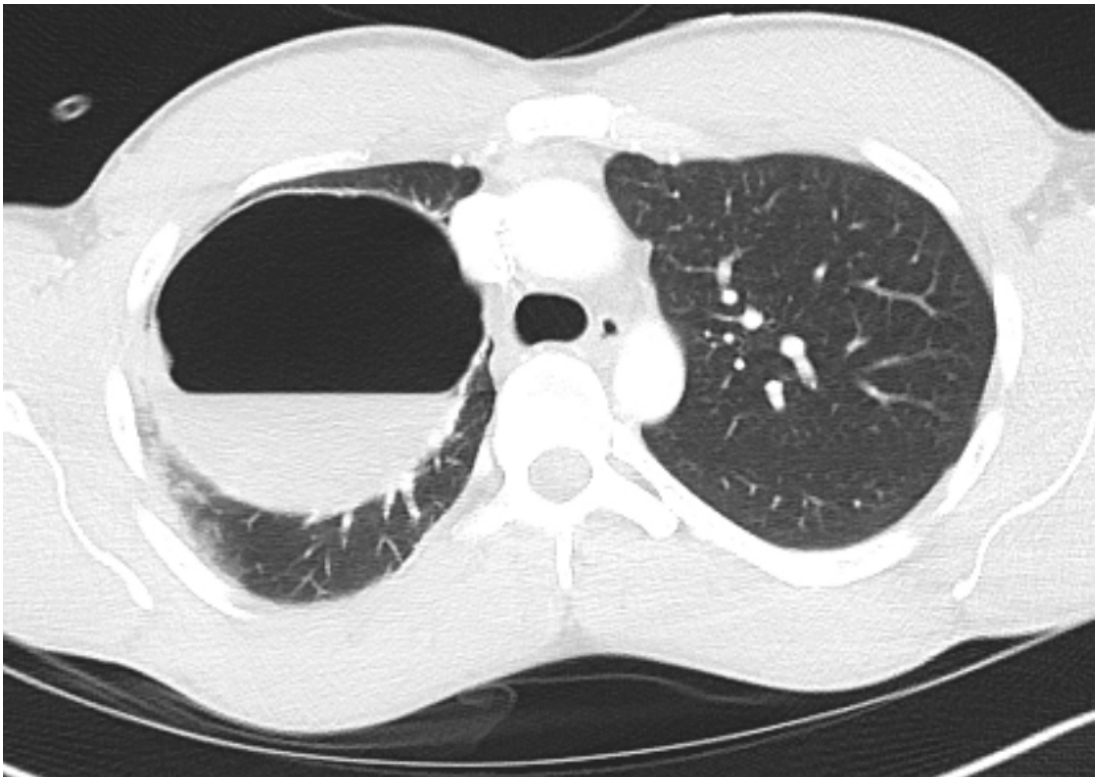
Diving and Hyperbaric Medicine

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

SPUMS

Volume 49 No. 2 June 2019

EUBS



Bullous disease and cerebral arterial gas embolism

Does closing a PFO reduce the risk of DCS?

A left ventricular assist device in the hyperbaric chamber

The impact of health on professional diver attrition

Serum tau as a marker of decompression stress

Are hypoxia experiences for rebreather divers valuable?

Nitrox vs air narcosis measured by critical flicker fusion frequency

The effect of medications in diving

E-ISSN 2209-1491 ABN 29 299 823 713

CONTENTS

Diving and Hyperbaric Medicine Volume 49 No.2 June 2019

Editorials

Original articles

Review article

Technical report

Case report

Obituary

SPUMS notices and news

EUBS notices and news

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

PURPOSES OF THE SOCIETIES

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

---

DIVING AND HYPERBARIC MEDICINE

www.dhmjournal.com

Editor
Simon Mitchell editor@dhmjournal.com
European (Deputy) Editor
Lesley Blogg euroeditor@dhmjournal.com
Associate Editor
Michael Davis assoceditor@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

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

Editorial

Risk mitigation in divers with persistent (patent) foramen ovale

In this issue, Anderson and colleagues report follow-up of divers who were found to have a persistent (patent) foramen ovale (PFO) or, in eleven cases, an atrial septal defect (ASD).[1] In most divers diagnosis followed an episode of decompression illness (DCI). The efficacy of closure of the PFO/ASD in preventing future DCI was compared with conservative diving. They reported that in the closure group the occurrence of confirmed DCI decreased significantly compared with pre-closure, but in the conservative group this reduction was not significant.

It is believed there are three requirements for a diver to suffer shunt-mediated DCI:

- A significant right-to-left shunt (usually a large PFO but sometimes an ASD or pulmonary arteriovenous malformation).
- Venous bubbles nucleated during decompression circumvent the lung filter by passing through the shunt.
- Target tissues are supersaturated with dissolved inert gas, so that they are able to amplify embolic bubbles.[2,3]

All three are required because DCI does not occur after contrast echocardiography when bubbles cross a right-to-left shunt.

Therefore, there are two ways that a diver who has suffered shunt-mediated DCI may continue to dive – either their shunt is sealed or future dives should be so conservative that venous bubbles are not liberated and/or critical tissues are not able to amplify embolic bubbles.[4]

PFO/ASD closure will give divers a risk of DCI comparable to the risk in others without a right-to-left shunt, if the procedure adequately seals the shunt. Closure of the shunt will not prevent a diver suffering DCI by other mechanisms, such as when there is arterial gas embolism (AGE) as a result of pulmonary barotrauma or when the dive profile is provocative (e.g., if there is rapid ascent or missed decompression stops). Conservative diving will be effective only if all the dives performed are truly conservative and prevent bubble nucleation and/or amplification.

The study by Anderson et al. has a number of serious limitations.[1] The study was small with only 62 self-selected divers, who self-reported outcomes. Eleven divers had not had DCI when their PFO or ASD was detected. Initially 36 divers were classified as closure and 26 as conservative treatment, but six subjects crossed from the conservative group to the closure group. Three of the six dived in the conservative group before having closure and are classified in both groups depending on whether the dives performed were before or after closure. As a result, there were 42 in the closure group and 23 in the conservative group.

Randomisation to the treatment groups was not possible and its absence results in imbalance. Because the closure group is approximately twice as large as the conservative group, similar changes in incidence would have a greater probability of achieving statistical significance in the former. Large shunts were present in more than three-quarters of the closure group but fewer than half of the conservative group. The authors have three definitions of a 'large' PFO, so the definition of large was inconsistent. All ASDs were considered to be large.

When dealing with small numbers, one needs patient-level data, but that is lacking and may mask inconsistency in management. The divers were investigated and treated in at least 38 hospitals (some divers did not state where they were treated). We do not know what devices were used for PFO/ASD closure, and closure effectiveness varies, or what tests were performed to assess the effectiveness of closure.[5]

The primary end-point was not different between the two groups because only two episodes of confirmed DCI occurred in each group. The authors also considered a softer and subjective end-point, possible DCI.

Crucially we are not told what the divers in the conservative group were told constitutes a conservative dive and whether it was consistent. Nor are we told whether they followed the advice given. That is important because it appears that incidence of possible DCI increased considerably in only the conservative group, which means either that the advice they were given on what constitutes a conservative dive was flawed, that the divers failed to follow good advice or that they frequently reported innocent symptoms as possible DCI, because knowledge that they had a PFO may have increased their reporting – introducing further bias.

There should be assessment of whether DCI after the intervention was shunt-mediated or had another cause. For that assessment, one needs to know details of the dives resulting in symptoms, clinical manifestations and latency of onset.[6]

I have investigated 20 divers who had DCI after PFO closure. In five divers, a contrast echocardiogram showed a significant residual shunt. Typically, the diver had their closure procedure by a cardiologist lacking knowledge of diving medicine and no post-closure contrast echocardiogram was performed. In one case, the diver's PFO was closed but they had a residual pulmonary shunt that was not detected. In those cases where there is a significant residual shunt, the dive profiles, clinical manifestations and latencies of onset were typical of shunt-mediated DCI.[6]

Three divers, who had PFO closure with no residual shunt, subsequently had neurological symptoms with manifestations consistent with AGE secondary to pulmonary barotrauma. High resolution CT scans of their chests showed pulmonary bullae and emphysema.

The remaining divers seen had no residual shunt but had performed highly provocative dives, usually much deeper than 50 metres' sea water (msw). The most recent case that I saw had dived to 102 metres' fresh water (mfw) in a lake at high altitude breathing trimix.

In contrast, several hundred divers in whom I diagnosed a PFO and who elected to dive conservatively had not reported further DCI. I advised them that I have never seen shunt-mediated DCI after dives breathing air to depths of 15 msw or less provided no rules were broken. So I set that as the depth limit or allow them to dive to greater depths breathing nitrox so that there are equivalent partial pressures of nitrogen (e.g., 19 msw with nitrox 32 or 23 msw with nitrox 40) provided they use an air decompression table/algorithm. Alternatively, one can dive using the DCIEM recreational air diving table.

Recurrence of DCI after PFO closure may be the result of a residual shunt or may have other causes. It is difficult to draw conclusions about the safety of 'conservative' diving unless one knows what the divers were advised constitutes conservative dives and whether they adhered to the advice.

References

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

2 Wilmshurst PT, Davidson C, O'Connell G, Byrne C. Role of cardiorespiratory abnormalities, smoking and dive characteristics in the manifestations of neurological decompression illness. Clin Sci. 1994;86:297–303.

3 Mitchell SJ, Doolette DJ. Selective vulnerability of the inner ear to decompression sickness in divers with right-to-left shunt: the role of tissue gas supersaturation. J Appl Physiol. 2009;106:298–301. doi: 10.1152/japplphysiol.90915.2008. PMID: 18801958.

4 Smart D, Mitchell S, Wilmshurst P, Turner M, Banham N. Joint position statement on persistent foramen ovale (PFO) and diving. South Pacific Underwater Medicine Society (SPUMS) and United Kingdom Sports Diving Medical Committee (UKSDMC). Diving Hyperb Med. 2015;45:129–31. PMID: 26165538.

5 Thaman R, Faganello G, Gimeno JR, Szantho GV, Nelson M, Curtis S, et al. Efficacy of percutaneous closure of patent foramen ovale: comparison among three commonly used occluders. Heart. 2011;97:394–9. doi:10.1136/hrt.2010.203950.

6 Wilmshurst PT. The role of persistent foramen ovale and other shunts in decompression illness. Diving Hyperb Med. 2015;45:98–104. PMID: 26165532.

Dr Peter Wilmshurst, Consultant Cardiologist, Royal Stoke University Hospital, Stoke-on-Trent, ST4 6QG, UK
peter.wilmshurst@tiscali.co.uk

doi: 10.28920/dhm49.2.77-78. PMID: 31177512.

Submitted: 02 May 2019; revised 13 May 2019
Accepted: 15 May 2019

Conflicts of interest: nil

Funding: nil

Key words
Decompression illness; Decompression sickness; Persistent (patent) foramen ovale; Atrial septal defect; Right-to-left shunt; Trans-catheter closure

The Editor's offering

This issue of the journal contains a range of articles addressing issues of high practical and contemporary relevance to diving medicine.

The striking cover photo comes from the case report describing a cerebral arterial gas embolism (CAGE) event occurring on only the second ever dive in a diver with a primary lung bulla.[1] While not a unique report, it raises the unresolved dilemma of how to choose the path of least risk in managing CAGE following pulmonary barotrauma in a patient with predisposing structural lung disease, and particularly where the circumstances of the accident (e.g., second ever dive,[1] or first ever hyperbaric oxygen treatment[2]) imply a high risk of a repeat event during a recompression, even with a slow decompression in a hyperbaric chamber. The issue of recompression management in such patients would make a stimulating topic for a consensus workshop discussion. Another case report describes how a left ventricular assist device controller and battery system have been cleverly adapted for use in a hyperbaric chamber.[3] The single review article in this issue addresses the perennially debated topic of the safety of medications in diving.[4]

There are several intriguing original studies in this issue.

Biomarkers of decompression stress or injury are one of our field's holy grails. Preliminary evidence is presented that repeated deep trimix dives are associated with a significant rise in serum levels of tau protein; a biomarker correlated with outcome or severity in some chronic brain diseases and acute brain injuries.[5] There remains a long way to go

in evaluating the significance and cause of this observation in diving, but this finding may translate to an exciting line of related research.

There are still limited data on the efficacy of closure of a persistent (patent) foramen ovale (PFO) in preventing subsequent decompression sickness (DCS) in those continuing to dive after the procedure. In this issue, the rate of DCS is compared in divers with a PFO who either had the PFO closed or continued diving without closure.[6] As in a previous study,[7] the authors report that PFO closure was associated with a reduction in the rate of new cases of DCS. There are few medical issues that are discussed more often among divers than whether to be screened for a PFO, and how to manage it if one is found. Given the importance of the topic, Peter Wilmshurst discusses in his editorial the strengths, weaknesses and implications of this study.[8]

Critical flicker fusion frequency is increasingly being studied to measure the effects of inert gas narcosis on cerebral function. The narcotic effects of nitrogen, and how these effects change if nitrox40 (40% oxygen) rather than air is breathed are compared here with cognitive function testing.[9] In a fascinating finding, an increase in both brain activation and cognitive ability occurred on arrival at depth, and was followed by the more expected deterioration during time spent there. This initial enhancement of cognitive ability was greater when nitrox was respired.

Whether health problems are an important reason for employed divers to leave the industry is examined in an interrogation of the New Zealand occupational divers database.[10] Only a tiny proportion of occupational divers who leave the industry appear to do so because of health issues which, therefore, are not the key determinant of attrition from the diving industry.

Hypoxia training has been advocated for rebreather divers. However, in the study reported in this issue, no benefits were found to cognitive performance or subsequent accuracy in recall of performance in an hypoxic experience that followed five weeks after a previous one.[11] The authors discuss the substantial challenges to performing a valid study to determine whether prior hypoxia experience training would help a diver self-rescue in a subsequent hypoxic event during diving.

References

1 Goffinet CMJ, Simpson G. Cerebral arterial gas embolism in a scuba diver with a primary lung bulla. Diving Hyperb Med. 2019;49:141–4. doi: 10.28920/dhm49.2.141-144. PMID: 31177521.

2 Rivalland G, Mitchell SJ, van Schalkwyk JM. Pulmonary barotrauma and cerebral arterial gas embolism during hyperbaric oxygen therapy. Aviat Space Environ Med. 2010;81:888–90. doi: 10.3357/ASEM.2783.2010. PMID: 20824998.

3 Kot J, Siodalski P, Lenkiewicz E. The Hyperbaric Protective Tube: A housing for a left ventricular assist device (LVAD) in a multiplace hyperbaric chamber. Diving Hyperb Med. 2019;49:137–40. doi: 10.28920/dhm49.2.137-140. PMID: 31177520.

4 Hoencamp E, van Dongen TTCF, van Ooij P-JAM, Wingelaar TT, Vervelde ML, Koch DA, et al. Systematic review on the effects of medication under hyperbaric conditions: consequences for the diver. Diving Hyperb Med. 2019;49:127-36. doi: 10.28920/dhm49.2.127-136. PMID: 31177519.

5 Rosén A, Oscarsson N, Kvarnström , Gennser M, Sandström G, Blennow K, et al. Serum tau concentration after diving – an observational pilot study. Diving Hyperb Med. 2019;49:88–95. doi: 10.28920/dhm49.2.88-95. PMID: 31177514.

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

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

8 Wilmshurst P. Risk mitigation in divers with persistent foramen ovale. Diving Hyperb Med. 2019;49:77–8. doi: 10.28920/dhm49.2.77-78. PMID: 31177512.

9 Lafere P, Hemelryk W, Germonpré P, Matity L, Guerrero F, Balestra C. Early detection of diving-related cognitive impairment of different nitrogen-oxygen gas mixtures using critical flicker fusion frequency. Diving Hyperb Med. 2019;49:119–26. doi: 10.28920/dhm49.2.119-126. PMID: 31177518.

10 Sames C, Gorman DF, Mitchell SJ, Zhou L. The impact of health on professional diver attrition. Diving Hyperb Med. 2019;49:NN–nn. doi: 10.28920/dhm49.2.107-111. PMID: 31177516.

11 Mitchell SJ, Green HM, Reading SA, Gant N. The utility and safety of hypoxia experiences for rebreather divers. Diving Hyperb Med. 2019;49:112–8. doi: 10.28920/dhm49.2.112-118. PMID: 31177517.

Simon Mitchell

Front cover image is from a computed tomography scan of the chest showing a large thin-walled fluid-containing bulla in the right upper lobe of a diver presenting with cerebral arterial gas embolism (with permission from Goffinet and Simpson – see case report in this issue).

Original articles

The effectiveness of risk mitigation interventions in divers with persistent (patent) foramen ovale

George Anderson[1], Douglas Ebersole[2], Derek Covington[3], Petar J Denoble[1]

[1]*Divers Alert Network, Durham NC, USA*
[2]*Watson Clinic, Lakeland FL, USA*
[3]*Department of Anesthesiology, University of Florida, Gainesville FL, USA*

Corresponding author: *Petar J Denoble, Divers Alert Network, 6 West Colony Place, Durham, NC 27705, USA*
pdenoble@dan.org

Key words
Cardiovascular; Decompression sickness; Decompression illness; Right-to-left shunt; Trans-catheter closure

Abstract
(Anderson G, Ebersole D, Covington D, Denoble PJ. The effectiveness of risk mitigation interventions in divers with persistent (patent) foramen ovale. Diving and Hyperbaric Medicine. 2019 June 30;49(2):80–87. doi: 10.28920/dhm49.2.80-87. PMID: 31177513.)

Introduction: Persistent (patent) foramen ovale (PFO) is a recognized risk for decompression sickness (DCS) in divers, which may be mitigated by conservative diving or by PFO closure. Our study aimed to compare the effectiveness of these two risk mitigation interventions.

Methods: This was a prospective study on divers who tested positive for PFO or an atrial septal defect (ASD) and either decided to continue diving without closure ('conservative group'), or to close their PFO/ASD and continue diving ('closure group'). Divers' characteristics, medical history, history of diving and history of DCS were reported at enrollment and annually after that. The outcome measures were the incidence rate of DCS, frequency and intensity of diving activities, and adverse events of closure.

Results: Divers in both groups dived less and had a lower incidence rate of confirmed DCS than before the intervention. In the closure group ($n = 42$) the incidence rate of confirmed DCS decreased significantly. Divers with a large PFO experienced the greatest reduction in total DCS. In the conservative group ($n = 23$), the post-intervention decrease in confirmed DCS incidence rate was not significant. Of note, not all divers returned to diving after closure. Seven subjects reported mild adverse events associated with closure; one subject reported a serious adverse event.

Conclusions: PFO closure should be considered on an individual basis. In particular, individuals who are healthy, have a significant DCS burden, a large PFO or seek to pursue advanced diving may benefit from closure.

Introduction

Persistent (patent) foramen ovale (PFO), a remnant of foetal interatrial communication which persists after birth in about 30% of people, has been suspected as a risk factor for decompression sickness (DCS) for nearly four decades.[1–3] The role of a PFO as a conduit that enables arterialization of post-dive venous gas emboli (VGE) and occurrence of DCS is feasible in cerebral, spinal, cutaneous and vestibular manifestations of DCS.[4–6]

The prevalence of PFO in divers is probably similar to that in the general population.[7] However, very few divers experience DCS. The risk of DCS in recreational divers in the United States is 3.4 per 10,000 dives and less than 1 per 10,000 dives for neurological DCS.[8] Research suggests that only about 10% of divers experience some form of DCS in their lifetime.[9,10] However, for divers with a PFO the overall risk of DCS doubles, for neurological DCS it increases four-fold, and for divers with a large PFO, it increases six-fold.[11,12] In order for DCS associated with PFO to occur, at least three conditions need to be met:

- Post-dive venous gas emboli must be present.
- A right-to-left shunt must occur, whether spontaneous or due to a provocation factor such as Valsalva or breathing effort.
- The target tissue must be saturated with inert gas.[13–15]

Although a large PFO is associated with an increased risk of DCS, testing of divers for PFO is only deemed necessary if divers have a history of cerebral, spinal, vestibular or cutaneous DCS, migraine with aura, cryptogenic stroke or a history of PFO or ASD in a first-degree relative.[16,17] The obvious risk mitigation strategy for such divers is to stop diving or to reduce the probability of post-dive venous gas bubbles by diving more conservatively.[18]

Since the trans-catheter closure of PFO was approved for secondary prevention of stroke, interventional cardiologists have begun to offer it to divers as a risk-mitigation strategy

for DCS. The closure of a PFO ablates the major pathway for arterialization of venous bubbles.[19] However, at the time this study was initiated the indications and practice of screening for (and closure of) PFO had not been standardized, and not all interventional cardiologists willing to provide these services had extensive experience with divers or were familiar with diving medicine. Also, divers were not always properly educated about how a PFO affects the risk of DCS and what their options were to mitigate this risk. The present study aimed to establish the effectiveness of conservative diving versus the closure of PFO for risk mitigation of DCS in this environment.

Methods

This study was approved by the Institutional Review Board of the Lakeland Regional Medical Center, Lakeland, Florida. The study combined retrospective data about the period before enrolment and prospective data collected after enrollment in the study.

SUBJECTS

Subjects were eligible for this study if they were adult certified divers diagnosed with PFO regardless of their DCS history, and if they intended to continue diving. Subjects responded to study advertisements in social media or were referred by other divers. All participants were volunteers who provided written informed consent.

The subjects provided anthropometric data, PFO testing data, a medical and diving history before the intervention*, and an annual report* about their diving activities and related outcomes after that.

Divers were classified as 'conservative' if after diagnosis with a PFO they decided to continue diving without undergoing closure, or 'closure' if they decided to get their PFO closed. In the conservative group, the intervention was the diagnosis of PFO and the post-intervention period began with that diagnosis. In the closure group, the intervention was the closure of PFO and the post-intervention period began with the closure. Subjects who dived with a diagnosed PFO before they underwent closure were included in both the conservative and the closure group. For the subjects in the conservative group, the pre-intervention period included history up to the diagnosis and the post-intervention period was from the diagnosis until closure. For the subjects in the closure group, the pre-intervention period included history up to the closure and the post-intervention period was from the closure until the end of the study.

Subjects were further classified based on their reported diving practice as recreational or technical divers. For this study, divers who performed more than 40% of their air dives at depths greater than 30 metres, used mixed gas (other than enriched air nitrox), closed circuit rebreather (CCR) or engaged in cave diving, were classified as technical divers.

The PFO was classified as 'large' if the reported diameter was 5 mm or larger, if bubble contrast used in diagnosis arterialized spontaneously, or if a cardiologist qualified it 'large' without an explicit report of PFO diameter. Divers with an ASD were also classified in the 'large' group because of the continuous patency of that lesion.

OUTCOMES

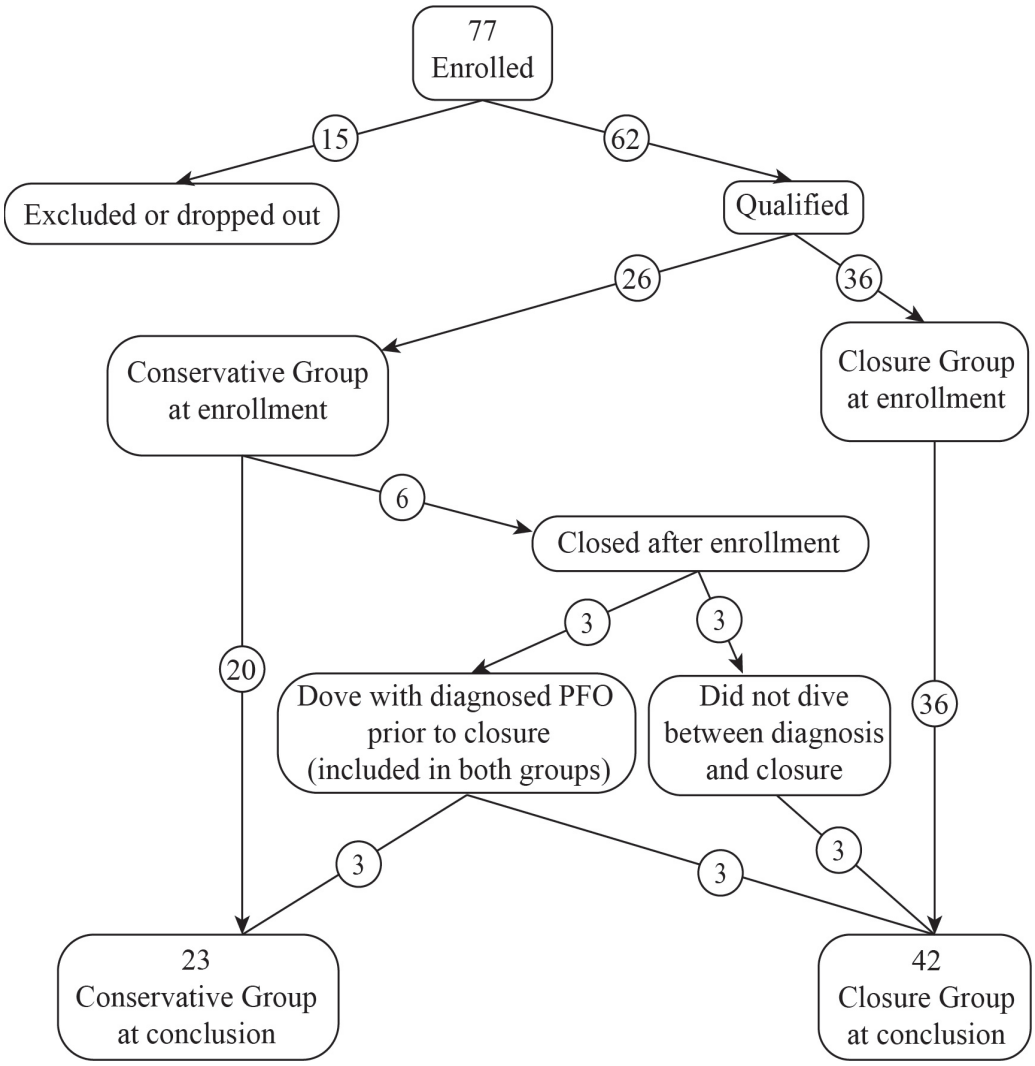
The main outcome of interest was DCS. The primary outcome was 'confirmed DCS', defined as cases diagnosed by a medical professional and treated in a recompression chamber. The secondary outcome was 'possible DCS' which was based on solicited subjective reports of the presence of symptoms usually associated with DCS and explicitly listed in the list of reportable symptoms. Examples of reportable symptoms were instances of vertigo, joint pain, skin itching and rash, post-dive skin mottling, breast swelling, muscular weakness, or use of in-water recompression or surface oxygen to alleviate symptoms. Isolated instances of a headache, fatigue or nausea were not considered possible DCS. Other outcomes were return to diving, frequency and intensity of diving after the intervention and possible adverse events related to the closure.

Subjects were determined to have returned to diving in one year if they had reported doing any dives in the year following the intervention. Frequency and intensity of diving after the intervention were classified as either: 'diving less', if they reported fewer dives per year (less than 70% of pre-intervention dives per year), or switched from technical to recreational diving; or 'diving same or more', if they reported the same or more dives per year (greater than or equal to 70% of pre-intervention dives per year), or switched from recreational to technical diving. Individuals who stopped diving were included in the 'diving less' group.

The group incidence rate of DCS before and after the intervention was calculated per 10,000 dives, based on the sums of reported dives and of DCS cases. These calculations were completed for both confirmed DCS and possible DCS. These calculations were also performed while stratifying groups based on PFO size. Individuals who stopped diving were excluded from these calculations. Changes in confirmed DCS and possible DCS were considered on an individual basis before and after the intervention.

*** Footnote:**
The baseline survey and annual dive symptom report forms are available on request from the authors at pdenoble@dan.org

Figure 1
Enrollment and group allocation pathway



Reported adverse events of closure were classified as mild, such as minor bleeding, bruising, temporary palpitations or atrial fibrillation. Adverse events were classified as severe if they required surgical intervention, caused a serious threat to life, or resulted in permanent consequences.

STATISTICAL ANALYSIS

The difference in the incidence rate of DCS before and after intervention in each group was tested by calculating the risk ratio. The difference in the proportion of subjects in each group who dived the same or more was tested by calculating the odds ratio.

Continuous characteristics of subjects in the two groups were compared using the Mann-Whitney rank sum test. Discrete characteristics of subjects in the two groups were tested by calculating odds ratios.

Results

CHARACTERISTICS OF DIVERS BEFORE INTERVENTION

In the period from 2011 to 2017, 77 subjects enrolled in this study. During this time, 15 subjects were excluded for the following reasons: three subjects reported a PFO but its presence could not be confirmed during repeated testing after enrolment, five subjects were lost to follow up, and seven subjects asked to be removed from the study. The total number of remaining subjects was 62. Fifty-two subjects were treated in 38 different medical centres. Four subjects did not report the name of the centre they were treated in but provided sufficient detail about the findings. Eleven divers were diagnosed with a PFO without a history of previous DCS. Four of these were diagnosed while undergoing tests for non-DCS related medical issues and

Table 1
Characteristics of divers in conservative and closure groups before intervention; CI – confidence interval; PFO – persistent foramen ovale; SD – standard deviation

Characteristics	**Conservative** (n = 23)	**Closure** (n = 42)	***P*-value**
Age [median (95% CI)]	52 (43–55)	45.5 (40–50)	NS
Male/female ratio	12/11	22/20	NS
Height, cm [mean (SD)]	175 (8)	173 (10)	NS
Weight, kg [mean (SD)]	81 (14.5)	83 (18)	NS
Body mass index, $kg \cdot m^{-2}$ [mean (SD)]	26.3 (3.8)	27.4 (4.7)	NS
Years diving at enrollment [median (95% CI)]	7.0 (6–12)	8.5 (6–11.6)	NS
Total dives at enrollment (n) [median (95% CI)]	213 (129–461)	231 (142–363)	NS
Number of dives per year [median (95% CI)]	41 (22–49)	33 (24–49)	NS
Number of technical divers	8	17	NS
Number of subjects with large PFO	8/18	26/34	< 0.05
DCS prior to intervention			
Possible [median (range)]	0.0 (0–6)	2.0 (0–60)	< 0.05
Confirmed [median (range)]	1.0 (0–1)	1.0 (0–2)	NS

Table 2
Diver practice in conservative and closure groups after intervention; bottom two rows refer to comparisons with diving prior to the intervention; no differences between groups were significant; CI = confidence interval

Outcome	**Conservative**	**Closure**
Years diving [median (95% CI)]	5 (3–8)	6 (5–7)
Dives per year [median (95% CI)]	16 (12–19)	20 (15–29)
Dived less (n)	16/23	23/42
Dived the same or more (n)	7/23	19/42

seven asked for testing to comply with the requirements of their technical diving associations or because of personal concerns. Initially, 36 subjects were classified as closure, and 26 subjects were classified as conservative. During the follow-up period, six of the subjects from the conservative group underwent closure and were subsequently reclassified into the closure group. Three of those subjects executed dives between diagnosis and closure and they were included in both groups as described in the methods. As a result, the study yielded 42 subjects in the closure group and 23 in the conservative group. The classification algorithm is shown in Figure 1 and the characteristics of divers in each group are shown in Table 1.

Age, years diving, the total number of dives, and the number of DCS instances were not distributed normally. Divers in both groups were similar in body characteristics and dive history, although the number of reported possible DCS cases was significantly greater in the closure group while

Table 3
Incidence rate of confirmed and possible DCS per 10,000 dives in the conservative and closure groups before and after the intervention; values in brackets are 95% confidence intervals

Group	DCS	Before	After	Relative risk	*P*-value
Conservative	Confirmed	12.8 (6–23)	6.2 (0.3–23)	0.49 (0.05–2.24)	NS
	Possible	31.3 (21–46)	131.2 (95–177)	4.2 (2.5–7.1)	< 0.0001
Closure	Confirmed	13.1 (9–19)	2.7 (0.3–10)	0.21 (0.02–0.83)	< 0.05
	Possible	144.5 (129–162)	42.1 (29–60)	0.3 (0.2–0.4)	< 0.0001

Table 4
Number of subjects in the conservative and closure groups reporting episodes of DCS before and after the intervention

Group	DCS	Before	After
Conservative	Confirmed	12	2
	Possible	10	11
Closure	Confirmed	24	2
	Possible	30	10

the number of confirmed DCS cases was similar. Divers in the closure group appeared younger than those in the conservative group, but the difference was not significant.

The median follow-up period after the intervention was five years (95% confidence interval (CI) 3–8) for the conservative group and six years (95% CI 5–7) for the closure group. These were not significantly different. In about half of the subjects (22 closure subjects, ten conservative subjects) intervention occurred years before enrolment in the study. Within one year, 85% of subjects in the conservative group and 90% of subjects in the closure group returned to diving (NS). Details of their diving practices are shown in Table 2.

Fifty-two subjects had adequate information to classify the size of their PFO. Thirty-three were classified as large; including 11 divers in whom the diagnosis was that of an ASD. A significantly greater number of subjects in the closure group (26 of 34) had a large PFO compared to the conservative diving group (8 of 18) (OR = 3.7, 95% CI 1–13.5, $P < 0.05$).

Before the intervention, the group incidence rate of confirmed DCS per 10,000 dives was similar in both groups while the incidence rate of possible DCS was greater in the closure group (Table 3). However, the incidence rate of confirmed DCS before intervention (12.8 and 13.1 per 10,000 dives) in both groups was greater than in the general recreational diving population.

In three cases, subjects originally decided to dive conservatively, but after executing dives decided to opt for closure. One diver experienced two episodes of possible DCS while diving conservatively, which lead them to pursue closure. A second did not originally pursue closure because their insurance would not cover it but after experiencing two episodes of possible DCS and one of confirmed DCS, elected for closure. The third did not experience any DCS while diving conservatively but wished to pursue more aggressive diving and elected for closure.

OUTCOMES

The number of subjects who experienced confirmed DCS decreased in both groups (see Table 4). The number of subjects experiencing possible DCS decreased in the closure group and remained the same in the conservative group.

The incidence rate of confirmed DCS after the intervention was reduced in the closure group to 2.7 and in the conservative group to 6.2 (Table 3). In the closure group, this was a nearly five-fold reduction in comparison to the pre-intervention value, which was statistically significant, and a two-fold reduction in the conservative group which was not statistically significant.

The median dives per year after intervention decreased in comparison to the pre-intervention period (conservative: from 33 to 20; closure: from 41 to 16). Four subjects stopped diving. Seven subjects in the conservative group and 19 subjects in the closure group maintained or increased their diving in comparison to pre-intervention levels (Table 2), which was not significantly different.

The incidence rate of reported possible DCS (Table 3) increased significantly in the conservative group (RR = 4.2, 95% CI 2.5–7.1; $P < 0.0001$) and decreased significantly in the closure group (RR = 0.3, 95% CI 0.2–0.4; $P < 0.0001$).

Table 5
Incidence rate of possible DCS per 10,000 dives before and after the intervention stratified by size of the atrial defect; values in brackets are 95% confidence intervals except where indicated

Group *(n)*	PFO *(n)*	Before	After	Relative risk	*P*-value
Conservative (17)	Large (7)	45 (16–99)	445 (296–643)	9.7 (4.0–23)	< 0.0001
	Small (10)	30 (17–49)	131 (72–221)	4.4 (2.1–8.9)	< 0.05
Closure (34)	Large (26)	219 (194–247)	48 (31–70)	0.2 (0.1–0.3)	< 0.0001
	Small (8)	38 (25–55)	31 (9–79)	0.8 (0.3–2.3)	NS

LARGE VS SMALL PFO

Of the subjects with available PFO size information, 18 had small, and 33 had large PFOs. Of the 18 subjects with a small PFO, ten were in the conservative group, and eight were in the closure group. Of the 33 subjects with a large PFO, seven were in the conservative group, and 26 were in the closure group. There were only four cases of confirmed DCS, and we could not calculate the incidence rate of stratified data.

The incidence rate of possible DCS stratified by the group and by PFO size is shown in Table 5. Divers with a small PFO in the conservative group had a greater incidence rate of possible DCS after the intervention, while divers with a small PFO in the closure group experienced no significant change in possible DCS incidence rate after the intervention. Divers with a large PFO in the conservative group had a greater incidence rate of possible DCS after the intervention, while divers with a large PFO in the closure group had a decreased incidence rate of possible DCS after the intervention.

ADVERSE EVENTS ASSOCIATED WITH CLOSURE

Adverse events associated with PFO/ASD closure occurred in eight out of the 42 subjects who went for closure. These included post-surgical bleeding, transient atrial fibrillation, migraines with aura, dysrhythmia, heart palpitations, premature atrial and ventricular contractions, supraventricular tachycardia and an allergic reaction to a muscle relaxant used in surgery.

Discussion

Our study included self-enrolled subjects with widely varied personal diving histories. Before the intervention, some subjects frequently suffered post-dive symptoms such as skin mottling but did nothing about them for a long time, whilst others underwent preventive testing and even closure without experiencing any DCS. Furthermore, the indications for testing, the testing procedures and the description of findings in our sample varied widely and were not always in line with current recommendations, which were published after the start of our study.[16,17]

As reported in the only other study of this type,[20] we found that confirmed DCS was reduced after intervention in the closure group. In the conservative group, the incidence rate after intervention decreased by nearly 50%, but this was not statistically significant as reported by other studies.[18] Interestingly, the incidence rate of possible DCS in the conservative group increased after the intervention, on account of five individuals who reported more cases of skin itch and rash (not mottling) and received first-aid oxygen more often. They may have become more vigilant and anxious after having been diagnosed with PFO, leading them to report subjective symptoms and seek assistance more readily. On the other hand, this also may have been owing to regression to the mean.

When stratified by size, it appeared that individuals with large PFOs would reduce their possible DCS from closure, while those with small PFOs would not. However, individuals with small PFOs started with a lower incidence rate in the first place, and their DCS may not have been related to a PFO at all.

On average, divers in both groups reported fewer dives per year after intervention. In the conservative group, most subjects reported shallower dives and used more nitrox. In the closure group, some subjects who previously had frequent post-dive symptoms reported being able to continue -diving as before or even more aggressively without any problems. Some divers who underwent closure started diving more conservatively, used nitrox more frequently and dove shallower.

In the closure group, one subject suffered a severe vestibular DCS hit resulting in hearing loss before closure and did not continue diving after the procedure. Another subject stopped diving for undisclosed reasons. In the conservative group, one subject stopped diving because he had not been able plan a dive trip, and another stopped for undisclosed reasons.

One diver in the closure group experienced a serious adverse event and seven experienced minor adverse events. The incidence rate of adverse events was more than reported in clinical trials of closure for stroke.[21]

In a prospective, single-centre study including non-PFO divers, divers with PFO and divers with closed PFO, the incidence rate of treated DCS (what corresponds to 'confirmed' DCS in our study) was reduced in both PFO groups in the post-intervention period.[20] However, the total burden of subjectively reported DCS increased in the PFO group after intervention while in the no-PFO and the closed-PFO groups the incidence rates decreased, as in our study. In both studies, the increase in reported post-dive symptoms in divers with an unclosed PFO may have been due to the subject's increased vigilance after being diagnosed.[20]

Another prospective study evaluated the incidence rates of DCS in divers with PFO who received instructions on how to dive conservatively.[18] Both the divers with PFO and with closed PFO benefited from these instructions, and either did not suffer DCS, or their DCS incidence rate was reduced to the overall incidence rate in recreational divers.

The weaknesses of our study include small sample size, bias due to self-enrolment, subjective reporting of DCS burden, differences in clinical practices and deficiencies in the available medical documentation. The sample size was smaller than we originally planned and the study is underpowered for some outcome measures. An extension of the study was not a practical solution due to slow enrolment.

Self-enrolment potentially introduces a selection bias. The sample may not have been representative of all divers who had been diagnosed with PFO and who had undergone closure. It is possible that participants were in better health, had a lesser burden of previous DCS, had a stronger motivation to continue diving and, in general, had better outcomes of the intervention. However, the sample was not homogenous and included both success and failure stories. The study started before the consensus recommendations on investigation and management of PFO in diving were published,[16,17] and instead of imposing stringent selection criteria the study explored implicit criteria for testing and closure in real life. These varied widely. Personal motivations of divers seemed to have been the influencing factor on decisions for undergoing testing and for the election of closure or conservative diving. Despite this, the closure of PFO appeared to be effective in the reduction of DCS burden for most but not for all subjects, and some subjects fared worse either due to adverse events of closure or they stopped diving due to undisclosed causes. If the current consensus criteria had been applied, the success rate could have been higher.

Conclusion

While we could not establish the risk-benefit ratios or relative risk ratios for the two interventions with confidence, we have identified subsets of subjects that could benefit from closure. These are healthy divers with a significant DCS burden and a large PFO who seek to pursue advanced diving.

References

1 Wilmshurst PT, Ellis BG, Jenkins BS. Paradoxical gas embolism in a scuba diver with an atrial septal defect. Br Med J (Clin Res Ed). 1986;293(6557):1277. PMID: 3096463. PMCID: PMC1342110.

2 Wilmshurst PT, Byrne JC, Webb-Peploe MM. Relation between intertrial shunts and decompression sickness in divers. Lancet. 1989;2(8675):1302–6. PMID: 2574256.

3 Moon RE, Camporesi EM, Kisslo JA. Patent foramen ovale and decompression sickness in divers. Lancet. 1989;1(8637):513–4. PMID: 2564057.

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

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

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

7 Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc. 1984;59:17–20. PMID: 6694427.

8 Moon RE, Bove AA. Transcatheter occlusion of patent foramen ovale: a prevention for decompression illness? Undersea Hyperb Med. 2004;31:271–4. PMID: 15568413.

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

10 Klingmann C, Gonnermann A, Dreyhaupt J, Vent J, Praetorius M, Plinkert P. Decompression illness reported in a survey of 429 recreational divers. Aviat Space Environ Med. 2008;79:123–8. PMID: 18309910.

11 Bove AA. Risk of decompression sickness with patent foramen ovale. Undersea Hyperb Med. 1998;25:175–8. PMID: 9789338.

12 Lairez O, Cournot M, Minville V, Roncalli J, Austruy J, Elbaz M, et al. Risk of neurological decompression sickness in the diver with a right-to-left shunt: literature review and meta-analysis. Clin J Sport Med. 2009;19:231–5. doi: 10.1097/JSM.0b013e31819b0fa2. PMID: 19423977.

13 Mitchell SJ, Doolette DJ. Selective vulnerability of the inner ear to decompression sickness in divers with right-to-left shunt: the role of tissue gas supersaturation. J Appl Physiol. 2009;106:298–301. doi: 10.1152/japplphysiol.90915.2008. PMID: 18801958.

14 Wilmshurst PT, Davidson C, O'Connell G, Byrne C. Role of cardiorespiratory abnormalities, smoking and dive characteristics in the manifestations of neurological decompression illness. Clin Sci (Lond). 1994;86:297–303. PMID: 8156740.

15 Moses KL, Seymour M, Beshish A, Baker KR, Pegelow DF, Lamers LJ, et al. Inspiratory and expiratory resistance cause right-to-left bubble passage through the foramen ovale. Physiol Rep. 2018;6(12):e13719. doi: 10.14814/phy2.13719. PMID: 29952137. PMCID: PMC6021277.

16 Smart D, Mitchell S, Wilmshurst P, Turner M, Banham N. Joint position statement on persistent foramen ovale (PFO) and diving. Diving Hyperb Med. 2015;45:129–31. PMID: 26165538.
17 Moon R, Bove AA, Mitchell SJ. PFO Statement. In: Denoble PJ, Holm JR, editors. Patent foramen ovale and fitness to dive consensus. Durham, NC 27705: Divers Alert Network; 2015. p. 142–6. Available from: https://www.diversalertnetwork.org/research/Conference/2015PFOFTDProceedings/2015-pfo-workshop-proceedings.pdf. [cited 2019 February 13].
18 Klingmann C, Rathmann N, Hausmann D, Bruckner T, Kern R. Lower risk of decompression sickness after the recommendation of conservative decompression practices in divers with and without a vascular right-to-left shunt. Diving Hyperb Med. 2012;42:146–50. PMID: 22987461.
19 Honěk J, Šrámek M, Šefc L, Januška J, Fiedler J, Horváth M, et al. Effect of catheter-based patent foramen ovale closure on the occurrence of arterial bubbles in scuba divers. JACC Cardiovasc Interv. 2014;7:403–8. doi: 10.1016/j.jcin.2013.12.199. PMID: 24630875.
20 Billinger M, Zbinden R, Mordasini R, Windecker S, Schwerzmann M, Meier B, et al. Patent foramen ovale closure in recreational divers: effect on decompression illness and ischaemic brain lesions during long-term follow-up. Heart. 2011;97:1932–7. doi: 10.1136/heartjnl-2011-300436. PMID: 21917666.
21 Kheiri B, Abdalla A, Osman M, Ahmed S, Hassan M, Bachuwa G. Patent foramen ovale closure versus medical therapy after cryptogenic stroke: An updated meta-analysis of all randomized clinical trials. Cardiol J. 2019;26:47–55. doi: 10.5603/CJ.a2018.0016. PMID: 29512097.

Funding and conflicts of interest: nil

Submitted: 15 December 2018; revised 8 January and 15 February 2019
Accepted: 12 March 2019

Serum tau concentration after diving – an observational pilot study

Anders Rosén[1], Nicklas Oscarsson[2], Andreas Kvarnström[1], Mikael Gennser[3], Göran Sandström[4], Kaj Blennow[5,6], Helen Seeman-Lodding[1], Henrik Zetterberg[5,6,7,8]

[1]*Department of Anesthesia and Intensive Care Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden*
[2]*Department of Surgery, Angered Hospital, Gothenburg*
[3]*Department of Environmental Physiology, School of Chemistry, Biotechnology and Health, Royal Institute of Technology, KTH, Stockholm, Sweden*
[4]*Swedish Armed Forces, Center for Defence Medicine, Gothenburg*
[5]*Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Gothenburg*
[6]*Department of Psychiatry and Neurochemistry, Sahlgrenska Academy at the University of Gothenburg, Mölndal, Sweden*
[7]*Department of Neurodegenerative Disease, UCL Institute of Neurology, London, United Kingdom*
[8]*UK Dementia Research Institute at UCL, London*

Corresponding author: *Anders Rosén, Department of Anesthesia and Intensive Care Medicine, Sahlgrenska University Hospital, Göteborgsvägen 31, S-431 80 Mölndal, Sweden*
anders.rosen@vgregion.se

Key words
Tau protein; Decompression sickness; Venous gas emboli; Diving research; Biomarkers; Central nervous system; Stress

Abstract
(Rosén A, Oscarsson N, Kvarnström , Gennser M, Sandström G, Blennow K, Seeman-Lodding H, Zetterberg H. Serum tau concentration after diving – an observational pilot study. Diving and Hyperbaric Medicine. 2019 June 30;49(2):88–95. doi: 10.28920/dhm49.2.88-95. PMID: 31177514.)
Introduction: Increased concentrations of tau protein are associated with medical conditions involving the central nervous system, such as Alzheimer's disease, traumatic brain injury and hypoxia. Diving, by way of an elevated ambient pressure, can affect the nervous system, however it is not known whether it causes a rise in tau protein levels in serum. A prospective observational pilot study was performed to investigate changes in tau protein concentrations in serum after diving and also determine their relationship, if any, to the amount of inert gas bubbling in the venous blood.
Methods: Subjects were 10 navy divers performing one or two dives per day, increasing in depth, over four days. Maximum dive depths ranged from 52–90 metres' sea water (msw). Air or trimix (nitrogen/oxygen/helium) was used as the breathing gas and the oxygen partial pressure did not exceed 160 kPa. Blood samples taken before the first and after the last dives were analyzed. Divers were monitored for the presence of venous gas emboli (VGE) at 10 to 15 minute intervals for up to 120 minutes using precordial Doppler ultrasound.
Results: Median tau protein before diving was 0.200 pg·mL^{-1} (range 0.100 to 1.10 pg·mL^{-1}) and after diving was 0.450 pg·mL^{-1} (range 0.100 to 1.20 pg·mL^{-1}; $P = 0.016$). Glial fibrillary acidic protein and neurofilament light protein concentrations analyzed in the same assay did not change after diving. No correlation was found between serum tau protein concentration and the amount of VGE.
Conclusion: Repeated diving to between 52–90 msw is associated with a statistically significant increase in serum tau protein concentration, which could indicate neuronal stress.

Introduction

Diving is a widespread recreational and professional activity. While diving using air as the breathing gas, the body accumulates nitrogen due to an elevated ambient pressure. The amount of nitrogen or other inert gases taken up in the tissue depends on diving depth and time spent underwater. When the diver ascends towards the surface and decompresses, the ambient pressure falls and nitrogen leaves the tissues. If decompression is too rapid, then there is a risk that nitrogen could come out of solution, forming bubbles in blood and tissues. Intravascular nitrogen bubbles mainly form in the venous system and they are therefore named venous gas emboli (VGE).[1]

The formation of VGE in the body is considered to be a cause of decompression sickness (DCS). VGE passing into the arterial circulation through veno-arterial shunts in either the heart or the lungs could occlude arteries, disrupting both blood supply and normal tissue function. Disparity in bubble location could explain the varied clinical symptoms associated with DCS, which range from itchy skin, fatigue and pain, to neurological lesions, seizures, coma, and death.[2] Even uneventful dives, without clinical signs of DCS, can give rise to VGE; these so-called 'silent bubbles' can be regarded as a normal phenomenon after diving. Analyses of large groups of divers show that DCS is more common when the VGE load is high after diving. Conversely, when no VGE can be detected, the risk of DCS seems low.[3] VGE

load can be quantified by Doppler ultrasound examination of the heart or major vessels using the Kisman-Masurel (KM) grading system. This is an ordinal scale based on categorical data describing amplitude, frequency and duration of VGE.[4]

High partial pressures of both oxygen and nitrogen are known to disturb normal function of the human brain. Oxygen can be harmful to the central nervous system (CNS) at partial pressures exceeding 160 kPa, 66 metres' sea water (msw) when a diver breathes air, with the toxic effect increasing with partial pressure and length of exposure. Signs of oxygen toxicity include sensory and behavioural changes, dizziness, and seizures.[5] The narcotic effect of nitrogen becomes increasingly apparent at depths exceeding 30 msw when a diver breathes air, but individual susceptibility varies. Nitrogen narcosis manifests as impaired cognitive and neuromuscular performance.[6] In order to regulate the partial pressures of oxygen and nitrogen and their effects at greater depths, gas mixtures containing nitrogen, oxygen and helium are used and commonly referred to as 'trimix'.

Exposure to high ambient pressure, equivalent to diving depths of more than 150 msw, can cause neuromuscular dysfunction, a condition termed the high-pressure neurological syndrome (HPNS). Nausea, dizziness and tremors are common symptoms. With increasing depth, myoclonic episodes appear. Factors such as individual susceptibility, compression rate and breathing gas mixture affect the clinical manifestations. The causal mechanism of HPNS is partly unknown though it has been shown to be independent of elevated gas pressure.[7]

Tau protein (tau) is a microtubular protein abundant in neuronal axons, predominantly in thin unmyelinated axons of the cortex. It can also, to a lesser extent, be detected in the liver, kidneys and testes.[8] Increased tau levels are found in blood serum in conjunction with dementia, traumatic brain injury (TBI),[8–10] cerebral concussion, boxing,[11,12] and hypoxic brain injury, where it correlates with outcome.[13,14] Tau levels in blood serum rise early, within 24 hours, after cerebral damage. A delayed secondary peak appears a few days after an hypoxic injury.[14] A recent study on patients undergoing surgery and general anesthesia showed a transient rise of serum tau levels.[15] High intensity interval training can also lead to increased serum tau levels in the bloodstream; however, a two-week period of such training is alleged to blunt the tau release during subsequent training sessions.[16] Transient hypoxia during breath-hold diving has been associated with elevated tau levels, but a small pilot study on divers with DCS found no statistically significant elevation of tau concentration in cerebrospinal fluid (CSF).[17,18]

Neurofilament light protein (NfL) is a structural axonal protein which is found mainly in myelinated subcortical axons.[8] Serum NfL levels correlate with outcome in patients with TBI, but their rise is slower than that for tau, reaching a maximum beyond 10 days following the insult.[19] Glial fibrillary acidic protein (GFAp) is expressed almost solely in astrocytes. Elevated blood serum levels of GFAp have been reported within 24 hours after TBI.[8]

The potential influence of diurnal variation on neuronal fluid biomarker results has been a subject of scientific discussion.[20–22] However, a study including patients with Alzheimer's disease and older healthy volunteers concluded that there was no circadian pattern for tau in CSF.[23] Another study on neurosurgical patients showed no diurnal variation in CSF tau levels.[24] Likewise, there was no significant diurnal variation in CSF tau levels among older patients with idiopathic normal pressure hydrocephalus or pseudotumor cerebri, when studied through sequential CSF sampling.[25] Most likely serum tau levels reflect those in CSF. It is not known whether a hyperbaric exposure alone, without hypoxia, is associated with a rise in serum tau levels.

We hypothesized that diving, by way of the previously discussed consequences of exposure to an elevated ambient pressure, affects the central nervous system and causes a rise in serum tau protein concentration in blood. Our primary objective was to investigate changes in serum tau concentration after diving to depths of up to 90 msw. The secondary objective was to investigate if there was an association between serum tau concentration and VGE load after the same dives.

Methods

The study was prospective and observational. It was conducted in accordance with the Declaration of Helsinki, approved by the regional ethical committee in Gothenburg, Sweden (Dnr 292-17) and registered at ClinicalTrials.gov (NCT03190252).

SUBJECTS

Ten male military divers participating in professional naval dive training on the Swedish west coast from 12–15 June 2017 took part in the study. Subject characteristics are described in Table 1. All subjects gave their written informed consent. A control group containing non-diving military divers was initially planned. However, difficulties in subject recruitment meant that an appropriate control group could not be formed.

DIVING PROTOCOL

The participants performed one or two dives a day over four days, as shown in Figure 1. Dive depths were planned to increase with each subsequent dive. One diver did not dive on the third day. Eight subjects dived to 50–52 msw on the first day and reached 82–90 msw on the fourth day. For the two remaining divers, maximal depth ranged between 34 msw on the first day and 52 msw during the last dive.

Figure 1
Diving protocol. Divers 7–10 performed two 65–66 msw dives on the 13 June; divers 1 and 2 performed two 52 msw dives on the 15 June; diver 10 did not dive on the 14 June

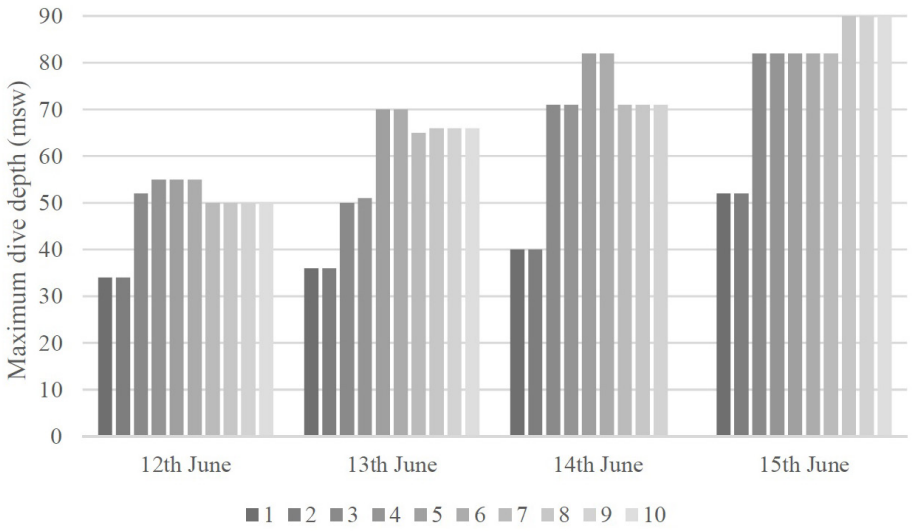


Table 1
Baseline and demographic data; for categorical variables *n* is presented; for continuous variables mean (SD) and median (range) are presented

Male	10
Age (years) Mean (SD) Median (range)	 38.4 (8.2) 39.5 (27.0–52.0)
BMI (kg·m^{-2}) Mean (SD) Median (range)	 25.6 (1.2) 25.4 (24.4–28.1)
Prior DCS	4
Excessive physical activity or diving ≤ 48 hours prior:	
No	6
One dive 15–20 msw	4
Medication:	
No	8
Diclofenac	1
Phenylpropanolamine (only on 1st dive day)	1

Median time spent at maximum depth during the first three days was 20 min (range 10 to 25 min). On the fourth day, time spent at maximum depth was 10 min for dives to 52 msw and 20 min for dives to 82–90 msw. All subjects used electronically controlled closed circuit rebreathers. Air was used as the diluent gas for dives less than 40 msw and trimix was used for all dives deeper than 40 msw. For dives between 40–65 msw the trimix diluent gas contained 15% oxygen, 50% helium, 35% nitrogen. During dives deeper than 65 msw the diluent contained 10% oxygen, 70% helium and 20% nitrogen. The rebreather equipment maintained a constant oxygen partial pressure of 130 kPa while the divers descended and were at depth. During the final decompression phase, an oxygen partial pressure of 160 kPa was allowed. Decompressions were planned according to the VPM-B algorithm with conservatism factor 2.[26] Immediately after dives deeper than 60 msw 100% oxygen was breathed for 10 minutes.

DATA COLLECTION

Venous blood samples were obtained from all participants before the first dive (Sample 1, baseline, 12 June 2017 between 11:30–12:50) and approximately two to three hours after the last dive (Sample 2, 15 June 2017 between 15:35–17:05). Samples were collected in gel tubes (Vacuette no. 454420, Hettish Labinstrument AB, Sweden) and immediately centrifuged for 10 minutes at 2,200 rpm and 20ºC (Sorvall ST 8/8R Centrifuge, Thermo Scientific, Germany). Directly afterwards, aliquots of 500 µL serum were frozen on dry ice and then stored at -78ºC until analyzed. Tau concentration was measured using the Human Neurology 4-Plex A assay (N4PA) on an HD-1 single molecule array (Simoa) instrument according to instructions from the manufacturer (Quanterix, Lexington MA, USA). For quality control (QC) samples, with tau concentrations of 0.70 pg·mL^{-1}, 1.4 pg·mL^{-1} and 24.1 pg·mL^{-1}, coefficients of variation (CVs) were 8.1%, 11.9% and 6.2%, respectively. The N4PA assay is designed to measure four biomarkers, namely tau, GFAp, NfL and ubiquitin carboxy-terminal hydrolase L1 (UCHL-1). Therefore, results for all these

Table 2
Serum tau protein values before (sample 1) and after (sample 2) diving; the mean (SD) and median (range) are presented for each parameter; for comparison the Wilcoxon signed-rank test was used

Sample 1 (pg·ml^{-1}) *n* = 9 Mean (SD) Median (range)	 0.322 (0.315) 0.200 (0.10–1.10)	
Sample 2 (pg·ml^{-1}) *n* = 10 Mean (SD) Median (range)	 0.500 (0.337) 0.450 (0.10–1.20)	
Delta-tau (pg·ml^{-1}) *n* = 9 Mean (SD) Median (range)	0.211 (0.145) 0.300 (0.0–0.40)	*P* = 0.016
Delta-tau (%) *n* = 9 Mean (SD) Median (range)	98.8 (96.0) 100 (0.0–300)	*P* = 0.016

Figure 2
Serum tau protein values before and after diving (*n* = 9). One diver is not included due to a missing sample 1 before diving. For two divers, increase in serum tau protein value (0.2 pg·mL^{-1} – 0.5 pg·mL^{-1}) was identical. They are represented by one line

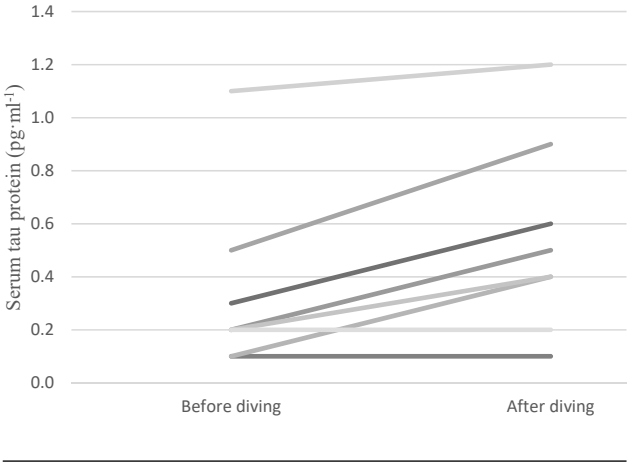


Table 3
Serum GFAp and NfL values before (sample 1) and after (sample 2) diving; for continuous variables mean (SD) and median (range) are presented; for comparison the Wilcoxon signed-rank test was used

	GFAp	*P*-value	NfL	*P*-value
Sample 1 (pg·ml^{-1}) *n* = 9 Mean (SD) Median (range)	 68.644 (24.086) 59.0 (41.0–108.5)		 9.956 (7.663) 7.800 (5.4–30.0)	
Sample 2 (pg·ml^{-1}) *n* = 10 Mean (SD) Median (range)	 65.090 (13.834) 62.9 (45.2–86.6)		 8.960 (5.830) 7.200 (5.7–25.3)	
Delta (pg·ml^{-1}) *n* = 9 Mean (SD) Median (range)	-3.644 (25.834) -0.400 (-39.4–32.6)	0.678	-1.056 (1.982) -1.400 (-4.7–1.6)	0.173
Delta (%) *n* = 9 Mean (SD) Median (range)	3.5 (37.0) 0.0 (-39.9–62.0)	0.678	-5.9 (19.7) -15.7 (-26.9–28.1)	0.173

four biomarkers were obtained. For QC samples, with NfL concentrations of 101.2 pg·mL^{-1}, 8.0 pg·mL^{-1} and 14.8 pg·mL^{-1}, CVs were 5.0%, 9.5% and 3.5%, respectively and for QC samples, with GFAp concentrations of 75.3 pg·mL^{-1}, 95.6 pg·mL^{-1} and 118.9 pg·mL^{-1}, CVs were 2.2%, 9.4% and 4.9%. The results of UCHL-1 analyses were discarded due to an unacceptably high level of imprecision as CVs were 44.9% and 121.0% for QC samples with UCHL-1 concentrations of 8.4 pg·mL^{-1} and 9.7 pg·mL^{-1} respectively.

Within 20 minutes after surfacing, each diver was monitored for the presence of VGE, at 10 to 15 minute intervals for up to 120 minutes, using precordial Doppler ultrasound (DBM9008; Techno Scientific Inc., Ontario, Canada). VGE load was assessed while the subjects lay in the left lateral decubitus position at rest and measurements were also made following movement (knee bends made whilst still lying down) and graded according to the KM scale.

The Kisman integrated severity score (KISS) algorithm[27] was used to convert KM grade measurements collected during the four-day study period into one mean score for each diver (VGE-KISS).

Figure 3
Serum tau protein after the last dive versus maximal KM grade at rest (n = 8); Spearman rank correlation coefficient 0.2, P-value: 0.6

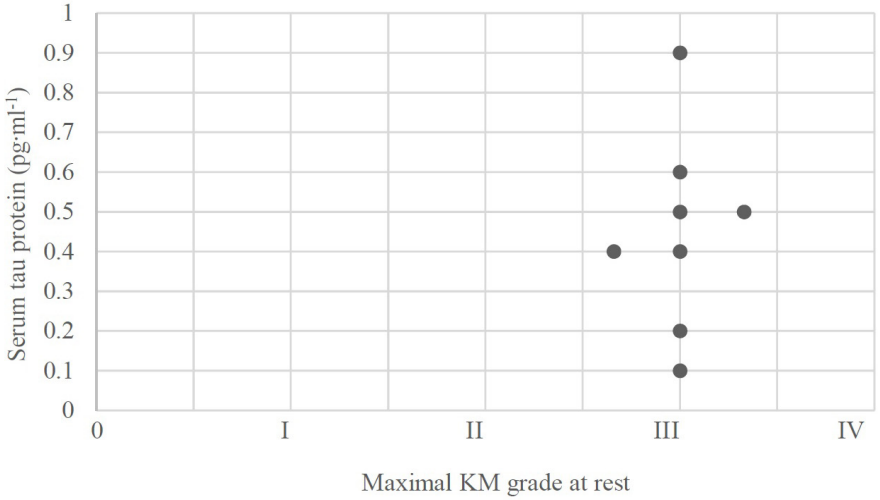
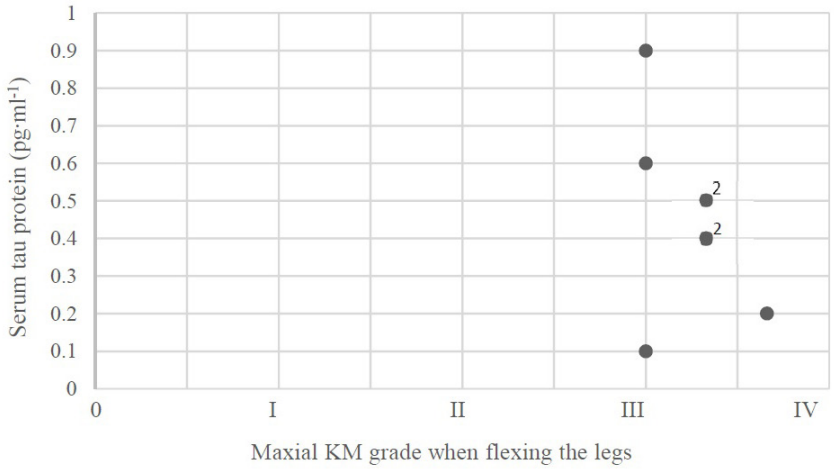


Figure 4
Serum tau protein after the last dive versus maximal KM grade when flexing the legs (n = 8); Spearman rank correlation coefficient -0.4, P-value: 0.33



STATISTICS

Results for tau and its association with VGE, were compiled by an independent statistical company (Statistiska Konsultgruppen, Gothenburg, Sweden) using SAS® v9.3 (Cary, NC, USA). Statistical analysis for GFAp and NfL were performed using IBM SPSS® v24 (IBM, Armonk NY, USA) and Spearman's correlation tests involving VGE KISS were performed using Microsoft© Office Excel 2018 (Microsoft Corporation, Redmond WA, USA). The study group was small and serum levels of tau, GFAp and NfL before diving were not normally distributed. Therefore, a non-parametric statistical technique was used for statistical inference.

Primary outcome

Serum tau levels before and after diving are presented as both mean (SD) and median (range: min–max) values. Differences in the tau levels between sample 1 and sample 2 (delta-tau) were presented both as an absolute (pg·mL^{-1}) and a relative change (%). Statistical significance was tested using the Wilcoxon signed-rank test.

Secondary outcome

Correlation between the maximum VGE loads measured after the last dive and the sample 2 serum tau concentrations was tested using Spearman's correlation test and presented as scatter plots.

Following the initial compilation of the results, correlation between the KISS scores and the sample 2 serum tau concentrations, and between KISS and delta tau, was tested using the Spearman correlation test.

GFAp and NfL

GFAp and NfL levels before and after diving were presented as both mean (SD) and median (range: min–max) values. Differences in the GFAp and NfL levels between sample 1 and sample 2 (delta-values) were presented both as an absolute ($pg \cdot mL^{-1}$) and a relative change (%). Statistical significance was tested using the Wilcoxon signed-rank test.

Missing data

Tau sample 1 was missing for one diver. Over the first three days, VGE data were not available for any dives and no VGE data were collected for the pair of divers who were diving no deeper than 52 msw.

Results

PRIMARY OUTCOME

Among the nine divers with baseline samples, seven had increased serum tau concentrations after four days of diving and none showed a decrease. Both the absolute and the relative changes in median serum tau concentration between sample 1 and sample 2 were statistically significant (Table 2, Figure 2).

SECONDARY OUTCOME

Eight of the 10 divers were monitored for VGE after the last dive of the series; across these subjects the median KM grade was III at rest and III+ following the knee bends. With regard to maximum KM grades, six subjects had grade III, one III- and one III+ measurements at rest. Following knee bends, three were graded KM III, four III+ and one IV-. With the observed narrow distribution of KM grades, no statistical correlation was found between serum tau protein concentration and maximum VGE load after diving (Figure 3 and Figure 4). Similarly, there was no statistically significant correlation between the VGE-KISS scores and sample-2 serum tau concentration ($R^2 = 0.15$, $t = 1.02$) nor between VGE-KISS and delta-tau ($R^2 = 0.002$, $t = 0.12$).

GFAp AND NfL

Neither GFAp nor NfL concentrations changed significantly after diving (Table 3).

Discussion

In this prospective pilot study, diving over a four-day period was associated with a statistically significant rise in serum tau concentration. The median tau value increased 2.5 times. This serum tau change is comparable to changes in plasma tau and CSF tau observed in earlier studies in athletes and after mild concussion injuries.[8,9] Causality between diving and serum tau concentrations is still uncertain, due to the lack of a control group and the small number of observations. Yet, as the divers' tau values after diving were compared to values obtained shortly before the first dive, the results are consistent with causation.

The KM grading system is the gold standard method of assessing VGE load after diving, as confirmed in a recent concensus,[28] but it is subjective and non-linear. Furthermore, all categorization results in a loss of information and reduced precision. A majority of KM grades after diving were III at rest and III or III+ following knee bends. In this study, there was no statistically significant correlation between maximum VGE load and tau levels nor between VGE-KISS scores and tau levels, but the narrow distribution of KM grades and the small set of observations precludes conclusions. A future study involving a larger cohort of divers, with a wider range of KM grades, would make it possible to investigate if there is a correlation between tau and VGE.

Our objective was to investigate changes in serum tau concentration after diving, but the assay used for measurement also provided us with results for GFAp and NfL. The absence of change in NfL concentration was expected, as NfL is a slow biomarker for axonal injury, reaching its maximum no earlier than 10 days following a traumatic injury.[19] GFAp, a protein highly expressed in astrocytes, appears to have similar kinetics in blood as tau.[8] The unchanged GFAp concentrations may thus suggest a limited involvement of astrocytes in response to diving exposure, though the small size of the study makes such a conclusion speculative.

High partial pressures of oxygen could potentially affect the CNS negatively. Oxygen partial pressure in the breathing gas did not exceed 160 kPa during the study. This is considered a safe limit during diving and does not give rise to subjective symptoms. Despite this, even a modest increase in oxygen partial pressure could be a contributing cause of elevated serum tau protein after diving and furthermore, nothing is known about any relevant effects of breathing gases containing helium. Studies investigating HPNS have shown that exposure to increased ambient pressure affects the nervous system through mechanisms unrelated to the partial pressures of breathing gases and VGE. It is possible that the CNS is affected by pressure at depths shallower than those associated with manifestations of HPNS and this could be a cause of elevated tau.

The lack of a control group is a shortcoming of this study. There was a difference between the time of day when samples 1 and 2 were taken. Studies show no diurnal variation in CSF tau levels,[23–25] making it improbable that

they should fluctuate in the blood significantly during the day. Nevertheless, a representative control group could have ensured that no confounding factors, such as diurnal variation, were responsible for changes in serum tau. Ideally in future studies, tau should be sampled at the same times of day and the results compared to a representative control group. In the context of hypoxic brain injury, studies have shown that the increase in serum tau levels reach a maximal elevation within 24 hours, though sometimes there is a delayed peak at about 72 hours.[14] The change in serum tau levels after a far milder but prolonged impact, such as repeated diving, are unknown. Additional sampling of venous blood at other points might have yielded even higher serum tau values.

The small size of the study was an important limitation. Mean values were potentially unreliable and misleading. For that reason, both mean and median values were presented and a non-parametric statistical technique was used for inference. Another limitation was that only serum samples were available. Tau concentrations are, for unknown reasons, higher in plasma than in serum, but the ultrasensitive method employed still allows accurate measurement of serum tau concentrations. Meaningful associations of serum tau concentrations and neuronal injury in other conditions have been reported before.[13,29] Therefore, we consider this limitation minor.

No subject reported excessive physical activity within the 48 hours before the study, but it is possible that dives made by four of the participants shortly before the study did influence their results. None of the dives prior to the study were reported to be deeper than 20 msw, which could be considered at most moderately stressful for a trained diver. No strenuous physical activity was performed during the study dives. Therefore, it is unlikely that the results were confounded by either prior diving or physical exertion during the study dives.

The study group consisted exclusively of trained male navy divers. Even though there was a considerable age difference between participants, they all met the physical and medical demands required by the navy and so in this respect the group was homogenous. Four of the 10 subjects had a past history of DCS. This is potentially the result of a professional diving career and not necessarily due to an increased individual susceptibility of the nervous system to hyperbaric exposure.

Conclusion

Despite its limitations, this pilot study showed that repeated diving to depths between 52–90 msw using a trimix breathing gas was associated with a statistically significant rise in tau protein levels in serum. A larger, controlled study is needed both to validate these results and to investigate the relationship between VGE and tau. Further studies on tau and diving should ideally also be carried out on divers with DCS.

References

1 Mitchell SJ. Decompression sickness: pathophysiology. In: Edmonds C, Bennett M, Lippmann J, Mitchell SJ. Diving and subaquatic medicine, 5th ed. Boca Raton, FL: Taylor and Francis; 2016.

2 Francis TJR, Mitchell SJ. Pathophysiology of decompression sickness. In: Brubakk AO, Neumann TS, editors. Bennett and Elliott's physiology and medicine of diving, 5th ed. Edinburgh: Saunders; 2003.

3 Nishi RY, Brubakk AO, Eftedal OS. Bubble detection. In: Brubakk AO, Neumann TS, editors. Bennett and Elliott's physiology and medicine of diving, 5th ed. Edinburgh: Saunders; 2003.

4 Blogg SL, Gennser M, Møllerløkken A, Brubakk AO. Ultrasound detection of vascular decompression bubbles: the influence of new technology and considerations on bubble load. Diving Hyperb Med. 2014;44:35–44. PMID: 24687484.

5 Bennett M. Oxygen toxicity. In: Edmonds C, Bennett M, Lippmann J, Mitchell SJ. Diving and subaquatic medicine, 5th ed. Boca Raton, FL: Taylor and Francis; 2016.

6 Bennett P, Rostain JC. Inert gas narcosis. In: Brubakk AO, Neumann TS, editors. Bennett and Elliott's physiology and medicine of diving, 5th ed. Edinburgh: Saunders; 2003.

7 Mitchell S. High pressure neurological syndrome. In: Edmonds C, Bennett M, Lippmann J, Mitchell SJ. Diving and subaquatic medicine, 5th ed. Boca Raton, FL: Taylor and Francis; 2016.

8 Zetterberg H, Blennow K. Fluid biomarkers for mild traumatic brain injury and related conditions. Nat Rev Neurol. 2016;12:563–74. doi: 10.1038/nrneurol.2016.127. PMID: 27632903.

9 Shahim P, Tegner Y, Wilson DH, Randall J, Skillbäck T, Pazooki D, et al. Blood biomarkers for brain injury in concussed professional ice hockey players. JAMA Neurol. 2014;71:684–92. doi: 10.1001/jamaneurol.2014.367. PMID: 24627036.

10 Zetterberg H. Review: Tau in biofluids – relation to pathology, imaging and clinical features. Neuropathol Appl Neurobiol. 2017;43:194–9. doi: 10.1111/nan.12378. PMID: 28054371.

11 Neselius S, Brisby H, Theodorsson A, Blennow K, Zetterberg H, Marcusson J. CSF-biomarkers in olympic boxing: diagnosis and effects of repetitive head trauma. PLoS One. 2012;7(4):e33606. doi: 10.1371/journal.pone.0033606. PMID: 22496755. PMCID: PMC3319096.

12 Zetterberg H, Hietala MA, Jonsson M, Andreasen N, Sturyd E, Karlsson I, et al. Neurochemical aftermath of amateur boxing. Arch Neurol. 2006;63:1277–80. doi: 10.1001/archneur.63.9.1277. PMID: 16966505.

13 Mattsson N, Zetterberg H, Nielsen N, Blennow K, Dankiewicz J, Friberg H, et al. Serum tau and neurological outcome in cardiac arrest. Ann Neurol. 2017;82:665–75. doi: 10.1002/ana.25067. PMID: 28981963. PMCID: PMC5725735.

14 Randall J, Mörtberg E, Provuncher GK, Fournier DR, Duffy DC, Rubertsson S, et al. Tau proteins in serum predict neurological outcome after hypoxic brain injury from cardiac arrest: results of a pilot study. Resuscitation. 2013;84:351–6. doi: 10.1016/j.resuscitation.2012.07.027. PMID: 22885094.

15 Evered L, Silbert B, Scott DA, Zetterberg H, Blennow K. Association of changes in plasma neurofilament light and tau levels with anesthesia and surgery: results from the CAPACITY and ARCADIAN studies. JAMA Neurol. 2018;75:542–7. doi: 10.1001/jamaneurol.2017.4913. PMID:

29459944. PMCID: PMC5885271.
16 Di Battista AP, Moes KA, Shiu MY, Hutchison MY, Churchill N, Thomas SG, et al. High-intensity interval training is associated with alterations in blood biomarkers related to brain injury. Front Physiol. 2018;9:1367. doi: 10.3389/fphys.2018.01367. PMID: 30323770. PMCID: PMC6172320.
17 Gren M, Shahim P, Lautner R, Wilson DH, Andreasson U, Norgren N, et al. Blood biomarkers indicate mild neuroaxonal injury and increased amyloid beta production after transient hypoxia during breath-hold diving. Brain Inj. 2016;30:1226–30. doi: 10.1080/02699052.2016.1179792. PMID: 27389622.
18 Shahim P, Arnell P, Kvarnström A, Rosén A, Bremell D, Hagberg L, et al. Cerebrospinal fluid markers of central nervous system injury in decompression illness – a case-controlled pilot study. Diving Hyperb Med. 2015;45:240–3. PMID: 26687311.
19 Shahim P, Gren M, Liman V, Andreasson U, Norgren N, Tegner Y, et al. Serum neurofilament light protein predicts clinical outcome in traumatic brain injury. Sci Rep. 2016;6:36791. doi: 10.1038/srep36791. PMID: 27819296. PMCID: PMC5098187.
20 Bateman RJ, Wen G, Morris JC, Holtzman DM. Fluctuations of CSF amyloid-beta levels: implications for a diagnostic and therapeutic biomarker. Neurology. 2007;68:666–9. doi: 10.1212/01.wnl.0000256043.50901.e3. PMID: 17325273.
21 Cicognola C, Chiasserini D, Parnetti L. Preanalytical confounding factors in the analysis of cerebrospinal fluid biomarkers for Alzheimer's disease: the issue of diurnal variation. Front Neurol. 2015;6:143. doi: 10.3389/fneur.2015.00143. PMID: 26175714. PMCID: PMC4483516.
22 Lucey BP, Fagan AM, Holtzman DM, Morris JC, Bateman RJ. Diurnal oscillation of CSF Aβ and other AD biomarkers. Mol Neurodegener. 2017;12:36. doi: 10.1186/s13024-017-0161-4. PMID: 28478762. PMCID: PMC5421331.
23 Slats D, Claassen JA, Spies PE, Borm G, Besse KT, van Aalst W, et al. Hourly variability of cerebrospinal fluid biomarkers in Alzheimer's disease subjects and healthy older volunteers. Neurobiol Aging. 2012;33:831.e1–9. doi: 10.1016/j.neurobiolaging.2011.07.008. PMID: 21880396.
24 Cicognola C, Chiasserini D, Eusebi P, Andreasson U, Vanderstichele H, Zetterberg H, et al. No diurnal variation of classical and candidate biomarkers of Alzheimer's disease in CSF. Mol Neurodegener. 2016;11:65. doi: 10.1186/s13024-016-0130-3. PMID: 27605218. PMCID: PMC5013624.
25 Moghekar A, Goh J, Li M, Albert M, O'Brien RJ. Cerebrospinal fluid Aβ and tau level fluctuation in an older clinical cohort. Arch Neurol. 2012;69:246–50. doi: 10.1001/archneurol.2011.732. PMID: 22332192. PMCID: PMC3310240.
26 Yount DE, Hoffman DC. On the use of a bubble formation model to calculate diving tables. Aviat Space Environ Med. 1986;57:149–56. PMID: 3954703.
27 Nishi RY, Jankowski LW, Tikuisis P. Effect of exercise on bubble activity during diving. In: RTO Meeting Proceedings 62. Operational medical issues in hypo- and hyperbaric conditions. RTO Human Factors and Medicine Panel, 16-19 October 2000, Toronto, Canada (RTO-MP-062). National Technical Information Service, United States 2001, session IV Hyperbaric operations issues, 34-1 to 34-6. ISBN 92-837-0019-8. Available from: https://apps.dtic.mil/dtic/tr/fulltext/u2/a395680.pdf. [cited 2018 December 14].
28 Møllerløkken A, Blogg SL, Doolette DJ, Nishi RY, Pollock NW. Consensus guidelines for the use of ultrasound for diving research. Diving Hyperb Med. 2016;46:26–32. PMID: 27044459.
29 Thompson AG, Luk C, Heslegrave AJ, Zetterberg H, Mead SH, Collinge J, et al. Neurofilament light chain and tau concentrations are markedly increased in the serum of patients with sporadic Creutzfeldt-Jakob disease, and tau correlates with rate of disease progression. J Neurol Neurosurg Psych. 2018:89:955–61. doi: 10.1136/jnnp-2017-317793. PMID: 29487167. PMCID: PMC6109239.

Acknowledgements

The authors would like to thank the Swedish Navy, The Swedish Society for Military Medical Officers, participating individuals, Dr Lesley Blogg of SLB Consulting (for Doppler ultrasound measurements and manuscript editing), Daniel Reinemann and research personnel for their contribution to this study.

Funding

The Swedish Society for Military Medical Officers, and the Herbert and Karin Jacobssons Foundation provided financial contribution for this study. HZ is a Wallenberg Academy Fellow supported by grants from the Knut and Alice Wallenberg Foundation, the Swedish Research Council, the European Research Council, Swedish State Support for Clinical Research (ALFGBG), the UK Dementia Research Institute at UCL, Hjärnfonden and Frimurarestiftelsen.

Conflicts of interest

HZ has served at scientific advisory boards for Roche Diagnostics, Wave, Samumed and CogRx and is a co-founder of Brain Biomarker Solutions in Gothenburg AB, a GU Ventures-based platform company at the University of Gothenburg. KB has served on scientific advisory boards for Roche Diagnostics, Fujirebio Europe, IBL International, Eli Lilly and Alzheon and is a co-founder of Brain Biomarker Solutions in Gothenburg AB. No other authors have reported any conflicts of interest.

Submitted: 17 December 2018; revised 31 January 2019
Accepted: 12 March 2019

A survey of scuba diving-related injuries and outcomes among French recreational divers

David Monnot[1], Thierry Michot[2], Emmanuel Dugrenot[1], François Guerrero[1], Pierre Lafère[1]

[1] *EA4324 ORPHY, Institut Brestois Santé Agro Matière, Université de Bretagne Occidentale, Brest, France*
[2] *EA3149 LABERS, Institut Brestois des Sciences de l'Homme et de la Société, Université de Bretagne Occidentale, Brest*

Corresponding author: *François Guerrero, EA4324 ORPHY, 6 Av. Le Gorgeu CS 93837, 29238 Brest Cedex 3, France*
francois.guerrero@univ-brest.fr

Key words
Diving incidents; Epidemiology; Barotrauma; Decompression illness; First aid; Hyperbaric oxygen therapy

Abstract
(Monnot D, Michot T, Dugrenot E, Guerrero F, Lafère P. A survey of scuba diving-related injuries and outcomes among French recreational divers. Diving and Hyperbaric Medicine. 2019 June 30;49(2):96–106. doi: 10.28920/dhm49.2.96-106. PMID: 31177515.)
Introduction: Few studies are available to appreciate the broad spectrum of dive-related injuries (DI), which are not limited to decompression illness (DCI) and fatalities. Studies supporting injury-management efficacy from early recognition to first-aid, final treatment and outcome are also lacking. This study aims at making an epidemiologic inventory of DI among French scuba divers.
Methods: This online, retrospective, cross-sectional survey analyzed self-reported symptoms, context of occurrence, initial response and outcome. The relationships between symptoms and diver characteristics were assessed and severity scores created from the reports.
Results: A total of 799 divers responded, of whose questionnaires 784 were sufficiently complete to be analyzed. Approximately one-third (35%) of respondents had never experienced a DI. DCI-like symptoms represent a small fraction of DIs, the most commonly reported being ear barotrauma. Self-reported symptom rates decreased with increasing age and male sex. The ranking dive leader was the primary care provider in 58% of reports and 32% of injured divers never sought help. Management decisions (first aid and/or hyperbaric oxygen treatment) were related to the severity score. Complete resolution was achieved in 84 (74%) of 114 DCI cases, whilst mild ($n = 22$, 19%) and severe ($n = 8$, 7%) residual symptoms were reported. One in 10 divers who did not seek treatment for symptoms believed to be related to DCI declared some residual symptoms.
Conclusion: Based on these results, diving injury rates may be higher than previously reported. However, the most frequent symptoms appear to be of only a modest nature.

Introduction

Although generally a safe sport, scuba diving is associated with a spectrum of injury severity. Data from the French Federation of Undersea Studies and Sports (FFESSM), the main diver training organization in France, indicate roughly proportional increases in numbers of French divers undergoing advanced training and the numbers of recorded injuries, from 170 in 1991 to 412 in 2013.[1] Reports on dive-related injuries (DI) have concentrated on acute and/or severe injuries, primarily decompression illness (DCI) and fatalities.[2–4] However, DI are not limited to DCI and fatalities but, rather, cover a much broader spectrum, with other injuries remaining largely unaccounted for.[5] Owing to a paucity of data regarding the risk and prevalence of DI among recreational divers,[5–7] it is difficult to provide an overview of the situation. This occurs because the reporting of recreational diving accidents is not mandatory unlike the protocols for military or scientific diving.[8–10] According to the few readily available reports on DI, the most common insults do not involve DCI. For example, mild ear barotrauma and sinus barotrauma were common amongst a sample of 709 divers.[11,12] These symptoms were experienced on more than one occasion by 369 (52%) and 245 (35%) divers, respectively. Only a small proportion (4%) of divers reported symptoms of DCI. More recently, 20 diving-related injuries of sufficient concern to be logged in the dive boat manifest were reported out of 97,144 dives, 11 being non DCI-related incidents, including ear and sinus barotraumas.[13]

Accurate data concerning incident management, from the recognition of a DI by divers to the implementation of a treatment, first aid and/or hyperbaric oxygen treatment (HBOT), are also lacking.[14] Indeed, even if DCI may be tracked through hyperbaric treatment records, less is known regarding how divers respond to a problem. A significant proportion of sports divers in Orkney either failed to identify DCI or underestimated the potential consequences if left untreated.[14] According to data from 183 injured recreational divers treated in Corsica between 1996 and 2000, 54% of

cases involved a delay of more than one hour before the emergency medical services were activated.[15]

First aid and adjunctive therapies for DI are mainly supported by accumulated experience over decades or by clinical judgement,[16] rather than being evidence-based. For example, surface oxygen is widely employed in the treatment of DI, but its use is supported by animal experiments only,[17] with few human studies supporting its efficacy.[18,19] More importantly, it seems from those studies that administration of first-aid oxygen serves to reduce the number of recompressions required but cannot necessarily improve the odds of recovery.

Improving knowledge of the pattern, frequency, management and outcome of DI is of importance to provide better insights for prevention and treatment. The aim of this study was to create an epidemiologic inventory of recreational diving injuries and their consequences among individuals that dived in French territorial waters (metropolitan and overseas territories).

Methods

Experimental procedures, conducted in accordance with the Declaration of Helsinki, were approved by the local correspondent of the Western Brittany University for informatic database and individual liberties (European Directive 95/46/EC).[20] Participation was voluntary, and responses were confidential. No identifying information was collected.

A cross-sectional study of French recreational divers used a questionnaire (Google Form) to investigate:

- Diver demographic data, including dive experience;
- Self-reported symptoms and the context of the incident;
- First aid, medical intervention and outcome.

This self-reported online survey was conducted from 21 November 2017 to 05 March 2018 inclusive. In order to obtain a representative sample of the diving population, diving organizations and their national representatives were identified and contacted by email. The questionnaire was further disseminated through social networks and diving forums to allow us to also contact unaffiliated divers.

The retrospective survey focused on participant diving exposures and diving-related injuries. It was designed to address the presence of clinical symptoms rather than the presence of a type of accident (e.g., 'ear barotrauma' or 'neurological DCS'). The development of questions was based on the current literature regarding dive-related epidemiology.[5–7,21] In total, 28 symptoms were investigated. When a symptom was reported, contextual parameters (optional questions), such as dive environment and profiles, were also recorded. Finally, first aid, medical intervention and outcomes were also investigated. All questions were written to be understandable regardless of any previous knowledge of diving physiology and/or diving medicine. A draft version was sent to 10 divers of different certification levels (instructors and medical staff included) and from three different regions of France, and some questions which could be misinterpreted or not understood (e.g., a complicated medical term) were modified. A second validation was made in 'real' conditions by sending a beta version through social networks and email (which was the final mode of dissemination). In this manner, 69 responses were obtained, of which 67 contained sufficient information to be analyzed. This led us to additional minor adjustments to ensure that the survey avoided ambiguity.

STATISTICAL ANALYSIS

Most responses were analyzed descriptively. The relationship between the presence/absence of symptoms and divers' characteristics were calculated from all self-reported dive-related symptoms using Pearson's Chi-squared Test. Since all discrete data, except the number of dives, passed the Kolmogorov-Smirnov test, allowing us to assume a Gaussian distribution, comparison between variables was carried out with unpaired *t*-tests. We used Chi-square tests to compare the number of dives. Statistical analysis was conducted with Statistica© software (ver. 10, StatSoft France, 2011). A probability of $P < 0.05$ was considered statistically significant. However, in case of multiple comparisons, this *P*-value was divided by the number of independent tests. Indeed, when the influence of sex on the age of divers, dive experience and certification level was tested, a *P*-value of 0.016 was considered statistically significant, whereas a probability of $P < 0.007$ was considered statistically significant for the influence of sex, age, dive experience, certification level, time spent in physical activity, dive location and seasonal rhythm of diving.

Results

Because of the method used for the dissemination of the questionnaire, the number of divers who accessed the questionnaire is unknown. A total of 799 divers responded during the study period, of whose questionnaires 784 were analysable. The respondents were geographically widespread within France and included both inland and coastal areas. All the French territories were represented except for French Guiana.

DESCRIPTION OF THE RESPONDENTS

Characteristics are described in Table 1. The majority of divers were men (n = 586, 75%) while women (n = 198) represented 25% of the total sample. The sex distribution within the different age categories was significantly different ($\chi^2 = 35.25$, df = 5, $P < 0.001$); in men, the most representative age group was 46–55 years old (25.3%), then 36–45 years old (20.3%) second, whilst in women the age groups were represented more evenly (26–35 years old, 6.3%; 36–45, 5.8%; 46–55, 6.9%). Most respondents were experienced

Table 1

Respondent profiles (n = 784); missing values in the table refer to the missing data from the respondents; * – diving certification: Basic = EN 14153-1/ISO 24801-1 level 1 'supervised diver'; Autonomous = EN 14153-2/ ISO 24801-2 level 2 'autonomous diver'; Advanced and dive guide = EN 14153-3/ ISO 24801-3 level 3 'dive leader'; Instructor = EN 14413-1/ ISO 24802-1 level 1 scuba instructor or EN 14413-2/ ISO 24802-2 level 2 scuba instructor. For simplicity of presentation, categories were pooled for the following components: Age, physical activity, experience (years) and experience (number of dives)

		Male (n = 586)			**Female** (n = 198)			**Total** (n = 784)	
		n	%	% of total	n	%	% of total	n	%
Age (years)	18–35	101	17.2	12.9	71	35.9	9.1	172	22.0
	36–45	159	27.1	20.3	46	23.2	5.8	205	26.1
	46–55	198	33.8	25.3	54	27.3	6.9	252	32.2
	> 56	127	21.7	16.2	26	13.1	3.3	153	19.5
	Missing	1	0.2	0.1	1	0.5	0.1	2	0.2
Physical activity (h/week)	< 2 h	348	59.4	44.4	136	68.7	17.3	484	61.8
	> 2 h	238	40.6	30.4	62	31.3	7.9	300	38.2
Dive certification*	Basic	10	1.7	1.2	20	10.1	2.6	30	3.8
	Autonomous	65	11.1	8.3	47	23.7	6.0	112	14.3
	Advanced	97	16.6	12.4	46	23.2	5.9	143	18.3
	Dive guide	54	9.2	6.9	11	5.6	1.4	65	8.3
	Instructor	358	61.1	45.7	74	37.4	9.4	432	55.1
	Missing	2	0.3	0.2	0	0.0	0.0	2	0.2
Open *vs* closed-circuit	Open-circuit	506	86.4	64.5	189	95.5	24.1	695	88.6
	Rebreather	71	12.1	9.1	8	4.0	1.0	79	10.1
	Missing	9	1.5	1.2	1	0.5	0.1	10	1.3
Breathing gas	Air	458	78.2	58.4	173	87.4	22.1	631	80.5
	Nitrox	101	17.2	12.9	22	11.1	2.8	123	15.7
	Trimix	24	4.1	3.0	3	1.5	0.4	27	3.4
	Missing	3	0.5	0.4	0	0.0	0.0	3	0.4
Experience (years)	< 6 months	0	0	0	4	2.0	0.5	4	0.5
	1 to 5	104	17.7	13.3	57	28.8	7.3	161	20.6
	5 to 10	112	19.1	14.3	33	16.7	4.2	145	18.5
	10 to 20	151	25.8	19.2	65	32.8	8.3	216	27.5
	> 20	218	37.2	27.8	38	19.2	4.9	256	32.7
	Missing	1	0.2	0.1	1	0.5	0.1	2	0.2
Experience (number of dives)	< 50	35	5.9	4.5	34	17.2	4.3	69	8.8
	51 to 300	157	26.8	20.0	79	39.9	10.1	236	30.1
	301 to 1,000	160	27.4	20.4	45	22.7	5.7	205	26.1
	1,001 to 3,000	108	18.4	13.8	17	8.6	2.2	125	16.0
	> 3,000	34	5.8	4.3	8	4.0	1.1	42	5.4
	Missing	92	15.7	11.7	15	7.6	1.9	107	13.6

scuba divers, the majority being certified instructors (55%) or with advanced level certifications (41%); 4% having only a basic certification. However, sex distribution among all certification levels was significantly different ($\chi^2 = 142.72$, df = 5, $P < 0.001$); the higher the certification level, the lower the proportion of women.

Eighteen training organizations were represented with the vast majority of divers belonging to three, namely FFESSM (n = 664, 85%), Professional Association of Diving Instructors (n = 135, 17%), and Scuba Schools International (n = 43, 5 %). Most divers declared more than one affiliation, while others (n = 21, 3%), although trained and certified according to the ISO 24801/24802 standards were unaffiliated.

A total of 683,171 dives were reported over a period ranging from less than six months to over 30 years (median 400 per diver, interquartile range (IQR) 150–1,000 dives). Dive experience in years of practice was significantly lower in females than males ($\chi^2 = 45.58$, df = 7, $P < 0.001$). The number of dives undertaken per year ranged from five to 230 (median 40, IQR 19–95).

SELF-REPORTED SYMPTOMS AND CONTEXT OF OCCURRENCE

Self-reported diving-related symptoms covered a 43-year span (from 1974 to 2017) and are summarised in Table 2. A total of 513 respondents (65%) reported at least one symptom, whilst 274 (35%) had not experienced any symptoms since the beginning of their diving career. The maximum number of symptoms reported by a diver was 23; however, the median was 1 (IQR 0–2) injury per diver. The primary symptom was related to the ears (ear pain in 44.8% at least once). After context analysis of self-reported symptoms through the optional questions, it appeared that the most common injuries incurred by divers were barotrauma (n = 320, 63% of the injured divers) followed by DCI (n = 146, 28% of injured divers). In 47 cases (9% of injured divers) a formal diagnosis could not be made.

The proportion of women who declared no dive-related symptoms was significantly lower than in men ($\chi^2 = 11.29$, df = 1, $P < 0.001$). A significant relationship between self-declared symptoms and age ($\chi^2 = 36.28$, df = 5, $P = 0.001$) was also found; the older the diver the lower the ratio of respondents declaring a probable DI, based on symptoms. This ratio was independent of both dive experience ($\chi^2 = 11.78$, df = 7, $P = 0.108$) and certification level ($\chi^2 = 6.03$, df = 5, $P = 0.303$). The presence of symptoms after a dive and therefore, the probable occurrence of a dive injury, was independent of the time spent in physical activity ($\chi^2 = 3.04$, df = 3, $P = 0.385$) or the dive location ($\chi^2 = 4.03$, df = 4, $P = 0.401$). Finally, the relationship of symptoms to the seasonal rhythm of diving did not quite reach statistical significance ($\chi^2 = 9.38$, df = 2, $P = 0.009$).

Injured respondents (n = 513) engaged in various types of diving (Table 3) depending on the purpose. Most DI were related to recreational diving (30% training and 59% exploration dives) while technical diving (rebreather, cave or deep trimix diving) accounted for 6%. No difference was observed between men and women in total dive time (45 ± 27 vs. 41 ± 18 minutes, paired t-test, $P = 0.07$, df = 511). However, male divers made significantly deeper dives than females (32 ± 17 vs. 25 ± 12 metres, paired t-test, $P < 0.0001$, df = 511). Most of the reported dives were decompression dives. It is noteworthy that 2% of the injured divers did not use any decompression tool, either because it was a no-decompression dive or because they completed the decompression required by following their dive buddy or instructor.

ANALYSIS OF DCI CASES

After contextual analysis, 114 datasets of DCI injuries (from the initial 799 questionnaires) were available for a complete analysis, including a severity score calculation,[22] first aid, HBOT and outcome.

First aid

As described in Table 4, 70% of divers were symptomatic within 30 minutes. The ranking dive leader was the primary care provider in 58% of cases. Thereafter, 59% of these divers received care from a physician. In these cases, referral to the physician depended on the severity score (< 7: 47%; 7–13: 82%; > 13: 100%; $\chi^2 = 10.23$, df = 2, $P = 0.004$). In only 10% of cases did divers seek help directly from a physician. The severity of the symptoms ($\chi^2 = 23.34$, df = 2, $P < 0.0001$) as well as their duration ($\chi^2 = 9.97$, df = 2, $P = 0.007$) were the primary triggers for seeking help directly from a physician, while severity had no influence on the activation of the ranking dive leader ($\chi^2 = 0.36$, df = 2, $P = 0.43$) (Figure 1). Surprisingly, 32% of the injured divers did not activate an emergency response and none of these were treated. Again, low severity seemed to be the primary factor for not seeking help (severity score < 7: 36%; 7–13: 27%; > 13: 0%; $\chi^2 = 8.45$, df = 2, $P = 0.014$).

Amongst the 66 divers who informed the ranking dive leader of symptoms, 86% received oxygen at a minimal rate of 15 L·min^{-1} and fluids were given in 65%. Despite it being a recommended procedure in France, unlike most other places, only 29% of injured divers recalled receiving oral acetylsalicylic acid.

Treatment and outcome for DCI cases

The decision to administer HBOT was made according to the severity score (< 7 32%; ≥ 7 100%; $\chi^2 = 25.66$, df = 2, $P < 0.0001$), not based on the presence of continuing symptoms (< 24 hours 64%; ≥ 24 hours 60%; $\chi^2 = 0.10$, df = 2, $P = 0.949$). However, the chosen protocol was not

Table 2
Self-reported symptoms after a dive; although some respondents may have declared several episodes, percentage calculations are made on the first episode

	Male (*n* = 586)			**Female** (*n* = 198)			**Total** (*n* = 784)	
	n	%	% of total	*n*	%	% of total	*n*	%
No symptom reported	**222**	**37.9**	**28.3**	**49**	**24.7**	**6.3**	**271**	**34.6**
Self-reported symptoms	**364**	**62.1**	**46.4**	**149**	**75.3**	**19.0**	**513**	**65.4**
Ear pain	240	40.9	30.6	111	56.0	14.2	351	44.8
Sinus pain	144	24.6	18.4	60	30.3	7.6	204	26.0
Toothache	58	9.9	7.4	26	13.1	3.3	84	10.7
Loss of hearing or ringing in ears	50	8.5	6.4	19	9.6	2.4	69	8.8
Headache	28	4.8	3.6	25	12.6	3.2	53	6.8
Dizziness	37	6.3	4.7	11	5.6	1.4	48	6.1
Tingling	36	6.1	4.6	11	5.6	1.4	47	6.0
Joint pain	37	6.3	4.7	9	4.6	1.1	46	5.8
Unusual fatigue	30	5.1	3.8	13	6.6	1.7	43	5.5
Loss of strength	29	5.0	3.7	14	7.1	1.8	43	5.5
Muscle pain	33	5.6	4.3	8	4.0	1.0	42	5.3
Shortness of breath	27	4.6	3.4	14	7.1	1.8	41	5.2
Numbness	29	4.9	3.7	9	4.6	1.1	38	4.8
Stomach pain	23	3.9	2.9	12	6.1	1.5	35	4.4
Chest pain	23	3.9	2.9	10	5.0	1.3	33	4.2
Decreased/absent sensation	25	4.3	3.2	7	3.6	0.9	32	4.1
Breathing disorders	19	3.2	2.4	12	6.1	1.5	31	3.9
Nausea/vomiting	19	3.2	2.4	10	5.0	1.3	29	3.7
Thoracic oppression	16	2.7	2.0	13	6.6	1.6	29	3.7
Visual disturbances	18	3.1	2.3	10	5.0	1.3	28	3.6
Itchy skin	21	3.6	2.7	7	3.6	0.9	28	3.6
Coughing up blood	16	2.7	2.0	8	4.0	1.0	24	3.0
Balance disorders	17	2.9	2.2	5	2.5	0.6	22	2.8
Eye pain	9	1.5	1.2	8	4.0	1.0	17	2.2
Back pain	11	1.9	1.4	6	3.0	0.8	17	2.2
Confusion/unusual behaviour	7	1.2	0.9	2	1.0	0.3	9	1.2
Language disorders	5	0.8	0.6	2	1.0	0.3	7	0.9
Urinary disorders	2	0.3	0.3	2	1.0	0.3	4	0.6

Table 3
Dive parameters for injured divers (n = 513). Missing values in the table refer to missing data from the respondents.
(* $P < 0.0001$, men vs. women, paired t-test, df = 511)

		Male (n = 364)			Female (n = 149)			Total (n = 513)	
		n	%	% of total	n	%	% of total	n	%
Type of dive	Single	218	59.9	42.5	90	60.4	17.5	308	60.0
	Interrupted	2	0.5	0.4	0	0	0.0	2	0.4
	Repetitive	98	27.0	19.1	35	23.5	6.9	133	26.0
	≥ 3rd dive/day	36	9.9	7.0	17	11.4	3.3	53	10.3
	Missing	10	2.7	1.9	7	4.7	1.4	17	3.3
Purpose	Introductory	4	1.1	0.8	3	2.0	0.6	7	1.4
	Exploration	210	57.7	40.1	91	61.1	18.6	301	58.7
	Training	112	30.8	21.8	40	26.8	8.4	152	29.6
	Technical	27	7.4	5.2	6	4.0	1.2	33	6.4
	Missing	11	3.0	2.1	9	6.1	1.8	20	3.9
Decompression	Dive computer	320	87.9	62.4	135	90.6	26.3	455	88.7
	Dive table	26	7.2	5.1	8	5.4	1.6	34	6.7
	None	8	2.2	1.6	3	2.0	0.5	11	2.1
	Missing	10	2.7	2.0	3	2.0	0.5	13	2.5
Diving depth (msw [mean ± SD])*		32.1 ± 16.6			25.0 ± 11.6			30.2 ± 15.8	
Total dive time (min [mean ± SD])			45 ± 27			41 ± 18		44 ± 25	

related to severity and included short 284 kPa treatment tables (14%; US Navy Treatment Table 5 or Comex 18C), long 284 kPa tables (64%; USN TT6 or Comex 18L) and a 405 kPa table (Comex 30). Complete resolution was reported by 84 (74%) divers, mild residual symptoms such as mild paresthesia, weakness, residual pain or some impairment of daily activities by 22 (19%). Eight (7%) divers self-declared severe residual symptoms, such as difficulty walking, paralysis, uncompensated vertigo or speech disorders. The final outcome was related to the initial severity score ($\chi^2 = 58.58$, df = 4, $P < 0.0001$) and also to symptom duration ($\chi^2 = 27.28$, df = 4, $P < 0.0001$), which did not appear to be a treatment choice criterion. Three out 31 divers who did not seek help reported having some residual symptoms.

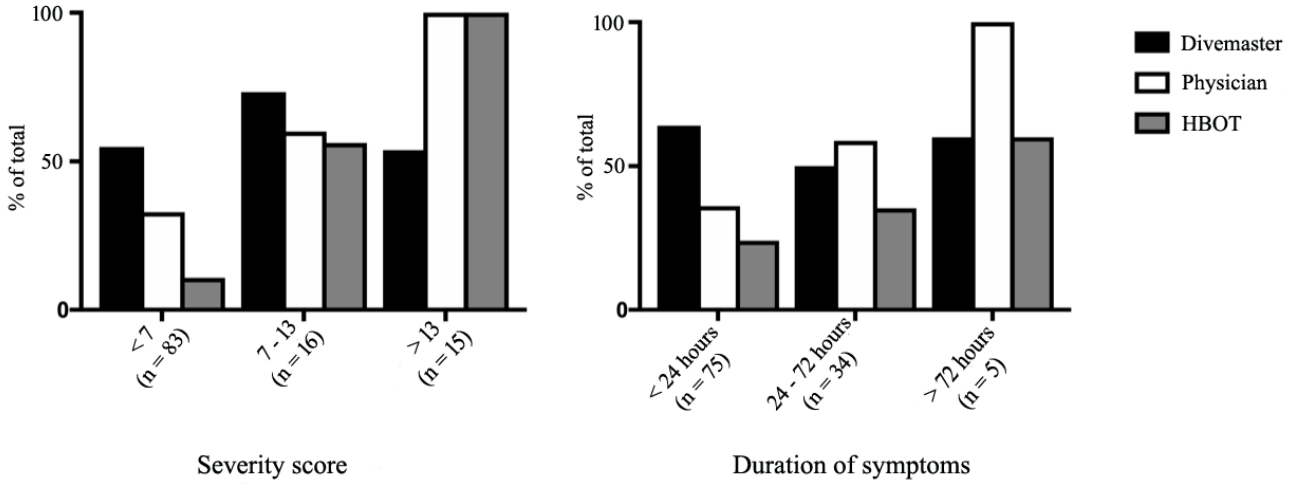
Discussion

The characteristics of the general French diving population have been previously estimated by two French marketing studies, one conducted on behalf of the French diving organizations[23] and one conducted by the French government.[24] According to those studies, the average diver is a man aged 38 ± 10 (mean +/- SD) years (median 37, IQR 32–47), with a low certification level and for whom scuba diving is an occasional activity (8 ± 6 dives per year; median 12.5, IQR 5–16), despite an activity span of 7.1 ± 4.4 years (median 6.5, IQR 5.5–11.5). Women account for 32% of the total population and 25% of dive leaders and instructors. As far as sex, age and occupational categories are concerned, our sample is consistent with these general diving population characteristics. However, it differs markedly in its certification breakdown and diving activity, with high-level certification (82%) over-represented compared to the general diving population, as only one-third of the latter has a certification level higher than EN 14153-2/ ISO 24801-2 'autonomous diver'. This would also explain the reported greater diving activity. Therefore, these observations cannot evaluate the effect of relative inexperience on the occurrence of DI-related symptoms.

Table 4
Diver responses to DCI-like symptoms according to onset, severity score and duration of symptoms (n = 114) (DM = Divemaster)

Onset	Severity score	Duration of symptoms	Men (n = 73)			Women (n = 41)			Total (n = 114)			
			n	DM	Medic	n	DM	Medic	n	DM	Medic	HBO
In water	<7	<24h	7	4	0	8	0	3	15	7	3	0
		24–72h	6	5	1	4	1	3	10	6	4	2
	7–13	<24h	3	1	1	-	-	-	3	1	1	1
	>13	<24h	2	2	2	1	1	1	3	3	3	3
		24–72h	1	1	1	2	1	2	3	2	3	3
<5 min	<7	<24h	13	9	3	4	2	0	17	11	3	1
		24–72h	6	4	2	2	1	0	8	5	2	1
		>72h	4	3	4	1	0	1	5	3	5	3
	7–13	<24h	1	1	0	-	-	-	1	1	0	0
	>13	<24h	1	1	1	-	-	-	1	1	1	1
5–10 min	<7	<24h	2	1	0	1	0	0	3	1	0	0
		24–72h	1	0	1	-	-	-	1	0	1	1
	>13	<24h	1	1	1	-	-	-	1	1	1	1
11–30 min	<7	<24h	2	2	0	2	2	0	4	4	0	0
		24–72h	1	1	0	1	1	1	2	2	1	0
	7–13	<24h	-	-	-	2	2	2	2	2	2	2
		24–72h	1	1	1	-	-	-	1	1	1	1
31–60 min	<7	<24h	3	3	0	1	1	0	4	4	0	0
		24–72h	1	0	1	-	-	-	1	0	1	0
	7–13	<24h	2	2	2	-	-	-	2	2	2	2
	>13	<24h	1	1	1	-	-	-	1	1	1	1
		24–72h	1	0	1	-	-	-	1	0	1	1
1–3 h	<7	<24h	2	1	1	4	0	2	6	1	3	0
		24–72h	1	0	1	3	1	2	4	1	3	1
	7–13	<24h	3	2	1	2	2	2	5	4	3	2
	>13	<24h	1	1	1	1	1	1	2	2	2	2
3– >24 h	<7	<24h	2	0	1	-	-	-	2	0	1	0
		24–72h	1	0	1	-	-	-	1	0	1	0
	7–13	<24h	-	-	-	1	0	0	1	0	0	0
	>13	<24h	2	0	2	-	-	-	2	0	2	2
		24–72h	1	0	1	1	0	1	2	0	2	2

Figure 1
Activating triggers among injured divers (n = 114) for seeking help and determining hyperbaric oxygen treatment (HBOT)



This is especially true for ear barotrauma, which is known to be associated with less experienced and intermediate divers.[25] Nonetheless, barotrauma accounted for the vast majority of the recorded DI in our study. It is likely that this is partly explained by the questionnaire design, which was meant to explore the whole diving career of respondents to mitigate this particular risk of bias. It could also be considered that the survey methods helped to reach those who dive more actively and so more frequently expose themselves to a possible DI. Therefore, the results give a fair picture of probable DI among more experienced French recreational divers.

Several factors, such as age, sex and lack of continuity of diving influenced the self-reporting of DI symptoms. For instance, women declare more DI symptoms than men, either because they are more willing to report a DI or owing to physiological differences, either genetic or hormonal. This relationship has been mostly studied in relation to DCI, with contradictory results. Although a lower risk has been reported in female professional divers owing to more conservative dive conditions,[26] other studies have reported an increased risk of DCI in women.[27] When it comes to the global risk of DI (not limited to DCI), to the best of our knowledge, only one study has assessed the influence of sex and several other factors.[5] Consistent with this previous survey, our data support the hypothesis that women could be more susceptible to DI than men. However, the possible reasons for this are unknown.

Age is a well-documented risk factor both for diving fatalities[28] and DCI.[27] However, our results indicate that when considering all types of DI, self-reporting of dive-related symptoms tended to decrease with increasing age. The absence of a relationship with diving experience or certification level suggests that age is paramount in this relationship. No definitive explanation is possible for such a counter-intuitive relationship, but this may be related to either a selection effect or, since it is a self-reported survey, a psychological difference in the perception of symptom severity. Indeed, divers who experience repeated symptoms, even minor, or comorbidities ('healthy diver' effect) might not continue to dive. As a result, the proportion of divers who never experienced injury increases with age. Alternatively, older divers might not declare symptoms considered as 'normal' or not sufficiently important to note. In the latter case, the question arises as to whether a diver's training should include teaching on the potential impact of 'minor' injuries on long-term health issues.[29]

Although physical fitness and exercise are known to exert a protective effect for DCI,[30] this was not supported in this survey. One explanation could be that the beneficial effect of physical fitness may only be related to DCI but not to other DI, mainly barotrauma. Less than a third of divers who reported DCI-like symptoms reported neurological signs, a proportion less than in previous studies.[31,32] This discrepancy probably relates to a reporting bias, respondents only reporting what they remember retrospectively rather than being tested formally. Alternatively, this difference might also come from the absence of the less severe cases of DCI in these previous studies, as suggested by the number of divers in our survey who declared DCI-related symptoms but did not seek care from a physician.

After context analysis, the most common self-reported injuries were barotraumas (n = 320, 62% of injured divers), consistent with previous data.[5] This poses questions regarding prevention and overall knowledge of this particular issue. Barotrauma, except for pulmonary[33] and inner ear barotrauma,[34] are largely ignored by the scientific community. For instance, a recent review could only identify 44 relevant papers that constituted primary literature related to otology and scuba diving.[35]

Table 5

Final outcome and applied treatment among DCI cases (n = 114); mild residual symptoms are mild paresthesia, weakness, residual pain or some impairment of daily activities. Severe residual symptoms are difficulty walking, paralysis, uncompensated vertigo, or speech disorders; 14 divers (13 with a severity score < 7, 1 between 7–13) had a spontaneous recovery with full resolution without any treatment, although they activated the emergency response system

	Severity score	After first HBOT			Final outcome		
		Complete resolution	Mild residual	Severe residual	Complete resolution	Mild residual	Severe residual
Received first-aid and HBOT	<7 (n = 9)	8	1	0	8	1	0
	7–13 (n = 8)	2	4	2	4	2	2
	>13 (n = 16)	2	6	8	1	9	6
	(n = 33)	**12**	**11**	**10**	**13**	**12**	**8**
Received first-aid	<7 (n = 31)	–	–	–	25	6	0
	7–13 (n = 2)	–	–	–	1	1	0
Not seeking help	<7 (n = 30)	–	–	–	29	1	0
	7–13 (n = 4)	–	–	–	2	2	0
Total					**84 (74%)**	**22 (19%)**	**8 (7%)**

Reduction of sequelae after DCI is based on early recognition of symptoms and signs, the initiation on site of first aid and swift evacuation to a hyperbaric chamber. Nonetheless, several studies have demonstrated that on-site first aid was often inadequate, with only 17 to 59% of injured divers receiving oxygen or fluids at some stage prior to recompression.[18,31,36] This survey is consistent with these observations. Permanent complete relief or improvement was reported in 59% of all treated cases, which is consistent with previous reports (65%[19] and 57%[18]). This raises questions about appropriate education on accident management, a concept commonly misunderstood and which is different from treatment.[12] Since the majority of the injured divers (70%) were symptomatic within 30 minutes of surfacing, consistent with the existing literature,[37] it also raises the question of how divers react to diving incidents. Injury severity did not appear to be a factor in reporting events to dive leaders, but it was a factor in medical referrals. Indeed, there is a high proportion of divers who fail to identify DCI owing to many factors (non-specific presentation, hope that symptoms will settle spontaneously, denial, underestimation of the potential consequences of untreated DCI,[31] unwillingness of fellow divers to acknowledge the evidence[15] and poor education on the diversity of symptomatology of DCI). These behaviours potentially may explain the large proportion of injured divers (32%, including those with DCI-like symptoms) who never sought help. Therefore, more emphasis should be given in divers' training to the varied, atypical symptomatology and unpredictable evolution of DCI, making pre-hospital diagnosis difficult. This is paramount since one out of 10 divers with DCI symptoms, who never sought treatment, reported some residual symptoms.

In France, transfer to a referral centre is required by law, and is under the responsibility of the CROSS (Search and Rescue Regional Centre).[38] It can be seen from this survey that the ranking dive leader often acts as a filter for referral to medical care. This indicates a need for better education of dive centres, instructors, boat skippers and deck hands in diving incident management. Fortunately, all but a few of the divers who did not receive oxygen or were not referred for medical assessment had complete resolution.

The decision to use HBOT seemed to be based solely on the severity score of the presenting symptoms and signs but this needs to be interpreted with caution since it is based only on patient self-reporting and not on the medical records. Since the time beyond which hyperbaric treatment is not effective has yet to be determined, this is of importance for triage

by telemedicine where consultation with a diving medical officer who is not present at the accident site is organized by telephone or some other means.[39]

LIMITATIONS

Firstly, like all surveys, our results depend on self-reported data. Self-reported surveys introduce recall bias and there is a chance of over- or under-reporting of the frequency and/or severity of symptoms. This could be intentional or owing to missed or incorrectly assessed symptoms. Secondly, owing to the nature of the distribution of this survey, the response rate is unknown, resulting in a non-responder bias. Thirdly, the ability to generalize the findings to the general French diving population is limited because of the high responder rate amongst highly qualified and experienced divers.

Conclusions

This online survey provides insights into diving injuries amongst experienced French recreational divers, based on retrospective self-reporting of symptoms on an electronic questionnaire. The most frequently reported symptoms suggest the mild nature of most injuries, with ear barotrauma seeming to be the most frequent. The survey provided evidence of the influence of female sex, younger age and lack of continuity of diving as potential risk factors for injury. The data question divers' knowledge about dive-related risks and showed the need for better information and education for recreational divers.

References

1 Henckes A. Enquête nationale accidents de plongée autonome sportive, bilan 2013 [Internet]. FFESSM; 2014. [cited 2018 July 13]. Available from: http://medical.ffessm.fr/wp-content/uploads/Bilan-ADP-2013.pdf. French.

2 Denoble PJ, Pollock NW, Vaithiyanathan P, Caruso JL, Dovenbarger JA, Vann RD. Scuba injury death rate among insured DAN members. Diving Hyperb Med. 2008;38:182–8. PMID: 22692749.

3 Van Hulst RA. Analysis of ten year diving casualties 1979–1989, diving medical centre. The Netherlands. Undersea Biomed Res. 1990;17:144.

4 Vinkel J, Bak P, Hyldegaard O. Danish diving-related fatalities 1999–2012. Diving Hyperb Med. 2016;46:142–9. PMID: 27723014.

5 Ranapurwala SI, Bird N, Vaithiyanathan P, Denoble PJ. Scuba diving injuries among Divers Alert Network members 2010-2011. Diving Hyperb Med. 2014;44:79–85. PMID: 24986725.

6 Hyun GS, Jee YS, Park JM, Cho NH, Cha JY. Injury survey in scuba divers of British Sub-Aqua Club: A retrospective study. J Exerc Rehabil. 2015;11:331–6. doi: 10.12965/jer.150252. PMID: 26730384.

7 Trevett AJ, Forbes R, Rae CK, Sheehan C, Ross J, Watt SJ, Stephenson R. Diving accidents in sports divers in Orkney waters. Scott Med J. 2001;46:176–7. doi: 10.1177/003693300104600608. PMID: 11852632.

8 Arness MK. Scuba decompression illness and diving fatalities in an overseas military community. Aviat Space Environ Med. 1997;68:325–3. PMID: 9096830.

9 Dardeau MR, Pollock NW, McDonald CM, Lang MA. The incidence of decompression illness in 10 years of scientific diving. Diving Hyperb Med. 2012;42:195–200. PMID: 23258455.

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

11 Taylor DM, O'Toole KS, Ryan CM. Experienced scuba divers in Australia and the United States suffer considerable injury and morbidity. Wilderness Environ Med. 2003;14:83–8. PMID: 12825881.

12 Taher A. Diving accident management, with special emphasis on the situation in the Red Sea. Wien Med Wochenschr. 1999;151:134–7. PMID: 11315412.

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

14 Trevett AJ, Forbes RF, Rae CK, Sheehan C. Reducing delays in treatment – how sports divers in Orkney respond to accidents. 2002. Available from: http://archive.rubicon-foundation.org/7262. [cited 2018 July 13].

15 Grandjean B. Peut-on améliorer le délai de traitement hospitalier des accidents de plongée sous-marine autonome de loisir? Table ronde de médecine de plongée de l'Océan Indien. October 10-11, 2001 Mauritius. French.

16 Moon RE. Adjunctive therapy for decompression illness: a review and update. Diving Hyperb Med. 2009;39:81–7. PMID: 22753201.

17 Lillo RS, Parker EC. Evaluation of oxygen and pressure in treatment of decompression sickness in guinea pigs. Undersea Hyperb Med. 1998;25:51–7. PMID: 9566087.

18 Lippmann J. First aid oxygen administration for divers. SPUMS J. 2003;33:192–8.

19 Longphre JM, Denoble PJ, Moon RE, Vann RD, Freiberger JJ. First aid normobaric oxygen for the treatment of recreational diving injuries. Undersea Hyperb Med. 2007;34:43–9. PMID: 17393938.

20 European Parliament. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). Off J Eur Union. 2016;59:89–131.

21 Ozyigit T, Egi SM, Denoble P, Balestra C, Aydin S, Vann R, Marroni A. Decompression illness medically reported by hyperbaric treatment facilities: cluster analysis of 1929 cases. Aviat Space Environ Med. 2010;81:3–7. PMID: 20058731.

22 Boussuges A, Thirion X, Blanc P, Molenat F, Sainty JM. Neurologic decompression illness: a gravity score. Undersea Hyperb Med. 1996;23:151–5. PMID: 8931282.

23 Chauveau M. Etude socio-économique relative à la plongée subaquatique de loisir en 2004–2005. Section Permanente du Comité Consultatif de l'Enseignement de la Plongée Subaquatique; 2005. Available from: https://ffessm.fr/ckfinder/userfiles/files/Etude_Eco_plongee.pdf. [cited 2018 July 13]. French.

24 Muller L. La pratique sportive en France, reflet du milieu social. Insee. 2006. French.

25 Jansen S, Meyer MF, Boor M, Volland R, Pracht ED,

Klünter HD, et al. Repetitive freshwater diving: risk factors and prevalence of barotrauma. Undersea Hyperb Med. 2017;44:407–14. PMID: 29116695.
26 Irgens Å, Troland K, Grønning M. Female professional divers. Similarities and differences between male and female professional divers. Int Marit Health. 2017;68:60–7. doi: 10.5603/IMH.2017.0010. PMID: 28357838.
27 Cialoni D, Pieri M, Balestra C, Marroni A. Dive risk factors, gas bubble formation, and decompression illness in recreational SCUBA diving: Analysis of DAN Europe DSL Data Base. Front Psychol. 2017;8:1587. doi: 10.3389/fpsyg.2017.01587. PMID: 28974936. PMCID: PMC5610843. [cited 2018 Jul 11]. Available from: http://journal.frontiersin.org/article/10.3389/fpsyg.2017.01587/full.
28 Denoble PJ, Pollock NW, Vaithiyanathan P, Caruso JL, Dovenbarger JA, Vann RD. Scuba injury death rate among insured DAN members. Diving Hyperb Med. 2008;38:182–8. PMID: 22692749.
29 Hemelryck W, Germonpré P, Papadopoulou V, Rozloznik M, Balestra C. Long term effects of recreational SCUBA diving on higher cognitive function: cognitive functions in SCUBA divers. Scand J Med Sci Sports. 2014;24:928–34. doi: 10.1111/sms.12100. PMID: 23902533.
30 Carturan D, Boussuges A, Vanuxem P, Bar-Hen A, Burnet H, Gardette B. Ascent rate, age, maximal oxygen uptake, adiposity, and circulating venous bubbles after diving. J Appl Physiol. 2002;93:1349–56. doi: 10.1152/japplphysiol.00723.1999. PMID: 12235035.
31 Bessereau J, Genotelle N, Brun PM, Aboab J, Antona M, Chenaitia H, et al. Decompression sickness in urban divers in France. Int Marit Health. 2012;63:170–3. PMID: 23129100.
32 Hart AJ, White SA, Conboy PJ, Bodiwala G, Quinton D. Open water scuba diving accidents at Leicester: five years' experience. J Accid Emerg Med. 1999;16:198–200. doi: 10.1136/emj.16.3.198. PMID: 10353047. PMCID: PMC1343334.
33 Lafère P, Germonpré P, Balestra C. Pulmonary barotrauma in divers during emergency free ascent training: review of 124 cases. Aviat Space Environ Med. 2009;80:371–5. PMID: 19378907.
34 Lechner M, Sutton L, Fishman JM, Kaylie DM, Moon RE, Masterson L, et al. Otorhinolaryngology and diving - Part 1: Otorhinolaryngological hazards related to compressed gas scuba diving: A review. JAMA Otolaryngol Head Neck Surg. 2018;144:252–8. doi: 10.1001/jamaoto.2017.2617. PMID: 29450472.
35 Livingstone DM, Smith KA, Lange B. Scuba diving and otology: a systematic review with recommendations on diagnosis, treatment and post-operative care. Diving Hyperb Med. 2017;47:97–109. doi: 10.28920/dhm47.2.97-109. PMID: 28641322. PMCID: PMC6147252.
36 Shinnick MA. Recognition of scuba diving accidents and the importance of oxygen first aid. J Emerg Nurs. 1994;20:105–10.
37 Hadanny A, Fishlev G, Bechor Y, Bergan J, Friedman M, Maliar A, et al. Delayed recompression for decompression sickness: retrospective analysis. PLoS ONE. 2015;10(4):e0124919. doi: 10.1371/journal.pone.0124919.
38 Coulange M, Hugon M, Blatteau JE. Prise en charge préhospitalière des accidents de plongée: de l'alerte à l'admission. In: Broussolle B, Méliet JL, Coulange M, editors. Physiol Médecine Plong. Paris: Ellipses; 2006. p. 417–24. French.
39 Mitchell SJ, Bennett MH, Bryson P, Butler FK, Doolette DJ, Holm JR, et al. Consensus guideline: Pre-hospital management of decompression illness: expert review of key principles and controversies. Diving Hyperb Med. 2018;48:45–55. doi: 10.28920/dhm48.1.10-16. PMID: 29557102. PMCID: PMC6467826.

Acknowledgements

We wish to thank the diving organizations' national representatives who spread the questionnaire through their networks.

Conflicts of interest and funding: nil

Submitted: 08 September 2018; final revision 08 May 2019
Accepted: 19 May 2019

The impact of health on professional diver attrition

Chris Sames[1], Desmond F Gorman[2], Simon J Mitchell[3], Lifeng Zhou[4]

[1] *Slark Hyperbaric Unit, Waitemata District Health Board, Auckland, New Zealand*
[2] *Department of Medicine, University of Auckland, Auckland*
[3] *Department of Anaesthesiology, University of Auckland*
[4] *Funding and Outcomes, Waitemata and Auckland District Health Boards, Auckland*

Corresponding author: *Chris Sames, Slark Hyperbaric Unit, Waitemata District Health Board, Stanley Point, Auckland 0624, New Zealand*
chris.sames@waitematadhb.govt.nz

Key words
Occupational diving; Occupational health; Diving industry; Diving at work; Medicals – diving; Smoking; Medical database

Abstract
(Sames C, Gorman DF, Mitchell SJ, Zhou L. The impact of health on professional diver attrition. Diving and Hyperbaric Medicine. 2019 June 30;49(2):107–111. doi: 10.28920/dhm49.2.107-111. PMID: 31177516.)
Introduction: Approximately 77% of professional divers leave the industry within five years of entry for reasons that are uncertain. One possibility is that attrition is due to ill-health. The health of New Zealand occupational divers is surveyed by a comprehensive medical examination every five years and by a health questionnaire in the intervening years. Divers are thereby confirmed 'fit' annually. The aim of this study was to determine if divers quit the industry due to a health problem not identified by this health surveillance system.
Method: 601 divers who had left the industry within five years of entry medical examination ('quitters') were identified from a computerised database. One hundred and thirty-six who could be contacted were questioned about their principal reason for quitting. Comparison was made between the health data of all those defined as 'quitters' and a group of 436 'stayers' who have remained active in the industry for over 10 years.
Results: Health was the principal reason for abandoning a diving career for only 2.9% of quitters. The overwhelming majority (97.1%) quit because of dissatisfaction with aspects of the work, such as remuneration and reliability of employment. Besides gender, the only significant difference between the health data of quitters and stayers was that smoking was four times more prevalent among quitters.
Conclusions: The key determinant of early attrition from the New Zealand professional diver workforce is industry-related rather than health-related. The current New Zealand diver health surveillance system detects the medical problems that cause divers to quit the industry.

Introduction

The impact of diving on health has been extensively investigated, but not the impact of health on diving. The registered professional diver workforce in New Zealand has remained relatively stable numerically, at approximately one thousand divers, for many years. However, a previous study of this group showed that over a five-year period there was an attrition rate of 77%, suggesting considerable flux, with the number of newly registered divers roughly matching those either retiring or leaving the profession to pursue other employment.[1] There are many possible explanations for such a high rate of attrition, but of primary interest, and the focus of the present study is whether health-related issues play a significant role in a diver's decision to leave the profession.

Diving is undeniably hazardous, with workers at risk of potentially catastrophic accidents, and also the possibility of long-term adverse health effects. Anxiety about such outcomes may be one of the drivers of the reported high attrition rate. However, many studies have reported minimal long-term adverse health effects, even in relation to respiratory and auditory function, both commonly believed to be the most likely targets for damage.[2–7] One of the limitations of such studies is a possible sampling bias caused by the lack of data from divers who are no longer working, and who may have left the industry for health reasons, leading to erroneous conclusions due to a 'healthy worker effect' of unknown magnitude. However, in New Zealand, where occupational diver health is monitored by a comprehensive medical examination every five years and by a health questionnaire in intervening years, very few divers are found to have a health condition that disqualifies them from occupational diving.[1,8] One could conclude that almost all who leave the industry do so for reasons unknown because of a lack of relevant data. However, there remains the possibility that diver attrition may be due to health issues that the health surveillance system is failing to detect.

The current study aims to establish the significance of health issues as a determinant of departure from the professional diver workforce, and to check that the current New Zealand

diver health surveillance system is not failing to detect medical problems that cause divers to quit the industry.

Method

Ethical approval for this study was granted by the Health and Disability Ethics Committee (HDEC), approval number 18/CEN/180. Professional divers were identified from a computerised database and categorised as either 'quitters' (with no derogatory implication intended) or 'stayers'. Quitters were defined as those who had remained registered for fewer than five years and had not re-registered in the last five years, while stayers were defined as current divers who have remained registered for 10 years or longer.

Quitters with a recorded email address were surveyed by asking them to complete a simple questionnaire designed to clarify whether or not they were still working as a diver (perhaps overseas), and if not, what type of diving they had been engaged in when they left, and, most importantly, whether they had quit diving for health reasons. Because of difficulties establishing communication with ex-divers, additional avenues of contact were attempted, namely by telephone and by social media (Facebook®). To give an indication of a desirable sample size, a power analysis based on a notional response distribution of 10% quitting for health reasons (agreed *a priori* based on clinician-author experience) demonstrated that a sample of 113 quitter-divers would be required to complete the survey, with a 5% margin of error, a 95% confidence limit (95% CL) and a total population of quitter-divers of 600. Any who reported that they were now employed as divers registered in another country were excluded from further analysis. The remaining group of respondents was compared with the group of non-respondent quitters to test for group homogeneity with the understanding that the non-respondents would also include an unknown number still working elsewhere as divers.

Any record of a health-related issue disclosed in initial or subsequent dive medical assessments was noted, and these results together with the category of occupational diving and other demographic data were compared between quitters and stayers.

Statistical analysis was performed using SAS® v9.4 software (SAS Institute Inc., Cary, North Carolina, USA). Frequency and proportion (%) were used for describing categorical variables, such as gender, smoking status and type of diving. Median with minimum and maximum were used to describe the continuous variables, such as years registered and body mass index (BMI), as they did not follow a normal distribution, whilst 95% confidence limits (CL) were estimated for the reported proportions quitting for health reasons and for those with a recorded history of a health condition. Comparisons were made between the quitter group and the stayer group, and between responder and non-responder groups. The Chi-squared test (and Fisher's exact test if suitable) and the Wilcoxon rank-sum test were used for categorical and continuous variables respectively. A P-value of < 0.05 was considered to be statistically significant.

Results

622 divers were identified as 'quitters' and 436 as 'stayers'. Quitters remained registered for a median of one year (range 1–5 years), compared with 14 years (range 10–25 years) for stayers. Record of either an email address or telephone number was available for 364 quitters, but many were either incorrect or no longer active. There were 53 responses to email, a further 67 to telephone calls and 37 to Facebook® contact, giving a total of 157 responses (response rate 25.2%). Twenty-one respondents (13.4%) were still active divers, but were registered and working in countries other than New Zealand. These divers were excluded from our analysis of health reasons for leaving the divers' register, and also from comparison of quitters with stayers, leaving a total of 601 quitters and 136 quitter-responders.

Of the quitter responders, four claimed that they had stopped diving because of a health issue (2.9% of responses, 95% CL = 0.8%, 7.4%). Two were aquaculture workers, one was a construction worker and one was a recreational diving instructor. The specific health reason was described as a sinus problem in all four cases. The most common reason for quitting (97% of responses) was simply to provide a change in job/life direction, usually prompted by dissatisfaction with aspects of professional diving, such as poor remuneration and lack of consistency of employment. A similar proportion of quitters (11.1%, 95% CL = 8.7%, 13.9%) and stayers (11.0%, 95% CL = 8.2%, 14.3%) had a recorded medical condition (most commonly obesity or abnormal hearing or lung function requiring regular surveillance), but none of the four who quit for health reasons had any notable medical condition (including the sinus problems that resulted in quitting) recorded from their health questionnaire or initial medical examination.

For all divers, smoking was almost four times more common in quitters than stayers (18.6% vs 5.3%) (Table 2). The proportion of scientific divers who were current smokers was consistently low in both groups (1.6%), while the proportion of instructors and commercial divers who were current smokers was significantly higher in the quitter than the stayer group (17.7% vs 3.9%, and 31.2% vs 4.7% respectively). This smoking association was particularly pronounced for commercial divers, who represented a similar proportion in both quitter and stayer groups (23.0% vs 19.7%), but the proportion who smoked decreased six-fold in the stayer group.

Quitters were almost twice as likely as stayers to be female (20.6% vs 11.2%) and also more than twice as likely to be an instructor (38.4% vs 17.4%). In fact, 53.2% of females who quit and 26.5% who stayed, were instructors. Quitters were significantly less likely to be a scientific diver. These

Table 1

Comparison of characteristics of New Zealand professional divers who have either quit diving within five years of starting (quitters) or continued diving for > 10 years (stayers); * values were taken from the most recent medical examination and are presented as median (and range) where not expressed as a percentage; percentages are rounded to nearest whole number; *n* (%) for all variables except where stated otherwise; ** 'Reason for leaving' values are not applicable for 'stayers' and not available for 'all quitters' (N/A)

Characteristics	**All quitters** (*n* = 601)		**Quitter responders** (*n* = 136)		**Stayers** (*n* = 436)	
Male/female ratio (%)	477/124	(79/21)	108/28	(79/21)	387/49	(89/11)
Height [cm (range)]*	177	(152–200)	178	(152–200)	178	(154–204)
Weight [kg (range)]*	81	(47–153)	83	(52–145)	85	(48–150)
BMI [$kg \cdot m^{-2}$ (range)]*	26	(18–51)	26	(18–41)	27	(19–42)
Age at last medical [years (range)]*	29	(16–62)	28	(16–56)	43	(23–72)
Years registered [years (range)]	1	(1–5)	1	(1–5)	14	(10–25)
Non-smoker	326	(54)	83	(61)	317	(73)
Ex-smoker	163	(27)	35	(26)	96	(22)
Current smoker	112	(19)	18	(13)	23	(5)
Medical issue on record	67	(11)	17	(12)	48	(11)
Type of diving						
Instructor	231	(39)	54	(40)	76	(17)
Commercial	138	(23)	15	(11)	86	(20)
Scientific	65	(11)	16	(12)	126	(29)
Aquaculture	49	(8)	16	(12)	24	(6)
Military/Police/Customs	53	(9)	26	(19)	56	(13)
Construction	41	(7)	3	(2)	55	(13)
HBU attendant	12	(2)	5	(4)	4	(1)
Film	12	(2)	1	(< 1)	9	(2)
Medical issue on record	67	(11)	17	(12)	48	(11)
Reason for leaving**						
Dissatisfaction	N/A		132	(97)	N/A	
Health	N/A		4	(3)	N/A	

results are summarised in Tables 1 and 2. Comparison of the responder and non-responder groups showed no significant differences apart from the proportions of the various diver sub-groups.

Discussion

The impact of health status on the attrition rate of professional divers was investigated by identifying and surveying a group of divers who left the industry within five years of joining.

Table 2
Prevalence of smoking amongst the principal categories of New Zealand professional divers who have either quit diving within five years of starting (quitters) or continued diving for > 10 years (stayers); number (%) are shown; * $P < 0.0001$

Diver Category	**Quitters** (n = 601)		**Stayers** (n = 436)	
Scientific	1 (1.6)	(n = 65)	2 (1.6)	(n = 126)
Instructor	41 (17.7)	(n = 231)	3 (3.9)	(n = 76)
Commercial	43 (31.2)	(n = 138)	4 (4.7)	(n = 86)
Aquaculture	15 (30.6)	(n = 49)	3 (12.5)	(n = 24)
Military/Police/Customs	4 (7.5)	(n = 53)	5 (8.9)	(n = 56)
Construction	7 (17.1)	(n = 41)	6 (10.9)	(n = 55)
All*	112 (18.6)		23 (5.3)	

The reasons given for leaving were almost entirely related to the diving work environment, such as dissatisfaction with aspects of the job or just wanting a change in career, rather than anything to do with health. This finding will not surprise clinicians who have experience working with professional divers, but the purpose of the study was to quantify the impact of health on diver attrition, and we are not aware of any previous studies that address this issue.

The finding that only 2.9% of responding professional divers leave the industry for health reasons undetected during formal health surveillance provides strong support for the integrity of the current system of health surveillance for this group of workers. This is particularly so since in every case the undetected medical problem responsible for the divers' decisions to leave the industry was highly unlikely to result in a life or limb-threatening event. In contrast, a high percentage quitting for undetected health reasons, particularly health problems with significant implications for diver safety, would have suggested an inadequate surveillance process and an unacceptably high false negative rate (if we define 'negative' as absence of health-related findings that would preclude safe diving).

These results are relevant to the many previous studies investigating the converse issue, the impact of diving on health, which could be criticised for sampling bias due to the omission of data from ex-divers. Our findings suggest that a 'healthy worker effect' is unlikely to have a significant impact on the validity of such studies of working divers, especially in relation to the possibility that serious diving-induced health problems might be significantly over-represented among divers who have left the industry. Although there might be potential for diving to have exacerbated the condition in the four divers we found who ceased diving because of sinus problems, it is more likely that diving unmasked a chronic predisposition to such problems.

The reasons for recreational diving instructors being more likely to quit than any other category of diver are speculative, but we suggest that instructors may, in general, be a more itinerant group, perhaps comprising those who consider instructing as a short-term, interim or secondary occupation. Work as an instructor may also be less consistent and more seasonal than some of the more 'stable' diving careers such as scientific, construction or military diving. We also noted a correlation between smoking and quitting diving, such that smokers were more likely to quit diving, and, as a corollary, non-smokers were far more common amongst stayers than quitters (72.7% vs 54.2% respectively). The proportion of instructors in the quitter group was more than twice that in the stayer group, and the proportion of instructors who smoked in the quitter group was more than four times that in the stayer group.

The six-fold decrease in the proportion of commercial divers who smoked in the stayer group compared to the quitters might be explained simply on the basis of age. The median age of the stayer group was 15 years older than the quitter group, but although smoking prevalence rates in the general population decrease with age, the large difference we found between quitters and stayers emphasised a stayers' smoking prevalence rate significantly lower than the age-related New Zealand and international population norms.[9,10] The quitters who responded to this survey were not asked their current smoking status, but further research could resolve the question of whether diving may act as a motivation to quit smoking, or conversely, that smoking possibly contributes to a departure from diving. If the former were true, however, we would have expected to find a higher proportion of ex-smokers in the stayers group.

LIMITATIONS

Firstly, the study surveyed only those divers who quit early in their career, whereas there are likely to be some who leave for health reasons after a career spanning longer than five

years. We agree that research including the more experienced group would be worthwhile, but note that a high rate of attrition has been reported in the first five years of the divers' careers. In addition, the results of many previous studies of the long-term health effects of diving suggest that clinically evident diving-related health reasons for quitting are very unlikely.[2–7] That said, one must accept that lack of a diving-related health reason for quitting diving does not necessarily exclude the possibility of delayed development of a diving-related clinical condition (e.g., dysbaric osteonecrosis).

Secondly, these results are not necessarily generalisable to populations of professional divers in other countries. The characteristics, including health status, of professional divers may vary depending on local certification and health surveillance protocols. Therefore, it is conceded that early career attrition rates probably vary internationally.

Thirdly, we found that 13% of the group of quitter-responders were, in fact, working as divers, but registered in other countries. Therefore, it is possible that a similar proportion of the quitter-non-responders were also still active divers. Our inability to determine this number reduces the accuracy of our comparison of quitter-responder and non-responder groups. Nevertheless, this had no effect on the primary outcome of the study, the influence of health status on the decision to quit diving.

Finally, as there was a relatively low quitter response rate, despite our employment of three methods to contact the ex-divers, we accept the possibility of a non-response bias. It could be argued that there might be a higher rate of leaving for health reasons among the non-responders. On the other hand, our reported response rate of 25.2% should be considered conservative, as the majority of non-responders were unable to be contacted and so had no opportunity to respond. However, the fact that there was not a single report of a diver quitting because of a clearly diving-related health condition suggests that health status is a minimal contributor to the professional diver attrition rate.

Conclusions

Diving-related health reasons are of minimal significance in determining attrition rates of professional divers. The low rate of health-related attrition from the professional diver workforce supports the integrity of the current diver health surveillance system. Conclusions drawn from studies of the health effects of diving on working divers are unlikely to be significantly affected by the absence of those who have left the industry.

References

1 Sames C, Gorman D, Mitchell SJ, Gamble G. Utility of regular examinations of occupational divers. Intern Med J. 2009;39:763-6. doi: 10.1111/j.1445-5994.2009.02055.x. PMID: 19912402.

2 Sames C, Gorman DF, Mitchell SJ, Gamble G. The long-term effects of compressed gas diving on lung function in New Zealand occupational divers: a retrospective analysis. Diving Hyperb Med. 2009;39:133–7. Available from: http://archive.rubicon-foundation.org/9339. [cited 2018 September 28]. PMID: 22753243.

3 Sames C, Gorman DF, Mitchell SJ, Zhou L. Long-term changes in spirometry in occupational divers: a 10–25 year audit. Diving Hyperb Med. 2018;48:10–16. doi: 10.28920/dhm48.1.10-16. PMID: 29557096. PMCID: PMC6467824.

4 Hope A, Lund T, Elliott DH, Halsey MJ, Wiig H. Long-term health effects of diving. An international consensus conference. Godøysund 6–10 June 1993. Bergen: John Greig forlag A/S;1994:387-91. Cited by: Thorsen E. In: Brubakk AO, Neuman TS, editors. Bennett and Elliott's physiology and medicine of diving, 5th ed. Edinburgh: Saunders; 2003. p. 656.

5 Pougnet R, Pougnet L, Lucas D, Uguen M, Henckes A, Dewitte J, et al. Longitudinal change in professional divers' lung function: literature review. Int Marit Health. 2014;65:223–9. doi: 10.5603/IMH.2014.0042. PMID: 25522707.

6 Tetzlaff K, Thomas PS. Short- and long-term effects of diving on pulmonary function. Eur Respir Rev. 2017;26:160097. doi: 10.1183/16000617.0097-2016. PMID: 28356403.

7 Sames C, Gorman DF, Mitchell SJ, Zhou L. The impact of diving on hearing: a 10–25 year audit of New Zealand professional divers. Diving Hyperb Med. 2019;49:2–8. doi: 10.28920/dhm49.1.2-8. PMID: 30856661.

8 Sames C, Gorman D, Mitchell S, Sandiford P. An evidence-based system for health surveillance of occupational divers. Intern Med J. 2016;46:1146–52. doi: 10.1111/imj.13204. PMID: 27507783.

9 Annual update of key results 2016/17: New Zealand Health Survey. [cited 2018 October 30]. Available from: https://www.health.govt.nz/publications/annual-update-key-results-2016-17-new-zealand-health-survey.

10 WHO global report on trends in prevalence of tobacco smoking 2015. [cited 2018 October 30]. Available from: https://www.who.int/tobacco/publication/surveillance/reportontrendstobaccosmoking/en/index4.html.

Acknowledgements

We thank Murray Polson (CEO, Erudite Software Ltd) for developing and maintaining the electronic database for New Zealand occupational divers, and retrieving much of the data required for this study. We also thank Amanda Main and Caitlin Williams for assistance in contacting ex-divers.

Funding sources: nil

Conflicts of interest

Simon Mitchell is the Editor of *Diving and Hyperbaric Medicine*. He had absolutely no involvement in the peer-review and decision-making processes for this paper, which were managed entirely by the Associate Editor, Associate Professor F Michael Davis.

Submitted: 18 December 2018; revised 26 February 2019
Accepted: 21 March 2019

The utility and safety of hypoxia experiences for rebreather divers

Simon J Mitchell[1,2], Hayden M Green[3], Stacey A Reading[3], Nicholas Gant[3]

[1] *Department of Anaesthesiology, University of Auckland, Auckland, New Zealand*
[2] *Department of Anaesthesia, Auckland City Hospital, Auckland*
[3] *Department of Exercise Sciences, University of Auckland*

Corresponding author: *Associate Professor Nicholas Gant, Department of Exercise Sciences, University of Auckland, Private Bag 92019, Auckland, New Zealand*
n.gant@auckland.ac.nz

Key words
Diving; Aviation; Brain; Near infrared spectroscopy; Performance; Training; Oximetry

Abstract
(Mitchell SJ, Green HM, Reading SA, Gant N. The utility and safety of hypoxia experiences for rebreather divers. Diving and Hyperbaric Medicine. 2019 June 30;49(2):112–118. doi: 10.28920/dhm49.2.112-118. PMID: 31177517.)
Background: Aircrew training often includes an hypoxic experience aimed at improving symptom recognition and self-rescue in a subsequent hypoxic event. Similar training has been advocated for rebreather divers. We investigated the effect of a prior hypoxic experience on actual and perceived cognitive function during subsequent hypoxia and measured the physiological responses to severe progressive hypoxia.
Methods: Twenty-five subjects underwent two hypoxic hypoxia experiences (trials one and two) approximately five weeks apart. Subjects breathed 5.5% oxygen whilst performing a playing card recognition test. The primary endpoint was the time taken to make three consecutive errors in the card recognition test (time of useful consciousness, TUC). Secondary endpoints were the total number of errors made, accuracy of error recollection and physiological variables.
Results: Mean (SD) TUC was 166 seconds (37) and 169 s (35), and subjects made 8.9 (2.4) and 7.8 (2.0) errors in trials one and two respectively. Error recall was identical between trials with participants failing to recall 6 (3) and 6 (2) errors made in trials one and two respectively. Across both trials mean nadir arterial blood and cerebral oxygen saturations were 52% and 49% respectively. The mean (SD) increase in heart rate was 42 (16) beats·min^{-1}.
Conclusion: An hypoxic experience did not improve cognitive performance or subject insight into performance in a second exposure five weeks later. Hypoxia imposes a significant physiological stress which may be hazardous in unscreened, non-medically supervised subjects. Hypoxia experience training is not recommended for rebreather divers at this time.

Introduction

Unanticipated severe hypoxia can occur in both aircrew and scuba divers with disastrous consequences. In aviation, hypoxia may arise because of cabin decompression or failure of oxygen (O_2) supplementation devices in unpressurised aircraft.[1] In diving, hypoxia may arise because of inadvertent breathing of an hypoxic gas mix at shallow depth, or failure of closed circuit 'rebreather' devices to maintain a safe inspired PO_2 (> 21 kPa) in the breathing loop.[2] In both settings the precipitating circumstances may not be obvious, distracted victims may fail to perceive encroaching symptoms of hypoxia, and consequent decrements in cognitive performance (and ultimately loss of consciousness) can lead to fatal accidents.

In aviation, there is a well-established practice of conducting periodic training experiences to familiarize aircrew with the symptoms of impending hypoxia. Participants are decompressed in a hypobaric chamber to pressures equivalent to high altitude (typically around 37.6 kPa, 25,000 feet) whilst wearing masks which deliver supplemental O_2. Removal of the masks exposes the subjects to hypobaric air and, therefore, hypobaric hypoxia. The demonstration of consequent failure both in simple cognitive tasks and in following instructions is considered a valuable illustration of the dangers of hypoxia. Several studies have demonstrated that an individual's hypoxic symptoms remain relatively constant between widely separated exposures (years).[3–5] Based on these experimental observations, coupled with some weak but supportive real-world evidence,[6] it is believed that better hypoxia symptom recognition prepares participants to recognize impending hypoxia and, thus, intervene in a timely manner in any subsequent event. In addition, although there is no substantive hypothesis that would explain better cognitive performance during hypoxic events occurring after previous hypoxia training, one small study reported a 10–20% higher (but statistically insignificant) probability of retaining useful consciousness in the latter stages of eight minutes (min) of hypobaric hypoxia conducted eight months after a prior hypoxic training exposure.[7]

Use of hypoxic training in aviation has motivated advocacy for hypoxia experiences for divers using closed circuit rebreathers.[8] It has been suggested that hypoxic experiences

could take place in dive training facilities or even private homes with participants breathing on a rebreather (effectively a closed-circuit breathing loop) with no oxygen addition until significant symptoms occur.[8] No established rebreather diving training agencies presently recommend this practice, the utility of which is uncertain and its safety questionable.

A recent negative study of creatine loading as a means of prolonging useful cognitive function during hypoxia conducted in our laboratory (unpublished observations) has provided certain insights into the value and safety of hypoxic experiences for rebreather divers. First, the question could be addressed as to whether a hypoxic exposure could result in prolongation of useful cognitive function during a subsequent hypoxic event. Second, observations were made of arterial blood and cerebral oxygen saturations and the cardio-respiratory responses during severe progressive hypoxia in humans. Such data are surprisingly difficult to find in the medical or physiological literature. This provided insights into the potential for medical complications of hypoxic training experiences in typical rebreather divers. Finally, the study afforded the opportunity for discussion of the complexity and difficulty in investigating whether a prior hypoxic training experience does or does not improve the chances of effective self-rescue during a subsequent real-world hypoxic event.

Methods

The study protocol was approved by the University of Auckland Human Participants Ethics Committee (reference 019199). The parent study was an investigation of the effect of creatine loading on cognitive performance during hypoxia. The relevant data will be reported independently. However, the lack of any effect of creatine on cognitive performance allowed us to re-evaluate the data as an investigation of the effect of a prior hypoxic exposure on cognitive function during subsequent hypoxia, and to appraise the physiological data in the context of conducting hypoxia experiences for rebreather divers. For simplicity, we will henceforth omit references to creatine administration from the narrative.

TRIAL DESIGN

This was an interventional cohort study that took place at the Exercise Metabolism Laboratory, University of Auckland from July to September 2017. Twenty-five subjects underwent cognitive function testing during two hypoxia experiences conducted approximately five weeks apart (a total of 50 hypoxia exposures).

PARTICIPANTS

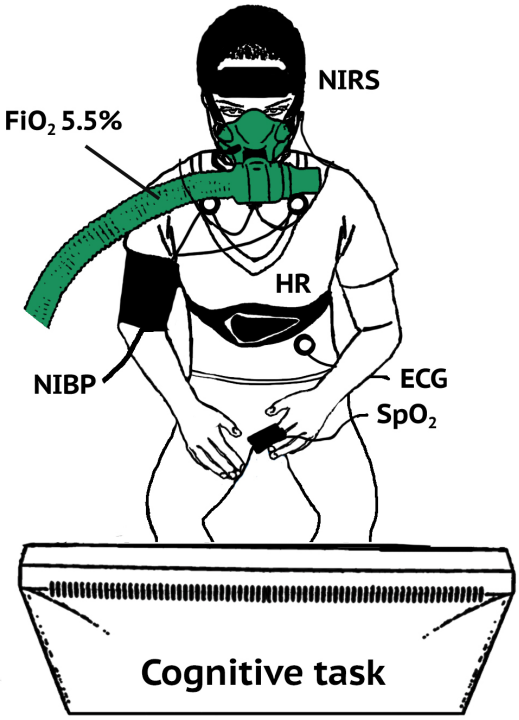
Subjects were 25 volunteers (15 male), mean age 28 years [11 SD], range 20–57 solicited from the local student and diving communities. All subjects received a participant information sheet, a verbal explanation of the study, and provided written informed consent. They completed a pre-participation medical screening questionnaire designed to exclude those with known cardiac, metabolic, neurological or respiratory disease or associated risk factors. The questions were similar to those on a standard pre-participation screening form for scuba diving and were chosen by a specialist anaesthesiologist (SJM).

EXPERIMENTAL SETUP

Subjects were comfortably seated and monitoring was established as follows: 3-lead electrocardiogram (standard limb lead II displayed), finger pulse oximetry (SpO_2; arterial haemoglobin oxygen saturation), and end tidal carbon dioxide (CO_2) (all components of an S5 anesthesia monitoring system; GE Electronics, USA); continuous measurement of inspired O_2 and CO_2 concentrations (via a ML206 Gas Analyzer, ADInstruments, Dunedin, New Zealand); ventilation (tidal volume and respiratory rate) via a Respiratory Flow Head (MLT1000 L, ADInstruments, New Zealand) and single-channel near infra-red spectroscopy (NIRS) (PortaLite, Artinis, The Netherlands) with optodes placed over the left pre-frontal cortex (Fp1 position, international 10–20 system).[9] NIRS is a non-invasive continuous measurement of cerebral (pre-frontal cortex) oxygenation influenced mainly by haemoglobin O_2 saturation in the cerebral venous blood. As in its use during clinical monitoring of patients, both the absolute O_2 saturation value and the percentage reduction from baseline saturation were utilized to measure the impact hypoxia on cerebral oxygenation. Blood pressure was measured via an automated non-invasive blood pressure cuff (NIBP) (GE Electronics, USA) before and after the experiment, but not during the trial because the discomfort of periodic cuff inflation would have been distracting. All experiments were attended throughout by a specialist anesthesiologist (SJM) for safety purposes.

Subjects breathed via a tight-fitting oronasal mask (7450, Hans Rudolpf Inc., USA) connected to a two-way valve (2700, Hans Rudolph Inc., USA) with the delivery of inspired gas controlled by a pneumatic controller and balloon-type valve (8200, Hans Rudolph, USA) which could be switched to deliver either room air or a premixed gas (5.5% O_2 94.5% nitrogen (N_2); inspired oxygen (PiO_2) 38.7 mmHg (SD 1.3)) drawn from a Douglas bag. Hypoxic gas mixtures were prepared within 10 min of each experiment by combining compressed medical grade O_2 and N_2 (BOC, Auckland, New Zealand) in 150 L Douglas bags. The O_2 fraction within each bag was verified using two independent gas analyzers (ML206 Gas Analyzer, ADInstruments, Dunedin, New Zealand). Prior to each experiment, the mask seal was confirmed by leak-free negative pressure generation by the subjects. Maintenance of the seal during the experiment was verified by continuous monitoring of the PiO_2. The experimental set-up is depicted in Figure 1.

Figure 1
Illustration of the experimental setup. ECG – electrocardiography; FiO_2 – fraction of inspired oxygen; NIBP – non invasive blood pressure cuff; NIRS – near infrared spectroscopy; SpO_2 – finger oxygen saturation; HR – heart rate



Cognitive function testing was via a card recognition protocol in which playing cards between numbers 4 and 10 (inclusive), of all four suits and with numbers removed were displayed in front of the subject on a bright LCD screen. The card changed every four seconds (s) irrespective of the accuracy of the subject's answer or absence of an answer. Subjects were required to verbalize the number and suit of each new card. Subjects completed a familiarization version of the test on four occasions under normoxic conditions, in order to confirm perfect test-retest reliability (r = 1) and 100% accuracy.

EXPERIMENTAL PROCEDURE

Each exposure began with the subject breathing air via the mask. The mask gas supply could be switched between air and the hypoxic mix without moving the mask using the balloon-operated valve (8200, Hans Rudolph, USA). The dead space in the hose supplying the mask from the gas switching point was 880 ml and would be effectively cleared within two breaths of switching (< 10 s). A two-minute preliminary period of card recognition (during air breathing) was conducted to establish task baseline measurements and provide a final familiarization with the task. Upon error-free completion of the preliminary task any questions that arose were answered before starting the hypoxic exposure.

The hypoxic exposure began with a three second countdown followed by switching from air to 5.5% O_2 breathing, at which time the card recognition test and measurement of time of useful consciousness (TUC) began. The subject continued breathing 5.5% oxygen until he or she made three consecutive card recognition errors. An error was defined as wrongly identifying the suit of the card and/or the card value, or failure to provide any answer within the 4 second period over which the card was displayed. When three consecutive errors occurred, the inspired gas was switched back to air and the TUC recorded. The card recognition test was continued during recovery of normoxia until SpO_2, ventilation, and heart rate recovered to pre-test levels. All experiments were videoed and later reviewed to verify the results recorded in real time.

Five minutes after completion of the protocol, subjects were asked how many errors they recalled making during the test, and they completed a post-trial questionnaire* adapted from the aviation literature in which the severity of potential hypoxia symptoms was rated on a 125 mm visual analogue scale (VAS) from "*not at all*" to "*severe*" where severe was further defined as meaning "*greatest intensity possible*".[10]

OUTCOMES AND ANALYSIS

The primary endpoint in each exposure was the TUC, defined as the duration from switching to the hypoxic gas supply to committal of the third of three consecutive card recognition errors. Data are presented as mean (standard deviation) and with ranges, as appropriate. The mean times of useful consciousness in the two hypoxic exposures were compared, as were the mean number of errors actually made with the mean number of errors that the subjects recollected making in the two exposures. Finally, the mean severity ratings of individual hypoxia symptoms between the two trials were compared. Comparisons of TUC, errors made, errors recalled, and ratings of symptom severity between the first and second hypoxic experiences were made using two-tailed paired *t*-tests (Prism 7, Graphpad, USA). A *P*-value ≤ 0.05 was considered to indicate statistical significance. No corrections for multiplicity were applied.

Results

All 25 enrolled subjects completed two hypoxia exposures (referred to as trial one and trial two) separated by an average 39 day interval (range 35–42 days). There were no adverse events.

* **Footnote:**
The post-trial questionnaire is available on request to the authors from n.gant@auckland.ac.nz

Figure 2
Time of useful consciousness (TUC) (seconds) for individual subjects in two hypoxic experiences (Trials 1 and 2) separated by approximately five weeks; group means ± SD shown beneath

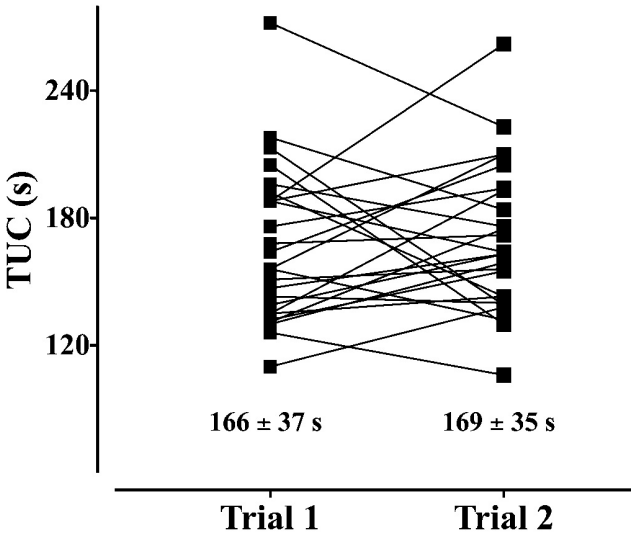
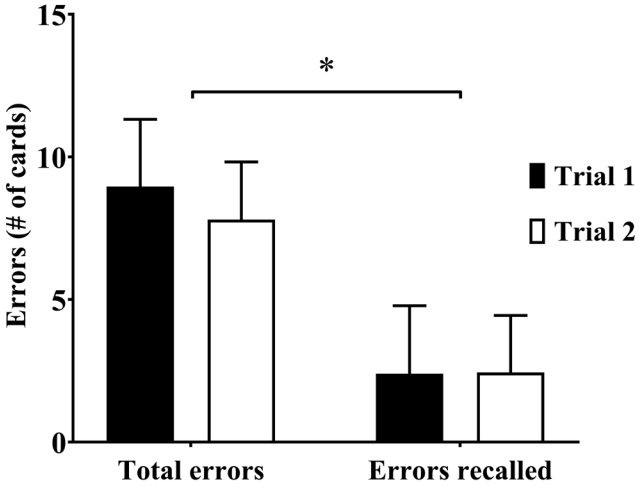


Figure 3
Mean (SD) card identification errors (total errors) made and errors recalled by the subjects in trials 1 and 2; * $P = 0.087$ for number of errors and $P = 0.91$ for recall of errors between the two trials



TUC

The TUC for individual subjects in trials one and two is shown in Figure 2. Mean TUC was 166 s (SD 37) and 169 s (SD 35) respectively ($t_{24} = 0.38$, $P = 0.70$). On average, subjects made 8.9 (SD 2.4) and 7.8 (SD 2.0) errors in trials one and two respectively ($t_{24} = 1.79$, $P = 0.087$) (Figure 3). Subjects exhibited poor perception or recall of the number of errors they made whilst hypoxic. Recall bias was virtually identical between trials with participants, on average, failing to recall 6 (SD 3) errors made in trial one and 6 (SD 2) errors made in trial two ($t_{24} = 0.12$, $P = 0.91$) (Figure 3).

SYMPTOM PERCEPTION

Perception of the 24 individual hypoxic symptoms listed in the post-trial symptoms questionnaire was very similar between trials one and two. The mean ± SD visual analogue scores for each symptom in each trial are shown in Figure 4. There were no statistically significant differences between trials in the ratings of symptom severity for all 24 symptoms (all $P > 0.05$).

PHYSIOLOGICAL CHANGES

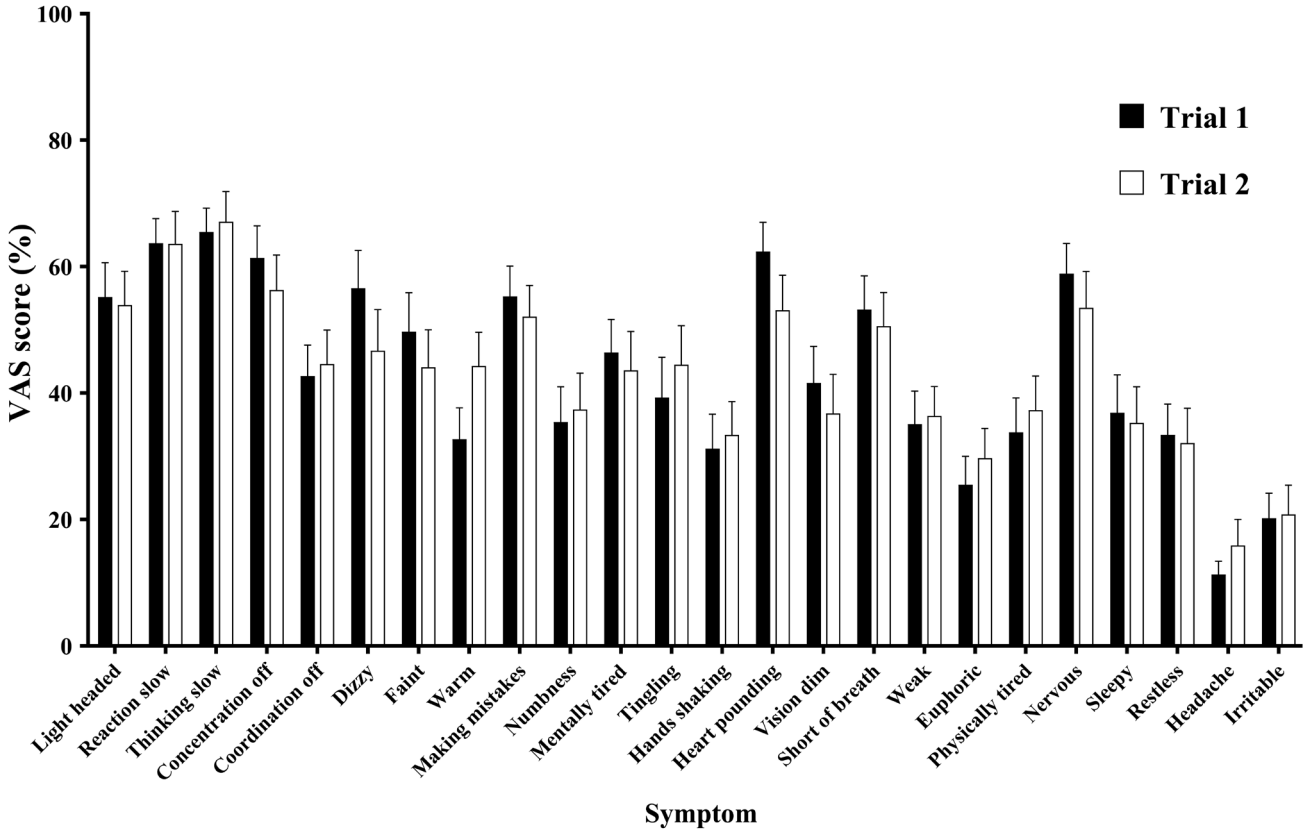
The physiological changes associated with breathing 5.5 % O_2 are shown in Figure 5. By the end of TUC mean heart rate and minute ventilation had increased by a mean of 42 beats·min^{-1} (SD 16) and 10.0 L·min^{-1} (SD 5.1), respectively. Conversely, SpO_2 reduced by 48% (SD 16). Subjects typically exhibited a nadir SpO_2 near 50% at the end of TUC. Prefrontal cortex tissue O_2 saturation (designated 'tissue saturation index' in Figure 5) decreased on average by an absolute value of 16 % (SD 4), but this represents a 25% decrease from the initial mean baseline value of 63%. The mean nadir in pre-frontal cortex tissue O_2 saturation was below 50%.

Discussion

Subjects were exposed to two episodes of severe hypoxia separated, on average, by 39 days and there was no evidence that the first exposure resulted in greater TUC during the second. There was extremely poor post-exposure insight into cognitive impairment during hypoxia, and no evidence that this improved after the second exposure. The lack of any difference in TUC between the two exposures helps clarify the finding of the one previous small study of the effect of repeat hypobaric hypoxia exposures on cognitive performance.[7] That study reported a statistically insignificant trend to (10–20%) higher probability of retaining useful consciousness during the latter stages of eight min of severe hypobaric hypoxia conducted eight months after a prior hypoxic exposure. However, there is no obvious physiological hypothesis which would predict that a hypoxic experience would improve TUC during subsequent hypoxia. One could speculate that a process of psychological adaptation or learning to cope with the impairment might have a positive influence, but our data confirm this does not occur (at least in the context of a one-month interval between events), even when subjects are well aware that they are experiencing hypoxia for a second time.

Consistent with previous studies in sequential widely separated exposures to hypobaric hypoxia,[3–5] the present study found that ratings of severity of potential hypoxia symptoms remained relatively constant between the two exposures. Largely on the basis of this previously reported within-subject consistency of hypoxic symptoms, hypoxia experience training has been recommended for flight crews

Figure 4
Mean (SD) symptom severity ratings during trials one and two recorded using a visual analogue scale (VAS); 0% = asymptomatic; 100% = most severe possible



for the purpose of facilitating appropriate early responses to hypoxia events in flight. The implicit assumption is that knowledge of one's 'hypoxic symptom signature' occurring in a prior hypoxic exposure could result in earlier symptom recognition and initiation of self-rescue in a second hypoxic event.

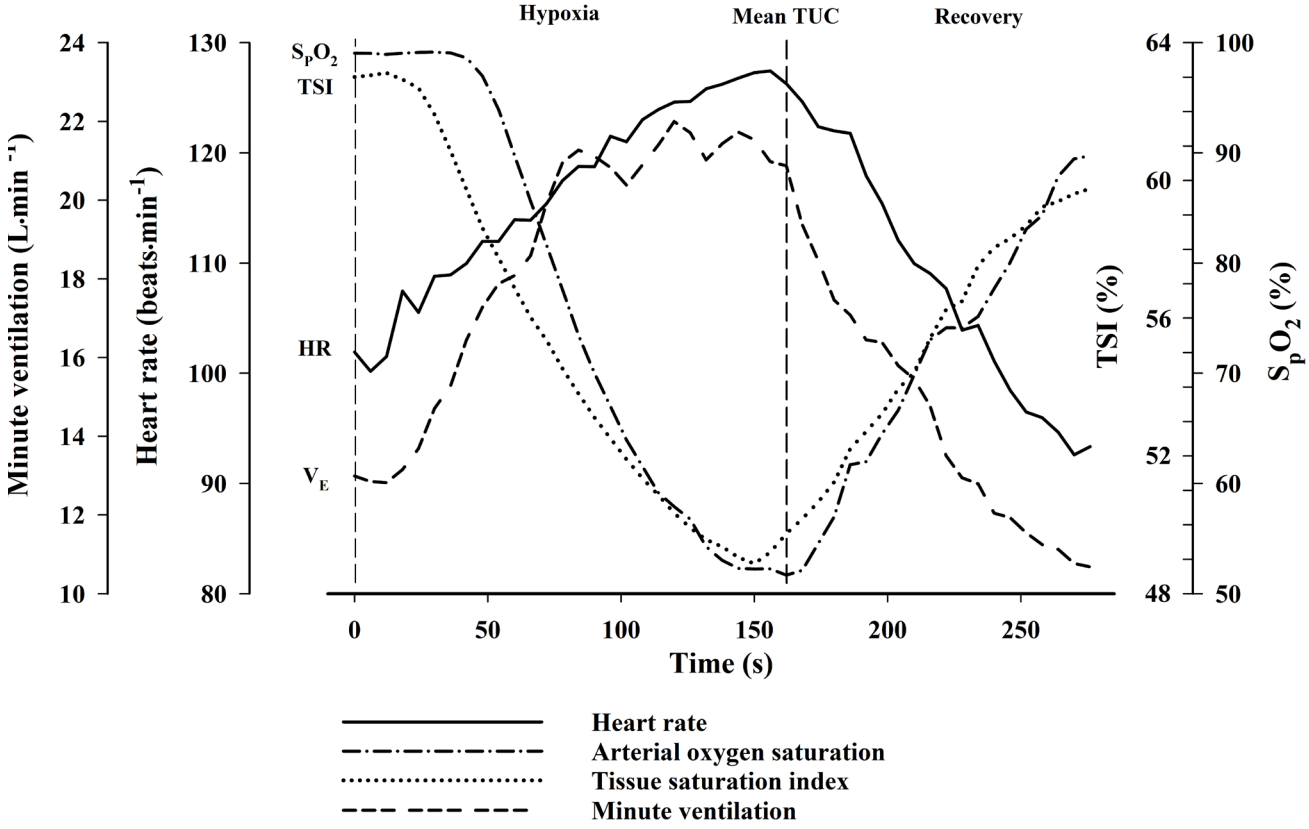
This assumption may be correct, but it has not been proven. A review of in-flight hypoxic events showed a dramatic difference in the incidence of loss of consciousness between aircrew who had received hypoxia training and untrained passengers.[6] However, there are other differences between trained aircrew and passengers (and their in-flight circumstances) that could at least partly account for this result. Our finding of very poor recall of errors during hypoxia is clear evidence of failure to accurately perceive the severity of impairment during hypoxia, or failure to form accurate memories of it, or both. Similarly, our subjects generally gave only mid-range VAS ratings of those hypoxia symptoms related to cognitive function despite their invariably severe objective cognitive impairment. These findings raise the suspicion that prior knowledge of hypoxic symptoms might not help a task-loaded and significantly distracted aviator or diver to self-rescue during a subsequent hypoxic event as reliably as seems to be believed.

This question is of high relevance to both rebreather diving and aviation but resolving it in an experimental setting would require a complex study. One would have to begin with subjects randomized into groups receiving initial hypoxic training (Group H – hypoxia) or not (Group N – no hypoxia). Then after some predetermined interval, both groups would then need to be randomized again to perform an objectively measurable and highly distracting task during either hypoxia or normoxia while blinded to their hypoxia/normoxia allocation, with an instruction to perform a secondary self-rescue task if they perceived impairment during the test. One would then compare the timing and execution of the self-rescue task in those Group H and Group N subjects randomized to hypoxia on the second exposure. The use of a valid task providing similar levels of motivation and distraction to flying a plane or operating a rebreather in the dynamic underwater environment would be a crucial component of such a study, as would blinding participants to their allocation (normoxia or hypoxia) in the second exposure. The difficulty in conducting such a study probably explains why it has not been done to date.

Our cautious interpretation of the benefits of hypoxia familiarization training should not be interpreted as suggesting that we disagree with current practices within

Figure 5

Mean responses from 50 hypoxic hypoxia exposures showing changes in arterial oxygen saturation of haemoglobin (S_pO_2) measured by pulse oximetry; TSI – near infrared cerebral tissue saturation index; V_E – minute ventilation; HR – heart rate; the hypoxia phase (ending at the point of mean TUC) represents the period of breathing 5.5% oxygen and the recovery phase represents the period of recovery during air breathing



aviation. We see little potential for harm in the aviation industry practice of exposing properly screened and medically supervised aircrew to hypobaric hypoxia as a training exercise. Experience has proven that there is little risk and there may be benefits (albeit incompletely quantified at this time).

However, in respect to rebreather diving we do not believe these benefits have been adequately demonstrated to recommend hypoxia experiences in diver training facilities or in divers' homes. Unlike the highly supervised aviation setting, there is no experience or safety data for hypoxia exposures provided to unscreened and non-medically supervised divers and based on first principles there are multiple risks. First, failure to terminate the exposure quickly enough could result in loss of consciousness with associated complications such as loss of airway patency or aspiration of stomach contents into the lungs. Second, the physiological changes seen with breathing 5.5% O_2 were predictable though nevertheless dramatic. The induction of a significant tachycardia at a time when blood oxygen carriage is extremely poor, as demonstrated in our data (Figure 5), effectively constitutes a myocardial stress test, and in an unscreened population there is an unknown, and possibly unacceptable risk of precipitating an ischaemic myocardial event or dysrhythmia.

LIMITATIONS

First, as in the only previous study of hypoxia training which provided blood oxygenation data,[10] measurement of blood oxygenation was with pulse oximetry. Pulse oximetry may become less accurate (though usually not grossly so) during severe hypoxia[11] and recordings in the study were not verified against a gold standard method such as arterial blood gas measurements (P_aO_2). However, the latter is invasive and, we would argue, unnecessary for the primary purpose of the study. The endpoint was functionally severe cognitive impairment rather than a specific P_aO_2 or S_pO_2. In addition, NIRS measurements are considered valid during hypoxia, and absolute values < 50% or a 20% fall from individual baseline values are commonly considered as intervention triggers in clinical practice.[12] The subjects often crossed either or both thresholds. We believe that it is valid to characterize these hypoxic exposures as severe.

Second, unlike attempts to demonstrate adaptation to cognitive impairment in other settings such as inert gas narcosis,[13] only the effect of a single exposure was evaluated. The possibility cannot be excluded that subjects might learn to cope better with hypoxia over a greater number of exposures. However, such a finding would be of doubtful practical value because training programmes with multiple exposures are unlikely to be considered acceptable.

Third, the definition of TUC used was the duration from switching to the hypoxic gas supply to the point where three consecutive card recognition errors were made. This included a very short initial period (< 10 sec) of clearance of non-hypoxic dead space gas from the gas supply tubing. Therefore, the true TUC during hypoxic gas breathing is correspondingly shorter. However, since the goal was to compare a measure of performance between two standardized sequential trials rather than to explicitly define a true hypoxic TUC, this small error is inconsequential.

Finally, as alluded to above, neither our study nor others conducted previously provide a definitive answer to the key question of whether prior hypoxic experience enhances the chances of effective self-rescue in a subsequent hypoxic event. Our conclusions in respect of the value of such experiences for rebreather divers must therefore be regarded as interim, pending the conduct of a definitive study.

Conclusions

A prior hypoxic experience did not improve cognitive performance or subject insight into performance in a second exposure five to six weeks later. Therefore, it is unlikely that cognitive acclimation or learning contributes to the ability to self-rescue during hypoxia, and any benefit of hypoxic training must lie solely in improved symptom recognition. However, at the present time there is no definitive proof that such training enhances self-rescue during hypoxia. With this in mind, we conclude that the potential risks associated with both hypoxic loss of consciousness and the physiologic changes that occur during hypoxia training are sufficiently concerning that we do not recommend such training for rebreather divers.

References

1 Cable GG. In-flight hypoxia incidents in military aircraft: causes and implications for training. Aviat Space Environ Med. 2003;74:169–72. PMID: 12602449.

2 Mitchell SJ, Doolette DJ. Recreational technical diving part 1. An introduction to technical diving. Diving Hyperb Med. 2013:43:86–93. PMID: 23813462.

3 Smith AM. Hypoxia symptoms in military aircrew: long term recall vs. acute experience in training. Aviat Space Environ Med. 2008:79;54–7. PMID: 18225780.

4 Woodrow AD, Webb JT, Wier JS. Recollection of hypoxia symptoms between training events. Aviat Space Environ Med. 2011;82:1143–7. PMID: 22195396.

5 Johnston BJ, Iremonger GS, Hunt S, Beattie E. Hypoxia training: symptom replication in experienced military aircrew. Aviat Space Environ Med. 2012;83:962–7. PMID: 23066618.

6 Island RT, Fraley EV. Analysis of USAF hypoxia incidents January 1976 through March 1990. In: Proceedings of the 31st Annual SAFE Symposium. Creswell, OR: SAFE Association; 1993. p.100–2.

7 Izraeli S, Avgar D, Glikson M, Shochat I, Glovinski Y, Ribak J. Determination of the "time of useful consciousness" (TUC) in repeated exposures to simulated altitude of 25,000 ft (7,620 m). Aviat Space Environ Med. 1988;59:1103–5. PMID: 3202796.

8 Sutton D. Dry hypoxia training for rebreather divers. Discussion thread on website CCR Explorers [Online]. [cited 2018 July 02]. Available from: https://www.ccrexplorers.com/community/threads/dry-hypoxia-training-for-rebreather-divers.14442/.

9 Klem GH, Lüders HO, Jasper HH, Elger C. The ten-twenty electrode system of the International Federation. The International Federation of Clinical Neurophysiology. Electroencephalogr Clin Neurophysiol Suppl. 1999;52:3–6. PMID: 10590970.

10 Singh B, Cable GG, Hampson GV, Pascoe GD, Corbet M, Smith A. Hypoxia awareness training for aircrew: a comparison of two techniques. Aviat Space Environ Med. 2010;81:857–63. PMID: 20824992.

11 Severinghaus JW, Naifeh KH, Koh SO. Errors of 14 pulse oximeters during profound hypoxia. J Clin Monit. 1989:5:72–81. PMID: 2723709.

12 Scheeren TWL, Shober P, Schwarte LA. Monitoring tissue oxygenation by near infrared spectroscopy (NIRS): background and current applications. J Clin Monit Comput. 2012;26:279–87. doi: 10.1007/s10877-012-9348-y. PMID: 22467064. PMCID: PMC3391360.

13 Rogers WH, Moeller G. Effect of brief repeated hyperbaric exposures on susceptibility to nitrogen narcosis. Undersea Biomed Res. 1989;16:227–32. PMID: 2741255.

Acknowledgements

We are grateful to Andrew Cosgrove and Cullen Le Roy for providing assistance with data collection and analysis.

Funding: This study was funded by the University of Auckland.

Conflicts of interest

Simon J Mitchell is Editor of *Diving and Hyperbaric Medicine*. He took no part in the peer-review and decision-making processes for this paper, which were managed entirely by the Associate Editor, Associate Professor F Michael Davis. There were no other conflicts of interest.

Submitted: 25 October 2018; revised 06 February and 07 April 2019
Accepted: 08 April 2019

Early detection of diving-related cognitive impairment of different nitrogen-oxygen gas mixtures using critical flicker fusion frequency

Pierre Lafère[1,2,3], Walter Hemelryck[1,3], Peter Germonpré[1,4], Lyubisa Matity[5], François Guerrero[1,2], Costantino Balestra[1,3,6,7,8]

[1] *DAN Europe Research Division, Roseto, Italy*
[2] *Laboratoire ORPHY, EA 4324, UFR sciences et techniques, Université de Bretagne Occidentale, Brest, France*
[3] *Environmental, Occupational, Ageing (Integrative) Physiology Laboratory, Haute Ecole Bruxelles-Brabant (HE2B), Brussels, Belgium*
[4] *Centre for Hyperbaric Oxygen Therapy, Military Hospital 'Queen Astrid', Brussels*
[5] *Hyperbaric Unit, Mater Dei Hospital, Msida, Malta*
[6] *Anatomical Research and Clinical Studies (ARCS), Vrije Universiteit Brussel (V.U.B.), Brussels*
[7] *Anatomical Research Training and Education (ARTE), Vrije Universiteit Brussel (V.U.B.)*
[8] *Motor Sciences, Université Libre De Bruxelles (U.L.B.), Brussels*

Corresponding author: *Pierre Lafère, Laboratoire ORPHY, EA 4324, UFR sciences et techniques, Université de Bretagne Occidentale, 6 Avenue Le Gorgeu - CS 93837, 29238 Brest Cedex 3, France*
doc.lafere@sfr.fr

Key words
Enriched air – nitrox; Narcosis; Oxygen; Risk management; Near-infrared spectroscopy

Abstract
(Lafère P, Hemelryk W, Germonpré P, Matity L, Guerrero F, Balestra C. Early detection of diving-related cognitive impairment of different nitrogen-oxygen gas mixtures using critical flicker fusion frequency. Diving and Hyperbaric Medicine. 2019 June 30:49(2):119–126. doi: 10.28920/dhm49.2.119-126. PMID: 31177518.)
Introduction: Cognitive impairment related to inert gas narcosis (IGN) is a threat to diving safety and operations at depth that might be reduced by using enriched air nitrox (EANx) mixtures. Using critical flicker fusion frequency (CFFF), a possible early detection of cognitive abilities/cerebral arousal impairment when breathing different oxygen (O_2) fractions was investigated.
Methods: Eight male volunteers performed, in random order, two dry chamber dives breathing either air or EANx40 (40% O_2–60% nitrogen) for 20 minutes (min) at 0.4 MPa. Cognition and arousal were assessed before the dive; upon arrival at 0.4 MPa; after 15 min exposure at 0.4 MPa; on surfacing and 30 min post-dive using behavioural computer-based testing psychology experiment building language (PEBL) and by CFFF while continuously recording brain oxygenation with near-infrared spectroscopy.
Results: In both breathing conditions, CFFF and PEBL demonstrated a significant inverse correlation (Pearson r of -0.90, $P < 0.0001$), improved cognitive abilities/cerebral arousal occurred upon arrival at 0.4 MPa followed by a progressive deterioration. Initial brain activation was associated with a significant increase in oxyhaemoglobin (HbO_2) and a simultaneous decrease of deoxyhaemoglobin (HHb). The magnitude of the changes was significantly greater under EANx ($P = 0.038$).
Conclusions: Since changes were not related to haemodynamic variables, HbO_2 and HHb values indicate a significant, O_2-dependent activation in the prefrontal cortex. Owing to the correlation with some tests from the PEBL, CFFF could be a convenient measure of cognitive performance/ability in extreme environments, likely under the direct influence of oxygen partial pressure, a potent modulator of IGN symptoms.

Introduction

Although considered safe, there are some inherent risks to scuba diving. For instance, under hyperbaric conditions, nitrogen accumulates within the human body and is responsible for a neurologic syndrome that includes alterations of cognitive functions, motor control and mood states. Individual susceptibility varies widely but all divers eventually will be impaired.[1] As a consequence, these associated cognitive and motor impairments may increase the risks of injury and reduce working performance. According to *Project Stickybeak*, seeking to document all diving fatalities in Australia, inert gas narcosis (IGN) was directly responsible for 9% of those fatalities.[2]

No accurate depth of onset of IGN has ever been proven satisfactorily because of a wide individual variation in onset and/or divers' lack of insight into behavioural manifestations of narcosis in themselves during diving. For instance, it was demonstrated recently, that although objectively impaired as assessed by a computerized test battery, it was not possible for blinded divers to identify the gas they

had just breathed.[3] Narcosis is not simply an objective measurable phenomenon; it also has a subjective facet.[4] Indeed, metacognitive awareness (defined as cognition about cognition) and cognitive performance can become dissociated.[5] However, although divers may be aware of this impairment, and could potentially compensate for it, the ability or willingness of divers to implement control procedures was not as good at deeper depths.[5] This has major safety implications. Indeed, individuals unable to either accurately assess whether they are impaired, or unable to implement compensatory control procedures in response to a preserved accurate metacognitive judgment, are at risk of failing to adopt compensatory strategies and behaviours to avoid accidents. Therefore, reliable indices to quantify the effects or identify pre-symptomatic effect of IGN are needed but not yet available.

Based on animal models,[6] it is now commonly accepted that the narcotic action of inert gases is responsible for an impairment of cognitive abilities and control, where cognitive control is defined as a system of processes that maintain the ability to interact with the environment in a goal-driven manner, with flexibility and constantly adapting behaviour to the changing environment.[7] Behavioural studies have indeed confirmed a progressive deterioration with increasing pressure. Although amenable to mitigation through study design, many of these tests have been criticized because of the influences of motivation, experience and learning which may improve task performances over the course of testing.[8] A computer-based cognitive approach may now be possible underwater,[9] although its assessment has been limited to shallow depth and might not be practical in operational circumstances. Hence there is a need for a simple, non-invasive but objective tool.

Since a recent study using event-related brain potentials suggested that cerebral arousal influenced both proactive and reactive cognitive control, an alternative measurement such as critical flicker fusion frequency (CFFF) may prove useful. Indeed, it has been demonstrated that CFFF could follow the recovery of cognitive function after propofol sedation earlier than psychometric testing.[10] This kind of correlation between mental state, CFFF and electroencephalography (EEG) has also been proposed recently in a world-class chess player, who showed parallel increases in CFFF threshold and theta Fz/alpha Pz ratio.[11] In another recent study CFFF and attentional performance were closely related, with a tight relationship between the CFFF and occipital gamma band activity both in frequency and power.[12] Under normobaric conditions, CFFF has been correlated to a computer-based assessment of cognitive function obtained from the psychology experiment building language battery test (PEBL), but with a less complicated set-up.[13]

Testing the CFFF device under hyperbaric condition was then an opportunity to question some divers' habits. Although air is the most commonly used breathing gas during diving, alternative gas mixtures, such as enriched air nitrox (EANx) are increasingly used in scuba diving. This alternative employs a lower nitrogen (N_2) content and higher oxygen (O_2) content than air, partly justified to reduce the risks of IGN. Interaction between O_2 and N_2 is poorly understood. One study suggests a correlation between individual sensitivity to nitrogen narcosis and protection by N_2 against cerebral O_2 toxicity in rats,[14] which allows the hypothesis of an individual O_2 limit in mixed-gas diving based on the diver's sensitivity to IGN. However, few comparative studies of air and EANx on IGN are available. Some human studies have reported worse psychomotor performance when using pure O_2 or EANx,[15] whilst others reported that narcotic impairment was the same, EANx and air being only differentiated on the basis of metacognitive assessment.[16]

The aims of this study were twofold; firstly, to understand cognitive performance variation under several standardized hyperbaric breathing conditions with different oxygen partial pressures (PO_2) and secondly, to investigate the value of CFFF under hyperbaric conditions as a potential early warning tool useful for the working diver.

Materials and methods

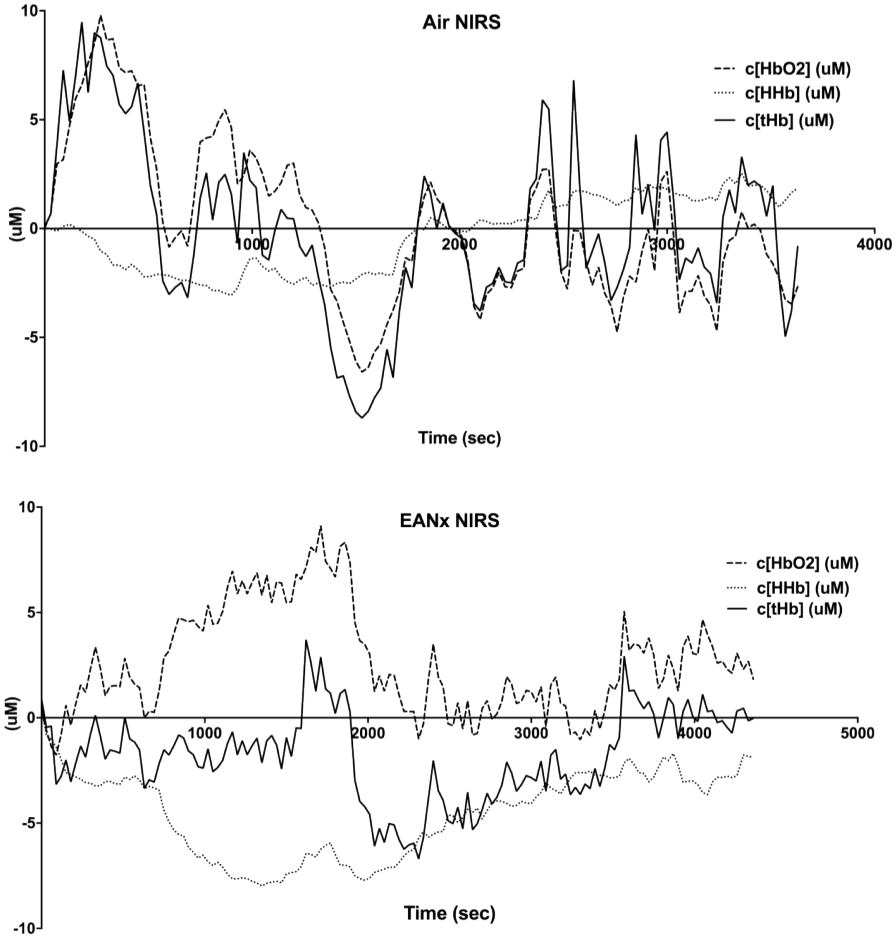
Experimental procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Academic Ethical Committee of Brussels (Belgium) (Ethic committee B 200-2011-5). The study protocol has also passed all Clinical Trial Application validation rules (EudraCT Number: 2011-004596-37). All subjects were recruited from a large sports diver population (age between 30 and 40 years, body mass index (BMI) between 20 and 25 $kg \cdot m^{-2}$ and in good health) as described in detail previously.[8] Methods and potential risks were explained to the eight selected male volunteers (certified according to European norm EN 14153-2 or ISO 24801-2 and for EANx-diving) who gave their written, informed consent prior to the experiment. Divers taking psychoactive drugs, or who had dived 72 hours prior to the experimental dive or had imbibed alcoholic or caffeinated beverages within four hours before the experimental dive were excluded.

EXPERIMENTAL PROTOCOL

All dives were dry dives, simulated in the hyperbaric chamber (Haux-Starmed 2800, Haux-Life-Support Gmbh, Karlsbad-Ittersbach, Germany) at the Centre of Hyperbaric Oxygen Therapy, Military Hospital 'Queen Astrid', Brussels, Belgium. On separate occasions, each subject performed, in random order, either a compressed air dive or an EANx40 (40% oxygen–60% nitrogen) dive. The inspired gases were delivered via a tight-fitting mask connected to the Haux-Oxymaster system which includes inspiratory and expiratory regulators. To avoid any bias, gas composition was monitored using a Haux-Oxysearch (Haux-Life-Support Gmbh, Karlsbad-Ittersbach, Germany). Subjects were blinded to the breathing gas.

Figure 1

Example of time plot of cerebral oxygenation after elimination of artefacts measured through oxyhaemoglobin (HbO_2 – dashed line), deoxyhaemoglobin (HHb – dotted line) and total haemoglobin (tHb – solid line) while breathing either air or enriched-air nitrox (EANx); the average of each value is calculated on a sample of 120 seconds (test time) concurrent with other measures



The dive profile was designed to produce narcosis: a seven-minute (min) compression time to 0.405 MPa; a 22-min bottom time and a 12-min linear decompression (0.033 MPa·min^{-1}) to the surface including a 3-min safety stop at 0.13 MPa. This profile is within accepted 'no-decompression' and O_2 toxicity limits for both gas mixes. The profile was managed by an experienced chamber technician according to the procedure described previously.[3]

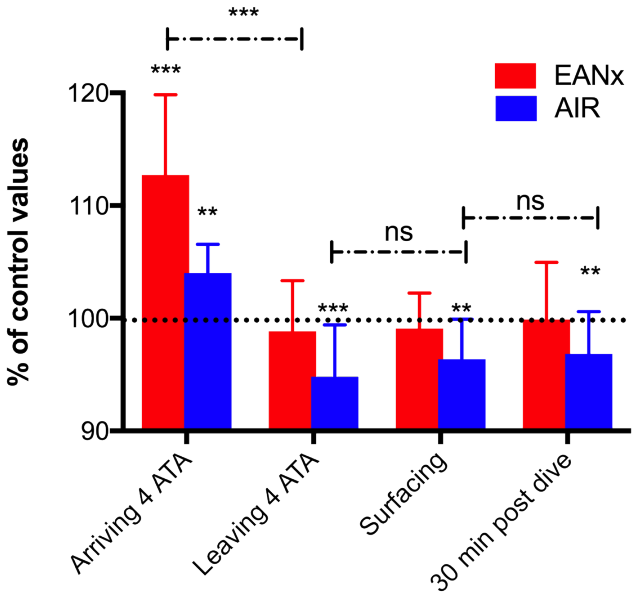
Divers were assessed, in the seated position, for higher cognitive functions using CFFF with a specifically designed watertight device (Human Breathing Technology, Trieste, Italy) as fully described previously,[8] and a computerized test battery (the psychology experiment building language - PEBL) specifically chosen to track deterioration in visual-perceptual organization, visual-motor coordination as well as integration, and visual memory. The tests (maths-processing, trail-making and perceptual vigilance) were chosen based on previous work.[3,13]

Divers were tested immediately before the dive (baseline), immediately upon arriving at 0.4 MPa, after 15 min at depth, when surfacing (i.e., at atmospheric pressure), and 30 min after surfacing. Since divers usually breathe EANx only during the dive, both baseline and 30 min post-dive measurements were made while breathing atmospheric air for all dives (air and EANx).

NEAR-INFRARED SPECTROSCOPY (NIRS)

Oxygenation of the prefrontal cortex, which plays an important role in cognitive control, in the ability to orchestrate thought and action in accordance with internal goals, was assessed with continuous recording of brain NIRS (Nimo [laser continuous wave near-infrared tissue oxymeter], NIROX srl, Brescia, Italy). NIRS data analysis is adapted from technical data established for functional magnetic resonance imaging (MRI). There are substantial differences between the two methods in particular the impact of the specific noise related to NIRS methodology. In the context of functional MRI related to task execution, error or noise is defined as all non-correlated activities in particular those related to head movements. They represent a critical obstacle to reliable statistical inference with a consequent

Figure 2
Percentage variation of CFFF during and after a dry chamber dive for 22 minutes at 0.4 MPa (4 ATA) breathing either air or enriched-air nitrox (EANx); pre-dive values normalized to 100%; each subject is compared to his own pre-dive value; ** $P < 0.01$; *** $P < 0.001$; ns – not significant ($n = 8$, means and SDs shown)



significant statistical bias toward false positives.[17] Therefore, for each individual recording (Figure 1), the curve was inspected to remove all artefacts in order to achieve effective statistical inference.[18] Then, the average of each value is calculated on a sample of 120 seconds concurrent with other measures. Functional challenge of the brain by task execution is accompanied by regional changes in cerebral blood flow, volume and oxygenation which can be monitored through the use of NIRS. When the brain is stimulated, in this case by the PEBL testing, this induces an increase in oxyhaemoglobin (HbO_2) and a decrease in deoxyhaemoglobin (HHb). According to the literature, brain activation is occurring when, compared to the baseline value, a two to threefold increase of HbO_2 accompanied by a similar decrease in HHb is observed.[19] Therefore, the whole literature reports HHb/HbO_2 changes as variations in percentage compared to a normalized baseline observation. We assumed the same method to report concurrent CFFF changes. The total O_2 index (TOI), defined as the ratio of oxygenated to total tissue haemoglobin, was also recorded. This measure reflects cerebral oxygenation to a high degree of sensitivity and specificity.[20]

ULTRASONIC MONITORING AND HAEMODYNAMICS

Finally, bubble load was evaluated 30 min post dive according to the Brubakk-Eftedal classification,[21] using a Vivid 7 echograph equipped with a GE 3S-RS sector array ultrasound probe (GE Healthcare, UK). The machine was used in harmonic imaging mode (2.0/4.0 MHz) to reduce noise in the cardiac cavities. Haemodynamic variables (blood pressure and heart beat) were also monitored through the whole experimentation.

STATISTICAL ANALYSIS

Since all data passed the Kolmogorov-Smirnov test, allowing us to assume a Gaussian distribution, they were analysed by means of repeated measures ANOVA with Bonferroni's multiple comparison tests comparing the effects of pressure (0.4 MPa vs. 15 min at 0.4 MPa vs. upon surfacing vs. 30 min post-dive) and breathing gas (Air vs. EANx), two-ways ANOVA and paired *t*-tests. After normalising the pre-dive values to 100%, percentage changes were calculated for each parameter, allowing an appreciation of the magnitude of change between each measurement rather than the absolute values. Existence of a correlation was assessed through a Pearson test and linear regression. All tests were performed using a standard computer statistical package, GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego California USA). A threshold of $P < 0.05$ was considered statistically significant. All data are presented as mean ± standard deviation (SD).

Results

The mean age of the eight subjects was 35.38 ± 3.59 years; BMI 23.68 ± 1.15 kg·m^{-2}, weight 71.4 ± 9.5 kg and height 1.77 ± 0.06 m.

CRITICAL FLICKER FUSION FREQUENCY

The evolution of CFFF during and after the dive is illustrated in Figure 2. When breathing air, each single measurement is statistically different from the baseline (one-sided *t*-test $P < 0.01$ or lower), while with EANx, only the first measurement is statistically different from baseline (one sample t test, $P < 0.0001$). When breathing air, there was an increase in CFFF when arriving at maximal pressure (104 ± 9.8 % of baseline) followed 15 min later by a decrease (95 ± 4.6 % of baseline). This impairment in CFFF persisted when surfacing (97 ± 3.5 % of baseline) and 30 min after surfacing, being still decreased to 97 ± 3.8 % compared to the pre-dive CFFF (100 %). When breathing EANx, similar changes were seen, with an increase (113 ± 7.1 % of baseline) followed by a decrease. However, this decrease was followed by a return back to baseline (99 ± 3.3%).

Repeated measures ANOVA followed by paired t-tests with a Bonferroni adjustment demonstrated a statistical difference between the first and second measurement at 'depth' in both conditions ($P < 0.001$, F (9, 171) = 16.6), but no statistical difference between the following measurements ($P > 0.05$). A two-way ANOVA analysis shows that gas accounted for 11.6% of the total variance ($P = 0.0001$, F (1.56) = 17) while time accounted for 47% of the total variance ($P < 0.0001$, F (3.56) = 23.15). Gas mix had the same effect at all time values as interaction accounted for a mere 3% of the total variance ($P = 0.218$, F (3.56) = 1.52).

Figure 3
Correlation calculation and linear regression of the magnitude of CFFF change and time to complete in a math processing and a trail-making task during air (A) or enriched-air nitrox (EANx) (B) breathing under pressure (0.4 MPa)

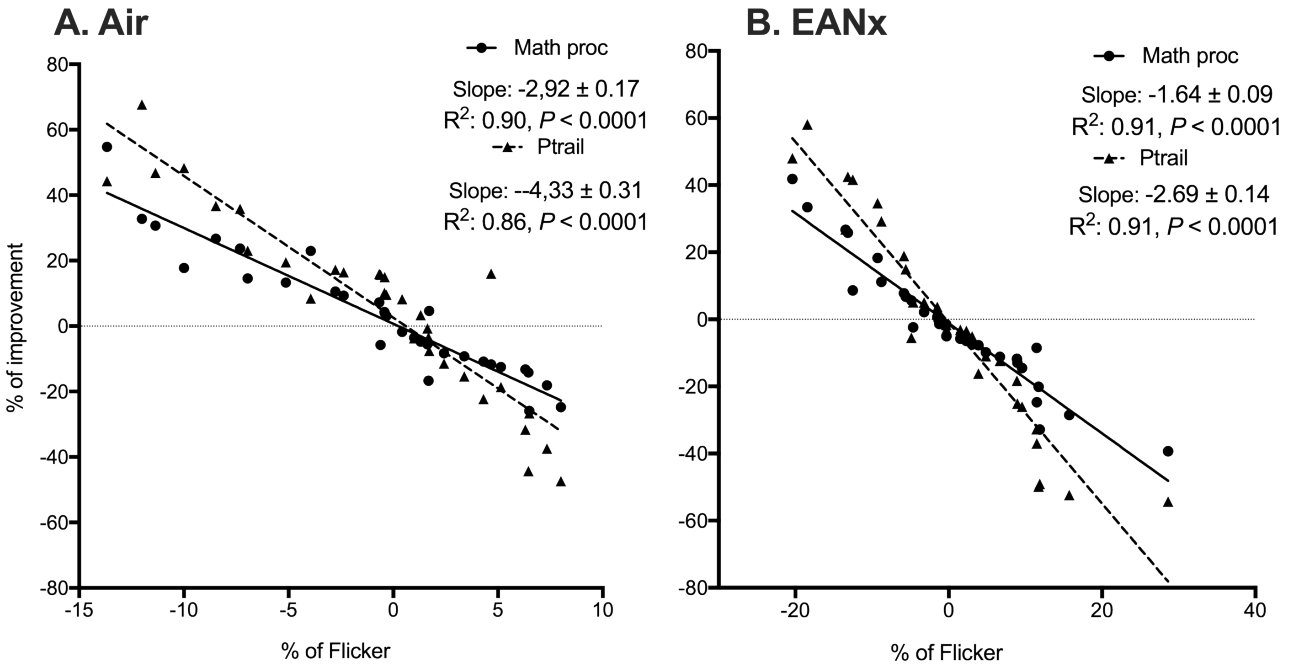
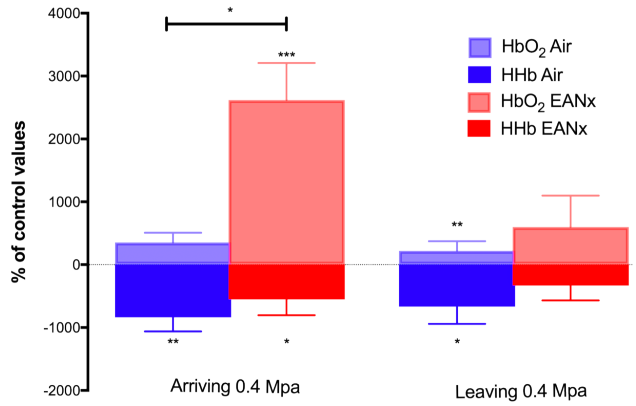


Figure 4
Variation of HbO_2 and HHb under pressure (0.4 MPa); pre-dive values normalized to 100%; each subject is compared to his own pre-dive value; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; ($n = 8$, means and SDs shown)



PSYCHOLOGY EXPERIMENT BUILDING LANGUAGE

PEBL results have already been published in detail elsewhere.[3] For all three tests (maths-processing, trail-making and perceptual vigilance) the error rates were stable throughout the whole experiment for both gas mixes. After an initial improvement in the times to complete the three tasks there were progressive deteriorations (increased time to complete) that lasted up to the 30-min post-dive test. The magnitude of CFFF changes and the times to completion in both the maths-processing and trail-making tasks were inversely correlated with air (Pearson r -0.90 and -0.86 respectively, $P < 0.0001$ in both tests; Figure 3A) and with EANx (Pearson r -0,91, $P < 0.0001$ in both tests; Figure 3B). This relation is further confirmed by linear regression (Figure 3).

NEAR-INFRARED SPECTROSCOPY

Arrival at maximal pressure is associated with a significant brain activation while breathing EANx was characterized by an increase in HbO_2 (2619 ± 590%, $P < 0.001$) and a simultaneous decrease in HHb (550 ± 253%, $P = 0.027$). These results are, by definition, associated with brain activation.[19] Similar activation is present while breathing air (HbO_2 354 ± 154% increase; HHb 836 ± 225% decrease). However, only the decrease of HHB is significant ($P < 0.01$, F (15, 72) = 1.377). The difference between the two gases is significant, EANx being associated with greater brain activation than air (ANOVA, $P = 0.038$, F (3, 19) = 0.785). Data collection beyond the measurements at depth was incomplete owing to a technical problem related to the Nimo Device buffer memory, with a loss of almost 40% of the data for the 30-min post dive measurement. Whilst there appears to be a trend thereafter characterized by a progressive return to baseline followed by brain inhibition, these data are not reported, only the two observations at depth being shown in Figure 4. The TOI remained stable throughout the experiment (Air: 2.22 ± 1.3 µM; EANx 2.89 ± 4 µM, $P = 0.343$).

ULTRASONIC MONITORING AND HAEMODYNAMICS

Precordial cardiac echography at 30 min post dive failed to demonstrate any bubble production (Grade 0, Brubakk-

Eftedal classification[21]). Heart rate and mean blood pressure were essentially identical for the two dives (P = 0.99, ANOVA, F (5, 33) = 0.03).

Discussion

Since IGN can eventually lead to unconsciousness, there is a need for underwater neurocognitive performance testing to identify pre-symptomatic cognitive impairment, affording the diver at depth a tool to improve their safety. This is especially true since subjective assessment (metacognition) does not meet the criteria of reliability[3] or alternatively does not guarantee proper implementation of appropriate goal-directed behaviour/coping strategies.[5] To investigate such a tool, one needs to assume a correlation between cognitive performance, measured with task performance such as mental arithmetic, memory, reaction time or manual dexterity (PEBL in this study) with physiological indexes that more accurately monitor mental workload/arousal (CFFF in this study). This correlation has already been demonstrated under normobaric conditions.[13] In the present study, the regression graph also shows a significant inverse correlation between CFFF and the time to completion of the chosen PEBL tasks under hyperbaric conditions. This correlation should come as no surprise, as a recent study using event-related brain potentials as indicators of the use of cognitive control, demonstrated that arousal has the potential to influence both proactive (active maintenance of contextual information to optimally bias attention, perception and action systems in a goal-driven manner) and retroactive control (retrieval of context information mobilized only as needed, especially after detection of a high interference event).[22] High arousal has been reported to decrease proactive control and increase reactive control compared to low arousal.[22]

Altogether, this suggests that these tests (PEBL and CFFF) might be considered comparable in providing assessment of cortical functions in both conditions, air and EANx. One study demonstrated that CFFF was a unique predictor of executive function across different age groups (means 21.7 vs. 72.4 years) and accounted for unique variance in performance above and beyond age and global cognitive status.[23] Nonetheless, even if there were a direct relationship between cortical arousal as measured by CFFF and cognitive performance, there is ample evidence of the nonlinear (inverted U-shape) relationship between arousal and cognitive performance (Yerkes-Dodson Law[24]), predicting declining performance at higher than optimal arousal levels, particularly in more complex cognitive tasks.[25] However, this should not be seen as a limitation in the case of scuba diving as arousal and cognitive performance deteriorate progressively during exposure to pressure rather than improving.

Although, the understanding of the result is simple: the lower the CFFF threshold, the lower the cerebral arousal, some limitations might apply. Indeed, since CFFF measurements are influenced by many factors (intensity of ambient light, flicker frequency modulation, the amplitude of the modulation, the average intensity of the illumination, the wavelength or colour of the LED and the position of the stimulus on the retina), no conclusions can be made on absolute values, hence the choice of assessing the magnitude of change. This also implies that this method, in its present form, is only suitable for studies where each candidate is his own control. Moreover, to compare studies or start multicentre experiments, a standardised, easily available device is required, which is lacking currently.

Because a small cohort was used, further research is needed to identify a clinically relevant cut-off for CFFF, namely a variation value, individually parameterized, indicating a cognitive impairment incompatible with safety of the monitored diver. Once identified, this cut-off could be implemented in a robotic system such as the ROAD project (Robotics for Assisted Diving)[26] or the CADDY project (Cognitive Autonomous Diving Buddy),[27] which aims to develop an intelligent system able to supervise in a semi-automatic way the activities performed by underwater operators. This would allow, as in other situations where safety is of concern, reliable monitoring and assessment of the current status and performance of operational divers.

The observed changes are characterized by an initial increase of cerebral arousal when arriving at 0.4 MPa, which is followed 15 min later by a progressive deterioration. However, although similar in form, there was a significant difference between the two gases, EANx being associated with greater brain activation than air and likely less late-dive/post-dive impairment. Therefore, we hypothesized that a higher fraction of inspired oxygen (EANx40, PO_2 = 162 kPa; air, PO_2 = 81 kPa at 0.4 MPa) had a beneficial effect on arousal and cognitive performance. Indeed, short-term normobaric O_2 (maximum 101 kPa O_2) influenced cognitive abilities such as memory, visuospatial and verbal abilities in a positive manner,[28] whilst functional MRI studies have demonstrated that normobaric hyperoxia (30 kPa O_2) during verbal or visual tasks increases the activation of brain areas associated with cognitive processing.[29]

In divers, an association between changes in response times and changes in CFFF suggest that divers susceptible to IGN may also be susceptible to the effects of elevated PO_2.[30] Also, even a small reduction in PN_2, associated with a conservative dive profile, resulted in a modest beneficial effect of EANx28 (28% O_2–72% N_2) on performance that may contribute to diving safety.[31] This hypothesis is supported by the NIRS measurements, although it could be argued that these results do not correspond to cerebral activation but to a variation in haemodynamics. However, measurements of blood pressure and heart rate did not vary throughout or between the two dives.

Since the TOI remained stable throughout the experiment, this indicates that total haemoglobin was neither increased nor decreased, which, in the absence of variation in total blood volume, means that cerebral haemodynamics remained constant. The 'oxygen hypothesis' (above) is also consistent with experimental models of neurotransmission. Although the exact mechanisms are still debated, based on animal studies on neurochemical data on IGN,[6] it is now accepted that inert gases exert their effects by influencing the synthesis, secretion and recapture of neurotransmitters, mainly dopamine, glutamate and gamma-aminobutyric acid (GABA),[6] whilst O_2 facilitates nerve conduction and interacts with GABA neurotransmission.[32] Recent data obtained from trainee pilots using magnetic resonance spectroscopy demonstrated that higher striatal concentrations of GABA and glutamate/glutamine were related to superior performance in action control allowing differentiation between high and normal performers.[33]

However, given the available data on the subject, it would be an error to consider that O_2 only elicits brain activation. According to one study, the effects on neuronal excitability measured by CFFF of changes in PO_2 could be dose-dependent.[34] Oxygen at 93 kPa resulted in partial recovery of motor and memory reaction times in some hyperbaric conditions while caused incapacitation with amnesia in others.[35] In this latter study, even high PN_2 (up to 0.57 MPa) was well tolerated providing neither hypercapnia nor hyperoxia were present. These findings and those from the present study are not mutually exclusive, despite differences in study protocols (e.g., exercise vs. at rest). Given these limitations, future research should combine a computer-based approach (which is now possible underwater[9]) with objective measurements such as CFFF to study the effects of different inspired gas mixes on human cognitive performance and brain cortical function.

Conclusions

Under hyperbaric conditions, CFFF testing provided a global assessment of cerebral arousal/workload and correlated with some psychometric tests from the PEBL. CFFF could provide a convenient measure of cognitive performance/abilities in extreme environments and is simple to use. However, some limitations may apply, and confounding factors need to be controlled to ensure accuracy of the measurement. Oxygen appeared to be an important modulator of IGN. In accordance with the neurochemical theory of IGN, the net effect on cerebral performance appears to depend on a balance between the activating effects of O_2 and the inhibitory effects of N_2. However, other factors, such as carbon dioxide retention may be important and require further study.

References

1 Clark JE. Moving in extreme environments: inert gas narcosis and underwater activities. Extrem Physiol Med. 2015;4:1. doi: 10.1186/s13728-014-0020-7. PMID: 25713701. PMCID: PMC4337274.

2 Edmonds C, Walker D. Scuba diving fatalities in Australia and New Zealand: 1. the human factor. SPUMS J. 1989;19:94–104. Available from: http://archive.rubicon-foundation.org/xmlui/handle/123456789/9294. [cited 2019 May 17].

3 Germonpré P, Balestra C, Hemelryck W, Buzzacott P, Lafère P. Objective vs. subjective evaluation of cognitive performance during 0.4-MPa dives breathing air or nitrox. Aerosp Med Hum Perform. 2017;88:469–75. doi: 10.3357/AMHP.4608.2017. PMID: 28417835.

4 Harding S, Bryson P, Perfect T. Investigating the relationship between simulated depth, cognitive function and metacognitive awareness. Norwich: Health and Safety Executive; 2004.

5 Hobbs M, Higham PA, Kneller W. Memory and metacognition in dangerous situations: investigating cognitive impairment from gas narcosis in undersea divers. Hum Factors. 2014;56:696–709. doi: 10.1177/0018720813510737. PMID: 25029895.

6 Rostain JC, Lavoute C. Neurochemistry of pressure-induced nitrogen and metabolically inert gas narcosis in the central nervous system. Compr Physiol. 2016;6:1579–90. doi: 10.1002/cphy.c150024. PMID: 27347903.

7 Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. Conflict monitoring and cognitive control. Psychol Rev. 2001;108:624–52. PMID: 11488380.

8 Balestra C, Lafère P, Germonpré P. Persistence of critical flicker fusion frequency impairment after a 33 mfw SCUBA dive: evidence of prolonged nitrogen narcosis? Eur J Appl Physiol. 2012;112:4063–8. doi: 10.1007/s00421-012-2391-z. PMID: 22476770.

9 Steinberg F, Doppelmayr M. Executive functions of divers are electively impaired at 20-meter water depth. Front Psychol. 2017;8:1000. doi: 10.3389/fpsyg.2017.01000. PMID: 28676772. PMCID: PMC5476772.

10 Sharma P, Singh S, Sharma BC, Kumar M, Garg H, Kumar A, et al. Propofol sedation during endoscopy in patients with cirrhosis, and utility of psychometric tests and critical flicker frequency in assessment of recovery from sedation. Endoscopy. 2011;43:400–5. doi: 10.1055/s-0030-1256182. PMID: 21547878.

11 Fuentes JP, Villafaina S, Collado-Mateo D, de la Vega R, Gusi N, Clemente-Suarez VJ. Use of biotechnological devices in the quantification of psychophysiological workload of professional chess players. J Med Syst. 2018;42:40. doi: 10.1007/s10916-018-0890-0. PMID: 29350296.

12 Kahlbrock N, Butz M, May ES, Brenner M, Kircheis G, Häussinger D, et al. Lowered frequency and impaired modulation of gamma band oscillations in a bimodal attention task are associated with reduced critical flicker frequency. Neuroimage. 2012;61:216–27. doi: 10.1016/j.neuroimage.2012.02.063. PMID: 22405731.

13 Hemelryck W, Rozloznik M, Germonpré P, Balestra C, Lafère P. Functional comparison between critical flicker fusion frequency and simple cognitive tests in subjects breathing air or oxygen in normobaria. Diving Hyperb Med. 2013;43:138–42. PMID: 24122188.

14 Arieli R, Ertracht O, Oster I, Vitenstein A, Adir Y. Effects of nitrogen and helium on CNS oxygen toxicity in the rat. J Appl Physiol (1985). 2005;98:144–50. doi:10.1152/japplphysiol.00506.2004. PMID: 15322063.

15 Frankenhaeuser M, Graff-Lonnevig V, Hesser CM. Effects on psycho-motor functions of different nitrogen-oxygen gas mixtures at increased ambient pressures. Acta Physiol Scand.

1963;59:400–9. doi: 10.1111/j.1748-1716.1963.tb02756.x. PMID: 14082611.
16 Hobbs MB. Impairment from gas narcosis when breathing air and enriched air nitrox underwater. Aviat Space Environ Med. 2014;85:1121–4. doi: 10.3357/ASEM.4003.2014. PMID: 25329945.
17 Cui X, Bray S, Reiss AL. Functional near infrared spectroscopy (NIRS) signal improvement based on negative correlation between oxygenated and deoxygenated hemoglobin dynamics. Neuroimage. 2010;49:3039–46. doi: 10.1016/j.neuroimage.2009.11.050. PMID: 19945536. PMCID: PMC2818571.
18 Fekete T, Rubin D, Carlson JM, Mujica-Parodi R. The NIRS analysis package: noise reduction and statistical inference. PloS One. 2011;6:e24322. doi: 10.1371/journal.pone.0024322. PMID: 21912687. PMCID: PMC3166314.
19 Kleinschmidt A, Obrig H, Requardt M, Merboldt KD, Dirnagl U, Villringer A, et al. Simultaneous recording of cerebral blood oxygenation changes during human brain activation by magnetic resonance imaging and near-infrared spectroscopy. J Cereb Blood Flow Metab. 1996;16:817–26. doi: 10.1097/00004647-199609000-00006. PMID: 8784226.
20 Al-Rawi PG, Smielewski P, Kirkpatrick PJ. Evaluation of a near infrared spectrometer (NIRO 300) for the detection of intracranial oxygenation changes in the adult head. Stroke. 2001;32:2492–500. PMID: 11692006.
21 Blogg SL, Gennser M, Møllerløkken A, Brubakk AO. Ultrasound detection of vascular decompression bubbles: the influence of new technology and considerations on bubble load. Diving Hyperb Med. 2014;44:35–44. PMID: 24687484.
22 Cudo A, Francuz P, Augustynowicz P, Strozak P. The effects of arousal and approach motivated positive affect on cognitive control. An ERP Study. Front Hum Neurosci. 2018;12:320. doi: 10.3389/fnhum.2018.00320. PMID: 30233339. PMCID: PMC6128242.
23 Mewborn C, Renzi LM, Hammond BR, Miller LS. Critical flicker fusion predicts executive function in younger and older adults. Arch Clin Neuropsychol. 2015;30:605–10. doi: 10.1093/arclin/acv054. PMID: 26370250.
24 Balestra C, Kot J, Efrati S, Guerrero F, Blatteau JE, Besnard S. Editorial: extreme environments in movement science and sport psychology. Front Psychol. 2018;4:2391. doi: 10.3389/fpsyg.2018.02391. PMID: 30564171. PMCID: PMC6288169.
25 Gur RC, Gur RE, Skolnick BE, Resnick SM, Silver FL, Chawluk J, et al. Effects of task difficulty on regional cerebral blood flow: relationships with anxiety and performance. Psychophysiology. 1988;25:392–9. PMID: 3174905.
26 Conte G, Scaradozzi D, Sorbi L, Zanoli SM, D'Ippolito F, Fagi A, et al. ROAD project: Robotics for assisted diving, 22nd Mediterranean Conference on Control and Automation. Palermo, Italy: IEEE; 2014. p. 853–6. doi: 10.1109/MED.2014.6961480.
27 Miskovic N, Pascoal A, Bibuli M, Caccia M, Neasham JA, Birk A, et al. CADDY Project, Year 2: The first validation trials. IFAC-PapersOnLine. 2016;49:420–5. doi: 10.1016/j.ifacol.2016.10.440.
28 Moss MC, Scholey AB, Wesnes K. Oxygen administration selectively enhances cognitive performance in healthy young adults: a placebo-controlled double-blind crossover study. Psychopharmacology. 1998;138:27–33. PMID: 9694523.
29 Rocco M, Pelaia P, Di Benedetto P, Conte G, Maggi L, Fiorelli S, et al. Inert gas narcosis in scuba diving, different gases different reactions. Eur J Appl Physiol. 2019;119:247–55. doi: 10.1007/s00421-018-4020-y. PMID: 30350155.
30 Tikkinen J, Wuorimaa T, Siimes MA. A comparison of simple reaction time, visual discrimination and critical flicker fusion frequency in professional divers at elevated pressure. Diving Hyperb Med. 2016;46:82–6. PMID: 27334995.
31 Brebeck AK, Deussen A, Schmitz-Peiffer H, Range U, Balestra C, Cleveland S, et al. Effects of oxygen-enriched air on cognitive performance during SCUBA-diving - an open-water study. Res Sports Med. 2017;25:345–56. doi: 10.1080/15438627.2017.1314289. PMID: 28397524.
32 Rostain JC, Lavoute C. Dopamine, neurochemical processes, and oxygen toxicity at pressure. Compr Physiol. 2016;6:1339–44. doi: 10.1002/cphy.c140025. PMID: 27347895.
33 Yildiz A, Quetscher C, Dharmadhikari S, Chmielewski W, Glaubitz B, Schmidt-Wilcke T, et al. Feeling safe in the plane: neural mechanisms underlying superior action control in airplane pilot trainees – a combined EEG/MRS study. Hum Brain Mapp. 2014;35:5040–51. doi: 10.1002/hbm.22530. PMID: 24753040. PMCID: PMC4452896.
34 Kot J, Winklewski PJ, Sicko Z, Tkachenko Y. Effect of oxygen on neuronal excitability measured by critical flicker fusion frequency is dose dependent. J Clin Exp Neuropsychol. 2015;37:276–84. doi: 10.1080/13803395.2015.1007118. PMID: 25715640.
35 Freiberger JJ, Derrick BJ, Natoli MJ, Akushevich I, Schinazi EA, Parker C, et al. Assessment of the interaction of hyperbaric N_2, CO_2, and O_2 on psychomotor performance in divers. J Appl Physiol (1985). 2016;121:953–64. doi: 10.1152/japplphysiol.00534.2016. PMID: 27633739.

Acknowledgements

The authors wish to thank the technicians who operated the hyperbaric chamber during the experimentation and the divers who volunteered for this study.

Funding

This study was funded internally.

Conflicts of interest: nil

Submitted: 19 September 2018; final revision 27 February 2019
Accepted: 08 March 2019

Review article

Systematic review on the effects of medication under hyperbaric conditions: consequences for the diver

Erik Hoencamp[1], Thijs TCF van Dongen[2,3], Pieter-Jan AM van Ooij[4], Thijs T Wingelaar[4], Mees L Vervelde[5], Dave AA Koch[4], Rob A van Hulst[4,6], Rigo Hoencamp[2,3,7]

[1] *Institute of Psychology, Leiden University, Leiden, The Netherlands*
[2] *Defense Healthcare Organization, Ministry of Defense, Utrecht, The Netherlands*
[3] *Department of Surgery, Alrijne Hospital, Leiderdorp, The Netherlands*
[4] *Diving Medical Center, Royal Netherlands Navy, Den Helder, The Netherlands*
[5] *Central Military Hospital, Ministry of Defense, Utrecht*
[6] *Department of Anesthesiology, Academic Medical Center, Amsterdam, The Netherlands*
[7] *Division of Surgery, Leiden University Medical Center, Leiden*
Corresponding author: *Thijs TCF van Dongen, Department of Surgery, Alrijne Hospital, PO Box 4220, 2350 CC Leiderdorp, Simon Smitweg 1, 2353 GA Leiderdorp, The Netherlands*
ttcfvandongen@alrijne.nl

Key words
Diving; Drugs; Pharmacokinetics; Decompression sickness; Fitness to dive; Review article

Abstract
(Hoencamp E, van Dongen TTCF, van Ooij PJAM, Wingelaar TT, Vervelde ML, Koch DAA, van Hulst RA, Hoencamp R. Systematic review on the effects of medication under hyperbaric conditions: consequences for the diver. Diving and Hyperbaric Medicine. 2019 June 30;49(2):127–136. doi: 10.28920/dhm49.2.127-136. PMID: 31177519.)
Background: Physiological changes are induced by immersion, swimming and using diving equipment. Divers must be fit to dive. Using medication may impact the capacity to adapt to hyperbaric conditions. The aim of this systematic review is to assess the interaction of diving/hyperbaric conditions and medication and to provide basic heuristics to support decision making regarding fitness to dive in medicated divers.
Methods: This was a systematic review of human and animal studies of medications in the hyperbaric environment. Studies were subdivided into those describing a medication/hyperbaric environment interaction and those concerned with prevention of diving disorders. Studies without a relation to diving with compressed air, and those concerning oxygen toxicity, hyperbaric oxygen therapy or the treatment of decompression sickness were excluded.
Results: Forty-four studies matched the inclusion criteria. Animal studies revealed that diazepam and valproate gave limited protection against the onset of the high-pressure neurological syndrome. Lithium had a protective effect against nitrogen-narcosis and losartan reduced cardiac changes in repetitive diving. Human studies showed no beneficial or dangerous pressure-related interactions. In prevention of diving disorders, pseudoephedrine reduced otic barotrauma, vitamins C and E reduced endothelial dysfunction after bounce diving and hepatic oxidative stress in saturation diving.
Discussion and conclusions: Animal studies revealed that psycho-pharmaceuticals can limit the onset of neurologic symptoms and cardiovascular protective drugs might add a potential protective effect against decompression sickness. No evidence of significant risks due to changes in pharmacologic mechanisms were revealed and most medication is not a contraindication to diving. For improving decision making in prescribing medicine for recreational and occupational divers and to enhance safety by increasing our understanding of pharmacology in hyperbaric conditions, future research should focus on controlled human studies.

Introduction

Scuba diving is an increasingly popular sport with more than 15 million divers worldwide completing more than 250 million dives per year.[1] Certification for scuba diving can be obtained through diving certification organizations. These include, for example, the Professional Association of Diving Instructors (PADI) and Scuba Schools International (SSI). This certification typically involves online classes, classroom instruction, pool practice and open-water training. Since physiological changes are induced by immersion, swimming and using special equipment during diving, divers must be fit to dive.[2,3] The laws of physics that are important to take into consideration while diving are Boyle's law, Henry's law and Dalton's law. These laws provide explanations for the possible occurrences of barotrauma, decompression sickness (DCS), nitrogen narcosis and oxygen toxicity, amongst other pathophysiological impacts of the underwater environment.[4] Although the hazards of diving are principally identical for sport, commercial and military divers, the risks may vary depending on the varying diving procedures and equipment used. Appropriate training, skills and equipment can aid in

reducing the risk of diving and, depending on jurisdictions, regular medical assessment is required before diving.

Medical disorders or use of medication may have an impact on the capacity to adapt to hyperbaric conditions and could affect medical fitness to dive.[5] Illnesses, such as asthma or epilepsy, require a medical clearance. However, in most cases, evidence of causality is absent and it is not always straightforward to predict the effect of medication on cognitive and physical functioning in hyperbaric conditions. General health, specifics of the disorder, medication interaction and the hyperbaric conditions are all factors in this assessment process. Obviously, regulations concerning commercial divers are stricter, and illnesses prior to a diving career are a stronger contraindication than onset during a diving career. Many protocols have been written for selecting humans for work under hyperbaric conditions or (recreational) diving, however robust evidence to guide practice is limited.[6–7]

The primary aim of this systematic review of the current human and animal study literature was to assess the interactions between the hyperbaric environment and medications. The secondary aim was to provide a heuristic approach to support decision making regarding physical fitness for occupational health under hyperbaric conditions and (recreational) diving.

Methods

PROTOCOL

The protocol for objectives, literature search strategies, inclusion and exclusion criteria and outcome measurements was prepared *a priori*, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[8] statement and is described in this section.

LITERATURE SEARCH STRATEGY

This systematic review sought human and animal studies investigating pharmacodynamic/kinetic effects of the hyperbaric environment on medications or the effects of medications used while diving on the risk of diving disorders. An electronic database search of PubMed, Medline, Embase Science Citation Index Expanded, the Web of Science and World Wide Web search (key words '(scuba) diving', 'hyperbaric', 'medication', 'drugs') was performed up to 16 February 2018. These databases were searched for articles published using the medical subject headings (MeSH) or entry terms from Table 1. We focused on the disease entities and most common pharmacological agents. Studies pertaining to the treatment of decompression sickness (DCS), oxygen toxicity and hyperbaric oxygen therapy were excluded from this review because of the different objectives and subject inclusion methods of these studies.

The reference lists from the included studies were searched to identify additional studies. Two authors (TCFvD, EH) independently identified the studies for inclusion and exclusion and extracted the data. Any inconsistencies between the authors were discussed until consensus was reached. The accuracy of the extracted data was further confirmed by the senior author (RAvH).

Table 1
Search PUBMED

('Diving' [MeSH] OR 'dive' [tw] OR 'diving' [tw] OR 'diver' [tw] OR 'divers' [tw] OR 'scuba' [tw] OR 'hyperbaric' [tw] OR 'deep sea' [tw] OR 'aquanaut' [tw] OR 'aquanauts' [tw] OR 'frogman' [tw] OR 'frogmen' [tw]) AND 'Drug Therapy' [MeSH] OR 'drug' [tw] OR 'drugs' [tw] OR 'medication' [tw] OR 'medications' [tw] OR 'Pharmacological Actions Category' [MeSH] OR 'Pharmaceutical Preparations' [Mesh] OR 'pharmaceuticals' [tw] OR 'medicament' [tw] OR 'medicaments' [tw] OR 'pharmacological' [tw])

QUALITY ASSESSMENT

Studies were rated on the level of evidence provided according to criteria by the Centre for Evidence Based Medicine in Oxford. The methodological quality of observational comparative studies was assessed by the modified Newcastle-Ottawa Scale.[9,10]

Results

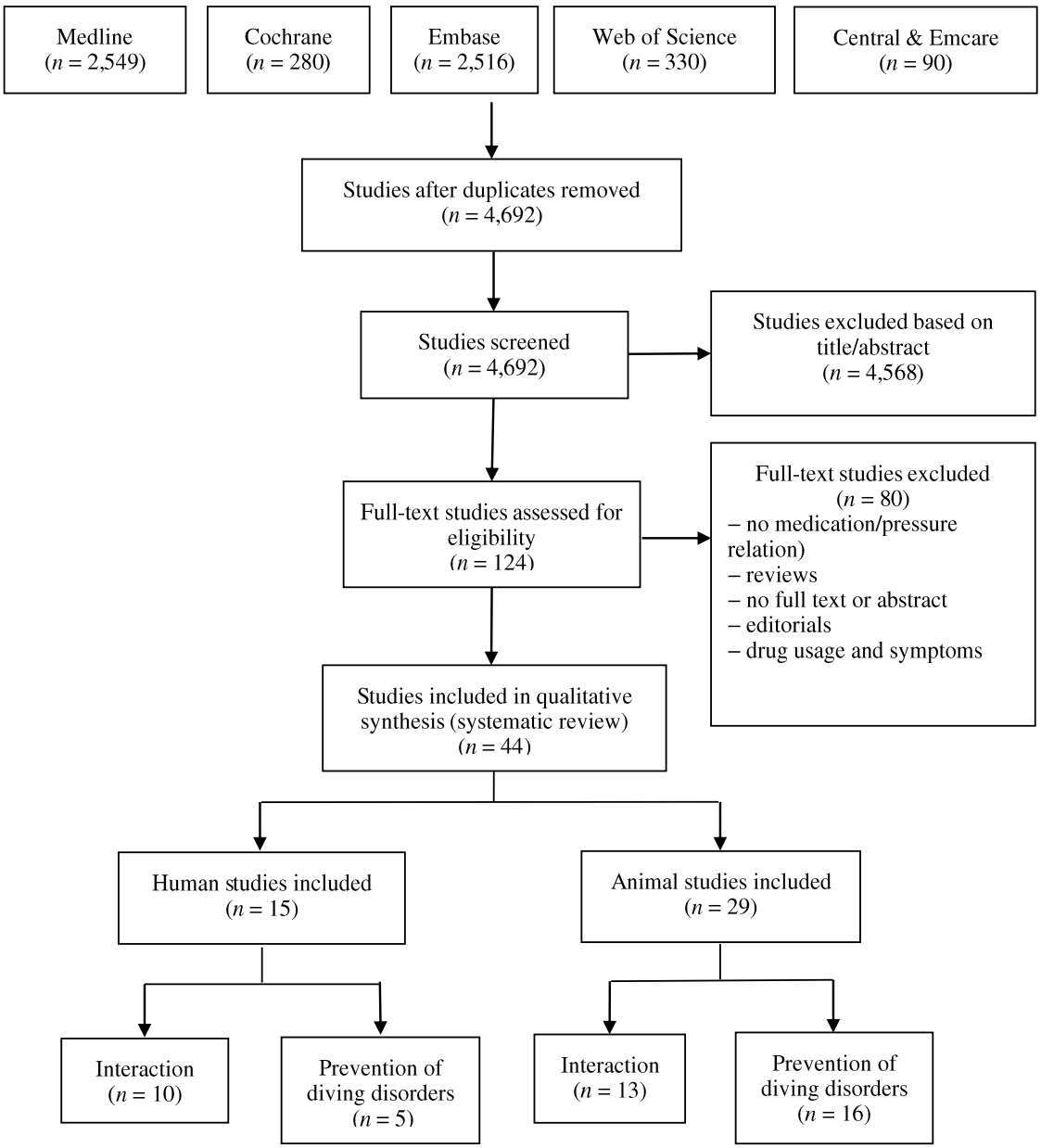
PRISMA FLOWCHART

The PRISMA flowchart quantitatively illustrates the search through to the final studies included in this review (Figure 1). The 44 included studies were subdivided between human and animal studies and further subdivided into two topics, being (1) medication and hyperbaric interaction, and (2) prevention of diving disorders.

MEDICATION AND HYPERBARIC INTERACTION

Table 2 shows the results of the human studies concerning interaction of drugs and hyperbaric pressure. Pharmacologic agents studied were aspirin, dipyridamole, scopolamine, clemastine, pseudoephedrine, dimenhydrinate, cyclizine, oral contraceptives, bleomycin and psychotropic drugs. Aspirin and dipyridamole accounted for some beneficial physiologic changes at a cellular level (preservation of platelet numbers) compared to a placebo following saturation dives.[11,12] No pressure-related interactions were found. No significant effects on diver performance from transdermal scopolamine were seen. Aggravation of mild symptoms of dry mouth and blurred vision compared to placebo was reported.[13,14] Dimenhydrinate adversely effected mental flexibility at depth.[15] Cyclizine had a potential small adverse effect on grammatical reasoning, which is increased at depth, but had no effect on a manual task.[16] These effects on various aspects

Figure 1
Literature search flow chart on the effects of medications under hyperbaric conditions



of diver performance, especially at depth, could possibly contribute to cyclizine worsening the risks of diving.[17] For all other agents studied, no beneficial or dangerous direct pressure-related interactions were found.[18–21]

Several animal studies showed significant beneficial effects of pharmacologic agents when animals were exposed to hyperbaric conditions (Table 3). Diazepam and valproate reduced the severity of the high-pressure nervous syndrome (HPNS) at depths beyond 150 metres' sea water (msw) in rats and baboons.[22,23] Lithium provided some protection against nitrogen narcosis in rats.[24] Lastly, losartan prevented deleterious changes in cardiac function seen after repeated hyperbaric exposures in rats.[25]

Conversely, some studies showed significant adverse effects. Sildenafil use showed an increased incidence of DCS combined with an exacerbated reduction in platelet numbers after hyperbaric exposure.[26] The antibiotics benzyl-penicillin, gentamycin and rifampicin were less effective at simulated depth.[27,28] Finally, lithium significantly potentiated the onset and severity of HPNS symptoms.[24] Studies of the use of salicylate, theophylline, meperidine, pentobarbital, and non-competitive N-methyl-D-aspartate receptor (NMDA) receptor antagonists did not show an interaction between the pharmacologic agents and the hyperbaric environment.[29–34]

Table 2

Interaction of hyperbaric pressure and the use of pharmacologic agents in human studies; ATA – atmospheres absolute pressure; DCT – decompression time; LoE – level of evidence; MTC – mega thrombocyte; *n* – number; OW(HL) – open water (Hydrolab); PC – pressure chamber; RBC – red blood cell count; resp – respiratory; VK744 – analogue of dipyridamole

Reference	*n*	Drug	Control	Pressure (ATA)	Bottom time	Location	Blinded	Outcome	Results	LoE
12	20	Aspirin	Placebo	2.4	60 h	OW(HL)	Yes	Platelet count	Reduced platelets in control group	Ib
12	12	VK744 (dipyridamole)	Placebo	2.4	5 days (incl. DCT)	OW(HL)	Yes	Platelet count	Greater elevation of MTC in VK744; reduced platelets in control group	Ib
11	24	Aspirin; Dipyridamole	Placebo	2.8	48 h	PC	Yes	Platelet count and function	Reduced platelets in dipyridamole and control groups	Ib
13	10	Scopolamine	Placebo	2.8	5.5 days	PC	Yes	Cognitive	No significant effects	Ib
14	24	Scopolamine	Placebo	4.8	11 min	PC	Yes	Cognitive	No significant effects	Ib
21	102	Clemastine fumarate	Placebo	6.1	20 min	PC	Yes	Cognitive	No significant effects	Ib
15	30	Pseudoephedrine; Dimenhydrinate	Placebo	3.0	30 min	PC	Yes	Cognitive	Pseudoephedrine nil effects; dimenhydrinate reduced performance	Ib
17	24	Pseudoephedrine; Cyclizine	Placebo	4.0	5 min	PC	Yes	Cognitive	Pseudoephedrine nil effects; cyclizine reduced performance	Ib
18	30	Oral contraceptives	None	3.5	25 min	OW	No	Bubble production	No differences	IV
19	1	Bleomycin	None	Multiple	Multiple	OW	No	Resp. distress or fatigue	No complications	V
20	1,608	Psychotropic drugs	None (survey)	Multiple	Unknown	OW	No	Narcosis (severe)	No significant effects	IIb

Table 3

Interaction of hyperbaric pressure and the use of pharmacologic agents in animal studies; ATA – atmospheres absolute pressure; 1 ATA – control group had drug but remained at 1 ATA; * denotes an additional control group without drug but at test pressure; ; DCS – decompression sickness; EC – Escherichia coli; He – helium; HPNS – high-pressure nervous syndrome; LoE – level of evidence; MIC – minimum inhibitory concentration; MK-801 – dizocilpine; *n* – number; N_2 – nitrogen; NA – not applicable; NR – not reported; PC – pressure chamber; PCP – phencyclidine; SA – Staphylococcus aureus; Salm – Salmonella sp; SKF – alazocine; U – unknown

Reference	*n*	Type	Drug	Control (ATA)	Pressure (ATA)	Bottom time (h)	Location	Blinded	Outcome	Results	LoE
29	138	Rats	Salicylate	1*	9	3.5	PC	Yes	Anti-pyretic effect	No interaction	Ib
28	U	SA, EC	Antibiotics	1	Multiple	16	OW	N/A	Antibiotic efficacy	Increased MIC: penicillin for SA	IIb
24	40	Rats	Lithium	1*	19.2	NR	PC	Yes	N_2 narcosis HPNS	Reduced narcosis; potentiation of HPNS	Ib
22	78	Rats	Diazepam	1	90	2.5	PC	NR	Anesthetic and anticonvulsive effect; HPNS	Prevention of convulsion; reduction of HPNS	IIb
30	U	Dogs	Theophylline	1	6	U	PC	No	Pharmacokinetics	No changes	IIb
31	U	Dogs	Meperidine	1	6	U	PC	No	Pharmacokinetics	No changes	IIb
33	U	Dogs	Pentobarbital	1	6	U	PC	No	Pharmacokinetics	No changes	IIb
32	U	Dogs	Salicylate	1	6	U	PC	No	Pharmacokinetics	Increased clearance at 2.8 ATA and 100% O_2	IIb
23	8	Baboons	Sodium valproate	* only	61	5	PC	Yes	Effect on HPNS	Reduced severity	Ib
34	25	Rats	NMDA antagonists	1*	till onset HPNS	several	PC	NR	Effect on HPNS	Little or no effect	Ib
27	U	SA, EC, Salm.	Antibiotics	1	36; 71	18	PC	N/A	Antibiotic efficacy	Increased MIC: penicillin for SA; gentamycin and rifampicin for EC + Salm	IIb
25	19	Rats	Losartan	1*	5	30 min x 40 d	PC	NR	Cardiac function	Prevention of change	Ib
26	67	Mice	Sildenafil	* only	10.2	45 min	PC	Yes	DCS	Increased incidence	Ib

Table 4

Effects of pharmacologic agents in prevention of diving disorders in human studies; ATA – atmospheres absolute pressure; LoE – level of evidence; *n* – number; OW(HL) – open water (hydro lab); PC – pressure chamber; Vit – vitamin

Reference	*n*	Drug	Control	Pressure (ATA)	Bottom time	Location	Blinded	Outcome	Results	LoE
35	116	Pseudoephedrine	Placebo	2.2	Several dives	PC	Yes	Otologic symptoms	Lower TEED score, less discomfort and blockage	Ib
39	15	Vitamin C and E	Placebo	1.4	30 min	OW	Yes	Eustachian tube function	No difference	Ib
38	10	Vitamin C and E tea catechins	None	41	30 days	PC	No	Oxidative stress (liver function)	Less oxidative stress	IIb
36	6	Vitamin C and E	Placebo	4.0	36 min	OW	Yes	Endothelial/cardiac function	Reversal of brachial artery endothelial dysfunction	Ib
37	16	Statins	Placebo	2.8	80 min	PC	Yes	Bubble formation	No difference	Ib

PHARMACOLOGICAL AGENTS IN PREVENTION OF DIVING DISORDERS

In human studies investigating protective effects of medications on diving disorders, pseudoephedrine, the anti-oxidants vitamin C and E and statins were tested (Table 4). The use of pseudoephedrine resulted in fewer otologic barotrauma symptoms in comparison to placebo.[35] In one study vitamins C and E showed reversal of brachial artery endothelial dysfunction, potentially diminishing bubble formation.[36] Statins did not reduce post-dive bubble formation.[37] Antioxidants (vitamins C, E and tea catechins) reduced hepatic oxidative stress in saturation diving,[38] but the same vitamins did not improve eustachian tube function after oxygen dives.[39]

Table 5 shows the results of pharmacologic DCS prevention in animal studies. When used before hyperbaric exposure, clopidogrel,[40] cyproheptadine,[41] dimethothiazine,[42] aspirin and levodopa,[43] and escin[44] showed a significant reduction of mortality and incidence of DCS. Combined use of aspirin with levodopa had an added beneficial effect. A significantly decreased incidence of DCS and reduction of symptoms was seen with fluoxetine, abciximab, hydrogen enriched saline and simvastatin.[45–48] A beneficial effect on DCS symptoms was seen also with dibutyryl cAMP[49] and cyclohexanone (with decompression beyond normobaric pressure to an equivalent of 26,000 feet).[50] Pre-treatment with terbutaline, heparin, superoxide dismutase, catalase or amphetamine exhibited no relevant effects.[51–53] The anti-depressant spadin, a sortilin-derived peptide, was the only medication that showed a negative effect in a simulated diving study, with increased susceptibility to neurologic DCS symptoms.[54]

Discussion

GENERAL

Animal studies revealed that slight benefits might be expected from some psychopharmaceutic agents against the onset of HPNS symptoms.[22–24] Also, several cardiovascular drugs could add a potential protective effect against DCS.[40,43,46,48] However, these pharmacologic agents were tested on small mammals. Studies using dogs were specifically aimed at pharmacokinetics of drugs under hyperbaric conditions.[30–33] Apart from an increased clearance of salicylate at depth, these studies did not reveal significant pharmacokinetic changes due to hyperbaric conditions. In contrast to the protective effect of theophylline found in guinea pigs,[55] a study in dogs showed that the use of a bronchodilator (aminophylline) before venous infusion of microbubbles resulted in an increased passage of these microbubbles across the pulmonary microvasculature.[56]

Studies of effects of pharmacological agents in hyperbaric conditions in humans are scarce. This is not surprising given the ethical considerations. Available studies showed few major effects of pharmacological agents in hyperbaric

Table 5

Effects of pharmacologic agents on DCS prevention in animal studies; ATA – atmospheres absolute pressure; 1 ATA – control group had drug but remained at 1 ATA; * denotes an additional control group without drug but at test pressure; PC – pressure chamber; DCS – decompression sickness; fb – followed by; ft – feet; H_2 – hydrogen; LoE – Level of Evidence; *n* – number; N/A – not applicable; NR – not reported; PC – pressure chamber; SOD – superoxide dismutase; RBC – red blood cell; SOD – superoxide dismutase; W/D ratio – wet/dry ratio

Reference	*n*	Type	Drug (group)	Control (ATA)	Pressure (ATA)	Bottom time	Location	Blinded	Results	LoE
55	138	Guinea pigs	Theophylline	* only	7.4	60 min	PC	Yes	50% mortality reduction (100% combined with 100% O_2)	Ib
50	110	Mice	Cyclohexanone	1*	6.3 fb 26,000 ft	6 h	PC	NR	Protective effect	Ib
42	200	Mice	Dimetotiazine	* only	6.3	6 h	PC	NR	Reduced mortality, manifestations and pathologic changes	Ib
51	7	Rabbits	Terbutaline	* only	2 fb 39,000 ft	NR	PC	NR	Reduced incidence	IV
41	500	Mice	Cyproheptadine	* only	6.3	6 h	PC	NR	Reduced mortality, manifestations and pathologic changes	Ib
53	64	Mice	Amphetamine + cyproheptadine	1*	6.3	6 h	PC	NR	No additive effect of amphetamine combined with cyproheptadine	IIb
43	202	Rats	Levodopa + aspirin	* only	7.0	30 min	PC	NR	Reduced incidence and mortality enhanced with combined therapy	Ib
52	44	Dogs	Heparin; SOD; catalase	1*	10	≥10 min	PC	NR	No effect	Ib
49	45	Rats	Dibutyryl cAMP	1*	6.3 / 7.0	120 / 60 min	PC	NR	Reduced inflammation and pulmonary oedema	Ib
47	84	Rats	H_2-enriched saline	1*	7.1	90 min	PC	NR	Reduced incidence	Ib
45	91	Mice	Fluoxetine	1*	10.2	45 min	PC	Yes	Reduced incidence and better neurological recovery; reduced loss of platelets and RBCs	Ib
40	111	Rats	Clopidogrel	1*	16.3	270 s	PC	NR	Reduced mortality and inflammatory lung injury	Ib
46	80	Mice	Antiplatelet drugs	1*	9.2	45 min	PC	NR	Reduced incidence with abciximab.	Ib
48	NR	Rats	Simvastatin	* only	7.1	100 min	PC	NR	Reduced incidence and inflammatory lung injury	Ib
54	280	Mice	Fluoxetine; spadin	1*	9.0	45 min	PC	NR	Fluoxetine protective; spadin increased susceptibility	Ib
44	90	Rats	Escin	* only	7	90 min	PC	Yes	Reduced incidence and mortality	Ib

conditions. Most evidence was gained through animal experiments with often extreme diving profiles (to provoke bubble formation). Extrapolation of animal studies to humans should be done with caution.[57]

Human studies are needed to examine whether the medications or vitamins used in the animal studies will have beneficial or harmful effects for healthy divers in wet circumstances. Besides the pharmacological effect, diving with medication affecting cardiovascular responses should be undertaken cautiously, lest there be unintended effects on life-threatening conditions such as immersion pulmonary oedema.[58–60] Immersion alters the balance between the sympathetic and parasympathetic nervous systems, thus affecting the responses to many physiological processes.[61,62] However, most research was conducted in recompression chambers, where subjects are exposed to hyperbaric pressure without immersion in water. These so called 'dry-dives' simulate hyperbaric conditions and accompanying hyperoxia or increased uptake of inert gases, but do not simulate immersion, hypothermia or the increased workload of fin swimming. Results from dry-dives should be interpreted cautiously when assessing the effects of pharmacologic interventions in scuba diving.

FITNESS TO DIVE

The primary aim of this systematic review was the assessment of available evidence on the effects of hyperbaric circumstances on use of medication, thereby enhancing heuristics supported by evidence-based medicine in the assessment of fitness to dive. Based on the outcomes of this study, being physically fit to dive remains the cornerstone of medical diving clearance. This judgment is often based on assumptions and risk analysis, when the risk is not easily assessed. In the medical examination of a diver, an understanding of the effects of medication, the disease being treated and the impact that the hyperbaric environment might have on both is essential. Any serious symptoms of illness or side effects of medication under normobaric circumstances are potentially a valid reason for rejection.

ENVIRONMENTAL AND HYPERBARIC CONDITIONS

Environmental conditions during a dive vary enormously, from relaxed scuba diving in calm, warm, shallow tropical waters, to professional divers at extreme depth for several weeks (i.e., saturation diving). Conditions can deteriorate rapidly, caused by change in the environment (waves, currents), technical apparatus malfunctions or problems with a diving buddy. In all these situations it becomes a challenge to adapt oneself physically and mentally to the new circumstances.

Apart from diving medical clearance, an individual diver should answer the following key questions before every dive:

- Is my physical condition sufficient to cope with the required strain?
- Am I mentally prepared to cope with the demanding situation?
- Do I (and my buddy) possess the skills for this activity?

Thus, a tailored assessment that encompasses more than medical conditions and medications is required. A diving medical clearance which imposes depth limitations is unjustified as circumstances can change rapidly.

LIMITATIONS

To our knowledge, this is the first systematic review focusing on the effects of the hyperbaric environment on medication, and the effects of medication on diving disorders. However, any conclusions are substantially limited by the poor quality of the available evidence. According to the Quality Assessment there is a risk of bias in most of the included animal studies. Also, protocols vary between studies, making it harder to compare them in a meta-analysis. Different hyperbaric pressures or lengths of exposure might influence the outcome. Furthermore, most studies used dry dives, whilst immersion is essential for a proper judgement of the effects of medication on safety during diving.

Conclusion

This systematic review revealed no evidence of significant risks due to changes in pharmacologic mechanisms in the hyperbaric environment. However, it is unlikely that hyperbaric conditions diminish any risks of medication encountered in non-hyperbaric conditions. Regarding prevention or treatment of DCS, pharmacologic agents targeted at cardiovascular diseases like aspirin, losartan, clopidogrel or simvastatin could add a potential protective effect although evidence is limited. The anti-depressant fluoxetine may also warrant further investigation. For decision making in prescribing medicine for recreational and occupational divers and to enhance safety by increasing our understanding of pharmacy and diving, future research should focus on human studies in submersed circumstances.

References

1 Germonpré P. The medical risks of underwater diving and their control. International Sportmed Journal. 2006;7(1):1–15.
2 Bosco G, Rizzato A, Moon RE, Camporesi EM. Environmental physiology and diving medicine. Front Psychol. 2018;9:72. doi: 10.3389/fpsyg.2018.00072. PMID: 29456518. PMCID: PMC5801574.
3 Wendling JED, Elliott DH, Nome T. Fitness to dive standards: guidelines for medical assessment of working divers. 2003. [cited 2018 March 1]. Available from: http://www.edtc.org/EDTC-Fitnesstodivestandard-2003.pdf.
4 Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. Lancet. 2011;377(9760):153–64. doi: 10.1016/S0140-6736(10)61085–9. PMID: 21215883.
5 British Thoracic Society, Fitness to Dive Group, Subgroup of the British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines on respiratory aspects of fitness for diving. Thorax. 2003;58:3–13. Epub 2003/01/04. doi: 10.1136/thorax.58.1.3. PMID: 12511710. PMCID: PMC1746450.

6 Challenor J. Medical Assessment of Working Divers. Fitness to Dive Standards of European Diving Technology Committee. In: Wendling J, Elliott D, Nome T, editors. European Diving Technology Committee; 2004. p. 216. Occupational Medicine. 2005;55:581. doi: 10.1093/occmed/kqi154.

7 Health and Safety Executive. The medical examination and assessment of commercial divers. London: Health and Safety Executive; 2015. [cited 2018 March 17]. Available from: http://www.hse.gov.uk/pubns/ma1.htm.

8 Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. BMJ 2009;339:b2535. doi: 10.1136/bmj.b2535

9 Centre for Evidence-Based Medicine. Oxford Centre for Evidence-based Medicine – Levels of evidence: 2009. [cited 2018 March 17]. Available from: https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/.

10 Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. [cited 2018 March 17]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

11 Philp RB, Bennett PB, Andersen JC, Fields GN, McIntyre BA, Francey I, et al. Effects of aspirin and dipyridamole on platelet function, hematology, and blood chemistry of saturation divers. Undersea Biomed Res. 1979;6:127–46. PMID: 531993.

12 Philp RB, Freeman D, Francey I, Bishop B. Hematology and blood chemistry in saturation diving: I. Antiplatelet drugs, aspirin, and VK744. Undersea Biomed Res. 1975;2:233–49. PMID: 1226582.

13 Schwartz HJC, Curley MD. Transdermal scopolamine in the hyperbaric environment. Navy Experimental Diving Unit Report, 1986 (No. 2-86). [cited 2018 March 19]. Available from: http://archive.rubicon-foundation.org/xmlui/handle/123456789/3528.

14 Williams TH, Wilkinson AR, Davis FM, Frampton CM. Effects of transcutaneous scopolamine and depth on diver performance. Undersea Biomed Res. 1988;15:89–98. PMID: 3363755.

15 Taylor D, O'Toole K, Auble T, Ryan C, Sherman D. The psychometric and cardiac effects of pseudoephedrine and antihistamines in the hyperbaric environment. SPUMS Journal. 2001;31:50–7. Available from: http://archive.rubicon-foundation.org/xmlui/handle/123456789/7711. [cited 2018 March 17].

16 McGeoch G, Davis FM, Fletcher L. The effects on performance of cyclizine and pseudoephedrine during dry chamber dives breathing air to 30 metres' depth. SPUMS Journal. 2005;35:178–82. [cited 2018 March 19]. Available from: http://archive.rubicon-foundation.org/xmlui/handle/123456789/9791.

17 Clark JE. Moving in extreme environments: inert gas narcosis and underwater activities. Extrem Physiol Med. 2015;4:1. doi: 10.1186/s13728-014-0020-7. PMID: 25713701. PMCID: PMC4337274.

18 Boussuges A, Retali G, Bodere-Melin M, Gardette B, Carturan D. Gender differences in circulating bubble production after SCUBA diving. Clin Physiol Funct Imag. 2009;29:400–5. doi: 10.1111/j.1475-097X.2009.00884.x. PMID: 19594770.

19 Gray RN Jr. Scuba diving post-bleomycin therapy: a case report. Undersea Hyperb Med. 2010;37:455–7. PMID: 21226396.

20 Krummel T, Thiery A, Villain M, Schittly B, Brouant B. Psychotropic drug use in recreational scuba divers and its effect on severe narcosis. Int J Sports Med. 2017;38:322–8. doi: 10.1055/s-0042-122336. PMID: 28249344.

21 Sipinen SA, Kulvik M, Leinio M, Viljanen A, Lindholm H. Neuropsychologic and cardiovascular effects of clemastine fumarate under pressure. Undersea Hyperb Med. 1995;22:401–6. PMID: 8574128.

22 Gran L, Coggin R, Bennett PB. Diazepam under hyperbaric conditions in rats. Acta Anaesthesiol Scand. 1980;24:407–11. PMID: 7468131.

23 Pearce PC, Clarke D, Doré CJ, Halsey MJ, Luff NP, Maclean CJ. Sodium valproate interactions with the HPNS: EEG and behavioral observations. Undersea Biomed Res. 1989;16:99–113. PMID: 2499971.

24 Bennett PB, Leventhal BL, Coggin R, Roby J, Racanska L. Lithium effects: protection against nitrogen narcosis, potentiation of HPNS. Undersea Biomed Res. 1980;7:11–6. PMID: 7385444.

25 Stuhr LE, Maehle BO. The effect of Losartan, an angiotensin II antagonist, on cardiac function, mass and morphology in rats after repeated hyperbaric exposures. Scand J Clin Lab Invest. 1997;57:253–61. PMID: 9238761.

26 Blatteau JE, Brubakk AO, Gempp E, Castagna O, Risso JJ, Vallée N. Sidenafil pre-treatment promotes decompression sickness in rats. PloS One. 2013;8:e60639. doi: 10.1371/journal.pone.0060639. PMID: 23580342. PMCID: PMC3620342.

27 Hind J, Attwell RW. The effect of antibiotics on bacteria under hyperbaric conditions. J Antimicrob Chemother. 1996;37:253–63. PMID: 8707735.

28 Wild JR. Induction of staphylococcal beta-lactamase in response to low concentrations of methicillin under simulated diving environments. Can J Microbiol. 1977;23:116–21. WOS:A1977CV60000016. Available from: https://www.nrcresearchpress.com/doi/pdf/10.1139/m77-01. [cited 2018 March 17].

29 Hart JL. The antipyretic effects of hyperbaric air and salicylate on rats. Undersea Biomed Res. 1974;1:83–9. PMID: 4469183.

30 Kramer WG, Gross DR, Fife WP, Chaikin BN. Theophylline pharmacokinetics during hyperbaria and hyperbaric hyperoxia in the dog. Res Commun Chem Pathol Pharmacol. 1981;34:381–8. PMID: 7323440.

31 Kramer WG, Gross DR, Moreau PM, Fife WP. Drug disposition under hyperbaric and hyperbaric hyperoxic conditions: meperidine in the dog. Aviat Space Environ Med. 1983;54:410–2. PMID: 6870734.

32 Kramer WG, Welch DW, Fife WP, Chaikin BN, Gross DR. Salicylate pharmacokinetics in the dog at 6 ATA in air and at 2.8 ATA in 100% oxygen. Aviat Space Environ Med. 1983;54:682–4. PMID: 6626074.

33 Kramer WG, Welch DW, Fife WP, Chaikin BN, Medlock C, Gross DR. Pharmacokinetics of pentobarbital under hyperbaric and hyperbaric hyperoxic conditions in the dog. Aviat Space Environ Med. 1983;54:1005–8. PMID: 6651725.

34 Wardley-Smith B, Wann KT. The effects of non-competitive NMDA receptor antagonists on rats exposed to hyperbaric pressure. Eur J Pharmacol. 1989;165:107–12. doi: 10.1016/0014-2999(89)90775-9. PMID: 2548878.

35 Brown M, Jones J, Krohmer J. Pseudoephedrine for the prevention of barotitis media: a controlled clinical trial in underwater divers. Ann Emerg Med. 1992;21:849–52. doi: 10.1016/s0196-0644(05)81033-9. PMID: 1610044.

36 Obad A, Palada I, Valic Z, Ivancev V, Baković D, Wisløff U, et al. The effects of acute oral antioxidants on diving-induced alterations in human cardiovascular function. J Physiol. 2007;578(Pt 3):859–70. doi: 10.1113/jphysiol.2006.122218.

PMID: 17110413. PMCID: PMC2151345.
37 Duplessis CA, Fothergill D, Schwaller D, Hughes L, Gertner J. Prophylactic statins as a possible method to decrease bubble formation in diving. Aviat Space Environ Med. 2007;78:430–4. PMID: 17484348.
38 Ikeda M, Nakabayashi K, Shinkai M, Hara Y, Kizaki T, Oh-ishi S, et al. Supplementation of antioxidants prevents oxidative stress during a deep saturation dive. Tohoku J Exp Med. 2004;203:353–7. PMID: 15297742.
39 Mutzbauer TS, Neubauer B, Mueller PH, Sigg O, Tetzlaff K. Can eustachian tube ventilatory function impairment after oxygen diving be influenced by application of free radical scavenger vitamins C and E? Laryngoscope. 2001;111:861–6. doi: 10.1097/00005537-200105000-00020. PMID: 11359167.
40 Bao XC, Chen H, Fang YQ, Yuan HR, You P, Ma J, et al. Clopidogrel reduces the inflammatory response of lung in a rat model of decompression sickness. Respir Physiol Neurobiol. 2015;211:9–16. doi: 10.1016/j.resp.2015.02.003. PMID: 25784626.
41 Chryssanthou C, Rubin L, Graber B. Amelioration of decompression sickness in mice by pretreatment with cyproheptadine. Undersea Biomed Res. 1980;7:321–9. PMID: 7233624.
42 Chryssanthou C, Teichner F, Koutsoyiannis M. Studies on dysbarism V. Prevention of decompression sickness in mice by dimethothiazine. Aerosp Med. 1974;45:279–82. PMID: 4816549.
43 Popovic P, Popovic V, Honeycutt C. Levodopa and aspirin pretreatment beneficial in experimental decompression sickness. Proc Soc Exp Biol Med. 1982;169:140–3. PMID: 7063493.
44 Zhang K, Jiang Z, Ning X, Yu X, Xu J, Buzzacott P, et al. Endothelia-targeting protection by escin in decompression sickness rats. Sci Rep. 2017;7:41288. doi: 10.1038/srep41288. PMID: 28112272. PMCID: PMC5256092.
45 Blatteau JE, Barre S, Pascual A, Castagna O, Abraini JH, Risso JJ, et al. Protective effects of fluoxetine on decompression sickness in mice. PLoS One. 2012;7(11):e49069. doi: 10.1371/journal.pone.0049069. PMID: 23145072. PMCID: PMC3493517.
46 Lambrechts K, Pontier JM, Mazur A, Theron M, Buzzacott P, Wang Q, et al. Mechanism of action of antiplatelet drugs on decompression sickness in rats: a protective effect of anti-GPIIbIIIa therapy. J Appl Physiol (1985). 2015;118:1234–9. doi: 10.1152/japplphysiol.00125.2015. PMID: 25792711.
47 Ni XX, Cai ZY, Fan DF, Liu Y, Zhang RJ, Liu SL, et al. Protective effect of hydrogen-rich saline on decompression sickness in rats. Aviat Space Environ Med. 2011;82:604–9. PMID: 21702310.
48 Zhang K, Wang D, Xu J, Li R, Cai Z, Liu K, et al. Simvastatin decreases incidence of decompression sickness in rats. Undersea Hyperb Med. 2015;42:115–23. PMID: 26094286.
49 Little TM, Butler BD. Dibutyryl cAMP effects on thromboxane and leukotriene production in decompression-induced lung injury. Undersea Hyperb Med. 1997;24:185–91. PMID: 9308142.
50 Chryssanthou C, Teichner F, Antopol W. Studies on dysbarism IV. Production and prevention of decompression sickness in "non-susceptible" animals. Aerosp Med. 1971;42:864–7. PMID: 5098578.
51 Balldin U, Linér M. Preventive effect of a vasodilator on the occurrence of decompression sickness in rabbits. Aviat Space Environ Med. 1978;49:759–62. PMID: 656001.
52 Catron PW, Thomas LB, McDermott JJ, Holt MA, Harabin AL, Flynn ET. Failure of heparin, superoxide dismutase, and catalase to protect against decompression sickness. Undersea Biomed Res. 1987;14:319–30. PMID: 3629744.
53 Chryssanthou C, Rodrigues L, Branden P. Amelioration of decompression sickness by combined cyproheptadine-amphetamine treatment: In Bachrach AJ, Matzen MM, editors. Underwater physiology VII: Proceedings of the seventh symposium on underwater physiology. Kensington (MD): Undersea and Hyperbaric Medical Society; 1981. p. 753–63. Available from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.852.3366&rep=rep1&type=pdf. [cited 2018 March 19].
54 Vallee N, Lambrechts K, de Maistre S, Royal P, Mazella J, Borsotto M, et al. Fluoxetine protection in decompression sickness in mice is enhanced by blocking TREK-1 potassium channel with the "spadin" antidepressant. Front Physiol. 2016;7:42. doi: 10.3389/fphys.2016.00042. PMID: 26909044. PMCID: PMC4755105.
55 Campbell SD, Spencer MP. Pharmacologic agents in the prevention of decompression sickness. J Occup Med. 1969;11:252–6. PMID: 5772734.
56 Butler BD, Hills BA. The lung as a filter for microbubbles. J Appl Physiol Respir Environ Exerc Physiol. 1979;47:537–43. doi: 10.1152/jappl.1979.47.3.537. PMID: 533747.
57 O'Collins VE, Macleod MR, Donnan GA, Horky LL, van der Worp BH, Howells DW. 1,026 experimental treatments in acute stroke. Ann Neurol. 2006;59:467–77. doi: 10.1002/ana.20741. PMID: 16453316.
58 Ng A, Edmonds C. Immersion pulmonary oedema and Takotsubo cardiomyopathy. Diving Hyperb Med. 2015;45:255–7. PMID: 26687314.
59 Peacher DF, Martina SD, Otteni CE, Wester TE, Potter JF, Moon RE. Immersion pulmonary edema and comorbidities: case series and updated review. Med Sci Sports Exerc. 2015;47:1128–34. doi: 10.1249/MSS.0000000000000524. PMID: 25222821.
60 Smart DR, Sage M, Davis FM. Two fatal cases of immersion pulmonary oedema - using dive accident investigation to assist the forensic pathologist. Diving Hyperb Med. 2014;44:97–100. PMID: 24986728.
61 Schipke JD, Pelzer M. Effect of immersion, submersion, and scuba diving on heart rate variability. Br J Sports Med. 2001;35:174–80. doi: 10.1136/bjsm.35.3.174. PMID: 11375876. PMCID: PMC1724326.
62 Shykoff BE. Pulmonary effects of six-hour dives:in-water or dry chamber exposure to an oxygen-partial pressure of 1.6 atm. Technical Report NEDU 05-19. Panama City (FL): Navy Experimental Diving Unit; 2005. [cited 2018 March 19]. Available from: https://apps.dtic.mil/docs/citations/ADA443182.

Funding: nil

Conflicts of interest: Rob van Hulst is a member of the DHM Editorial Board but played no part in the peer review for this paper.

Submitted: 28 July 2018; final revision 10 April 2019
Accepted: 15 April 2019

Technical report

The Hyperbaric Protective Tube: A housing for a left ventricular assist device (LVAD) in a multiplace hyperbaric chamber

Jacek Kot[1,3], Piotr Siondalski[2], Ewa Lenkiewicz[3]

[1]*National Centre of Hyperbaric Medicine in Gdynia, Medical University of Gdansk, Gdynia, Poland*
[2]*Department of Cardiac Surgery, Medical University of Gdansk*
[3]*Department of Hyperbaric Medicine and Sea Rescue, University Centre for Maritime and Tropical Medicine, Gdynia, Poland*

Corresponding author: *Jacek Kot, National Centre of Hyperbaric Medicine in Gdynia, Medical University of Gdansk, Poland*
jkot@gumed.edu.pl

Key words
Hyperbaric oxygen therapy (HBOT); Medical devices; Safety; Risk factors; Case reports

Abstract
(Kot J, Siodalski P, Lenkiewicz E. The Hyperbaric Protective Tube: A housing for a left ventricular assist device (LVAD) in a multiplace hyperbaric chamber. Diving and Hyperbaric Medicine. 2019 June 30;49(2):137–140. doi: 10.28920/dhm49.2.137-140. PMID: 31177520.)

Introduction: During a hyperbaric oxygen therapy (HBOT) session, every medical device that is used within the hyperbaric chamber is exposed to several hazards, including an increased ambient pressure and partial pressure of oxygen. In Europe, all medical devices marketed and/or sold for use in hyperbaric conditions must be tested by the manufacturer and marked 'CE' if approved. At the moment, no left ventricular assist device (LVAD) has been formally approved and CE-marked for HBOT.

Case: A 65-year-old male was referred to our Hyperbaric Centre for HBOT due to a persistent life-threating soft tissue infection of the non-removable wire connecting the external controller with the pump implanted into the left ventricle of the heart (Heartware LVAD). The aim of the intervention reported here was to safely conduct HBOT sessions with this non-CE marked medical device. After risk analysis, the decision was made to isolate the external part of the LVAD (controller and batteries) from the ambient conditions in the hyperbaric chamber by placing it in a pressure-resistant housing that was vented to the external atmosphere. The housing, a 'Hyperbaric Protective Tube' was built and tested, and the resulting operating procedures were practiced by personnel involved in the patient's care. Thirty uneventful HBOT standard sessions were conducted with subsequent clinical improvement of the soft tissue infection, resulting in an extended timeframe for awaiting heart transplantation.

Conclusion: An isolation housing that vents into the dumping system of the hyperbaric chamber allows for the safe use of critical medical devices without prior testing for their compatibility with the hyperbaric environment.

Introduction

Due to environmental conditions, mainly pressure and oxygen content, the use of medical devices in a hyperbaric chamber creates a risk of potential injury to, or even death of the patient in the event of a related malfunction and/or fire in the confined space. The main hazard intrinsically present in every hyperbaric session is the increase of ambient pressure and pressure changes during compressions and decompressions. This hazard can create the risk of malfunction or physical damage to the device. For the most critical devices, the clinical consequences to the patient can be life-threating.

The increased partial pressure of oxygen, arising from the combined fractional amount of oxygen in the hyperbaric air and the absolute pressure within the chamber, introduces the risk of fire if there is overheating or sparking within the device. Even in air-filled chambers, there is a possibility of building local 'oxygen clouds' due to small, but prolonged leakage of oxygen from the breathing units. Paradoxically, the risk of an unnoticed local increase in oxygen fraction can occur more easily in modern large chambers due to the long distance between the leak site (usually the patient's mask) and the oxygen sensor that is usually installed close to the chamber's exhaust. A fire ignited in the oxygen-rich environment is a life-threating situation to all chamber occupants, as well as chamber operators and external bystanders. Detailed reviews of the hazards and risks of introducing medical devices into hyperbaric chambers can be found in other publications,[1,2] or in the descriptive annex of the European Norm for multiplace hyperbaric chambers.[3]

In Europe, all medical devices marketed and/or sold for use in hyperbaric conditions must be tested by the manufacturer and marked 'CE' if approved for specific conditions. At the

Figure 1
Deployment of the HeartWare LVAD (sourced from: https://www.heartware.com/resources)

moment, there are only a few hyperbaric-certified medical devices on the market, all of which are used for intensive care, including monitors, ventilators and electronic pumps and syringe drivers. There is no left ventricular assist device (LVAD) which has been formally approved for hyperbaric use and CE-marked for those conditions.

In case of the need to expose any non-CE marked medical devices to a hyperbaric environment, the medical user should perform the risk assessment him or herself and take full responsibility for any residual risk created by using such a device.[4]

Aim

A 65-year-old male patient was referred to our hyperbaric centre for hyperbaric oxygen treatment (HBOT) to treat a persistent soft tissue infection of the non-removable wire connecting the external controller of the LVAD (HeartWare Inc., Framingham, MA, USA) with the magnetic pump implanted into the left ventricle of the heart. The LVAD was implanted to enhance left ventricular function which was critically impaired by an ischaemic cardiomyopathy. The aim was to bridge the patient to heart transplantation. Regardless of the good clinical status of the patient, the local infection was classified as life-threatening, since there was no physical possibility of replacing the line without replacing the complete set of implanted parts. The aim of this study was to prove that the in-chamber use of encapsulated equipment would allow effective function of this medical device not approved for hyperbaric exposure.

Methods

The HeartWare LVAD consists of the implanted magnetic pump, connection cable and an external controller with a power supply comprised of two independent, high-power batteries (Figure 1).

The implanted portion was not considered a risk for the patient, as it does not have any gaseous closed spaces. On the contrary, the external controller with the power supply, which cannot be safely disconnected for testing or therapeutic purposes, was considered potentially dangerous.

An extensive literature review was done, and only single-case reports published on the use of LVADs in patients treated with HBOT were found.[5–8] In all those cases, the manufacturers were included in the risk analysis, the power supply was removed and stayed outside the chamber, and the controller was exposed to the hyperbaric environment (up to 2.5 atmospheres absolute (atm abs), 253 kPa pressure). In our case, there was no direct contact with the manufacturer, and we had no access to a spare LVAD in case of malfunction of the controller during tests.

Therefore, a formal risk analysis was conducted according to published guidelines.[9] Due to the lack of detailed technical information about the external controller and the batteries, the risk of exposing it to hyperbaric pressure was considered unacceptably high. Therefore, the decision was made to separate the external part of the LVAD from the ambient conditions in the hyperbaric chamber. This would be done by enclosing the LVAD controller with the power supply in a pressure-resistant housing, the Hyperbaric Protective Tube (HPT), which was vented to the external atmosphere to keep the internal pressure at 101.3 kPa (1.0 atm abs). The facility staff prepared a general assembly diagram (Figure 2) for the housing with the following main properties:

- capable of enclosing the external controller with batteries within the housing;
- allowing the connection cable to pass through the housing wall without any mechanical damage;
- allowing connection to the hyperbaric chamber dump system opened to the external environment to ensure the internal pressure is kept at the normobaric level (101.3 kPa), regardless of any leak into the housing around the connection cable;
- include a valve to control the inflow of ambient air into the housing to decrease internal temperature;
- capable of monitoring internal pressure in order to alert the user in case pressure builds up over 121.6 kPa arbitrarily considered the safety cut-off point for any electronic device);
- designed so that the weakest point of the housing should be able to withstand 709 kPa (equivalent to 60 metres' sea water (msw) depth and the working pressure should be at least 253 kPa (equivalent to 15 msw).

Figure 2

Construction of the LVAD housing. 1 – transparent acrylic tube; 2 – tube base; 3 – tube flange; 4 – removable lid; 5 – hard synthetic seal; 6 – eight wingnut fasteners (for practical purposes replaced by hand-screws); 7 – quick connector to the dumping system; 8 – valve for venting; R in the View 'W' – machined conduit in the housing cover for connection cable

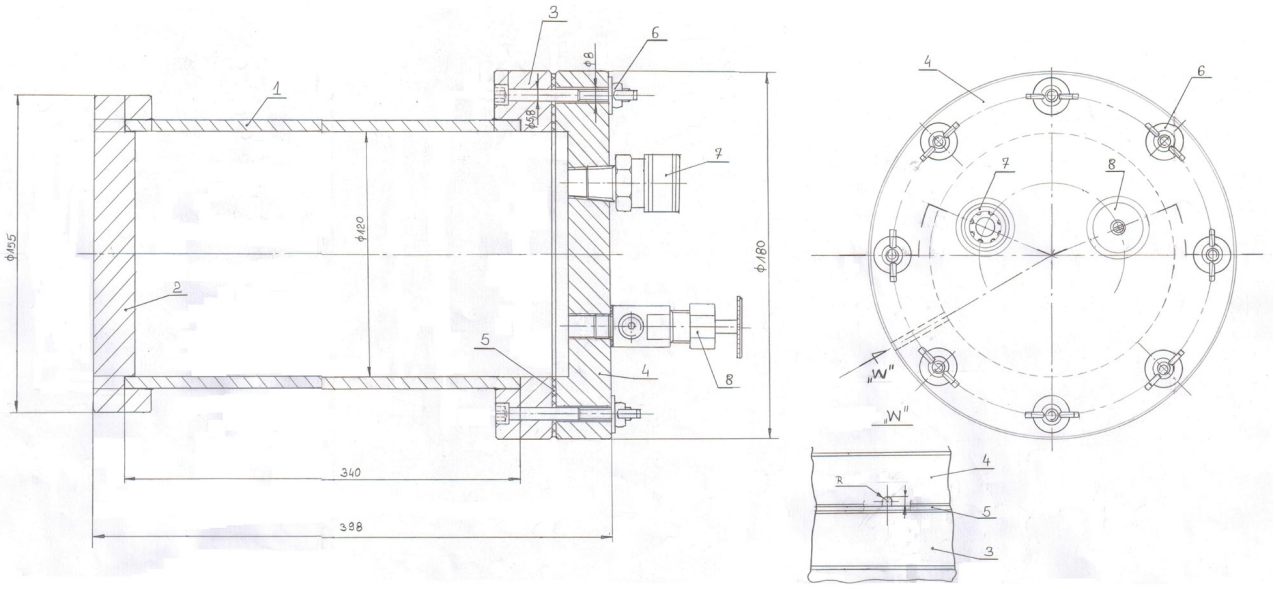


Figure 3

The housing with the enclosed HeartWare LVAD in the hyperbaric chamber. Inside there is the LVAD external controller with batteries and a diving computer showing only the date and time of exposure, which means that the internal pressure is in the normobaric range (1.0–1.2 atm abs). The other diving computer is located outside the housing confirming that the pressure inside hyperbaric chamber is 2.5 atm abs (14.9 msw on the display)

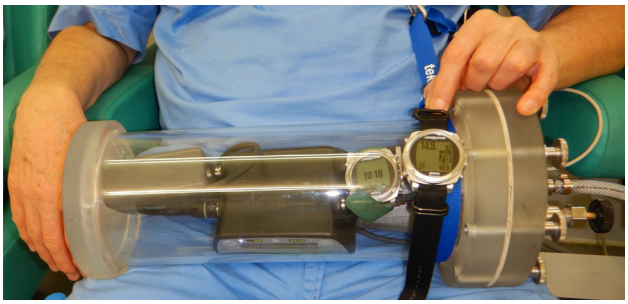
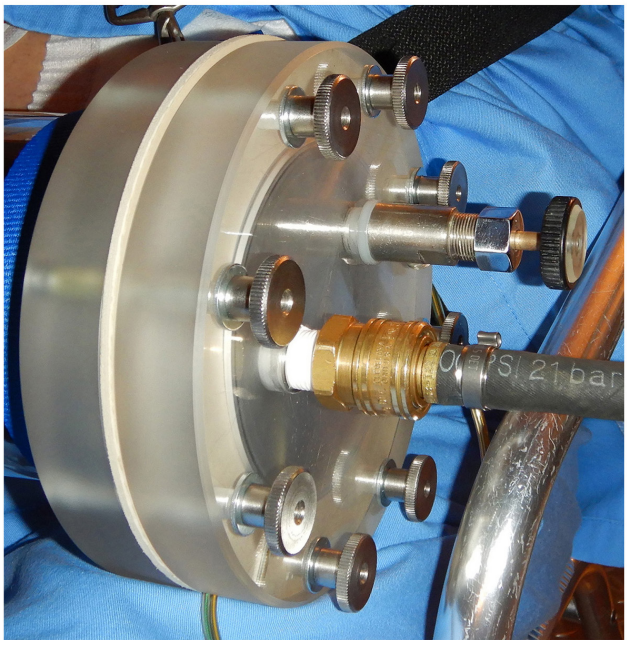


Figure 4

The housing lid. There are eight hand screws visible with a connector to the dumping system (black hose) and connection cable passing through the housing (at the lowest point)



An external commercial company manufactured the HPT from acrylic plastic according to the supplied drawings with internal dimensions that were capable of holding the HeartWare LVAD (cylindrical shape approximately 40 cm length and 12 cm diameter). Then, a full battery of tests was conducted internally by the hyperbaric facility staff, up to the test pressure of 6 atm abs (equivalent to 50 msw depth). A procedure for enclosing the LVAD in the housing unit in an uninterruptible manner without any disconnection was developed, and the staff were trained for standard and emergency situations. The patient was informed about the therapeutic plan and gave informed consent for the non-standard approach with unknown probability of critical failure.

Results

During each HBOT session, the LVAD controller with batteries and the diving computer used for monitoring the internal pressure were enclosed in the HPT (Figure 3), with staff double-checking that the connection cable was placed

in the machined conduit in the housing head to ensure there was no crushing. Eight screws were lightly tightened to avoid asymmetrical tension to the housing head (Figure 4).

The chamber was pressurized to 121 kPa, and the internal gauge (a diving computer) was checked to confirm that internal pressure was not increasing. The final check of the dumping system was done by opening the venting valve. The sound of air passing into the housing unit was heard with no indication of increasing internal pressure. Then, the venting valve was closed, and the chamber was pressurized to the treatment pressure (253 kPa). During proper operation at treatment pressure, the internal gauge in the HPT did not indicate any increase of pressure above atmospheric (1.0 atm abs) (see diving computers in Figure 3). Thirty uneventful standard HBOT sessions (100% oxygen for 70 minutes at 253 kPa, excluding compression and decompression) were conducted in an air-filled multiplace hyperbaric chamber with subsequent clinical improvement of the soft tissue infection. This facilitated an extended period to await heart transplantation.

Discussion

Where it is necessary to use a non-approved medical device in hyperbaric conditions exceeding those in the manufacturer's technical specification, there are several options available for the medical user, including: checking the resistance of a device to the external conditions (sealed medical devices, e.g., implantable devices); checking the compatibility of devices with specific hazards (e.g. syringe drivers/pumps, ventilators); and enclosing the device within an external case that is resistant to the in-chamber environment. In all cases, risk analysis and mitigation should be conducted by experienced personnel to keep the residual risks as low as possible. The process should be documented and approved by the facility or by hospital authorities. All problems should be discussed with the patient in detail to facilitate informed consent. Personnel must be informed and trained for both standard and emergency operating procedures.

Conclusions

Using the HPT, an external, not-perfectly-isolating housing unit with venting to the dumping system of the hyperbaric chamber allows the option of putting medical devices with unknown susceptibility to the environmental factors associated with HBOT into a pressurized environment.

After careful risk evaluation and training of personnel involved, such a housing allows for the safe use of critical medical devices, without prior testing for their compatibility with or exposure to the hyperbaric environment.

References

1 European Committee for Hyperbaric Medicine. European Code of Good Practice for Hyperbaric Oxygen Therapy. ECHM; 2004. [cited 2018 December 24]. Available from: http://www.echm.org/ECHM-Documents.htm.
2 Burman F. Risk Assessment guide for installation and operation of clinical hyperbaric facilities, 5th ed. San Antonio, TX: International ATMO; 2015.
3 CEN EN 14931. Pressure vessels for human occupancy (PVHO) - Multi-place pressure chamber systems for hyperbaric therapy - Performance, safety requirements and testing. 2006. [cited 2018 December 24]. Available for purchase from: https://www.en-standard.eu/din-en-14931.
4 Kot J, Houman R, Müller P. Hyperbaric chamber and equipment. In: Mathieu D, editor. Handbook on hyperbaric medicine. Dordrecht: Springer; 2006.
5 Churchill S, Weaver LK, Long JW, King CA. Left ventricular assist device performance in the monoplace hyperbaric chamber. Undersea Hyperb Med. 2004;31:323. Available from: http://archive.rubicon-foundation.org/xmlui/handle/123456789/1478. [cited 2018 December 24].
6 Goddard MK, Weaver LK, Churchill S, Bell J, Mason N. HeartMate II left ventricular assist device performance in a hyperbaric research chamber. Undersea Hyperb Med. 2010;37:353.
7 Snyder BK, Lathem EM, Duchnick JJ, Stahovich M, Dembitsky WP. Treatment of a patient with a left ventricular assist device (LVAD) with hyperbaric oxygen therapy. Undersea Hyperb Med. 2010;37:350.
8 Orwig D, Logue C, Hendriksen S, Westgard B, Walter J, Pullis M, et al. An approach to treating a patient with a HeartMate II left ventricular assist device in a multiplace hyperbaric chamber: a case report. Undersea Hyperb Med. 2018;45:89–93. PMID: 29571237.
9 Burman F, Sheffield R, Posey K. Decision process to assess medical equipment for hyperbaric use. Undersea Hyperb Med. 2009;36:137–44. PMID: 19462753.

Acknowledgments

We acknowledge Mr Ryszard Pisula, the Technical Director of the Department of Hyperbaric Medicine and Sea Rescue, University Centre for Maritime and Tropical Medicine, Gdynia, Poland for his involvement in design of the Hyperbaric Protective Tube and preparation of the technical drawings.

Funding sources: nil

Conflicts of interest: nil

Submitted: 05 January 2019
Accepted: 27 January 2019

Case report

Cerebral arterial gas embolism in a scuba diver with a primary lung bulla

Céline MJ Goffinet[1], Graham Simpson[1]

[1]*Department of Respiratory and Sleep Medicine, Cairns Hospital, Cairns, Queensland, Australia*

Corresponding author: *Céline MJ Goffinet, Department of Respiratory and Sleep Medicine, Cairns Hospital, PO Box 902, Cairns, Queensland 4870, Australia*
celine.m.goffinet@gmail.com

Key words
Pulmonary barotrauma; Recreational diving; Diving incidents; Case reports

Abstract

(Goffinet CMJ, Simpson G. Cerebral arterial gas embolism in a scuba diver with a primary lung bulla. Diving and Hyperbaric Medicine. 2019 June 30;49(2):141–144. doi: 10.28920/dhm49.2.141-144. PMID: 31177521.)
Primary lung bullae have been reported to cause pulmonary barotrauma and lead to cerebral arterial gas embolism (CAGE) in the context of diving; however, a lack of symptoms and often minimal radiographic findings often preclude a diagnosis of lung bullae prior to undertaking diving activity. We present the case of a healthy 27-year-old Caucasian male who presented following the second of two introductory resort dives with neurological symptoms attributable to CAGE. Investigations revealed a previously undiagnosed large primary lung bulla. This case highlights the clinical sequelae of primary lung bullae in the context of pulmonary barotrauma related to recreational diving activity.

Introduction

Primary lung bullae are air-filled, thin-walled spaces occurring within the lung in a patient free of airway obstruction or disease.[1] They are characteristically asymptomatic, and occur more frequently in patients with Marfan's syndrome and Ehlers-Danlos syndrome.[2,3] Bullous lung disease is an absolute contraindication to diving, however a lack of symptoms and often minimal radiographic findings often preclude a diagnosis of lung bullae prior to undertaking diving activity. We describe the case of a previously healthy 27-year-old Caucasian male who developed cerebral arterial gas embolism (CAGE) as a result of pulmonary barotrauma secondary to a previously undiagnosed primary lung bulla.

Case report

A 27-year-old Caucasian male tourist presented to the emergency department following an episode of transient neurological symptoms that developed after a dive ascent. His medical history was significant for a multinodular goitre requiring total thyroidectomy, inguinal hernia repair and testicular hydrocoele, with no history of respiratory disease. He was a non-smoker and had never had any chest imaging or lung function testing performed. This was his first dive experience and was a 'resort' dive with a reef company which did not require a dive medical to be performed. His first dive of the day was to 3–5 metres depth for 10 minutes, and was uneventful. His second dive occurred one hour later to 10 metres for 30 minutes, with a one-minute safety stop. He ascended slowly following the directions of the instructor, and there was no panic or breath holding. He began to feel dizzy on the last 1–2 metres of the ascent and began coughing one metre from the surface with a sensation of fullness of the chest. After reaching the surface he began to feel unwell, and on approaching the boat he was unable to lift himself unaided due to a left-sided hemiparesis involving his arm and leg. He also noted left-sided paraesthesiae and an expressive aphasia. He was helped into the boat and given high-flow oxygen, noticing an improvement in his symptoms within 10 minutes and complete resolution after 30 minutes.

His observations in the Emergency Department demonstrated an oxygen saturation of 98% on high-flow oxygen, blood pressure of 134/90 mmHg, heart rate of 77 beats per minute, and respiratory rate of 20 breaths per minute. Neurological examination was normal and cardiorespiratory examination was unremarkable. A chest X-ray was performed which revealed a large bulla in the right upper zone containing an air-fluid level (Figure 1). Computed tomography scanning of the chest confirmed the presence of a large thin-walled fluid-containing bulla in the right upper lobe with surrounding alveolar shadowing, likely representing pulmonary haemorrhage (Figure 2). There was also a smaller subpleural bulla in the left lower lobe (Figure 3). The diagnosis was of pulmonary barotrauma secondary to a primary lung bulla leading to CAGE. The patient was discussed with the

Figure 1
Chest radiograph of 27 year-old diver presenting with cerebral arterial gas embolism showing a large bulla in right upper zone containing an air-fluid level

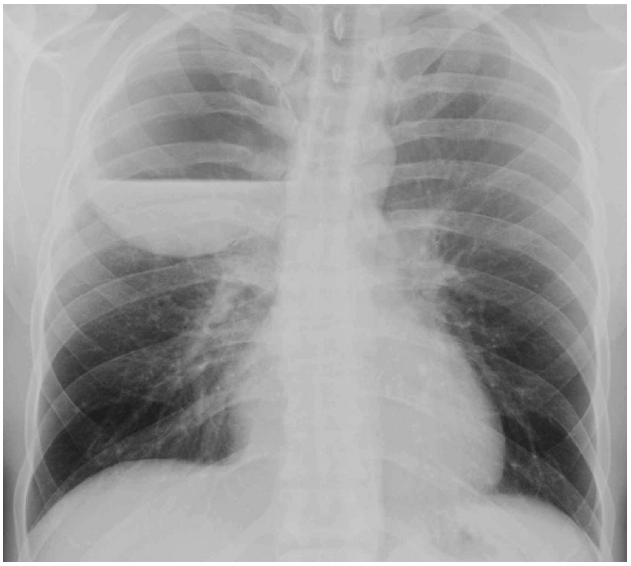


Figure 2
Computed tomography scan of the chest showing a large thin-walled fluid-containing bulla in the right upper lobe of a diver presenting with cerebral arterial gas embolism

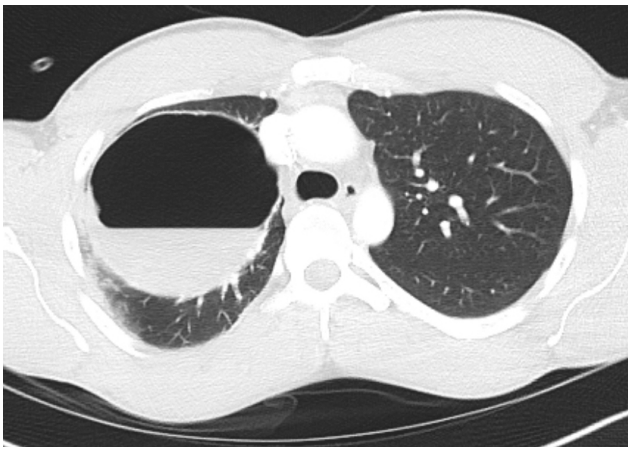
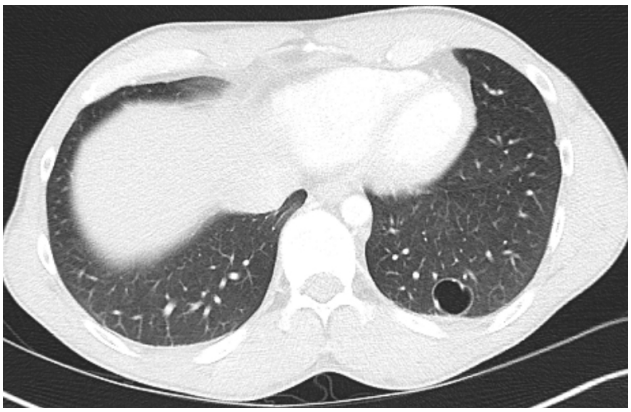


Figure 3
Computed tomography scan of the chest showing a smaller bulla in the left lower lobe of the same diver



nearest hyperbaric medicine unit, and recompression was not performed – partly because his symptoms had resolved, and partly due to concerns regarding possible further barotrauma on decompression. The patient fully recovered and returned home to be followed up in another centre. An MRI brain was performed several weeks later and was reportedly normal. He subsequently underwent a bullectomy. He was counselled never to dive again.

Discussion

Lung bullae are an absolute contraindication to diving. Since pressure is inversely related to volume (Boyle's Law), dangers arise when a poorly ventilated area of lung (such as that inside a primary lung bulla or cyst) takes up some gas during the time at depth, and is then subject to reduced pressure on ascent. If it is unable to be vented, possibly due to a one-way valve effect or intermittent plugging or obstruction, the gas that has accumulated within the bulla expands and may cause pulmonary barotrauma. The rate of change of pressure over the ascent will also affect the ability of the bulla to equilibrate the pressures. If the pulmonary parenchyma is damaged such that air enters the pulmonary vasculature, there may be systemic arterial gas embolism leading to stroke-like symptoms as bubbles reach the brain and/or myocardial ischaemia from coronary arterial air embolism.

It has been demonstrated previously that divers with pre-existing small lung cysts or bullae may be at risk of pulmonary barotrauma;[4] however as in our patient, owing to the frequent absence of chest imaging prior to the event, there is often uncertainty as to whether the bullae caused, or were the result of, the pulmonary barotrauma event. There are a few reports in the literature of pulmonary barotrauma related to primary lung bullae. A similar case to our patient has been described, wherein a 33-year-old, previously well female developed neurological symptoms attributable to CAGE shortly after ascending from an 18-metre dive, which was associated with a sensation of dyspnoea and pleuritic chest pain.[5] Subsequent investigations identified a giant emphysematous bulla in the left hemithorax. Her symptoms fully resolved, and recompression was not performed, as in our patient. Interestingly, the patient's previous chest imaging from five and three years prior was reviewed and demonstrated an area of hypertranslucency in the left lung, though the films were reported as normal at the time. This suggests that the bulla was indeed present prior to the dive.

In an interesting case series of three patients in whom a primary bulla was demonstrated radiographically, an increase in diameter of the bulla was attributed to diving activity, ultimately leading to a barotraumatic diving accident including CAGE.[6] Two of the cases demonstrated a marked increase in the size of the bulla immediately following the episode of CAGE when compared to previous imaging, which the authors supposed may have been a

consequence of the dive and contributory to the sequelae. Another series of three cases has been reported where unsuspected congenital lung bullae led to diving accidents without CAGE.[7] In two cases, the bullae ruptured causing spontaneous pneumothorax and in the third a tension bulla led to symptoms.

There are also case reports of pulmonary barotrauma and CAGE resulting from lung bullae during commercial air flight.[8–10] Our patient, in retrospect, recalled experiencing similar upper chest discomfort and dyspnoea four years previously following skydiving, which self-resolved after several minutes, as well as occasional upper chest discomfort during commercial air flights during the preceding several years. These symptoms were never investigated and were never associated with any neurological symptoms. That his respiratory symptoms developed most convincingly after skydiving, wherein he would have experienced a more sudden change in air pressure, is notable, and supports the notion that the bullae were pre-existing and not a consequence of the dive.

Thankfully the patient's symptoms resolved with supportive cares; however, this case raises the important question of whether recompression using hyperbaric oxygen treatment (HBOT) should be administered for persistent symptoms in cases of CAGE attributable to pulmonary barotrauma with underlying lung pathology. The dilemma is that while HBOT is the treatment of choice for CAGE,[11] it necessitates further recompression and, more importantly, decompression, which is the presumed mechanism of injury causing the pulmonary barotrauma in the first instance. There are two case reports of CAGE attributable to HBOT in the context of underlying lung pathology, such as bullous lung disease in a smoker[12] and diffuse interstitial pulmonary fibrosis with severe emphysema.[13] It is likely that recompression would have been offered to our patient if his neurological symptoms had persisted, on the basis that decompression from HBOT occurs at a much slower rate than the insult from the dive, and would therefore be less likely to cause further injury. The risks of recompression would, however, need to be openly and frankly discussed with the patient and/or next-of-kin, if possible, given the uncertainties.

This case also highlights the difficulties in screening an otherwise healthy population for underlying lung disease. Although our patient had experienced possible respiratory symptoms during previous flights and sky diving, he never underwent lung imaging and the screening medical questionnaire that he completed – the only form of assessment required for a leisure resort dive in Queensland – would not identify underlying bullous lung disease based on symptoms alone. Given the normal cardiorespiratory examination after the event, there is no certainty that a face-to-face diving medical would have identified the problem either. Further, as illustrated in several cases discussed above,[5,6] plain chest imaging is frequently inadequate for diagnosing primary lung bullae or cysts. The question of whether computed tomography of the chest should be incorporated into screening practices has been raised; however, this would unlikely be practical or cost effective.[14] Optimal screening practices for primary lung bullae is an area that warrants on-going study.

In summary, we have described the case of a healthy young male who developed CAGE secondary to pulmonary barotrauma owing to a previously undiagnosed primary lung bulla. This case highlights the need to maintain a degree of suspicion for pulmonary barotrauma in any patient who develops neurological symptoms following a dive.

References

1 Fraser RS, Muller NL, Colman NC, Paré PD, editors. Fraser and Paré's diagnosis of diseases of the chest, 4th ed. Philadelphia (PA): Saunders; 1999.

2 Wood JR, Bellamy D, Child AH, Citron KM. Pulmonary disease in patients with Marfan's syndrome. Thorax. 1984;39:780–4. PMID: 6495247. PMCID: PMC459918.

3 Ayers JG, Pope FM, Reudy JF, Clark TJ. Abnormalities of the lungs and thoracic cage in the Ehlers-Danlos syndrome. Thorax. 1985;40:300–5. doi: 10.1136/thx.40.4.300. PMID: 4023980. PMCID: PMC460052.

4 Tetzloff K, Reuter M, Leplow B, Heller M, Bettinghausen E. Risk factors for pulmonary barotrauma in divers. Chest. 1997;112:654–9. doi: 10.1378/chest.112.3.654. PMID: 9315797.

5 Mellem H, Emhjellen S, Horgen O. Pulmonary barotrauma and arterial gas embolism caused by an emphysematous bulla in a SCUBA diver. Aviat Space Environ Med. 1990;61:559–62. PMID: 2369396.

6 Germonpré P, Balestra C, Pieters T. Influence of scuba diving on asymptomatic isolated pulmonary bullae. Diving Hyperb Med. 2008;38:206–11. PMID: 22692754.

7 Simpson G. Primary lung bullae and SCUBA diving. SPUMS Journal. 1998;28:10–2.

8 Gudmundsdottir JF, Geirsson A, Hannesson P, Gudbjartsson T. Major ischaemic stroke caused by an air embolism from a ruptured giant pulmonary bulla. BMJ Case Rep. 2015;2015:bcr2014208159. doi: 10.1136/bcr-2014-208159. PMID: 25743863. PMCID: PMC4369024.

9 Farshchi Zarabi S, Parotto M, Katznelson R, Downar J. Massive ischemic stroke due to pulmonary barotrauma and cerebral artery air embolism during commercial air travel. Am J Case Rep. 2017;18:660–4. doi: 10.12659/AJCR.903354. PMID: 28607332. PMCID: PMC5478217.

10 Yeung JT, Ma JK, Mak YK, Lam VS. Fatal cerebral air embolism related to an air flight. Hong Kong Med J. 2013;19:352–3. doi: 10.12809/hkmj133898. PMID: 23918512.

11 Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. Diving Hyperb Med. 2017;47:24–32. doi: 10.28920/dhm47.1.24-32. PMID: 28357821. PMCID: PMC6147240.

12 Rivalland G, Mitchell SJ, van Schalkwyk JM. Pulmonary barotrauma and cerebral arterial gas embolism during hyperbaric oxygen therapy. Aviat Space Environ Med. 2010;81:888–90. doi: 10.3357/ASEM.2783.2010. PMID: 20824998.

13 Wolf HK, Moon RE, Mitchell PR, Burger PC. Barotrauma and air embolism in hyperbaric oxygen therapy. Am J Forensic

Med Pathol. 1990;11:149–53. PMID: 2343842.
14 Toklu AS, Kiyan E, Aktas S, Cimsit M. Should computed chest tomography be recommended in the medical certification of professional divers? A report of three cases with pulmonary air cysts. Occup Environ Med. 2003;60:606–8. doi: 10.1136/oem.60.8.606. PMID: 12883024. PMCID: PMC1740603.

Acknowledgement

We wish to thank the patient for giving formal written consent for his case to be reported.

Funding and conflicts of interest: nil

Submitted: 06 September 2018; final revision 14 February 2019
Accepted: 16 March 2019

Dr John Knight FANZCA, Dip DHM, Captain RANR

John Knight *was* the South Pacific Underwater Medicine Society. Having joined the Society in 1972, he went on to fill the roles at various times of Committee Member, Secretary, President, Public Officer (the predecessor of the Education Officer), Assistant Editor of the SPUMS Journal (Doug Walker as Editor) 1985–89, and then Editor of the Journal from 1990 to 2002. He was elected a Life Member of SPUMS in recognition of his enormous contributions. Our Journal would not exist today if not for John's efforts.

John passed away on 09 May, aged 89. A full obituary will appear in the September issue of *Diving and Hyperbaric Medicine*.

A Celebration of John's life will be held on Friday 7 June 2019 at 1.30 pm in the Newcomb Library Meeting Room, Geelong. RSVP to liz@legalpm.com.au

Notices and news

SPUMS society information and news is to be found mainly on the society website: www.spums.org.au

SPUMS Presidents message
David Smart

Over the past three years, SPUMS has undergone a transition which has been unprecedented in our history. Our banking processes have been overhauled and we have moved from St George to ANZ. Our website has been overhauled and rebuilt, to permit greater functionality (particularly with financial transactions) and security. The DHM website has also been overhauled and set up to permit general access to the non-embargoed editions, and member access to each new edition as it is produced. Our relationship with our EUBS colleagues has continued to flourish.

As per SPUMS purposes and rules, we have continued to provide high quality Scientific Meetings every year. This year's meeting with the theme 'Old divers, bold divers but no old bold divers'. Cardiovascular health risk assessment and diving" with keynote speaker Assoc. Prof. Nigel Stuart Jepson, promises to be a terrific update in the field. I offer my huge thanks to Cathy Meehan for organising this meeting, and also the support of Simon Mallender and Deborah Dickson-Smith from Diveplanit for the travel/ accommodation and organisational support. By the time of publication of this report, the meeting will have been completed.

Thanks to great work by SPUMS Treasurers' Peter Smith and Sarah Lockley over the last five years, our financial reporting fully meets modern accounting standards. I am particularly grateful to Sarah's husband Cal, who has voluntarily set up SPUMS and DHM finances on a professional accounting platform. Despite all of the above improvements and consolidation in processes, running of SPUMS still requires considerable volunteer input from all ExCom members. Without the continued volunteer input, SPUMS will cease to exist.

This AGM marks a transition point for SPUMS. Two positions are up for election. Nominations for the President Elect position have been called, and by the time of publication of this issue of DHM, the AGM will be complete and the position filled. The President Elect is for a period of 12 months, prior to assuming the role of SPUMS President for three years from 2020. This permits a smooth handover of the strategic leadership of SPUMS from one President to the next.

In addition to the President elect position, nominations for the Treasurer's position have been called. Sarah Lockley has stepped down from this role due to personal reasons. Her departure necessitates a mid-term election to be held. This is a key position for SPUMS and also for the ongoing viability of DHM. The work of the SPUMS Treasurer is highly valued, continuous but often not fully appreciated or understood by SPUMS or EUBS members. I am hopeful that we will have a member step up to the plate to take on this important role. I am personally of the opinion that we are at a pivotal point whereby SPUMS will need to transition obtaining professional support to run its finances, and the possibility of providing an honorarium to the treasurer (or book-keeper support) needs to be considered. The concept has been forwarded to EUBS for consideration, particularly in relation to the role of managing DHM finances and budget preparation.

I have stated my intention to resign as SPUMS President in 2020 when the next general election occurs. At that point I will have completed 17 years on SPUMS ExCom, six years as President. I will still be on ExCom after 2020, as the Immediate Past President. It is time for our members to step up to the plate and volunteer, so that SPUMS can continue its leadership role into the future.

Key words
Medical society; General interest

ANZHMG Report

The annual two week ANZHMG Introductory Course in Diving and Hyperbaric Medicine was held at the Esplanade Hotel in Fremantle and Fiona Stanley Hospital from 18 February to 01 March 2019 with 27 participants from Australia, New Zealand and overseas. The Unsworth Prize winner as dux of the course was Dr John Laughlin from Tasmania. Many thanks to Dr Ian Gawthrope, Course Convenor and to all the course faculty for their enthusiasm and commitment.

The next course is tentatively planned for 24 February – 06 March 2020.

The next meeting of the ANZHMG will be on Thursday 15 August 2019 at the Novotel Hotel Darling Harbour, Sydney at the beginning of the HTNA conference – all doctors working in diving and hyperbaric medicine in Australasia are welcome.

Dr Neil Banham, Chair ANZHMG

SPUMS 49th Annual Scientific Meeting

Diving Medical Support: Off the Beaten Track
19–24 April 2020

Venue: Oceans Resort, Tutukaka, New Zealand

The scientific programme for 2020 is coming together and looking good - "*Diving medical support: off the beaten track*", featuring our very own Richard Harris as Keynote Speaker. Add to that some of the best subtropical diving on the planet at the Poor Knights Islands Marine Reserve and this is an event not to be missed!

Conference website for more information and registration is here:
www.spums2020.nz

See you in Tutukaka in April 2020.

Guest Speaker: Richard Harris, Adelaide
Convenor: Greg van der Hulst
Scientific Convenors: Hanna van Waart and Xavier Vrijdag

Divers Emergency Service/DAN Asia Pacific Foundation Telemedicine Scholarship 2019

It is with great pleasure we announce that the winner of the 2019 Telemedicine Scholarship is Peter Watson. The award of AUD4,000 will support his attendance at the SPUMS ASM in the Solomon Islands in May.

The Divers Emergency Service (DES) telephone provides 24-hour advice for diving and underwater emergencies. Recognising that most doctors have no training in diving medicine, the volunteers providing this service have specific training and work in diving and hyperbaric facilities around Australia. This service has been in operation since 1986 and is supported by DAN.

Enquiries to:
david.wilkinson@sa.gov.au

The SPUMS website is at
www.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 http://www.anzca.edu.au/training/diving-and-hyperbaric-medicine.

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 2019

Viva voce TBC

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 enquries should be submitted to dhm@anzca.edu.au.

SPUMS Facebook page

Remember to 'like' us at:
http://www.facebook.com/pages/SPUMS-South-Pacific-Underwater-Medicine-Society/221855494509119

Royal Australian Navy Medical Officers' Underwater Medicine Course 2019

Dates: 14–25 October
Venue: HMAS Penguin, Sydney

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

Cost: AUD1,355 without accommodation
(tbc with accommodation and meals at HMAS Penguin)
For information and application forms contact:
Raj 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
E-mail: 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 to authors' available on the SPUMS website www.spums.org.au or at 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 January 2016, the SPUMS Academic Board consists of:

Dr David Wilkinson, Education Officer, Adelaide;
Professor Simon Mitchell, Auckand;
Dr Denise Blake, Townsville.

All enquiries and applications should be addressed to:
David Wilkinson
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 is now to be found mainly on the society's website: www.eubs.org

EUBS 45th Annual Scientific Meeting 2019

Dates: 09–12 September 2019
Venue: David Intercontinental Hotel, Tel Aviv, Israel

Main theme
Hyperbaric medicine and the brain

Emerging indications related to hyperbaric oxygen and the brain will be covered in depth by the world's leading investigators. In addition, new physiological data related to the effect of hyperbaric oxygen on sports performance and mitochondrial function will be presented. The preliminary programme is now online on the EUBS 2019 website, including all information on pre- and post-conference workshops and social events.

The conference will be jointly organised with the International Conference on Hyperbaric Oxygen and the Brain. The conference will be hosted by the Israeli Society for Hyperbaric and Diving Medicine.

This period has been chosen as it is after the summer break but just before the high holidays in Israel. Tel Aviv is an exciting hypermodern coastal city, with top-notch medical research and treatment facilities, but also bustling with beaches, restaurants and nightlife. Also, favourable airfares are dependent on early booking and hotel accommodation tends to be in high demand. Those who remember previous EUBS meetings organised in Israel will need no more motivation to attend! A number of pre- and post-conference diving workshops and other social events are available – create your own congress week tailored to your wishes and desires.

Please submit your abstract too, as your input is an important part of the success of our annual meeting.

There is still time to apply for a Student Travel Grants and other awards. You can find information on the conditions and application process on https://eubs2019.com/eubs-awards/.
You can find all the information regarding the conference on the website www.eubs2019.com, or by visiting the EUBS website www.eubs.org.

EUBS Elections – Member at Large

Around the time of publication of this issue of DHM, the election process for the 2019 ExCom members (Member-at-Large) of EUBS will have started.

Member-at-Large: we will be saying goodbye to Dr Med. Bengusu Mirasoglu as Member-at-Large 2016. ExCom extends their thanks to Bengu for the work she did within the ExCom, and we hope we will be able to continue counting on her support and help.

Candidates for the position of Member-at-Large 2019 will be available on the EUBS website with a picture and short CV, and you will receive soon, by email, an internet ballot where you can cast your vote. If you have not received such an email by the end of June, please notify us at secretary@eubs.org, and we will work with you to find out the reasons why. As the system works via email, it is possible for the message to end up in your spam folder. There may be other reasons but usually we are able to solve them.

EUBS Website

As always, please visit the EUBS website www.eubs.org for the latest news and updates. You will find information on planned and recruiting clinical trials, job offers and EUBS-endorsed documents and statements (all this under the menu item 'Activities').

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 to the Society. You can find their names, logo's and contact information on the Corporate Members page under menu item 'The Society'.

EUBS President's message

Ole Hyldegaard

EUBS ANNUAL SCIENTIFIC MEETING 2019

While I write these words, the annual EUBS scientific meeting is in its final preparation by our colleagues in Tel Aviv. Research made over recent years has put hyperbaric oxygen therapy and its possible effects on the brain for different disorders high on the agenda. Reports from Israel in particular, as well as the USA and others require that the clinical communities working with hyperbaric oxygen therapy invest more time and resources into the research of this field. A comprehensive program on pulmonary and CNS oxygen toxicity and exposure limits in both diving and clinical HBO – generously supported by the US Office of Naval Research – is also scheduled.

The organizers are to be complimented on putting together a very interesting program, with highlights including:

- World expert panel on traumatic brain injuries and post traumatic brain disorders, with focus on pathophysiology and the potential use of HBOT.
- World expert presentation and discussions on pulmonary and CNS oxygen toxicity and exposure limits in diving and hyperbaric medicine.
- Prospective clinical data on the physiological effects of HBOT on the healthy adult population, addressing pharmacodynamics effects of HBOT on the immune system, angio- and neurogenesis as well as HBOT effects on mitochondrial function and exercise capacity in athletes.
- A presentation of the challenging Tham Luang Cave Rescue mission in Thailand by Captain Natthasak Woracharonesri MD, will be part of the keynote lectures.

In addition, many interesting abstracts and scientific reports will be presented. I look forward to seeing you all at the Tel Aviv EUBS Scientific Meeting 2019.

Key words
Medical society; General interest

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

EUBS 46th Annual Scientific Meeting 2020

Preliminary Announcement

Dates: 16–19 September 2020
Venue: Prague, Czech Republic

Chairman of the Organising Committee and Secretary General of the Meeting: Michal Hajek, long-time member of EUBS and member of the Executive Board of ECHM.

Multiple collaborators include; the Czech Society of Hyperbaric and Aviation Medicine, the City Hospital of Ostrava and other academic institutions. Hyperbaric medicine has a long tradition in the Czech Republic – in 2020 it will be 55 years since this field of medicine was established in this country. Prague is the capital and largest city in theCzech Republic, with a long, rich history as a political, cultural and economic centre of central Europe.

More details will appear after the ASM in Tel Aviv.
Put the dates in your calendar now!

Hyperbaric oxygen lectures

Welcome to: http://www.hyperbaricoxygen.se/
This site offers publications and high-quality lectures from leading investigators in hyperbaric medicine. Please register to obtain a password via email. Once registered, watch online, or download to your smart device or computer for later viewing.
For information contact: folke.lind@gmail.se

German Society for Diving and Hyperbaric Medicine (GTÜM)

An overview of basic and refresher courses in diving and hyperbaric medicine, accredited by GTÜM according to EDTC/ECHM curricula, can be found on the website:
http://www.gtuem.org/212/Kurse_/_Termine/Kurse.html

The EUBS website is at <www.eubs.org>

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.

Scott Haldane Foundation

As an institute dedicated to education in diving medicine, the Scott Haldane Foundation has organized more than 250 courses all over the world over the past 22 years. SHF is targeting more and more on an international audience with courses world wide. Below are the upcoming SHF-courses in 2019.

The courses Medical Examiner of Diver (part I and II) 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).

SHF Course Calendar 2019
05 0ctober: Refresher course 'Organization diving medical', NL
09–16 November: Medical Examiner of Divers part 1 Nosy be, Madagascar
16–23 November: 27th SHF In-depth course diving medicine (2d), Nosy be, Madagascar
23–30 Novembe: 27th SHF In-depth course diving medicine (2d), Nosy be, Madagascar
On request: Internship HBOT (level 2d certification), NL/Belgium

The course calendar will be supplemented regularly.
For the latest information: www.scotthaldane.org

Capita Selecta Diving Medicine

The Capita Selecta Diving Medicine of the University of Amsterdam annually offers symposia presented by speakers of international renown to a multinational audience of diving physicians, paramedics and highly educated instructors. The level of the presentations is 'advanced' (1 and 2d of the European standard) and often beyond that. The lectures are in English.

Saturday 30 November 2019
Physiology and medicine of the metabolic and inert gases in diving

Topics include: O_2, CO_2, CO, He, N_2, Nitrox, He-mixtures, saturation, diagnosis, intoxications, HPNS, treatment.
Speakers include: Jean-Claude Le Péchon (FR) and Mattijn Buwalda (NL)

www.capitaselectaduikgeneeskunde.nl.
Info: n.a.schellart@amc.uva.nl

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

EUBS and SPUMS members are able to access the German Society's large database of publications in diving and hyperbaric medicine. EUBS members have had this access for many years. SPUMS members should log onto the SPUMS website, click on 'Resources' then on 'GTÜM database' in the pull-down menu. In the new window, click on the link provided and enter the user name and password listed on the page that appears in order to access the database.

Advertising in *Diving and Hyperbaric Medicine*

Companies and organisations within the diving, hyperbaric medicine and wound-care communities wishing to advertise their goods and services in *Diving and Hyperbaric Medicine* are welcome. The advertising policy of the parent societies appears on the journal website: www.dhmjournal.com

Details of advertising rates and formatting requirements are available on request from:
Email: editorialassist@dhmjournal.com

Copyright

DIVING HISTORICAL SOCIETY AUSTRALIA, SE ASIA

P O Box 347, Dingley Village
Victoria, 3172, Australia
Email: hdsaustraliapacific@hotmail.com.au
Website: www.classicdiver.org

20th International Congress on Hyperbaric Medicine 2020

Dates: 13–16 September 2020
Venue: Rio de Janeiro, Brazil
For preliminary information contact:
Dr Mariza D'Agostino Dias
Email: mariza@hiperbarico.com.br

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, members of the diving and hyperbaric industries, and divers. Manuscripts must be offered exclusively to *Diving and Hyperbaric Medicine*, unless clearly authenticated copyright exemption accompanies the manuscript. All manuscripts will be subject to peer review. Accepted contributions will also be subject to editing.

Address: The Editor, Department of Anaesthesiology, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand
Email: editor@dhmjournal.com
Mobile: +64-(0)27-4141-212
European Editor: euroeditor@dhmjournal.com
Editorial Assistant: editorialassist@dhmjournal.com
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 word count); structure of the article and abstract is at the author(s)' discretion.

Case reports, Short communications, Work in progress reports, etc: 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 and historical articles, Commentaries, Consensus and other meeting reports, etc., 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 requirements set out in the full instructions on the DHM website. Non-compliant manuscripts will be suspended whilst the authors correct their submission. Guidance on the general 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 2018
- DHM Mandatory Submission Form 2018
- 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)
+61-3-7018 3076 (International)

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

JAPAN – DAN
+81-3-3812-4999 (Japan)

EUROPE – DAN
+39-6-4211-8685 (24-hour hotline)

UNITED KINGDOM
+44-7740-251-635

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

USA – DAN
+1-919-684-9111

The DES numbers (except UK) are generously supported by DAN

Scholarships for Diving Medical Training for Doctors

The Australasian Diving Safety Foundation (ADSF) are proud to offer four 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 program. These scholarships are mainly available to doctors who reside in Australia. However, some 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 AUD3,000.

Interested persons should complete the Application Form at:
https://adsf.org.au/grants/scholarships/diving-medical-training and send it by email to johnl@adsf.org.au.

DISCLAIMER

Opinions expressed in this publication are given in good faith and in all cases represent the views of the authors and are not necessarily representative of the policies or views of SPUMS, EUBS or the Editor and Editorial Board.