induce pulmonary barotrauma.[1,10] The equivalent pressure of 1 mfw is 75 mmHg and it follows that pulmonary barotrauma in such shallow depths is certainly possible, if for example, the diver were to breathhold during ascent after a maximal inspiration. In the present case it is impossible to know exactly at what depth the injuring breath was taken, but it cannot have been deeper than 1.2 m and it seems clear that there was significant barotrauma with CAGE. It is notable that investigations did not find any obvious pulmonary predisposition to barotrauma. The sharp posterior headache after the second to last exercise might be an indication that pulmonary barotrauma had already occurred prior to the final exercise, but that is difficult to prove.

The instructors described clearly how the soldier was very motivated to complete the training but did have trouble breathing from the STASS and was uncomfourtable during the exercises. There was less time for the CV90 crews to do water exercises prior to the actual STASS training, in comparison to helicopter crews. This may have contributed to the accident. If the breatholding is initiated after the person has taken a very large breath the elasticity of the lung is already almost completely engaged and the added pressure required for pulmonary barotrauma can be quite small.

In this case the soldier exhibited altered consciousness for approximately 20 minutes after the initial CAGE. Each time she sat upright she lost consciousness completely, which might be due to re-embolisation when more air ascends to the brain or to lowered blood pressure in the affected vessels.

Patients presenting with initial neurological symptoms can improve without immediate recompression but might deteriorate clinically after a few hours.[11] It is important to treat patients even after a delay, since treatment initiated hours after the CAGE can still be beneficial.[7] The mechanism is uncertain, but resolution of residual bubbles or amelioration of inflammatory effects are possible. This patient had a delay to treatment of 11 hours and still improved in temporal relation to HBOT.

This case is illustrative of how important it is for divers and dive medical specialists to enter a dialogue with medical professionals at a receiving local hospital. Otherwise there is a great risk that HBOT will be delayed or completely withheld with possible serious consequences for a patient with barotrauma-induced CAGE.

Conclusions

Pulmonary barotrauma with CAGE is rare but possible during compressed gas diving in very shallow waters. A diver with symptoms such as loss of consciousness, confusion, focal neurological deficits, cardiac arrhythmias, or ischaemia, occurring immediately or within minutes of surfacing should be considered as a possible AGE and treated with HBOT. The risk of re-embolisation should be considered and the patient should not have the head or torso elevated during first aid management. Although this seems to be a rare occurrence with only two previous case-reports published,[8,9] it is important for divers and medical professionals to have sufficient knowledge concerning this possible injury even at shallow depths.

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Letters to the Editor

Commentary on using critical flicker fusion frequency to measure gas narcosis

We read with great interest the paper on using critical flicker fusion frequency (CFFF) for monitoring gas narcosis in divers.[1] We agree with the authors' general conclusion that the CFFF has many limits prohibiting its regular use for monitoring decrease of mental performance in divers exposed to pressure and increased partial pressure of gases, including nitrogen, helium, carbon dioxide and oxygen. However, we do not think that the experiments conducted were planned correctly for reaching such conclusions. We do not agree with some of the explanations of physiological phenomena presented in the text as a part of the literature review.

First, as reported in the text, each measurement was preceded by a five-minute acclimatisation period for the pressure and/or gas mixture. Such a short time is enough to reach the equilibrium for dissolving breathing gases in the lipid layers of the central nervous system, which is the basic assumption for inert gas narcosis based on the Meyer-Overton hypothesis, or for carbon dioxide acting of ion changes in the brain. But it is possibly too short to observe effects of other mechanisms potentially influencing gas narcosis, including oxygen effects on neurological tissues. Therefore, in our past experiments, referred to in the abovementioned paper, we did measurements of CFFF at different partial pressures of oxygen (0.7, 1.4, 2.8 atmospheres absolute [atm abs]) only after at least 25 minutes of breathing oxygen.[2] Also, general hyperbaric practice shows that oxygen seizures rarely occur before passing 20 minutes of breathing oxygen, even at high oxygen partial pressures (2.4–2.5 atm abs). This time-dependency is reflected in the cumulative risk of oxygen toxicity index.[3]

Second, while mentioning the use of CFFF for monitoring oxygen influence on CNS, the authors did not say that some of the 'conflicting' or 'paradoxical' reports from the literature can be easily explained if one considers subjects' experience with oxygen. Jammes et al. have already reported that the threshold for hyperbaric oxygen-induced neuromuscular hyperexcitability is elevated in divers repeatedly exposed to high oxygen pressure during their occupational activities as elite combat divers compared to recreational divers.[4] This can easily explain differences in CFFF readouts between recreational divers reported by Hemelryck et al.[5] and military combat divers reported by us.[2]

Third, Hesser et al. have already quantified the narcotic effect of oxygen to be 3 to 4 times as potent a narcotic as nitrogen.[6] This must be considered while dealing with 'inert' gas narcosis, but it cannot be explained based on the Meyer-Overton hypothesis as the solubility of oxygen in lipids is only 1.7 greater than nitrogen. Moreover, at some point, the oxygen effect converts to toxicity. Interestingly, Lavoute et al. demonstrated biphasic oxygen effect on dopamine release in the nigrostriatal pathway, at least in animal model.[7] Taken together, this may indicate that oxygen-induced brain poisoning and an increase in neuronal excitability measured by CFFF may use the same or intertwined cellular signaling pathways.[2]

To conclude, the CFFF is a recognised method to assess neuronal excitability influencing attention and alertness.[8] Hyperbaric exposure is a mixture of pressure effects per se, inert gas narcosis, additive/synergistic effects of metabolic gases (oxygen and carbon dioxide), physical environmental factors (immersion, temperature, stress) and many others. The limitation of measuring gas narcosis using the only single indicator for attention and alertness is an oversimplistic approach doomed to failure.

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Jacek Kot[1], Pawel J Winklewski[2]
[1] National Centre for Hyperbaric Medicine, Institute of Maritime and Tropical Medicine in Gdynia, Medical University of Gdansk, Poland
[2] Department of Human Physiology, Medical University of Gdansk, Poland

Address for correspondence: *Jacek Kot, National Centre for Hyperbaric Medicine, Institute of Maritime and Tropical Medicine in Gdynia, Medical University of Gdansk, Poland*
jkot@gumed.edu.pl

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Reply: Commentary on using critical flicker fusion frequency to measure gas narcosis

We wish to express our appreciation to Dr Jacek Kot and Dr Pawel Winklewski for their interest in our article.[1] We agree in general terms with the assertion that our critical flicker fusion frequency (CFFF) evaluations cannot be confidently extrapolated to measurements made after larger time intervals at pressure. However, as they point out, a 5-minute acclimatisation is sufficient for the onset of the phenomenon we were attempting to measure (nitrogen narcosis), based not only on kinetic models but also on studies that have shown onset after a 5-minute latency.[2,3] The remainder of their letter largely confirms our assertion that CFFF is confounded by so many other influences that it is likely incapable of reliably achieving our goal of isolating and measuring a short latency narcotic effect caused by hyperbaric nitrogen.

One such influence, emphasised by Kot and Winlewski, is the effect of elevated pressures of inspired oxygen, which can induce hyperexcitability. One point not noted in their letter is that hyperexcitability caused by oxygen has also been observed on arrival at elevated pressure.[2,4] Nevertheless, we agree that oxygen toxicity effects typically have an onset latency beyond the measurement period used in our study, but oxygen toxicity is obviously a different syndrome, and its measurement was not our goal. Therefore, we agree that studies comparing substantially different oxygen exposures might record very different findings when using an outcome measurement (such as CFFF) potentially affected by the duration of exposure to hyperbaric oxygen. This almost certainly explains the differences between our study and that of Kot et al.[5]

We note Kot and Winlewski's confident acceptance that oxygen is a narcotic gas and their invocation of the Meyer-Overton hypothesis in comparing narcotic potentials of gases. The Meyer-Overton hypothesis is still widely cited within the diving medicine community to predict the narcotic potency of the various gases used in diving. Conversely, in the field of anaesthesiology, progress has been made in understanding how narcotic agents cause their effect by binding to ligand-gated ion-channel proteins.[6] Related work has also helped explain why many gases, whose lipid solubility would predict a narcotic effect, have no such effect due to their incompatibility with receptor sites.[7] It has been shown that dopamine changes are only one among many neurophysiological pathways disturbed by oxygen,[8] both pre- and post-seizures. However, none of these pathways are similar to the pathways known to be implicated in the effect of narcotic agents. More recently, oxygen has been associated with the upregulating of the NMDA-receptor in a cellular model,[9] while nitrous oxide and ketamine inhibit the NMDA receptor.[10] This might explain the excitatory effect of hyperbaric oxygen. Hence, a narcotic effect of oxygen, preceding the hyperexcitability of oxygen seizures, seems very improbable.

In conclusion, we stand by our conclusion that research on CFFF as a measure of the narcotic effect exerted by hyperbaric gases has generated conflicting results, typically explained in each paper by invoking various confounding factors. We agree with Kot and Winlewski's conclusion that CFFF is poorly suited to monitoring hyperbaric gas narcosis. It is too sensitive to confounding effects that may obfuscate the cognitive impairment caused by gas narcosis.

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Xavier CE Vrijdag[1], Hanna van Waart[1], Jamie W Sleigh[1,2], Simon J Mitchell[1,3]

[1] Department of Anaesthesiology, University of Auckland, Auckland, New Zealand
[2] Department of Anaesthesia, Waikato Hospital, Hamilton, New Zealand
[3] Department of Anaesthesia, Auckland City Hospital, Auckland, New Zealand

Address for correspondence: *Xavier CE Vrijdag, Department of Anaesthesiology, School of Medicine, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand*
x.vrijdag@auckland.ac.nz

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Critical flicker fusion frequency; Narcosis; Nitrogen; Oxygen; Letters (to the Editor)

Science and Statistics

My first contact person within medical science in the field of experimentation was the head of an Institute of Physiology. He, coming from the Göttingen University, told me: "*If I am familiar enough within my particular area of physiology, and if I have a scientific issue, I should develop a hypothesis. In order to test the hypothesis, I need to develop, define and test an experimental model and then perform an experiment. If the data from the experiment are confirmative, I will publish my issue"*. This advice reaches back almost 50 years.

In the meantime, we had quite a few scientific issues, and we performed more than one experiment. We used descriptive statistics to present our data, having in mind that averaging was data murder. Still, we presented pre- and post-means ± SDs and graphs, and the journals were happy. (NB: At that time, our work was being paid by the publisher). Times changed and the situation has become more complex. The effects of different interventions were to be compared at different points in time, and we understood that our multiple *t*-testing was witches' brew. So, we learned to differentiate terms as ANOVA from MANOVA. If these analyses were not in the focus of our scientific activities, we needed to contact a statistical ambulance. Anyway, it took time prolonging the project.

In parallel, the statisticians' influence grew, such that the journals demanded the Methods section to be expanded by a statistics paragraph. We are now exhorted to include how the sample size was determined, why blinding and random assignment was warranted or not warranted, whether or not the groups were matched, and how the nature of the data distribution was tested. Finally, the climax of statistics – which test should the authors employ to determine whether the differences were significant with the *P*-value being ≤ 0.05.

Some journal's statisticians even wanted to read: the *P*-value was 0.034. How much does that contribute to a better understanding the effect of an intervention? To exemplify my displeasure: One study might compare the effects of air versus oxygen-enriched air (Nx) on the minute ventilation while intense fin swimming. The result: ventilation of air is higher over Nx, the difference being 0.3 $L \cdot min^{-1}$, i.e., has no clinical importance. How can this difference be statistically significant? Because of the 850 participants.

To remember: Researchers want to answer reasonable questions using reasonable experimental models. To do so, the researchers need to be creative, but also firmly founded in scientific reasoning. Statisticians at journals sometimes seem to misunderstand their role. They are important adjuncts, but they are not the protagonists. Nevertheless, often enough statistics became the Cerberus refusing admittance to the publication world.

Hope comes from the '*P*-value statement' of the American Statistical Society.[1] Ron Wasserstein (ASA's executive director) is to be admired in this context: the *P*-value was never intended to be a substitute for scientific reasoning. And he continues: Well-reasoned statistical arguments contain much more than the value of a single number with an arbitrary threshold. ASA is intended to steer research into a 'post $P < 0.05$ era'. As one result: The editors of *Basic and Applied Social Psychology* decided radically and banned *P*-values.

Expectedly, not all journals will react so radically. Maybe, the coming generation of statisticians will become ASA followers. A Nature article titled "*Scientific Method: Statistical Errors*"[2] might be helpful to step into the new era.

References

1 Wasserstein RL, Lazar NA. The ASA Statement on *P*-values: Context, process, and purpose. Am Stat. 2016;70:129–33. doi: 10.1080/00031305.2016.1154108.
2 Nuzzo R. Scientific method: statistical errors. Nature. 2014;506:150–2. doi: 10.1038/506150a.

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Jochen D Schipke
Research Group, Experimental Surgery, University Hospital Dusseldorf, Germany
j.schipke@gmx.org

Key words
Effect size; *P*-value; Scientific reasoning; Statistic; Letters (to the Editor)

Notices and news

SPUMS notices and news and all other society information can be found on:
https://spums.org.au/

SPUMS President's message

Neil Banham

This Annual General Meeting (AGM) marks the end of the first year of my Presidential term. I am writing this on the 50th Anniversary of the founding of our Society by Carl Edmonds, Bob Thomas, Douglas Walker, Ian Unsworth and Cedric Deal in the Wardroom of HMAS Penguin in Sydney on 03 May 1971. Our Society has certainly grown and evolved since then! This report was tabled at the SPUMS AGM on 22 May 2021.

Despite the interruption of COVID-19, which has resulted in the cancellation of our 2020 Annual Scientific Meeting (ASM), as well as our usual annual face-to-face (f2f) Executive Committee (ExCom) meeting, so much has been happening in the background.

Our AGM and f2f ExCom meetings were held virtually, with the usual business of our Society being successfully conducted. Despite these difficult times we have been able to manage a modest budget surplus. Our Treasurer Soon Teoh will present our 2020 Annual Accounts at the AGM. SPUMS member numbers for 2020 were 372, with 300 renewing already for 2021 and nine Educational Institution subscriptions. I encourage you all to promote SPUMS to your colleagues and encourage them to join or renew, such that we can grow and strengthen our Society for another 50 years.

We were pleased to be able to hold an ASM in 2021 at HMAS Penguin, which was a combination of virtual and in-person attendance, for those of you who live in Sydney, or were able to travel there.

Theme: *50 years of Diving Medicine (with an undercurrent of COVID medicine): Remembering the past and preparing for the future*

Our Keynote Speaker was Dr Richard Harris, who is known to all of you after his Thai cave rescue efforts resulting in him being awarded Australian of the Year in 2019 along with his co-rescuer and dive buddy Dr Craig Challen. 'Harry' is a very entertaining and accomplished speaker and his fascinating presentations were enjoyed by all who attended virtually or in person. Our thanks to our SPUMS Secretary Doug Falconer for organising this highly successful ASM.

The ExCom hope that the 2022 ASM will be able to be in-person, with diving again being a feature of the meeting. This is planned for Tutukaka, New Zealand in April 2022, the location for the cancelled 2020 ASM.

Our journal *Diving and Hyperbaric Medicine* continues to publish high quality material, maintaining its position as the pre-eminent journal in the field of diving and hyperbaric medicine, with an impressive Impact Factor of 1.5.

Our Editor Professor Simon Mitchell reports an increased volume of submissions during the last year, adding significantly to his and his teams' work load. Many thanks to Simon and his Editorial Assistant Nicky Telles for their efforts, as well as to the many reviewers and to the SPUMS members who have submitted to our journal.

The ANZHMG Introductory Course in Diving and Hyperbaric Medicine was able to be held in early 2020, before the commencement of lockdowns, and hopefully will proceed as planned in 2021 in Fremantle (24 May – 04 June) following a COVID-19 induced postponement in February. Dr Ian Gawthrope, Course Convenor, has successfully had this course accredited by ANZCA towards the ANZCA Diploma of Advanced Diving and Hyperbaric Medicine.

Dr David Cooper has succeeded Dr David Wilkinson OAM in the role of SPUMS Education Officer. I again thank '*Wilko*' for his many years of service in this role. The Education Officer, amongst other duties, has a vital role in the acceptance and review process for SPUMS Diploma candidates.

Finally, I would like to thank all my ExCom team for their hard work and ongoing support in these difficult times, and to members for staying engaged with SPUMS.

Neil Banham
SPUMS President

ANZHMG Chair's report

I would like to present my first report as chair of the ANZHMG committee.

Even though I have been in the position since late last year there is little to report, as we continue to grapple with the intermittent and unpredictable restrictions imposed by the pandemic

The most recent ANZHMG Introductory Course in Diving and Hyperbaric Medicine was held in Fremantle from the 24 May – 04 June 2021.

It was a highly successful course as judged by the excellent participant feedback. Despite the challenges there were 14 participants from around Australia. Congratulations to Dr Emma Tucker from Tasmania who was awarded the Unsworth Prize.

Thanks to the course convenor Dr Ian Gawthrope and to the course faculty who made this a success; Faculty SPUMS members: Dr Neil Banham, Professor David Smart, Dr Iestyn Lewis, Dr John Lippmann, Dr Peter Buzzacott, Dr Kavinda Senasinghe, Professor Mike Bennett, Dr David Wilkinson and Dr David McIlroy.

The tentative dates for the 2022 course are 21 February – 04 March, and again will be held at the Hougoumont Hotel in Fremantle. The Venue Meeting Room capacity will limit participant numbers to 15 so you will need to get in early when registrations open. The link to information on the SPUMS website is https://spums.org.au/content/approved-courses-doctors.

Stay safe as we continue to navigate a challenging time.

Bob Webb
Chairman, ANZHMG

The
SPUMS
website is at
https://spums.org.au/

Members are encouraged to log in and keep their personal details up to date.

The latest issues of *Diving and Hyperbaric Medicine* are via your society website login.

Australian and New Zealand College of Anaesthetists Diving and Hyperbaric Medicine Special Interest Group

The new Diploma of Advanced Diving and Hyperbaric Medicine was launched on 31 July 2017. Those interested in training are directed to the ANZCA website https://www.anzca.edu.au/education-training/anzca-diploma-of-advanced-diving-and-hyperbaric-me.

Training
Documents to be found at this site are:

- Regulation 36, which provides for the conduct of training leading to the ANZCA Dip Adv DHM, and the continuing professional development requirements for diplomats and holders of the ANZCA Certificate of DHM;
- ANZCA Advanced DHM Curriculum which defines the required learning, teaching and assessment of the diploma training programme; and
- ANZCA Handbook for Advanced DHM Training which sets out in detail the requirements expected of trainees and accredited units for training.

Examination dates for 2021

Written examination	11 August 2021
Viva examination	08 September 2021

Accreditation
The ANZCA Handbook for Advanced DHM accreditation, which provides information for units seeking accreditation, is awaiting approval by Standards Australia and cannot yet be accessed online. Currently six units are accredited for DHM training and these can be found on the College website.

Transition to new qualification
Transitional arrangements for holders of the ANZCA Certificate in Diving and Hyperbaric Medicine and highly experienced practitioners of DHM seeking recognition of prior experience lapsed on 31 January 2019.

All enquiries should be submitted to dhm@anzca.edu.au.

SPUMS Facebook page

Like us at:
http://www.facebook.com/pages/SPUMS-South-Pacific-Underwater-Medicine-Society/221855494509119

Royal Australian Navy Medical Officers' Underwater Medicine Course 2021

Date: 01–12 November 2021 and 14–25 March 2022

Venue: HMAS Penguin, Sydney

The MOUM course seeks to provide the medical practitioner with an understanding of the range of potential medical problems faced by divers. Emphasis is placed on the contraindications to diving and the diving medical assessment, together with the pathophysiology, diagnosis and management of common diving-related illnesses. The course includes scenario-based simulation focusing on the management of diving emergencies and workshops covering the key components of the diving medical.

Cost: The course cost remains at AUD$1,355.00 (ex GST), this is yet to be confirmed.

For information and application forms contact:
Rajeev Karekar, for Officer in Charge
Submarine and Underwater Medicine Unit
HMAS Penguin
Middle Head Rd, Mosman
NSW 2088, Australia
Phone:*+61 (0)2-9647-5572*
Fax: *+61 (0)2-9647-511*
Email: *rajeev.karekar@defence.gov.au*

SPUMS Diploma in Diving and Hyperbaric Medicine

Requirements for candidates (May 2014)

In order for the Diploma of Diving and Hyperbaric Medicine to be awarded by the Society, the candidate must comply with the following conditions: They must

1 be medically qualified, and remain a current financial member of the Society at least until they have completed all requirements of the Diploma;
2 supply evidence of satisfactory completion of an examined two-week full-time course in diving and hyperbaric medicine at an approved facility. The list of such approved facilities may be found on the SPUMS website;
3 have completed the equivalent (as determined by the Education Officer) of at least six months' full-time clinical training in an approved Hyperbaric Medicine Unit;
4 submit a written proposal for research in a relevant area of underwater or hyperbaric medicine, in a standard format, for approval before commencing the research project;
5 produce, to the satisfaction of the Academic Board, a written report on the approved research project, in the form of a scientific paper suitable for publication. Accompanying this report should be a request to be considered for the SPUMS Diploma and supporting documentation for 1–4 above.

In the absence of other documentation, it will be assumed that the paper is to be submitted for publication in *Diving and Hyperbaric Medicine*. As such, the structure of the paper needs to broadly comply with the 'Instructions for authors' available on the SPUMS website https://spums.org.au/ or at https://www.dhmjournal.com/.

The paper may be submitted to journals other than *Diving and Hyperbaric Medicine*; however, even if published in another journal, the completed paper must be submitted to the Education Officer (EO) for assessment as a diploma paper. If the paper has been accepted for publication or published in another journal, then evidence of this should be provided.

The diploma paper will be assessed, and changes may be requested, before it is regarded to be of the standard required for award of the Diploma. Once completed to the reviewers' satisfaction, papers not already submitted to, or accepted by, other journals should be forwarded to the Editor of *Diving and Hyperbaric Medicine* for consideration. At this point the Diploma will be awarded, provided all other requirements are satisfied. Diploma projects submitted to *Diving and Hyperbaric Medicine* for consideration of publication will be subject to the Journal's own peer review process.

Additional information – prospective approval of projects is required

The candidate must contact the EO in writing (or email) to advise of their intended candidacy and to discuss the proposed topic of their research. A written research proposal must be submitted before commencement of the research project.

All research reports must clearly test a hypothesis. Original basic and clinical research are acceptable. Case series reports may be acceptable if thoroughly documented, subject to quantitative analysis and if the subject is extensively researched in detail. Reports of a single case are insufficient. Review articles may be acceptable if the world literature is thoroughly analysed and discussed and the subject has not recently been similarly reviewed. Previously published material will not be considered. It is expected that the research project and the written report will be primarily the work of the candidate, and that the candidate is the first author where there are more than one.

It is expected that all research will be conducted in accordance with the joint NHMRC/AVCC statement and guidelines on research practice, available at: www.nhmrc.gov.au/_files_nhmrc/publications/attachments/r39.pdf, or the equivalent requirement of the country in which the research is conducted. All research involving humans, including case series, or animals must be accompanied by documentary evidence of approval by an appropriate research ethics committee. Human studies must comply with the Declaration of Helsinki (1975, revised 2013). Clinical trials commenced after 2011 must have been registered at a recognised trial registry site such as the Australia and New Zealand Clinical Trials Registry http://www.anzctr.org.au/ and details of the registration provided in the accompanying letter. Studies using animals must comply with National Health and Medical Research Council Guidelines or their equivalent in the country in which the work was conducted.

The SPUMS Diploma will not be awarded until all requirements are completed. The individual components do not necessarily need to be completed in the order outlined above. However, it is mandatory that the research proposal is approved prior to commencing research.

Projects will be deemed to have lapsed if:

- the project is inactive for a period of three years, or
- the candidate fails to renew SPUMS Membership in any year after their Diploma project is registered (but not completed).

For unforeseen delays where the project will exceed three years, candidates must explain to the EO by email why they wish their diploma project to remain active, and a three-year extension may be approved. If there are extenuating circumstances why a candidate is unable to maintain financial membership, then these must be advised by email to the EO for consideration by the SPUMS Executive. If a project has lapsed, and the candidate wishes to continue with their DipDHM, then they must submit a new application as per these guidelines.

The Academic Board reserves the right to modify any of these requirements from time to time. As of October 2020, the SPUMS Academic Board consists of:

Associate Professor David Cooper, Education Officer, Hobart
Professor Simon Mitchell, Auckland

All enquiries and applications should be addressed to:
Associate Professor David Cooper
education@spums.org.au

Key words
Qualifications; Underwater medicine; Hyperbaric oxygen; Research; Medical society

Notices and news

EUBS notices and news and all other society information can be found on:
https://www.eubs.org/

EUBS President's message

Ole Hyldegaard

Here's hoping for a time when our EUBS family can finally meet once again!

As the date for our next general assembly (GA) and Annual Scientific meeting approaches in September 2021, we are still in the grip of the COVID-19 pandemic and all of its consequences. Yet again, this year's Annual Scientific meeting scheduled for Prague, has been cancelled. Having had no annual meetings since our 2019 Tel-Aviv meeting, EUBS has been on a 'standby' situation with respect to our annual meeting and this temporary situation will hopefully end by 2022 and the meeting will be scheduled for Prague. On behalf of the EUBS ExCom I wish to express my appreciation for the flexibility and commitment of our local organizers – Dr Michal Hájek and his colleagues. Let us all hope that we will be able to meet again at a memorable event in Prague for 2022. As we approach summer and vacation time for most Europeans, I wish you all great holidays and safe diving for those of you lucky enough to embark on such a journey. So many of our colleagues have been experiencing a truly horrific year as front-line health care providers, especially in emergency medicine and intensive care with a large COVID-19 intake of patients. This said, positive developments are seen as vaccinations gradually take effect, many HBOT centers are starting to operate on a more normal schedule and travel is gradually becoming possible. Some tourist destinations have started to open up and we hope this industry, including the recreational diving industry, will soon be entering an positive trend after a long, hard shut-down.

As my term as EUBS president comes to an end around the time of our next virtual GA, I wish you all a splendid summer and stay safe.

Ole Hyldegaard
EUBS President

EUBS Notices and news

POSTPONED: EUBS2020 Scientific Meeting on Diving and Hyperbaric Medicine

The COVID-19 pandemic continues to wreak havoc and even though all over the world, vaccination campaigns are under way, it does not seem likely that unrestricted travel will be possible in the next six months. Even if travelling abroad may be allowed, the prospect of quarantine upon return to one's own country would make attending a three-day conference less attractive.

Combined with the decrease of hyperbaric and diving activities and the increased workload for most of the medical professionals as a consequence of COVID-19, the EUBS ExCom has decided to postpone our Annual Scientific Meeting for yet another year.

This means that the new calendar for EUBS meetings will now be:
2022 – Prague, Czech Republic
2023 – Porto, Portugal
2024 – Brest, France
2025 – Turku, Finland

In order to provide our membership and all interested professionals with scientific updates and education in the field of hyperbaric and diving medicine, EUBS will organise one or more Webinars in the second half of 2021, similar to the first Webinar on 10 March of this year. More information will be provided through the regular EUBS website news emails.

EUBS elections Member-at-Large and Vice President

Around the time of publication of this issue of DHM, the election process for the 2021 ExCom members (Member-at-Large and Vice President) of EUBS will have started.

Member-at-Large

We will be saying goodbye to Dr François Guerrero (Brest, France) as Member-at-Large 2018. ExCom extends their thanks to François for the work he did in ExCom, and hopes to be able to continue counting on his support and help.

Vice President

In September, Professor Jean-Eric Blatteau will take over the Presidency of our Society from Professor Ole Hyldegaard, after three years. Ole will remain in ExCom as Immediate Past President, and Professor Costantino Balestra will formally leave ExCom after a 'tour of duty' spanning 12 years. Of course, Tino will also remain active in the Research and Education Committee.

Candidates for the position of Member-at-Large 2021 and Vice President will be presenting themselves on the EUBS website with a picture and short CV, and you should by the time this journal issue is published, have received an internet ballot by email allowing you to cast your vote.

If you do not receive the email by the end of June, please notify us at secretary@eubs.org, and we will work with you to find out the reason why. As the system works via email, it is possible the message ended up in your spam folder. There may be other reasons but usually, we are able to solve them.

Website and social media

As always, please visit the EUBS Website (http://www.eubs.org/) for the latest news and updates.

On the 'Research Page' (http://www.eubs.org/?page_id=284) there is information on planned and recruiting clinical trials, including one on the 'use of HBOT for COVID-19'.

While we value the membership contributions of all our members (after-all, members are what constitutes our Society), EUBS ExCom would specifically like to thank our Corporate Members for their support of our Society. Their names, logos and contact information on the Corporate Members page under menu item "*The Society*".

Please follow us on Facebook, Twitter and Instagram. While we will continue to use our "*EUBS website news*" email messages as a way to communicate important information directly to our EUBS members, Twitter and Instagram will be used to keep both members and non-members updated and interested in our Society.

Here are the links to bookmark and follow:
Facebook: https://www.facebook.com/European-Underwater-and-Baromedical-Society-283981285037017/
Twitter: @eubsofficial
Instagram: @eubsofficial

Courses and meetings

Scott Haldane Foundation

As an institute dedicated to education in diving medicine, the Scott Haldane Foundation has organised more than 300 courses all over the world, over the past 28 years.

SHF is targeting on an international audience with courses world wide. Due to the COVID-19 Pandemic some courses are re-scheduled. Fortunately we were able to find new dates for all postponed courses. Below the upcoming SHF-courses in the second half of 2021.

The courses Medical Examiner of Diver (part 1 and 2) and SHF in-depth courses, as modules of the level 2d Diving Medicine Physician course, fully comply with the ECHM/EDTC curriculum for Level 1 and 2d respectively and are accredited by the European College of Baromedicine (ECB).

2021

11–18 Sept	Medical Examiner of Divers part 2 (level 1), Bonaire, Dutch Caribbean
01–02 Oct	Medical Examiner of Divers part 1 (level 1), Zeist, NL
07–09 Oct	Medical Examiner of Divers part 2 (level 1), Amsterdam Univ. Med. Centre, NL
Oct (5 hours)	Refresher course the diving medical in practice, NL
06–13 Nov	Medical Examiner of Divers part 1 (level 1), Manado, Indonesia
13–20 Nov	28th In-depth course diving and mental health (2d), Manado, Indonesia
20–27 Nov	28th In-depth course diving and mental health (2d), Manado, Indonesia
tbd	Internship different types of diving (2d), Royal Dutch Navy-Den Helder NL
On request	Internship HBOT (level 2d certification), NL/Belgium

The course calendar will be supplemented regularly. For the latest information see: https://www.scotthaldane.nl/en/. Please also check the COVID-19 news update on this website for the latest schedule changes.

The Science of Diving

Support EUBS by buying the PHYPODE book 'The science of diving'. Written for anyone with an interest in the latest research in diving physiology and pathology. The royalties from this book are being donated to the EUBS.
Available from: Morebooks
https://www.morebooks.de/store/gb/book/the-science-of-diving/isbn/978-3-659-66233-1

Hyperbaric Oxygen, Karolinska

Welcome to: http://www.hyperbaricoxygen.se/

This site, supported by the Karolinska University Hospital, Stockholm, Sweden, offers publications and high-quality lectures from leading investigators in hyperbaric medicine.

Please register to obtain a password via email. Once registered, watch on line, or download to your iPhone, iPad or computer for later viewing.

For further information contact via email:
folke.lind@karolinska.se

Publications database of the German Diving and Hyperbaric Medical Society (GTÜM)

German Diving and Hyperbaric Medical Society's (GTÜM) website is currently unavailable owing to a new website being built. They have advised that a notification will sent when their database will be available again, They apologise for any inconvenience this may cause.

Foundation of Diving Research, SDR

Saturday 26 March 2022, AMC, Amsterdam: Symposium to celebrate the 50 year anniversary of the Dutch Stichting Duik Research (SDR, Foundation of Diving Research).

Topics: 50 years research by SDR; diving cardiology; safety of professional diving; diving to perform coral biotope research and open sea under water archaeology; physiological adaptations of diving mammals. 4 cp.

Visit: http://www.duikresearch.org/ or
http://www.diveresearch.org/
For more information: n.a.schellart@amsterdamumc.nl

Historical Diving Society Australia - Pacific

P O Box 347, Dingley Village Victoria, 3172, Australia
Email: info@historicaldivingsociety.com.au
Website: https://www.historicaldivingsociety.com.au/

Diving and Hyperbaric Medicine: Instructions for authors (summary)

Diving and Hyperbaric Medicine (DHM) is the combined journal of the South Pacific Underwater Medicine Society (SPUMS) and the European Underwater and Baromedical Society (EUBS). It seeks to publish papers of high quality on all aspects of diving and hyperbaric medicine of interest to diving medical professionals, physicians of all specialties, scientists, members of the diving and hyperbaric industries, and divers. Manuscripts must be offered exclusively to *Diving and Hyperbaric Medicine*, unless clearly authenticated copyright exemption accompaniesthe manuscript. All manuscripts will be subject to peer review. Accepted contributions will also be subject to editing.

Address: The Editor, Diving and Hyperbaric Medicine, Department of Anaesthesiology, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand
Email: editor@dhmjournal.com
Phone: (mobile) +64 (0)27 4141 212
European Editor: euroeditor@dhmjournal.com
Editorial Assistant: editorialassist@dhmjournal.com
Journal information: info@dhmjournal.com

Contributions should be submitted electronically by following the link:
http://www.manuscriptmanager.net/dhm
There is on-screen help on the platform to assist authors as they assemble their submission. In order to submit, the corresponding author needs to create an 'account' with a user name and password (keep a record of these for subsequent use). The process of uploading the files related to the submission is simple and well described in the on-screen help provided the instructions are followed carefully. The submitting author must remain the same throughout the peer review process.

Types of articles

DHM welcomes contributions of the following types:

Original articles, Technical reports and Case series: up to 3,000 words is preferred, and no more than 30 references (excluded from word count). Longer articles will be considered. These articles should be subdivided into the following sections: an **Abstract** (subdivided into Introduction, Methods, Results and Conclusions) of no more than 250 words (excluded from word count), **Introduction, Methods, Results, Discussion, Conclusions, References, Acknowledgements**, **Funding** sources and any **Conflicts of interest**. **Legends/captions** for illustrations, figures and tables should be placed at the end of the text file.

Review articles: up to 5,000 words is preferred and a maximum of 50 references (excluded from word count); include an informative **Abstract** of no more than 300 words (excluded from total word count); structure of the article and abstract is at the author(s)' discretion.

Case reports, Short communications and **Work in progress** reports: maximum 1,500 words, and 20 references (excluded from word count); include an informative **Abstract** (structure at author's discretion) of no more than 200 words (excluded from word count).

Educational articles, Commentaries and **Consensus reports** for occasional sections may vary in format and length, but should generally be a maximum of 2,000 words and 15 references (excluded from word count); include an informative **Abstract** of no more than 200 words (excluded from word count).

Letters to the Editor: maximum 600 words, plus one figure or table and five references.

Formatting of manuscripts

All submissions must comply with the following requirements. Manuscripts not complying with these instructions will be suspended and returned to the author for correction before consideration. Guidance on structure for the different types of articles is given above.

The following pdf files are available on the DHM website to assist authors in preparing their submission:

- Instructions for authors (full version)
- DHM Key words
- DHM Mandatory Submission Form 2020
- Trial design analysis and presentation
- EASE participation and conflict of interest statement
- English as a second language
- Guideline to authorship in DHM 2015
- Helsinki Declaration revised 2013
- Is ethics approval needed?

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)

AFRICA – DAN
0800-020111 (in South Africa toll free)
+27-828-106010 (International call collect)

USA – DAN
+1-919-684-9111

JAPAN – DAN
+81-3-3812-4999 (Japan)

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.
