

Diving and Hyperbaric Medicine

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

SPUMS

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EUBS



Intensive care in the hyperbaric chamber

Recognising hypercapnia in a rebreather is difficult

Dark chocolate before diving may be good for you

Some divers 'bubble' when flying after diving

Divers with a history of DCS are more likely to 'bubble'

HBOT increases insulin sensitivity in obese males

PURPOSES OF THE SOCIETIES

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

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Editorial

Hyperbaric oxygen treatment for the critically ill patient

Lindell K Weaver

There are pros and cons with both the monoplace and multiplace chambers as used in intubated, critically ill patients.¹ In the multiplace chamber, staffing is a potential limitation because very few centres have sufficient numbers of intensive care unit (ICU) personnel and clinicians available 24/7, especially when offering HBO₂ twice per day or more than one critically ill patient per day.² The staffing demands for the treatment of critically ill patients in a monoplace chamber are less burdensome since inside attendants are not required. In addition, the staff in multiplace chambers incur a decompression risk, especially when exposed to the high pressures often used to treat critically ill patients, often up to 304 kPa. When multiplace chambers are operated at increased altitude, such as that in Salt Lake City, the decompression risk for inside attendants can be unacceptably high, but may be lessened by the attendant breathing supplemental oxygen, which may also have adverse consequences if done repetitively over many years.

Clearly a relatively smooth transition from the ICU to the hyperbaric centre can be accomplished by using multiplace chambers if the same IV pumps and ventilators (including modern-day ventilator modes) are used in the chamber as in the ICU.³ For monoplace chamber treatment of critically ill patients, their IVs must be changed to accommodate the IV pass-through and IV pump, which may be different to that of the ICU (and with different tubing), and ventilator support is much more challenging than what is possible in the multiplace chamber. Unfortunately, monoplace chamber ventilators are very limited in performance and features. These limitations often require the patient to be deeply sedated for HBO₂ and sometimes pharmacologically paralyzed, which can be independently risky. Nevertheless, with a skilled staff and specialized equipment, monoplace chamber use for very ill patients can be accomplished without evidence that adverse events are any greater than if

treated in multiplace chambers.

The bottom line is, if the critical care centre is fully committed to HBO₂ for critically ill patients, sufficient staff must be trained in HBO₂ and critical care, the chamber must be in close proximity to the ICU, equipment must work seamlessly with that in the ICU and there must be sufficient clinical workload to maintain staff skills. If these criteria are not satisfied, then monoplace chamber use for critically ill patients is a reasonable alternative, but close proximity to the ICU (or preferably inside the ICU) and a skilled staff fully aware of pitfalls and issues unique to HBO₂ are very important. Certainly the financial cost of implementing monoplace chambers for critically ill patients is a factor worthy of consideration too, since they are less expensive than fully equipped multiplace chambers. The ECHM position paper summarises all these various issues.⁴

References

- 1 Lind F. A pro/con review comparing the use of mono- and multiplace hyperbaric chambers for critical care. *Diving Hyperb Med.* 2015;45:56-60.
- 2 Kot J. Staffing and training issues in critical care hyperbaric medicine. *Diving Hyperb Med.* 2015;45:47-50.
- 3 Millar IL. Hyperbaric intensive care technology and equipment. *Diving Hyperb Med.* 2015;45:50-6.
- 4 Mathieu D. Hyperbaric oxygen therapy for intensive care patients: position statement by the European Committee for Hyperbaric Medicine. *Diving Hyperb Med.* 2015;45:42-6.

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Key words

Hyperbaric oxygen, hyperbaric medicine, intensive care medicine, editorials

The Editor's offering

This issue marks two important changes for *Diving and Hyperbaric Medicine* (DHM). The handling of submissions and their peer review has become increasingly challenging as the workload has grown (the number of papers submitted to DHM has nearly tripled in the past decade) and has resulted in mistakes and delays that are frustrating for all of us. Both Nicky McNeish and I work part-time to produce DHM from home offices; there is only so much we can do in that time and with the limited budget from subscriptions. Publishing costs have steadily increased, but the ExComs have worked hard to minimise the financial impact of this on members.

Over the years, a variety of changes have been made to improve efficiency of the office and the governance of the journal. As of the beginning of January, DHM has moved to a web-based platform called Manuscript Manager (MM) (<http://www.manuscriptmanager.com>) for submissions and peer review. In future, all submissions must be submitted on line through our new portal <<http://www.manuscriptmanager.com/dhm>>. E-mail submissions will no longer be accepted though we are still dealing with submissions from 2014 and before in the old manner. We recommend that everyone looks at the instructional videos on the MM website to see how the office will function and, especially, authors should watch video 5 and reviewers video 9. This software package can be tailored to the specific requirements of a journal and we are

still in the learning phase of how best to meet DHM's needs. The active participation of authors and reviewers in this process is welcomed. However, please do not cry "wolf" too often, try to solve the problem yourself before contacting us at <editorialassist@dhmjournal.com>; we all have the same goal – to create an interesting, diverse and readable journal.

The second important change is in the governance of the journal. Although communications between the two society executives has improved with time, there remain some frustrations both in my dealings with them as Editor and between the two organisations. As a result, a Journal Governance Group has been established to advise on publishing and financial matters and to create a vision for the future. The members are Peter Müller, former European Editor of DHM, Joerg Schmutz, former EUBS Secretary, the SPUMS Treasurer (currently Peter Smith), who manages the day-to-day finances of the Journal, and John Lippmann, DAN Asia Pacific Research Director, who has a long experience in the diving and medical publishing industry.

With Peter Müller's recent resignation as European Editor, it is with considerable regret that I also have to advise of Costantino Balestra's resignation from the Editorial Board. Peter and Tino will be greatly missed, but I am confident that we will find other doctors and scientists out there who will fill their shoes with honour.

This issue will suit chocoholic divers if the findings by Sigrid Theunissen et al are confirmed.¹ I know many divers who enjoy chocolate after a dive; now we have an excuse to eat it for breakfast too, before going diving!

Reference

- 1 Theunissen S, Balestra C, Boutros A, De Bels D, Guerrero F, Germonpré P. The effect of pre-dive ingestion of dark chocolate on endothelial function after a scuba dive. *Diving and Hyperbaric Medicine*. 2015 March;45(1):4-9.

Michael Davis

The Presidents' pages

David Smart, President SPUMS

I am pleased to report that SPUMS' new *Purposes and Rules* were accepted at the special general meeting 01 November 2014, and have now been submitted to Consumer Affairs Victoria for ratification. Our submission has been accepted and no further modifications will be required. The final copy is available on the SPUMS website. I extend a big thank you to all members who took the time to forward proxies to committee members, so that we could comply with our regulations with the voting. The SGM minutes are also posted on the website.

Over the past year, and especially the past three months, there has been lots of work done behind the scenes to migrate the SPUMS website to a new host server. Whilst there have been minor hiccups, this has generally gone without serious problems. I offer my thanks to Nicky McNeish and Joel Hissink for their continued great work. The functionality and capability of the website will be progressively improved to meet members' needs.

In this report I would like to touch upon and thank our volunteers. Our organisation is run by volunteers and I feel deeply indebted to everyone who contributes. Our executive committee undertakes a huge amount of background work to keep the society operational. The work undertaken by the SPUMS executive has increased over recent years due to modern compliance standards. Our conference convenors and ASM committees also volunteer their services to organise each year's annual scientific meeting – the quality of the scientific meeting has continued to go from strength to strength, and it was pleasing to see the large numbers

of members attending last year's meeting in Bali. We look forward to this year's ASM in Palau, organised by Cathy Meehan. The theme is *diabetes and diving*, with Neal Pollock as the keynote speaker. I would encourage as many members as possible to attend. Details are on our website. I would also encourage members to become involved in committee processes, and contribute as a volunteer. Further committee member places will be up for election this year at the AGM. Please volunteer your services to our organisation.

In addition to SPUMS as an organisation, we also have members volunteering on the Academic Board of SPUMS, with journal governance, on the Editorial Board of DHM and acting as scientific reviewers. The last three include our colleagues from EUBS, to whom we are very grateful. We also have volunteer members who join external committees such as Australian Standards, provide input to community organisations, or community ventures, provide teaching and contribute to statutory SPUMS committees such as the Australian and New Zealand Hyperbaric Medicine Group. I am sure I will have missed someone somewhere who has been assisting as a SPUMS volunteer. If I have, I apologise and offer my thanks to you for your contribution!

From time to time, SPUMS has received criticism of its strategic direction, or that certain groups are not represented in the activities we undertake. We are always grateful to receive constructive criticism and helpful suggestions/comments from our membership. All the Committee are contactable via e-mail addresses on the website, and we welcome your input/feedback. We need volunteers to assist

in the running of the Society, and who might roll their sleeves up to implement helpful suggestions for improvement. SPUMS is an open, inclusive organisation and it is our aim to provide services which are of benefit to all of our members. If you believe we are not representing your craft group or practice needs, or have ideas for change and improvement, please let us know. Better still, volunteer, please!

Key words

Medical society, general interest

Tino Balestra, President EUBS

Increasing membership of EUBS?

For a European scientific society, increasing membership nowadays is a challenging task. We have to keep in mind that almost every country in Europe has its own baromedical, hyperbaric or diving scientific society. Those who are already a member of these 'national' societies may not see a benefit to becoming a member of a 'supranational', European society in the same field. There may be linguistic difficulties, as not every European speaks English fluently; not to mention the currency differences, since not all countries have adopted the Euro. Nevertheless, in practice we often see that those differences are really not barriers at all – one only has to look at the attendees of EUBS meetings, in the meeting rooms, at the annual banquets and social events!

For a number of years we have seen a slight but steady increase in our membership numbers. A policy of 'group affiliation' has been proposed and, in some countries, the national baromedical societies have already applied this simple system: if a national society renews or joins up as a group of more than 15 members, the membership fee receives a 5% reduction. If the number of members reaches 25, the reduction goes up to 10%.

Surprisingly, only a few countries are using this group affiliation, despite it working well. Why not more? Perhaps it is time for a reminder, even though the concept is thoroughly explained on the EUBS Website and repeated during the General Assembly. Let this serve as a simple reminder to all national society administrators that this option exists.

Another big change for our Society is that we decided at last year's General Assembly to set the membership renewal date to 01 January each year. In fact, this means that any membership fee paid from September 2014 onwards will be valid for up to 16 months. For our loyal members this is a very good deal indeed! From 2016 on, we will have to increase our membership fee slightly (it has not changed since 2007), but this increase will (hopefully!) be no higher than the discount that is obtainable with a group affiliation!

Another very clear change in our membership profile is the proportion of members under 30 years of age. This may be

due to the recent European project on diving physiology research (PHYPODE) that, by design, involved young researchers. I recall that some years ago a former EUBS President (not to name him: Alf Brubakk) was constantly urging us to increase the number of youngsters in our community – Alf, they are coming in! We are very glad to see young researchers coming more and more to our meetings; the "Young Researchers Session", started some years ago will continue to be organised and we even have a proposition to constitute a "Young Researcher Committee" within the Executive. These are encouraging ideas and we will discuss them at the next ExCom face-to-face meeting.

Our future Annual Meetings are in the (advanced) planning stage and the organising committees are already working to achieve what is needed. Please bookmark our next meeting in Amsterdam, The Netherlands (in fact, it is high time to send an abstract and to register!). The meeting takes place earlier this year, on 19–22 August. Switzerland (Geneva) will organise the meeting in 2016 and, among proposals for the years beyond, another joint meeting together with SPUMS hopefully will be possible and we have Italy, Israel, Czech Republic, Portugal, etc. lining up, although proposals for definite locations or organising committees are not finalized for all yet. As you can see, we have a lot planned and we are very positive for the future.

Key words

Medical society, general interest

Erratum

In my December 2014 EUBS President's column, entitled "Hydrophobicity: the link between bubbles, bubblebers and autoimmunity?" (*Diving Hyperb Med.* 2014;44:185), the text in the first two paragraphs under the subheading "Surfactants act against proteins and cause autoimmune diseases" should have been attributed to:

Arieli R. Was the appearance of surfactants in air breathing vertebrates ultimately the cause of decompression sickness and autoimmune disease? *Resp Physiol Neurobiol.* 2015;206:15-18.

This paper was available on-line from November 2014.

Dr Arieli accepts that this omission was unintentional on my part and that the promulgation of his theories was done from the best of motives.

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Key words

Erratum, bubbles, decompression sickness, endothelium, surfactant, editorial, medical society

Original articles

The effect of pre-dive ingestion of dark chocolate on endothelial function after a scuba dive

Sigrid Theunissen, Costantino Balestra, Antoine Boutros, David De Bels, François Guerrero and Peter Germonpré

Abstract

(Theunissen S, Balestra C, Boutros A, De Bels D, Guerrero F, Germonpré P. The effect of pre-dive ingestion of dark chocolate on endothelial function after a scuba dive. *Diving and Hyperbaric Medicine*. 2015 March;45(1):4-9.)

Objective: The aim of the study was to observe the effects of dark chocolate on endothelial function after scuba diving.

Methods: Forty-two male scuba divers were divided into two groups: a control ($n = 21$) and a chocolate group ($n = 21$). They performed a 33-metres deep scuba-air dive for 20 minutes in a diving pool (Nemo 33, Brussels). Water temperature was 33°C. The chocolate group ingested 30 g of dark chocolate (86% cocoa) 90 minutes before the dive. Flow-mediated dilatation (FMD), digital photoplethysmography and nitric oxide (NO) and peroxynitrites (ONOO⁻) levels were measured before and after the scuba dive in both groups.

Results: A significant decrease in FMD was observed in the control group after the dive ($91 \pm 7\%$ (mean \pm 95% confidence interval) of pre-dive values; $P < 0.001$) while it was increased in the chocolate group ($105 \pm 5\%$ of pre-dive values; $P < 0.001$). No difference in digital photoplethysmography was observed between before and after the dives. No variation of circulating NO level was observed in the control group whereas an increase was shown in the chocolate group ($154 \pm 73\%$ of pre-dive values; $P = 0.04$). A significant reduction in ONOO⁻ was observed in the control group ($84 \pm 12\%$ of pre-dive values; $P = 0.003$) whereas no variation was shown after the dive with chocolate intake ($100 \pm 28\%$ of pre-dive values; *ns*).

Conclusion: Ingestion of 30 g of dark chocolate 90 minutes before scuba diving prevented post-dive endothelial dysfunction, as the antioxidants contained in dark chocolate probably scavenge free radicals.

Key words

Antioxidants, cardiovascular, hyperoxia, nitric oxide, diving research, scuba, circulation

Introduction

Endothelial dysfunction after scuba diving was first described in 2005, measured by flow-mediated dilatation (FMD).¹ Other authors have confirmed endothelial dysfunction after a scuba dive.² That FMD is nitric oxide-dependant is the commonly accepted assumption.³ Endothelial nitric oxide (NO) production is triggered by endothelial nitric oxide synthase (eNOS), the latter requiring several major cofactors such as tetrahydrobiopterin (BH₄). Endothelial-NOS is dependant on various activators (physiological and nutritional) such as polyphenols (red wine, cocoa or green tea) or Akt (also known as protein kinase B, PKB).⁴

Polyphenols contained in dark chocolate have the power to improve vascular health by stimulating the formation of vasoprotective factors such as NO, leading to vasodilatation. They also improve vascular smooth muscle function by reducing oxidative stress. Reduction of oxidative stress could reduce the NO degradation through superoxide anions and thus prevent vasoconstriction. Akt increases eNOS activity thus stimulating NO production through phosphatidylinositol kinase (PI3K)-dependent mechanisms.⁵ Peroxynitrites (ONOO⁻) have been used as a marker of oxidative stress following diving.⁶

Endothelial dysfunction is associated with poor cardiovascular outcome, leading to research into prevention measures. The aim of the study was to measure the effects of dark chocolate ingestion before a scuba dive on endothelial function.

Methods

STUDY POPULATION

All experimental procedures were conducted in accordance with the Declaration of Helsinki (2008 revision) and were approved by the Academic Ethical Committee of Brussels (B200-2009-039). All methods and potential risks were explained in detail to the participants. After written, informed consent, 42 non-smoking, experienced (at least four years of experience), male scuba divers volunteered for the study. All subjects needed to fulfil exercise criteria (at least 30 minutes of exercise two to three times per week). Prior to entering the study, they were assessed as fit to dive by a qualified diving physician. None of the subjects had a history of previous cardiac abnormalities and none of them were on any cardio-active medication. All participants were asked to refrain from strenuous exercise and nitrate-rich food for 48 h before the tests and not to dive for 72 h before testing. They were divided into a chocolate group (21 subjects) and a control group (21 subjects).

DIVE PROTOCOL

The subjects performed a 33-metre deep scuba dive for 20 minutes without a decompression stop in a calm, 8-m diameter pool (Nemo 33, Brussels, Belgium). Water and air temperature were 33°C and 29°C respectively. The chocolate group performed the identical dive in the same conditions as the control group 90 minutes after ingestion of 30 g of dark chocolate (86% cocoa). No exercise was undertaken during the dives.

ENDOTHELIAL FUNCTION

Arterial endothelial function was assessed before and after diving by measuring brachial artery FMD following a standardized protocol and guidelines.⁷ FMD was measured with a 5–10 MHz transducer (Mindray DP 6600, Mindray, China). The brachial artery diameter was measured on longitudinal images with the lumen/intima interface visualized on both the anterior and posterior walls. Boundaries for diameter measurement were identified automatically by means of boundary-tracking software (FMD-I software, FLOMEDI, Belgium) and manually adjusted by the same technician who performed all the vascular measurements and was blinded to the group assignment of the subjects. Once the basal measurements were obtained, the sphygmomanometer cuff, placed above the ultrasound testing region was inflated and held at 50 mmHg above systolic blood pressure for 5 min. Occlusion up to 5 min produces a transient arterial dilatation attributable to NO synthesis.⁸ After ischaemia, the cuff was deflated rapidly and the brachial artery was monitored for an additional four minutes. The FMD was computed as the percentage change in brachial artery diameter measured at peak dilatation.

ARTERIAL STIFFNESS

Arterial stiffness of small arteries was estimated from the pulse wave obtained at the finger by an infra-red sensor (Pulse Trace PCA 2, Micro Medical, UK). This non-invasive method is easy to use and reproducible.⁹ The waveform depends on vascular tone in the arterial tree. The contour of the wave exhibits two peaks. The first peak is formed by pressure transmitted along a direct path from the left ventricle to the finger. The second peak is formed in part by pressure transmitted along the aorta and large arteries to sites of impedance mismatch in the lower body.⁹ The peak-to-peak time (PPT) is the time taken for pressure to propagate along the aorta and large arteries to the major site of reflection in the lower body and back to the root of the subclavian artery. The waveform volume in the finger is thus directly related to the time it takes for the pulse waves to travel through the arterial tree. This PPT is proportional to subject height, and the stiffness index (SI) was formulated as h/PPT where h corresponds to the height expressed in metres and PPT is the peak-to-peak time expressed in seconds. Small artery stiffness decreases the time taken for pressure

waves reflected from the periphery to return to the aorta. Reflected waves arrive earlier in the cardiac cycle and may in part explain the change in pulse contour.

BLOOD ANALYSES

Blood samples were collected before diving and 15 minutes after the dive. Samples were drawn from an antecubital fossa vein into an EDTA tube and centrifuged according to a standard protocol (1,000 rpm for 15 min for NO and 3,500 rpm for 10 min for ONOO⁻ at 4°C) in order to separate blood cells and plasma. The plasma was then stored at -80°C and all analyses were performed within the following six months on the same microplate (one for each test) in order to analyse all the samples at the same time to avoid variance bias. Plasma levels of nitrite and nitrate, NO metabolites, were determined by a colorimetric method (Cayman, Ann Arbor, MI, USA) according to the manufacturer's instructions. Peroxynitrites were measured using the OxiSelect™ Nitrotyrosine ELISA kit (Bio-Connect BV, The Netherlands).

STATISTICAL ANALYSIS

For logistical reasons, a repeated measures study design was not possible. Power analysis for a 10% change in FMD, based on previous studies with a SD of approximately 7%, indicated a need for 18–20 subjects per group. Statistical analyses were conducted using GraphPad Prism 5 (La Jolla, California, USA). Data are reported as a percentage of pre-dive values. The difference between the percentage of pre-dive values and 100% was compared by a two-tailed, one-sample Student's *t*-test after normality of distribution of the sample was determined by the Kolmogorov-Smirnov test. Otherwise, the non-parametric Wilcoxon Rank Sum test was used. Statistical significance level was set at $P < 0.05$.

Results

All divers completed the study and no-one developed symptoms of decompression sickness. There were no statistical differences in demographics between the two groups. Mean age was 37 ± 6 years in the control group and 35 ± 6 years in the chocolate group. Height and BMI were respectively 178 ± 6 cm and 24 ± 1 kg·m⁻² in the control group and 176 ± 5 cm and 24 ± 2 kg·m⁻² in the chocolate group.

BRACHIAL ARTERY DIAMETER AND FLOW-MEDIATED DILATATION

An increase in pre-occlusion diameter of the brachial artery was observed after the dive in the control group ($105 \pm 9\%$ of pre-dive values, $P = 0.04$) whereas that of the chocolate group did not change ($99 \pm 3\%$ of pre-dive values). FMD was significantly reduced after the dive in the control group ($91 \pm 7\%$ of pre-dive values, $P < 0.001$) but significantly increased in the chocolate group ($105 \pm 5\%$, $P < 0.001$). The

Table 1

Absolute values of the pre-occlusion diameters of the brachial artery, of the flow-mediated dilatation, of the photoplethysmographic and haematological parameters before (pre-dive) and after (post-dive) a scuba dive to 33 metres' depth for 20 minutes for the control and the dark chocolate groups (mean \pm 95% confidence intervals (95% CI); * $P = 0.04$; † $P = 0.003$; ‡ $P < 0.001$)

| | Pre-dive | | Post-dive | | <i>n</i> |
|--|----------|------------------|-----------|------------------|----------|
| | Mean | CI ₉₅ | Mean | CI ₉₅ | |
| Control | | | | | |
| Pre-occlusion diameter (mm) | 4.8 | (4.6–5.1) | 5.0 | (5.8–5.3) | 21 |
| Flow-mediated dilatation (%)‡ | 110 | (105–115) | 100 | (97–103) | 21 |
| Peak-to-peak time (ms) | 199 | (180–217) | 210 | (188–232) | 21 |
| Stiffness index (m·s ⁻¹) | 9.3 | (8.5–10.1) | 8.9 | (8–9.9) | 21 |
| Nitric oxide (µM·L ⁻¹) | 1.4 | (0.7–2) | 1.4 | (0.8–2) | 10 |
| Peroxonitrites (µM·L ⁻¹) † | 188 | (157–218) | 160 | (124–196) | 10 |
| Dark chocolate | | | | | |
| Pre-occlusion diameter (mm) | 4.9 | (4.7–5.1) | 4.8 | (4.6–5.1) | 21 |
| Flow-mediated dilatation (%) ‡ | 107 | (105–109) | 113 | (110–115) | 21 |
| Peak-to-peak time (ms) | 198 | (186–210) | 201 | (189–213) | 21 |
| Stiffness index (m·s ⁻¹) | 9.1 | (8.5–9.6) | 8.9 | (8.4–9.4) | 21 |
| Nitric oxide (µM·L ⁻¹) * | 1.5 | (0.9–2.2) | 2.0 | (1.4–2.5) | 10 |
| Peroxonitrites (µM·L ⁻¹) | 192 | (158–227) | 190 | (147–233) | 10 |

difference between the control group and the chocolate group was statistically significant ($P < 0.001$). FMD changes are presented in Figure 1.

DIGITAL PHOTOPLETHYSMOGRAPHY

No variation in PPT between pre- and post-dive values was found in either group (106 \pm 15% of pre-dive values in the control group versus 103 \pm 11% in the chocolate group, n.s.). No variation was observed in the SI (96 \pm 15% of pre-dive values in the control group vs. 99 \pm 11% in the chocolate group, n.s.).

CIRCULATING NO AND ONOO⁻

No variation in circulating NO concentration was observed in the control group (103 \pm 18% of pre-dive values) whereas a significant increase was seen in the chocolate group (154 \pm 73%, $P = 0.04$). A significant reduction in plasma concentration of ONOO⁻ was observed in the control group (84 \pm 12% of pre-dive values, $P = 0.003$) whereas no variation in ONOO⁻ is shown in the chocolate group (100 \pm 28%).

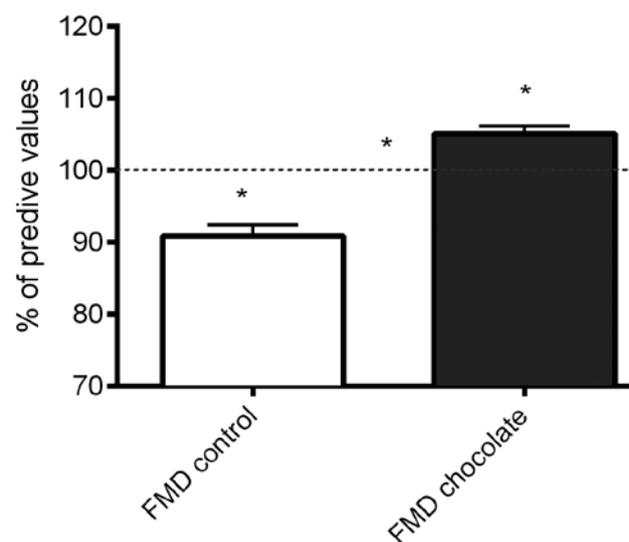
The absolute values of the various parameters measured are summarised in Table 1.

Discussion

All the dives occurred in thermoneutral waters (33°C) to blunt the physiological mechanisms induced by cold. Our results show a decrease in FMD after a standard scuba dive, consistent with the literature,^{1,10} whereas FMD increased post-dive after eating dark chocolate before diving.

Figure 1

Post-dive flow-mediated dilatation (FMD, expressed as % of pre-dive value) after scuba dives to 33 metres' depth for 20 minutes in two group of divers ($n = 21$ in each) with or without ingestion of 30 g of dark chocolate 90 minutes before the dive (mean \pm 95% confidence intervals); * $P < 0.001$ in both groups and for the post-dive difference between the groups

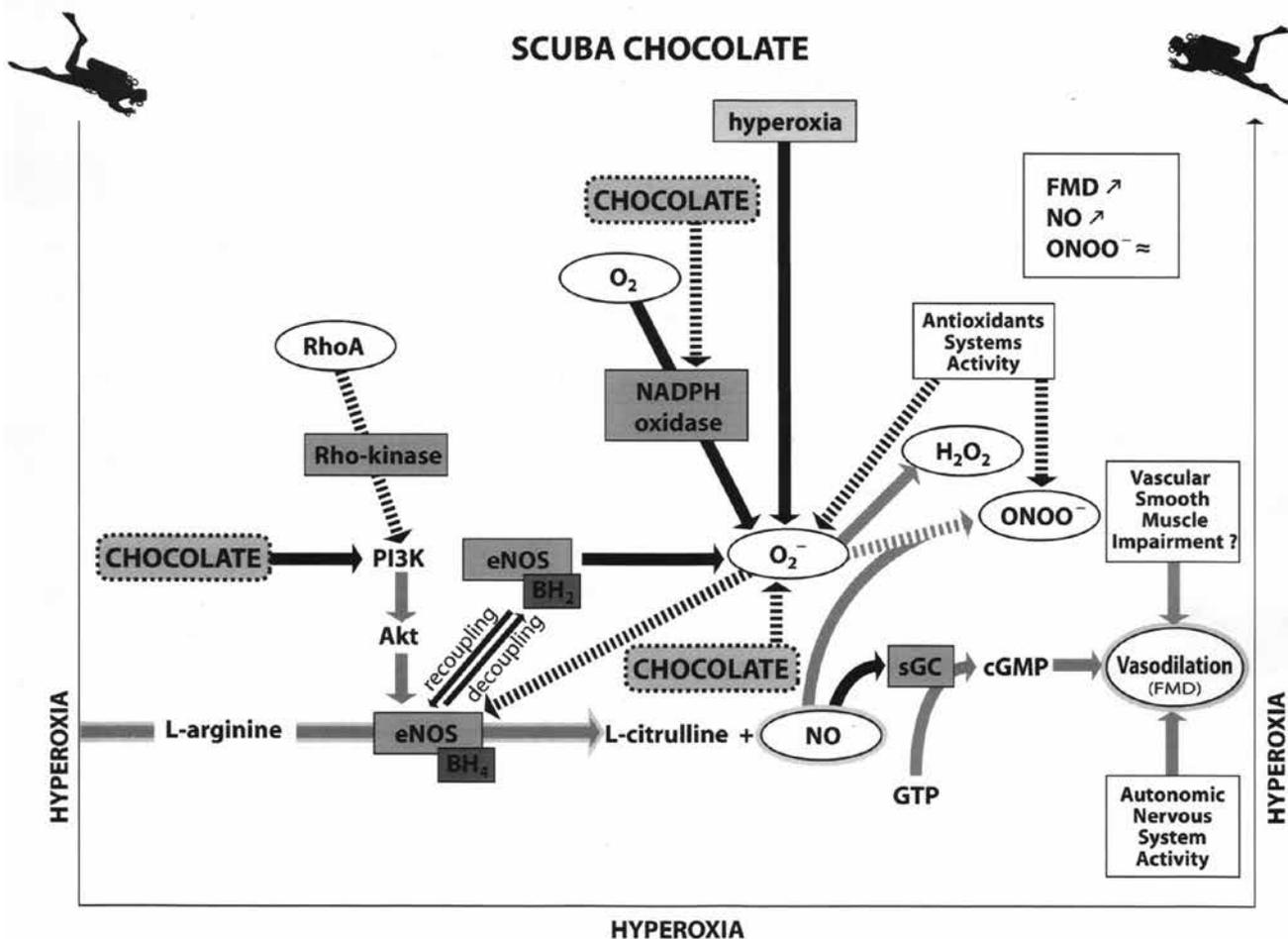


STANDARD SCUBA DIVE

One of the accepted hypotheses is that hyperoxia could be responsible for the decrease in FMD by increasing oxidative stress via superoxide anion production.¹¹ Furthermore, reactive oxygen species (ROS) not only react with NO to reduce its bioavailability, but also oxidize BH₄⁻, a major co-

Figure 2

Theoretical model of the influence of hyperoxia and antioxidants on nitric oxide (NO) bioavailability; chocolate decreases the amount of superoxide anions (O_2^-), decreasing the activity of NADPH oxidase and increasing the level of PI3K; these actions increase the activity of eNOS and thus the production of NO. Since superoxide anions are scavenged by the antioxidants of chocolate, it is possible that the amount of superoxide anions combined with NO may not be enough to increase the level of ONOO⁻. Continuous black lines: activation/production; discontinuous black lines: inhibition/scavenging; gray lines: transformation



factor of eNOS, which reduces NO production.¹² Indeed, the depletion of BH₄ in endothelial cells exposed to oxidative stress can lead to eNOS decoupling, leading to superoxide anion (free radical) production instead of NO.¹²

No variations were found in NO levels, indicating that eNOS activity was not modified. It has been reported that FMD is NO-dependant,³ so we should have seen a decrease in NO levels after a standard scuba dive. We believe that superoxide anions produced during diving interact with NO to produce ONOO⁻ thereby decreasing its availability to contribute to FMD,¹³ thus producing vasoconstriction.¹⁴ If so, we should have seen an increase in ONOO⁻ after diving, whereas our study showed a decrease in ONOO⁻ possibly suggesting that NO was not transformed to ONOO⁻. NO production was, thus, neither reduced nor was it transformed to ONOO⁻. This could explain why there was no NO variation in the control group, a result confirmed in the literature.¹⁵

Our ONOO⁻ measures did not seem to confirm the presence of oxidative stress in diving. This could be explained in three ways. Firstly, the levels of NO were not high enough to induce production of ONOO⁻. Secondly, diving-induced antioxidant systems neutralised ONOO⁻.¹⁶ Thirdly, oxidative stress was not present during the dives. The last hypothesis conflicts with previous studies demonstrating of oxidative stress during diving.^{10,17} This has been demonstrated with markers other than ONOO⁻, such as thiobarbituric acid reactive substances,¹⁶ superoxide dismutase (SOD) or glutathione peroxidase activity.¹⁸ For these reasons, ONOO⁻ may not be the best marker to study diving-induced oxidative stress, especially if a deficit in NO is suspected. Nevertheless, ONOO⁻ levels indicated that NO was probably not inactivated by oxidative stress.

During a scuba dive, FMD is decreased without any NO variation,¹⁵ as in our control group, and this could be due to cardiovascular adaptations,¹⁹ to change in vascular smooth

muscle²⁰ and/or to autonomic nervous system activity. Indeed ortho- or parasympathetic nervous system activity has been demonstrated during diving.²¹

CHOCOLATE DIVE

Antioxidants contained in dark chocolate are able to scavenge superoxide anions and therefore reduce oxidative stress, leading to reduced eNOS inhibition.²² Several studies have shown that an acute or chronic intake of dark chocolate reduced arterial stiffness and was thus beneficial for the vascular system.^{21,22} Also, accumulation of intracellular free radicals was reduced by a pretreatment containing cocoa procyanidins.²³ Pure cocoa contains between 12 and 18% polyphenols. An intake of 38 to 125 g of chocolate a day significantly increases the diameter of the brachial artery.²⁴ A small intake of dark chocolate rich in polyphenols as part of nutrition reduces arterial hypertension and promotes NO formation.²⁵

The antioxidants in dark chocolate are capable of reducing diving-induced oxidative stress. In autonomous scuba diving, chocolate acts directly on superoxide anions as well as on NADPH oxidase, reducing its activity thus enabling transformation of oxygen into superoxide anions. This leads to a decrease in BH_4 oxidation permitting eNOS to form NO. FMD follows the rise in NO concentrations. In our control group, we saw a reduction in FMD without any variation in NO, possible mechanisms for which are described above. Even if NO and FMD variations go in the same direction after dark chocolate ingestion, it does not mean that changes in vascular smooth muscle and/or to autonomic nervous system activity do not occur. Indeed, some studies link scuba diving and increased vagal activity associated with a decrease in the sympathetic tone of the heart.²¹ On the contrary, sympathetic activity is raised during the recovery phase,²¹ explaining why FMD does not always follow NO concentrations. The unchanged ONOO⁻ levels during scuba diving after chocolate intake could be explained by superoxide anions being trapped by antioxidants present in dark chocolate. This could sufficiently reduce their concentration, rendering combination with NO impossible and thus leaving unchanged ONOO⁻ concentrations. The possible mechanisms associated with chocolate intake in scuba diving are shown in Figure 2.

MICROCIRCULATION

There was no change in the stiffness index (SI) in small vessels in either group, whereas FMD decreased after a scuba dive but increased after the post-chocolate dive. An increase in endothelial function when measured by FMD, but without change in a tonometry-measured pulse wave, has been observed previously after cardiovascular training.²⁶ The use of post-occlusion reactive hyperaemia may be a better way of assessing short-term changes in endothelial function than the use of photoplethysmography which relies

on endothelial structure, the latter remaining unchanged during diving. Indeed, post-occlusion reactive hyperaemia has been shown to vary after a similar air dive.²

Extending this research to other domains such as to an older population, in whom increased oxidative stress and alterations in endothelial function occur, could be interesting. The literature shows interesting perspectives on the effects of dark chocolate reducing oxidative stress and thereby cardiovascular risks.²⁷

Conclusions

Dark chocolate inhibits post-dive endothelial dysfunction, suggesting the presence of oxidative stress. Peroxynitrites may not be the best biomarkers to evaluate this stress in the current setting. The generally accepted hypothesis is that FMD is NO-dependent, but we showed that FMD variations do not necessarily follow those of circulating NO. It seems that there are many potential factors that could contribute to variations in FMD. Dark chocolate could be an easy, inexpensive and tasty way to reduce the impact of diving on the cardiovascular system.

References

- 1 Brubakk AO, Duplancic D, Valic Z, Palada I, Obad A, Bakovic D, et al. A single air dive reduces arterial endothelial function in man. *J Physiol.* 2005;566(Pt 3):901-6.
- 2 Theunissen S, Guerrero F, Sponsiello N, Cialoni D, Pieri M, Germonpre P, et al. Nitric oxide-related endothelial changes in breath-hold and scuba divers. *Undersea Hyperb Med.* 2013;40:135-44.
- 3 Mullen MJ, Kharbanda RK, Cross J, Donald AE, Taylor M, Vallance P, et al. Heterogenous nature of flow-mediated dilatation in human conduit arteries in vivo: relevance to endothelial dysfunction in hypercholesterolemia. *Circ Res.* 2001;88:145-51.
- 4 Dimmeler S, Fleming I, Fisslthaler B, Hermann C, Busse R, Zeiher AM. Activation of nitric oxide synthase in endothelial cells by Akt-dependent phosphorylation. *Nature.* 1999;399(6736):601-5.
- 5 Papapetropoulos A, Garcia-Cardena G, Madri JA, Sessa WC. Nitric oxide production contributes to the angiogenic properties of vascular endothelial growth factor in human endothelial cells. *J Clin Invest.* 1997;100:3131-9.
- 6 Theunissen S, Schumacker J, Guerrero F, Tillmans F, Boutros A, Lambrechts K, et al. Dark chocolate reduces endothelial dysfunction after successive breath-hold dives in cool water. *Eur J Appl Physiol.* 2013;113:2967-75.
- 7 Corretti MC, Anderson TJ, Benjamin EJ, Celermajer D, Charbonneau F, Creager MA, et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. *J Am Coll Cardiol.* 2002;39:257-65.
- 8 Lieberman EH, Gerhard MD, Uehata A, Selwyn AP, Ganz P, Yeung AC, et al. Flow-induced vasodilation of the human brachial artery is impaired in patients <40 years of age with coronary artery disease. *Am J Cardiol.* 1996;78:1210-4.

- 9 Millasseau SC, Kelly RP, Ritter JM, Chowienczyk PJ. Determination of age-related increases in large artery stiffness by digital pulse contour analysis. *Clin Sci (Lond)*. 2002;103:371-7.
- 10 Obad A, Marinovic J, Ljubkovic M, Breskovic T, Modun D, Boban M, et al. Successive deep dives impair endothelial function and enhance oxidative stress in man. *Clin Physiol Funct Imaging*. 2010;30:432-8.
- 11 Jamieson D, Chance B, Cadenas E, Boveris A. The relation of free radical production to hyperoxia. *Annu Rev Physiol*. 1986;48:703-19.
- 12 Forstermann U. Nitric oxide and oxidative stress in vascular disease. *Pflugers Arch*. 2010;459:923-39.
- 13 Sureda A, Ferrer MD, Batle JM, Tauler P, Tur JA, Pons A. Scuba diving increases erythrocyte and plasma antioxidant defenses and spares NO without oxidative damage. *Med Sci Sports Exerc*. 2009;41:1271-6.
- 14 Demchenko IT, Boso AE, O'Neill TJ, Bennett PB, Piantadosi CA. Nitric oxide and cerebral blood flow responses to hyperbaric oxygen. *J Appl Physiol*. 2000;88:1381-9.
- 15 Marinovic J, Ljubkovic M, Breskovic T, Gunjaca G, Obad A, Modun D, et al. Effects of successive air and nitrox dives on human vascular function. *Eur J Appl Physiol*. 2012;112:2131-7.
- 16 Sureda A, Batle JM, Ferrer MD, Mestre-Alfaro A, Tur JA, Pons A. Scuba diving activates vascular antioxidant system. *Int J Sports Med*. 2012;33:531-6.
- 17 Vince RV, McNaughton LR, Taylor L, Midgley AW, Laden G, Madden LA. Release of VCAM-1 associated endothelial microparticles following simulated SCUBA dives. *Eur J Appl Physiol*. 2009;105:507-13.
- 18 Rousseau AS, Richer C, Richard MJ, Favier A, Margaritis I. Plasma glutathione peroxidase activity as a potential indicator of hypoxic stress in breath-hold diving. *Aviat Space Environ Med*. 2006;77:551-5.
- 19 Boussuges A. Immersion in thermoneutral water: effects on arterial compliance. *Aviat Space Environ Med*. 2006;77:1183-7.
- 20 Lambrechts K, Pontier JM, Balestra C, Mazur A, Wang Q, Buzzacott P, et al. Effect of a single, open-sea, air SCUBA dive on human micro- and macro-vascular function. *Eur J Appl Physiol*. 2013;113:2637-45.
- 21 Chouchou F, Pichot V, Garet M, Barthelemy JC, Roche F. Dominance in cardiac parasympathetic activity during real recreational SCUBA diving. *Eur J Appl Physiol*. 2009;106:345-52.
- 22 Karim M, McCormick K, Kappagoda CT. Effects of cocoa extracts on endothelium-dependent relaxation. *J Nutr*. 2000;130(8S Suppl):2105S-8S.
- 23 Cho ES, Jang YJ, Kang NJ, Hwang MK, Kim YT, Lee KW, et al. Cocoa procyanidins attenuate 4-hydroxynonenal-induced apoptosis of PC12 cells by directly inhibiting mitogen-activated protein kinase kinase 4 activity. *Free Radic Biol Med*. 2009;46:1319-27.
- 24 Kris-Etherton PM, Keen CL. Evidence that the antioxidant flavonoids in tea and cocoa are beneficial for cardiovascular health. *Curr Opin Lipidol*. 2002;13:41-9.
- 25 Taubert D, Roesen R, Lehmann C, Jung N, Schomig E. Effects of low habitual cocoa intake on blood pressure and bioactive nitric oxide: a randomized controlled trial. *JAMA*. 2007;298:49-60.
- 26 Cornelissen VA, Onkelinx S, Goetschalckx K, Thomaes T, Janssens S, Fagard R, et al. Exercise-based cardiac rehabilitation improves endothelial function assessed by flow-mediated dilation but not by pulse amplitude tonometry. *Eur J Prev Cardiol*. 2014;21:39-48.
- 27 Loffredo L, Perri L, Catasca E, Pignatelli P, Brancorsini M, Nocella C, et al. Dark chocolate acutely improves walking autonomy in patients with peripheral artery disease. *J Am Heart Assoc*. 2014;3(4).(pii):e001072.

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Flying after diving: should recommendations be reviewed? In-flight echocardiographic study in bubble-prone and bubble-resistant divers

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Abstract

(Cialoni D, Pieri M, Balestra C, Marroni A. Flying after Diving: should recommendations be reviewed? In-flight echocardiographic study in bubble-prone and bubble-resistant divers. *Diving and Hyperbaric Medicine*. 2015 March;45(1):10-15.)

Introduction: Inert gas accumulated after multiple recreational dives can generate tissue supersaturation and bubble formation when ambient pressure decreases. We hypothesized that this could happen even if divers respected the currently recommended 24 hour pre-flight surface interval (PFSI).

Methods: We performed transthoracic echocardiography (TTE) on a group of 56 healthy scuba divers (39 male, 17 female) as follows: first echo – during the outgoing flight, no recent dives; second echo – before boarding the return flight, after a multiday diving week in the tropics and a 24-hour PFSI; third echo – during the return flight at 30, 60 and 90 minutes after take-off. TTE was also done after every dive during the week's diving. Divers were divided into three groups according to their 'bubble-proneness': non-bubblers, occasional bubblers and consistent bubblers.

Results: During the diving, 23 subjects never developed bubbles, 17 only occasionally and 16 subjects produced bubbles every day and after every dive. Bubbles on the return flight were observed in eight of the 56 divers (all from the 'bubblers' group). Two subjects who had the highest bubble scores during the diving were advised not to make the last dive (increasing their PFSI to approximately 36 hours), and did not demonstrate bubbles on the return flight.

Conclusions: Even though a 24-hour PFSI is recommended on the basis of clinical trials showing a low risk of decompression sickness (DCS), the presence of venous gas bubbles in-flight in eight of 56 divers leads us to suspect that in real-life situations DCS risk after such a PFSI is not zero.

Key words

Echocardiography, Doppler, bubbles, altitude, flying (and diving), recreational diving, remote locations, travel

Introduction

The risk of decompression sickness (DCS) may increase when flying after diving.¹⁻³ The minimum safe pre-flight surface intervals (PFSI) between diving and exposure to altitude have been well studied;⁴⁻⁶ however, all the studies were not performed in real diving and flying conditions but in simulated hyperbaric and hypobaric chambers.⁷ It has been estimated that the incidence of DCS decreases as the PFSI increases and beyond 11 hours there appears to be no additional DCS risk after single no-stop dives and beyond 17 h after repetitive, no-stop dives.⁸ Current guidelines suggest a minimum PFSI of 12 h after a single, no-stop dive, 18 h after multiple dives per day or multiple days of diving, whilst intervals substantially longer than 18 h are suggested after dives requiring mandatory decompression stops.⁸⁻¹⁰

The steady increase in popularity of scuba diving has implied an increase in flights to and from tropical destinations and, as a consequence, the risk of DCS during the return flight may be increased. For this reason, we thought further research was due and well justified. Our recent work has shown that subjects who were particularly prone to develop post-dive bubbles (venous gas emboli, VGE) showed significant amounts of circulating bubbles in-flight after an intense recreational diving week, notwithstanding a 24-hour PFSI.¹¹ Although asymptomatic, these could be the reason for some hyperintense spots seen in the cerebrum of divers on MRI.¹² Our hypothesis was that inert gas could linger in

the tissues for longer than 24 hours after multiple, multi-day recreational diving and that the rapid decrease in cabin pressure with altitude, causing further tissue supersaturation, could trigger new bubble formation in some divers, even in those who respected the current recommendations to delay flying for 24 h. This could explain certain DCS occurring in flight despite a correct PFSI.

We performed Doppler-echocardiography during real commercial return flights on subjects whom we had studied during a previous week of diving to better understand any possible 'predisposition' to bubble formation in flight.

Methods

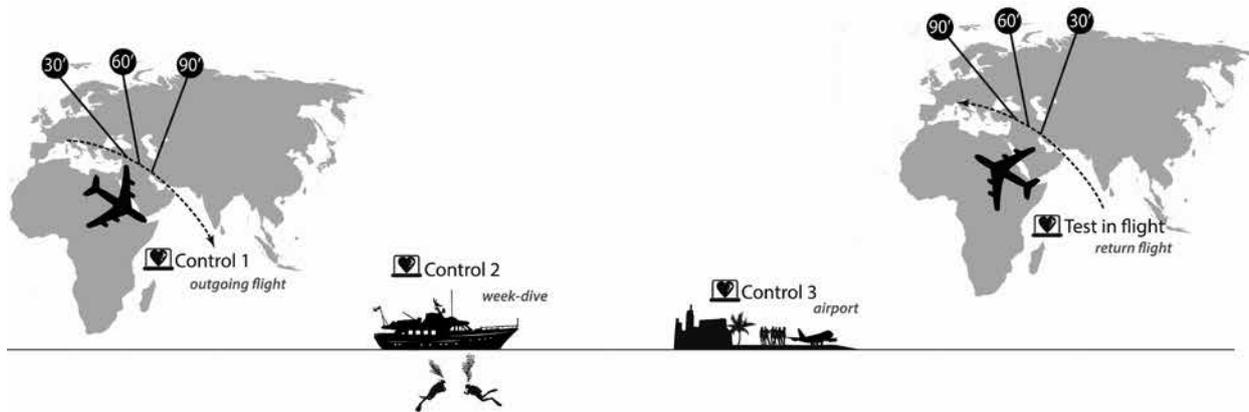
The study protocol was approved by the institutional ethics committee (Comite d'Ethique Hospitalier du CHU Brugmann, Brussels, Belgium; approval no: CE 2008/66). All participants were informed about the scope of the study, the procedures of the echocardiographic examination and gave their written informed consent.

SUBJECTS AND DIVES

We studied a group of 56 healthy, active, experienced divers. No subject had historical or clinical evidence of arterial hypertension, cardiac, pulmonary or any other significant disease. No subjects declared previous DCS. Information about age, gender and standard anthropometric data such as

Figure 1

Protocol description: Control 1 – trans-thoracic echocardiography (TTE) during the outgoing flight; Control 2 – TTE after every dive on every day of diving; Control 3 – TTE before boarding the return flight, after 24 hour pre-flight surface interval; test in flight – TTE during the return flight; TTE were performed at 30, 60 and 90 min after reaching cruising altitude



height and weight were recorded and the BMI calculated. Heart rate and arterial blood pressure were monitored, recorded daily and their means were calculated.

All divers concluded a full week of intensive recreational diving with 13 dives in total, two dives per day for five consecutive days plus one dive the day of arrival (check dive) one dive on the last day (24 hours before the return flight) and one night dive at mid-week. Two subjects did not make the last dive, therefore increasing their PFSI to approximately 36 hours. All divers made their planned dives without any restrictions or request imposed by the investigation protocol.

All divers did a safety stop of five minutes at 5 metres' sea water (msw) at the end of all dives. Dive computers (iDive pro, Dive system, Valpiana, Italy) provided by the Divers Alert Network (DAN-Europe) were used on every dive and all dive profiles were fully recorded.

Data about possible diving risk factors such as workload (light, moderate, heavy), current (absent or present) health problems (vertigo, seasickness, headache), problems during diving (difficulty in ear equalization, out of air, buoyancy, shared air, equipment problems) and alcohol use during the pre-dive 24 hours were collected by an ad-hoc questionnaire.

The gradient factor approach was used to measure the nitrogen supersaturation of the leading tissue at the end of each dive; this approach theoretically predicts the calculated maximum value allowed for all the 16 tissues included in the Buhlmann ZH-116 model C. All the gradient factor (GF) calculations were performed for each one of the 16 tissues and we reported the maximal GF value in the leading tissue. To estimate decompression stress we also calculated the Hennessy and Hempleman exposure factor (EF) ($p\sqrt{t}$; where p is the absolute pressure and t is the total time of diving).¹³

ECHOCARDIOGRAPHY

All the subjects were studied by trans-thoracic

echocardiography (TTE) after each dive during five diving trips and ten (five outgoing and five return) inter-continental Europe-Maldives flights on Boeing 767-300ER aircraft according to the protocol described below. TTE was performed by a commercially available instrument (MyLab 5, Esaote SPA, Florence, Italy) using a cardiac probe (2.5–3.5 MHz). All echocardiograms were recorded with the subjects lying motionless at rest on their left side breathing normally. Recordings were made for 20 sec and saved to the hard drive for subsequent analysis by two technicians with experience in transthoracic echocardiography. Analyses were performed frame by frame and, in cases of disagreement, the comparative analysis was repeated.

Bubbles were graded according to the Eftedal and Brubakk (EB) scale as follows:¹⁴

- 0 – no bubbles;
- 1 – occasional bubbles;
- 2 – at least one bubble per 4 heart cycles;
- 3 – at least one bubble per cycle;
- 4 – continuous bubbling;
- 5 – 'white out'; impossible to see individual bubbles.

After grading the divers, they were divided into three groups: non-bubblers (NB), occasional bubblers (OB) and bubblers (B). As well as those who never developed bubbles, subjects who only rarely showed solitary bubbles were included in the NB group. Subjects who usually showed only occasional low bubble grades were included in the OB group. Divers who consistently showed bubbles after every dive and only rarely showed low grade or no bubbles were included in the B group. We discriminated the three groups using a 'classic' EB grading scale. Differences in depth, diving time, GF and EF were analysed between the three groups (NB, OB and B).

STUDY PROTOCOL

The study used the following protocol (Figure 1):

- Control 1: during the outgoing flight to the Maldives, 30, 60 and 90 minutes after take-off;

- Control 2: during the diving week on every diving day; before diving and 30, 60 and 90 minutes after surfacing from each dive; if bubbles were detected, further scans were recorded;
- Control 3: before boarding the return flight, after a 24-hour interval from the last dive;
- In-flight test: during the return flight, 30,60 and 90 minutes after take-off (mean ambient pressure 850.4 +/- 1.60 mbar, approximately 0.84 atm).

The subjects who were found positive to in-flight bubbles were also monitored after the 90-minute recording and every 30 minutes until complete echocardiograph battery exhaustion. Bubble grades were compared with the possible risk factors listed above.

ELECTRO-MAGNETIC INTERFERENCE PROTOCOL

Specific tests to evaluate electromagnetic interference (EMI) were agreed with the Airline (NEOS) to ensure that in-flight use of the echocardiograph would not generate any interference with the aircraft instrumentation. EMI were evaluated during a 'ground EMI test' as per avionic guidelines concerning the use of portable electronic devices on board aircrafts.¹⁷ Some of the alternating current equipment was tested operationally by means of a special testing set (NAV402AP equivalent) in order to reproduce simulated flight conditions, thus ensuring EMI would not arise at any time. During in-flight echocardiography, the correct operation of the navigation, communications, identification and safety instruments of the aircraft was tested according to the above-cited avionics protocol. All tests were performed with the echocardiograph in the tail section of the aircraft in the last three rows (NEOS Engineering Order 12-00-001: "B767 – Ground EMI Test for Medical Portable Electronic Device (PED) Mylab").¹⁵ Tests were also aimed at ensuring the correct operation of the echocardiograph during flight using an internal device within the Mylab 5 itself. Avionics engineers and the echocardiography technicians also checked for any macroscopically visible interference or malfunction of the respective devices. In accordance with the airline's request, in-flight avionic conditions and aircraft configurations were repeatedly replicated to rule out any possible interference. The echocardiograph was then classified according to avionic safety procedures as not being detrimental to native aircraft instrumentation.

CABIN PRESSURE MEASUREMENT

Cabin pressure was monitored every 15 minutes from take-off until four hours after reaching cruising altitude using a modified dive computer (iDive Pro, Dive System, Valpiana) and compared with the aircraft's native altimeter data over the same four-hour time period. The modified dive computer used a barometric sensor that measured in millibar (mbar) with adjustment to a Boeing 767 cabin pressure variation ratio of 500 feet (152.4 metres) per minute as a maximum and an error tolerance up to +/- 80 m. Differences across

the 10 flights (five outgoing and five return) were evaluated for stability of the peak cabin pressure to determine whether similar hypobaric exposure conditions occurred during the flights.

STATISTICAL ANALYSIS

Data are presented as the mean ± standard deviation (SD) for parametric data and median and range for non-parametric data (e.g., bubble grades). The median bubble grades of the three groups (NB, OB and B) were calculated and statistical differences were tested by non-parametric analysis of variance (Kruskal-Wallis test), after normality testing (Kolmogorov-Smirnov test). Differences between NB, OB and B for age, height, weight, BMI, heart rate, diastolic and systolic blood pressure were calculated by analysis of variance (one-way ANOVA for parametric data with Neuman Keuls post hoc test and Kruskal-Wallis for non-parametric data) and by chi-square test for gender, workload, current, health problems, problems during dives and alcohol use. Differences between NB, OB, B and dive profile (depth, time, ascent rates, safety stops, gradient factor, surface intervals) were calculated by analysis of variance (Kruskal-Wallis test). Differences in aircraft cabin pressure between the ten flights were assessed in the same way. A probability of less than 5% was assumed as a threshold to reject the null hypothesis. The recommendations of Hochberg and Benjamini for multiple comparisons were employed,¹⁶ and statistical significance levels were set at $P < 0.05$, $P < 0.01$ and $P < 0.001$.

Results

A group of 56 subjects (39 male, 17 female); mean age 46 +/- 12.2 years (48 +/- 12.5 for men and 43 +/- 11.1 for women) (mean +/- SD), mean height 174 +/- 8.7 cm (177 +/- 7.6 for men and 165 +/- 4.7 for women); mean weight 74 +/- 14.1 kg (79 +/- 12.6 for men and 62 +/- 9.2 for women); body mass index (BMI) 24 +/- 3.2 (25 +/- 2.8 for men and 23 +/- 3.4 for women) was studied. The mean depth of the 726 dives recorded was 30.2 +/- 7.7 msw while the mean time was 47.8 +/- 10.3 min. All divers respected 'normal' ascent rates (not slower than 9 msw·min⁻¹ and not faster than 18 msw·min⁻¹, as confirmed by the electronic dive logs) and completed the safety stop. No dive required mandatory decompression stops. None of the divers showed symptoms of DCS during the study.

TTE during the five outgoing flights to the Maldives and at the airport immediately before boarding the five return flights did not show any bubbles in the right or left sides of the heart in any diver. During the diving week, TTE showed that 23 of the 56 subjects never developed bubbles (NB group), 17 subjects only occasionally developed bubbles (OB group) and 16 subjects produced bubbles every day and after almost every dive (B group). The median and range of EB bubble grades of the three groups during the diving were: NB 0 (0–1); OB 0 (0–3); B 3 (0–5).

Table 1

Relationship between potential anthropometric, physiological and diving exposure risk factors and bubble-prone divers; means and (SD) or number of divers or % shown; there were no statistical differences between the three groups except for age; * $P = 0.04$ for non-bubblers vs. occasional bubblers; † $P < 0.001$ for non-bubblers vs. bubblers

| Risk factor | Non-bubblers | Occasional bubblers | Bubblers |
|--|--------------|---------------------|-------------|
| Anthropometric | | | |
| Height (cm) | 174 (8.0) | 171 (9.3) | 175 (9.1) |
| Weight (kg) | 73 (13.5) | 72 (15.1) | 76.5 (14.5) |
| BMI (kg·m ⁻²) | 24 (2.9) | 24 (3.3) | 25 (3.6) |
| Males/females (n) | 15/8 | 11/6 | 13/3 |
| Age (yr) | 41 (8.8) | 45 (11.8) * | 55 (12.5) † |
| Physiological | | | |
| Heart rate (beats·min ⁻¹) | 76 (7.7) | 74 (10.4) | 75 (8.0) |
| Diastolic BP (mmHg) | 77 (7.4) | 75 (5.7) | 74 (10.4) |
| Systolic BP (mmHg) | 139 (24.0) | 134 (11.5) | 128 (12.6) |
| Diving factors | | | |
| Depth (msw) | 30 (7.2) | 31 (9.2) | 31 (6.5) |
| Diving time (min) | 47 (10.8) | 47 (11.0) | 49 (8.6) |
| Gradient factor (GF) | 0.7 (0.2) | 0.7 (0.2) | 0.8 (0.1) |
| Exposure factor (EF) | 27.2 (6.4) | 28.0 (7.9) | 28.4 (5.6) |
| Workload (% for each group from 726 reports) | | | |
| Light | 39 | 29 | 37 |
| Moderate | 48 | 53 | 50 |
| Heavy | 13 | 18 | 13 |
| Current (% for each group from 726 reports) | | | |
| Present | 39 | 41 | 44 |
| Absent | 61 | 59 | 56 |
| Diving problems (% for each group from 726 reports) | | | |
| No problem | 87 | 82 | 87 |
| Problem | 13 | 18 | 13 |
| Health problems during diving (% for each group from 726 reports) | | | |
| No problem | 91 | 88 | 94 |
| Problem | 9 | 12 | 6 |
| Alcohol (% daily use; 150 positive out of 390 reports) | | | |
| No | 55 | 71 | 62 |
| Yes | 45 | 29 | 38 |

The differences in bubble grade between the three groups were statistically significant (all $P < 0.001$). There were no differences between the three groups for any of the anthropometric, physiological or diving parameters (Table 1) excepting that our previous observations were confirmed with respect to age, with an increase in age in the B group (55 +/- 12.5 years) compared to the NB (41 +/- 8.8 yr, $P < 0.001$) and OB groups (45 +/- 11.8 yr, $P = 0.04$).¹¹ We also did not find any difference in diving exposure factors (depth, diving time, GF and EF) between the three groups. There was no relationship between the B group and the additional risk factors investigated (workload, current health problems, problems during diving, use of alcohol; Table 1).

During the return flights, bubbles were detected in 8 of the 56 subjects, all from the B group (median bubble score 1, range 0–3; one subject with grade 3). Subjects classified as B during the diving week and who also showed in-flight bubbles had a statistically higher mean bubble grade after

every dive compared to those who, although B, did not develop in-flight bubbles ($P < 0.001$). Two subjects in the B group, with high bubble grades during the diving (median 3, range 2–4 and 2, range 0–3) did not make the last dive of the series, thus increasing their PFSI to approximately 36 hours. Because of this, both were excluded from the comparative analysis. Neither showed any bubbles on the return flight. In-flight bubble grades decreased as the flight progressed and by 90 min after take-off no bubble-positive subjects showed any bubbling and there was no evidence of a reverse trend (increasing bubble grade over time). An example of in-flight bubbles in the right heart is shown in Figure 2.

No malfunction of or interference with the aircraft's instruments were found during the ground EMI test. Similarly no EMI interference or malfunction of the aircraft's instruments or of the MyLab 5 echocardiography machine were observed during the flights. Aircraft cabin pressure

Figure 2

Case of in-flight high-grade bubbles; the arrows indicate bubbles in the right heart as recorded in-flight after a 24-h pre-flight surface interval; no bubbles could be seen in this subject pre-flight



showed no statistically significant differences between the 10 flights; mean pressure 850 +/- 1.6 mbar.

Discussion

The purpose of this study was to investigate if divers who, during a week's intensive recreational diving, had consistently shown VGE after every, or nearly every dive (B – bubble) might respond to a new decrease in ambient pressure during flight with new circulating bubble formation, notwithstanding pre-flight computed non-critical inert gas tissue tensions and a 24-hour PFSI. To ensure that pre-flight diving was the only added variable and possible bubble trigger we had included TTE during the outgoing flight, without any diving for at least 72 hours pre-flight, and also before embarking on the return flight (after a 24-hour PFSI).

TTE performed after every dive on every diver during the diving allowed us to stratify the divers into three bubble groups (NB, OB and B). We discriminated the three groups using a 'classic' EB grading scale. This is consistent with our equipment, although we acknowledge that recent research indicates that, with newer echocardiography devices, it is common to observe EB Grade 4 bubbles in asymptomatic divers.¹⁷ Therefore, it would be more appropriate to use the 'expanded' EB grading scale with more modern devices to discriminate between the three groups more accurately.¹⁸

Statistical analysis across the three groups showed that the diving exposure for the divers was similar, even though we recognise that it is difficult to standardize real-world diving. This could be regarded as a limitation of the study. On the other hand, real conditions are not always perfectly

represented by simulated conditions.⁷ Our results show that, even if a 24-hour PFSI is respected, some subjects developed significant amounts of bubbles during the homeward flight, confirming our previous work.¹¹ The larger numbers of subjects investigated showed that only those subjects who consistently showed high bubble grades during the diving developed bubbles in-flight. Interestingly, the two highest bubble graders, who were advised to omit the last diving day, and boarded the plane about 36 hours after their last dive did not show any bubbles in-flight. This allows us to speculate that a longer PFSI is needed in divers with high bubble grades.

Lastly, the decrease in in-flight bubble grades as flight time elapses can be interpreted as indirect evidence that a certain level of possibly critical tissue super-saturation occurs shortly after take-off during a commercial flight; in fact, 90 min after take-off we did not find any difference in bubble grade with respect to the outgoing flight, or that immediately before take-off on the return flight.

This in-flight bubble formation could be explained in three different ways:

- Bubbles could persist in divers for a longer time than usually believed, and not be detectable by ultrasound before take-off because of their small size. Then, the in-flight decrease in ambient pressure may cause their growth and make them detectable again;
- Higher than estimated inert gas tensions could persist in the tissues for longer than believed and bubbles could be newly generated by the new supersaturation caused by flying. This could occur in predisposed subjects only or in all the divers, but the phenomenon might only be evident in the predisposed subjects;
- Genetically predisposed individuals may possess an endothelial blood vessel surface more prone to generate micronuclei and bubbles during the decompression/depressurization phase.^{19,20}

Pre-flight oxygen breathing to reduce bubble formation and/or decompression sickness incidence risk^{21,22} could be considered for bubble-prone divers to reduce the residual supersaturation of inert gas and the number of micronuclei, as previously hypothesised.²³

The authorization of the use of a medical device in flight, as in our investigation, opens new avenues for research, not only related to bubble formation but also to pathophysiological conditions which could be negatively affected by situations of mild hypoxia caused by altitude exposure in particularly predisposed subjects.^{24,25} Even though it is difficult to standardize real-life diving conditions, we believe this study provides useful data informing the safety of scuba diving. Our data suggest that 24 hours post multi-day, multiple no-decompression diving may be an insufficient delay before flying for some, bubble-prone divers. Further studies are already planned to validate our results on a larger number of subjects.

References

- 1 Millar I. Post diving altitude exposure. *SPUMS Journal*. 1996;26:135-40.
- 2 Pollock NW, Natoli MJ, Gerth WA, Thalmann ED, Vann RD. Risk of decompression sickness during exposure to high cabin altitude after diving. *Aviat Space Environ Med*. 2003;74:1163-8.
- 3 Freiburger JJ, Denoble PJ, Pieper CF, Ugucconi DM, Pollock NW, Vann RD. The relative risk of decompression sickness during and after air travel following diving. *Aviat Space Environ Med*. 2002;73:980-4.
- 4 Sheffield PJ, editor. *Flying after diving*. 39th Undersea and Hyperbaric Medical Society Workshop. Publication Number 77(FLYDIV). Bethesda: Undersea and Hyperbaric Medicine Society; 1989.
- 5 Sheffield PJ. Flying after diving guidelines: a review. *Aviat Space Environ Med*. 1990;61:1130-8.
- 6 Vann RD, Denoble P, Emmerman MN, Corson KS. Flying after diving and decompression sickness. *Aviat Space Environ Med*. 1993;64(9 Pt 1):801-7.
- 7 Vann RD. Diving at the no-stop limits: chamber trials of flying after diving. In: Vann RD, editor. *Flying after diving Workshop*. Durham, NC: Divers Alert Network; 2004. p. 32-7.
- 8 Vann RD, Gerth W, Denoble P, Pieper C, Thalmann E. Experimental trials to assess the risks of decompression sickness in flying after diving. *Undersea Hyperb Med*. 2004;31:431-44.
- 9 Pollock NW, Fitzpatrick DT. NASA flying after diving procedures. In: Vann RD, editor. *Flying after diving Workshop*. Durham, NC: Divers Alert Network; 2004. p. 59-64.
- 10 Freiburger JJ. Flying after multiday repetitive recreational diving. In: Vann RD, editor. *Flying after diving Workshop*. Durham, NC: Divers Alert Network; 2004. p. 38-44.
- 11 Cialoni D, Pieri M, Balestra C, and Marroni A; Flying after diving: in-flight echocardiography after a scuba diving week; *Aviat Space Environ Med*. 2014;85:993-8. doi: 10.3357/ASEM.3805.2014.
- 12 Balestra C, Marroni A, Farkas B, Peetrons P, Vanderschueren F, Duboc E, et al. The fractal approach as a tool to understand asymptomatic brain hyperintense MRI signals. *Fractals Journal*. 2004;12:67-72.
- 13 Hennessy TR, Hempelmann HV. An examination of the critical released gas volume concept in decompression sickness. *Proc R Soc Lond B Biol Sci*. 1997;197:299-313.
- 14 Eftedal O, Brubakk AO. Detecting intravascular gas bubbles in ultrasonic images. *Med Biol Eng Comput*. 1993;31:627-33.
- 15 Joint Aviation Authorities Administrative & Guidance Material. *Guidance concerning the use of portable electronic devices on board aircraft*. Hoofddorp, The Netherlands: Joint Aviation Authority; 2013. Leaflet 29.
- 16 Hochberg Y, Benjamini Y. More powerful procedures for multiple significance testing. *Statistics in Medicine*. 1990;9:811-8. doi:10.1002/sim.4780090710. PMID 2218183.
- 17 Ljubkovic M, Dujic Z, Møllerlökken A, Bakovic D, Obad A, Breskovic T, Brubakk AO. Venous and arterial bubbles at rest after no-decompression air dives. *Med Sci Sports Exerc*. 2011;43:990-5.
- 18 Blogg SL, Gennser M, Møllerlökken 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.
- 19 Papadopoulou V, Tang MX, Balestra C, Eckersley RJ, Karapantsios TD. Circulatory bubble dynamics: from physical to biological aspects. *Adv Colloid Interface Sci*. 2014;206:239-49.
- 20 Papadopoulou V, Eckersley RJ, Balestra C, Karapantsios TD, Tang MX. A critical review of physiological bubble formation in hyperbaric decompression. *Adv Colloid Interface Sci*. 2013;191-192:22-30.
- 21 Webb JT, Pilmanis AA. Preoxygenation time versus decompression sickness incidence. *SAFE Journal*. 199;29(2):75-8.
- 22 Ernsting J. Mild hypoxia and the use of oxygen in flight. *Aviat Space Environ Med*. 1984;55:407-10.
- 23 Balestra C, Germonpre P, Snoeck T, Ezquer M, Leduc O, Leduc A, et al. Normobaric oxygen can enhance protein captation by the lymphatic system in healthy humans. *Undersea Hyperb Med*. 2004;31:59-62.
- 24 Affleck J, Angelici A, Baker S. Cabin cruising altitudes for regular transport aircraft. *Aviat Space Environ Med*. 2008;79:433-9.
- 25 Hampson NB, Kregenow DA, Mahoney AM, Kirtland SH, Horan KL, Holm JR, Gerbino AJ. Altitude exposures during commercial flight: a reappraisal. *Aviat Space Environ Med*. 2013;84:27-31.

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The five-minute prebreathe in evaluating carbon dioxide absorption in a closed-circuit rebreather: a randomized single-blind study

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Abstract

(Deng C, Pollock NW, Gant N, Hannam JA, Dooley A, Mesley P, Mitchell SJ. The five-minute prebreathe in evaluating carbon dioxide absorption in a closed-circuit rebreather: a randomized single-blind study. *Diving and Hyperbaric Medicine*. 2015 March;45(1):16-24.)

Introduction: Closed-circuit underwater rebreather apparatus (CCR) recycles expired gas through a carbon dioxide (CO₂) 'scrubber'. Prior to diving, users perform a five-minute 'prebreathe' during which they self-check for symptoms of hypercapnia that might indicate a failure in the scrubber. There is doubt that this strategy is valid.

Methods: Thirty divers were block-randomized to breathe for five minutes on a circuit in two of the following three conditions: normal scrubber, partly-failed scrubber, and absent scrubber. Subjects were blind to trial allocation and instructed to terminate the prebreathe on suspicion of hypercapnia.

Results: Early termination was seen in 0/20, 2/20, and 15/20 of the normal, partly-failed, and absent absorber conditions, respectively. Subjects in the absent group experienced a steady, uncontrolled rise in inspired (P_ICO₂) and end-tidal CO₂ (P_{ET}CO₂). Seven subjects exhibited little or no increase in minute volume yet reported dyspnoea at termination, suggesting a biochemically-mediated stimulus to terminate. This was consistent with results in the partly-failed condition (which resulted in a plateaued mean P_ICO₂ near 20 mmHg), where a small increase in ventilation typically compensated for the inspired CO₂ increase. Consequently, mean P_{ET}CO₂ did not change and in the absence of a hypercapnic biochemical stimulus, subjects were very insensitive to this condition.

Conclusions: While prebreathes are useful to evaluate other primary functions, the five-minute prebreathe is insensitive for CO₂ scrubber faults in a rebreather. Partly-failed conditions are dangerous because most will not be detected at the surface, even though they may become very important at depth.

Key words

Scuba diving, rebreathers/closed circuit, carbon dioxide, hypercapnia, rebreathing, capnography, physiology

Introduction

Closed-circuit rebreathers (CCRs) are popular in advanced recreational diving owing to advantages such as the minimization of gas consumption, especially during deep diving, and optimization of decompression. Rebreathers recycle expired gas around a circle circuit with one-way valves. Expired carbon dioxide (CO₂) is removed as it passes through a 'scrubber' canister containing CO₂ absorbent that is most commonly soda lime (a mixture of sodium hydroxide and calcium hydroxide). Oxygen metabolised by the diver is replaced in the circuit to maintain a safe inspired partial pressure of oxygen (P_IO₂).

Rebreathers are more complex than open-circuit scuba equipment and more prone to operator errors.¹ Some of these relate to the CO₂ scrubber. The absorbent material has a finite capacity (approximately 12–15 L CO₂·100 g⁻¹) and must be changed regularly.² Errors include failing to replace the absorbent material in a timely manner, incorrect packing of the absorbent material into the scrubber canister, incorrect installation of the canister in the rebreather and, rarely, forgetting to install it entirely. Such errors may allow expired CO₂ to enter the inhaled gas which may in turn cause symptomatic hypercapnia (often referred to by

divers as CO₂ toxicity). There have been deaths during the use of rebreathers in which hypercapnia is thought to have contributed, one of which is comprehensively documented in the medical literature.³ Hypercapnia also enhances the toxicity of oxygen^{4,5} and the narcotic effect of nitrogen⁶ breathed at higher partial pressures.

Most rebreather units do not measure inspired CO₂, so most technical diver training agencies teach divers to conduct a five-minute 'prebreathe' as a means of checking scrubber function before entering the water. A prebreathe involves preparing the unit for diving, and then sitting quietly breathing on the circuit, ideally with the nose blocked. If the CO₂ scrubber is absent or faulty, the diver will re-inhale expired CO₂ and, in theory, should notice the early symptoms of hypercapnia such as dyspnoea and/or headache. The five-minute duration is assumed to be sufficiently long for early symptoms of hypercapnia to reliably manifest, but the validity of this practice has not been formally tested. Therefore, we measured the proportion of blinded subjects who could discern an absent or faulty CO₂ scrubber during a five-minute prebreathe test on a rebreather circuit. A secondary aim was to derive a physiological interpretation of the results.

Methods

TRIAL DESIGN AND PARTICIPANTS

This was a randomised, single-blind, controlled trial that took place at the Exercise Metabolism Laboratory, University of Auckland, in July 2014. The study protocol was approved by the University of Auckland Human Participants Ethics Committee (reference 012315).

The subjects were trained, certified and active adult divers. Preference was given to rebreather divers, but experienced open-circuit scuba divers were not excluded as they would be taught the same prebreathe technique and expected to use it if undertaking a rebreather training course. All subjects received a participant information sheet, a verbal briefing and provided written informed consent.

EXPERIMENTAL CONDITIONS & RANDOMIZATION

Twenty prebreathe tests were conducted on a rebreather in each of the following experimental conditions: normal scrubber; partly-failed scrubber and absent scrubber as described in more detail below. To achieve sufficient numbers of trials in each condition, 30 blinded subjects were block randomised to prebreathe in two of the three scrubber conditions with a rest period of at least 20 minutes between the two experiments. Subjects relaxed between trials in the presence of study personnel to prevent them discussing their experience until the study was complete. For each subject, the order of conditions was constrained so that the condition likely to result in less CO₂ rebreathing was first. This constraint was concealed from the subjects and was necessary to prevent an obvious hypercapnia experience on the first prebreathe from biasing perceptions of scrubber condition on the second. Similarly, we concealed the block randomization pattern from subjects who were told, again to avoid biasing, that any combination of the two conditions was possible, including breathing on a normal circuit twice.

EQUIPMENT CONFIGURATION

An Inspiration Evolution Plus rebreather (Ambient Pressure Diving, Helston, Cornwall) was assembled by the investigators for each prebreathe. The rebreather oxygen cylinder contained 100% oxygen and the diluent cylinder contained air. The rebreather oxygen controller was set to maintain a P_IO₂ at 0.7 atm (71 kPa) throughout each experiment. This is a standard setting used by rebreather divers when at the surface.

Rebreather assembly followed the standard procedure described by the manufacturer with several exceptions. First, the CO₂ scrubber was configured according to the allocated condition. In the normal condition, the absorbent canister was installed as recommended, with the soda lime material replaced each day (after approximately 80 minutes

of a maximum recommended 180 minutes use). In the partly-failed condition, the scrubber canister was installed, but a known assembly error was intentionally committed: a sealing O-ring that directs all gas flow through the canister was omitted from the circuit, allowing some expired gas to bypass the scrubber. In the absent condition, the absorbent canister was completely omitted.

Second, a disposable anaesthetic circuit antibacterial filter (Covidien DAR, MA, USA) was incorporated into the mouthpiece of the rebreather circuit. The filter had a dual purpose. It served to mask any changes in the circuit breathing resistance resulting from the scrubber condition (particularly the absent condition) by imposing a fixed resistance at the mouth. In addition, replacement of the mouthpiece and filter for each subject allowed use of the same rebreather circuit for multiple subjects. In a supplementary experiment using simple manometry, we evaluated the efficacy of the filter in masking changes in circuit resistance related to the scrubber condition and its contribution to any increase in circuit resistance. With the filter present or absent, and with the rebreather configured as for each of the three experimental conditions, we measured peak inspiratory and expiratory pressures (cm H₂O) at the mouthpiece with a respiratory pressure transducer (MLT844, AD Instruments, Dunedin) during sinusoidal mechanical ventilation (17050-2 Lung Simulator, VacuMed, Ventura, CA) over 1 minute (tidal volume V_T 1.5 L; respiratory rate RR 10 breaths·min⁻¹).

Third, a gas sampling line was attached to the dedicated port of the mouthpiece filter. This allowed continuous sampling for rapid response measurement of P_IO₂ with a paramagnetic O₂ analyser (S-3A, AEI Technologies, Pittsburgh, PA), inspired CO₂ (P_ICO₂), and end-tidal CO₂ (P_{ET}CO₂) with an infrared CO₂ analyser (CD-3A, AEI Technologies, Pittsburgh, PA). A three-point calibration was performed at routine intervals for O₂ and CO₂ using reference gases spanning the measurement range. A pneumotachometer (MLT1000L, AD Instruments, Dunedin) was interposed in the exhale limb of the rebreather circuit for measurement of V_T, RR and minute volume (V_E). The device was calibrated prior to each trial and removed from the circuit at regular intervals for comparison with an external standard (3L Calibration Syringe, Hans Rudolph, Shawnee, KS). For safety, heart rate (HR) and oxygen saturation (SpO₂) were monitored using a pulse oximeter (Rad-5, Masimo, Irvine, CA) with the audible signal silenced. All physiological parameters were sampled at 15 second intervals. The laboratory set-up is illustrated in Figure 1.

EXPERIMENTAL PROCEDURE

Subjects were briefed in a standardised manner prior to their first prebreathe. They were reminded of the symptoms of hypercapnia, and it was emphasised that this was an experiment to determine whether the subjects could detect

Figure 1

Laboratory set-up; the subject breathes from the modified rebreather whilst seated facing away from the monitors and recording equipment



a scrubber problem if present; not to determine whether they could tolerate hypercapnia. Accordingly, the subjects were asked to terminate the prebreathe test as they would in a real-world scenario if they detected relevant symptoms.

Subjects donned the rebreather in the sitting position, and faced away from the monitoring equipment. The breathing circuit hoses were passed over the shoulders as in normal use. At commencement of the prebreathe period the mouthpiece was placed in the subject's mouth and the nose was occluded using a nose clip, which is recommended as best practice. Each prebreathe either continued for five minutes or was terminated by the subject if he or she discerned symptoms of hypercapnia. Subjects who terminated the prebreathe early were asked to describe their symptoms.

OUTCOMES

The primary outcome was a comparison of the proportion of subjects who detected symptoms of hypercapnia and terminated the prebreathe in each condition. A secondary aim was to interpret these results in the context of the physiological data ($P_I\text{CO}_2$, $P_{ET}\text{CO}_2$, V_T , RR, and V_E).

POWER

We considered that 80% sensitivity for detection of a scrubber problem in the abnormal scrubber conditions would

indicate a potentially useful test. We anticipated that under the circumstances of the experiment, subjects might exhibit a high index of suspicion for CO_2 scrubber problems, resulting in some false positives in the group breathing on a normal rebreather loop. Thus, allowing for a 30% false positive rate in the normal rebreather condition, we calculated that to demonstrate a statistically significant difference between terminations in the normal condition and in each abnormal condition where the test appeared useful (80% sensitivity) with 90% power and an alpha value of 0.05, we would need 20 subjects in each group.

STATISTICAL ANALYSIS

Descriptive data are presented as mean \pm standard deviation (SD) or median with ranges, as appropriate. The proportion of subjects terminating the prebreathe in each condition was calculated, and these were compared using a two-tail Fisher exact test (GraphPad Prism ver 6.01, San Diego, CA). The sensitivity, specificity and positive predictive values of the prebreathe were calculated.

Results

Baseline characteristics of the groups are described in Table 1.

PRIMARY OUTCOME

Twenty prebreathe tests were completed in each condition. The proportion of subjects terminating the prebreathe in each of the three conditions is shown in Table 2. The sensitivity of the prebreathe was 10% for the detection of a partly-failed scrubber, and 75% for detection of an absent scrubber. The specificity of the prebreathe was 100% as there were no false positives in the normal condition. The positive predictive value (PPV) was 100% (albeit in a high prevalence setting), indicating that all subjects who terminated because of perceived symptoms of CO_2 toxicity were breathing on a loop with a faulty CO_2 scrubber. The negative predictive value was 80% for an absent scrubber and 53% for a partly-failed scrubber.

The mean time to termination in the absent scrubber group was 3 minutes and 41 seconds (range 2 min 1 s to 4 min 52 s). Among the 18 subjects who terminated the prebreathe, the most frequently reported symptoms of hypercapnia were

Table 1

Descriptive data for participants randomised to the three scrubber conditions; $n = 20$ for all three conditions

| | Normal scrubber | Partly-failed | Absent scrubber |
|---|-----------------|---------------|-----------------|
| Age (years) mean (SD) | 42 (8) | 44 (10) | 42 (9) |
| Sex (M/F) | 14/6 | 16/4 | 14/6 |
| Body mass index ($\text{kg}\cdot\text{m}^{-2}$) mean (SD) | 28.6 (3.2) | 27.7 (3.3) | 28.4 (3.7) |
| Years of diving median (range) | 18 (3–45) | 14 (1–45) | 15 (1–28) |
| Rebreather divers | 15 | 12 | 13 |

Figure 2

Normal scrubber condition (mean \pm SD); A – End-tidal (closed circles) and inspired (open circles) PCO₂; B – minute ventilation during the course of a five-minute prebreathe; note in both cases the first reading was made 30 s after commencement of the prebreathe

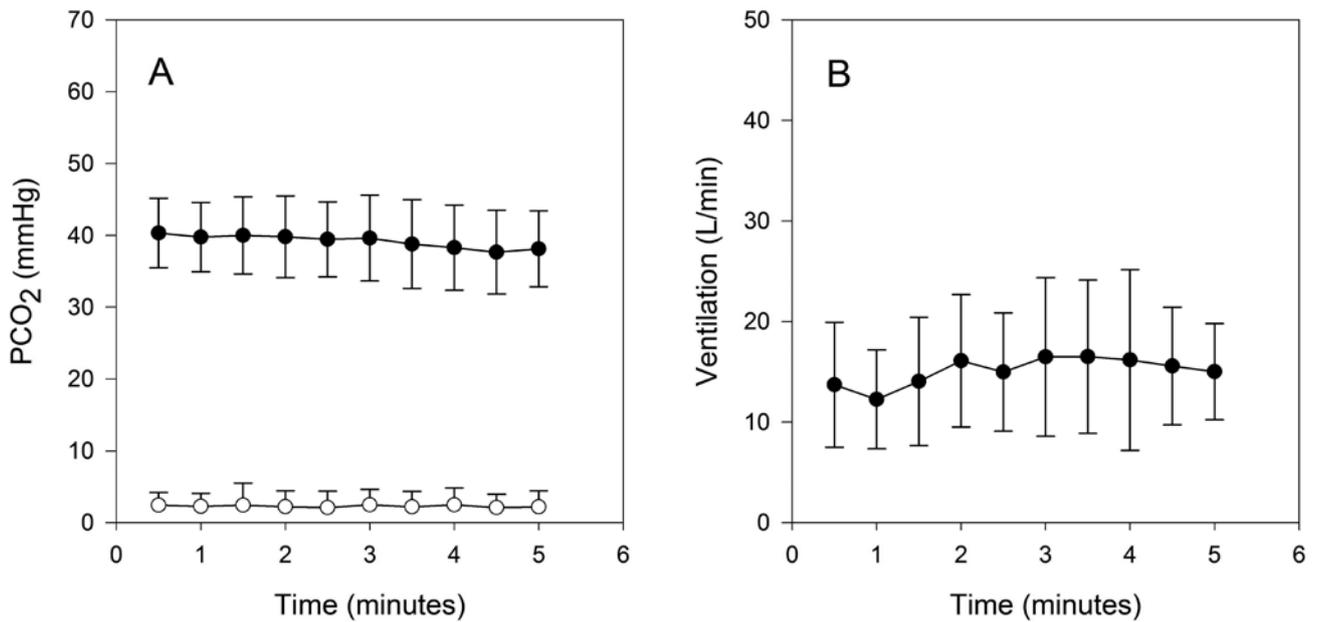


Figure 3

Partly-failed scrubber condition (mean \pm SD); A – End-tidal (closed circles) and inspired (open circles) PCO₂; B – minute ventilation during the course of a five-minute prebreathe; note in both cases the first reading was made 30 s after commencement of the prebreathe, therefore, these readings are not true baseline values; indicative baselines may be inferred from Figure 2 (normal scrubber condition)

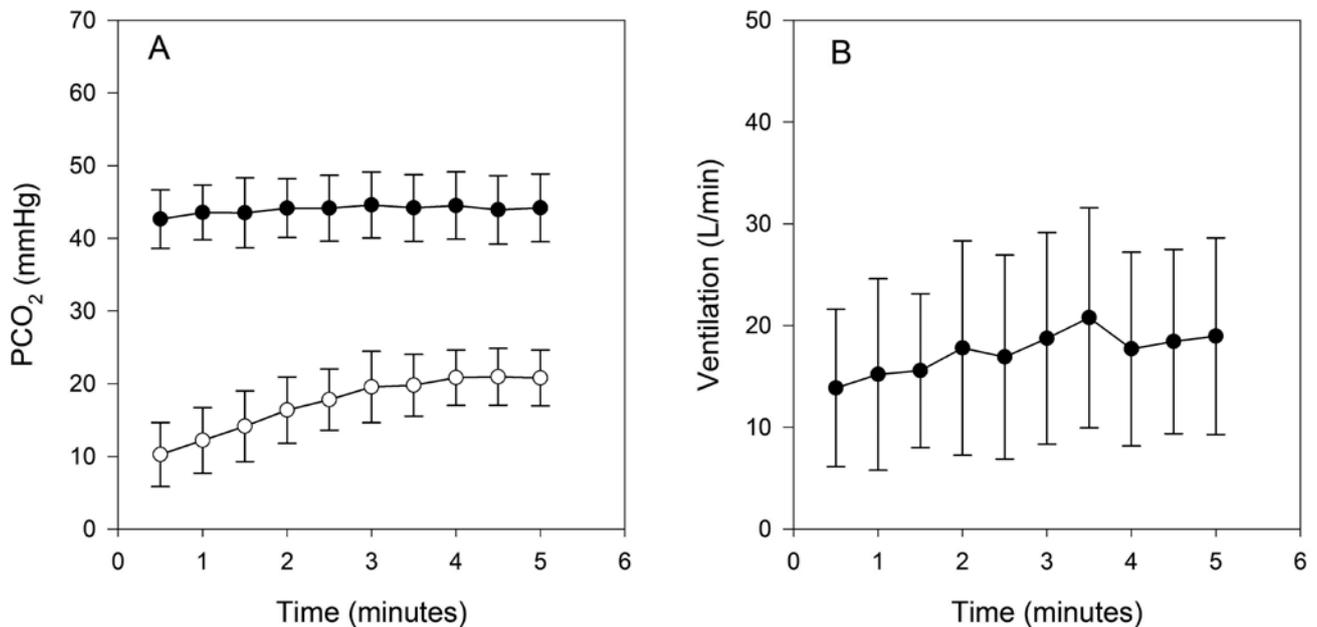


Table 2

Outcomes (numbers and proportion of subjects who terminated the prebreathe) for each of the three scrubber conditions; *P* values are for the comparison with the normal scrubber state

| | Terminated | Not terminated | <i>P</i> -value |
|---------------|------------|----------------|-----------------|
| Normal | 0 | 20 | |
| Partly failed | 2 | 18 | 0.487 |
| Absent | 15 | 5 | < 0.0001 |

Figure 4

Absent scrubber condition (mean \pm SD); A – End-tidal (closed circles) and inspired (open circles) PCO_2 and B – minute ventilation during the course of a five-minute prebreathe. Note, in both cases the first reading was made 30 s after commencement of the prebreathe, therefore, these readings are not true baseline values, indicative baselines may be inferred from Figure 2 (normal scrubber condition)

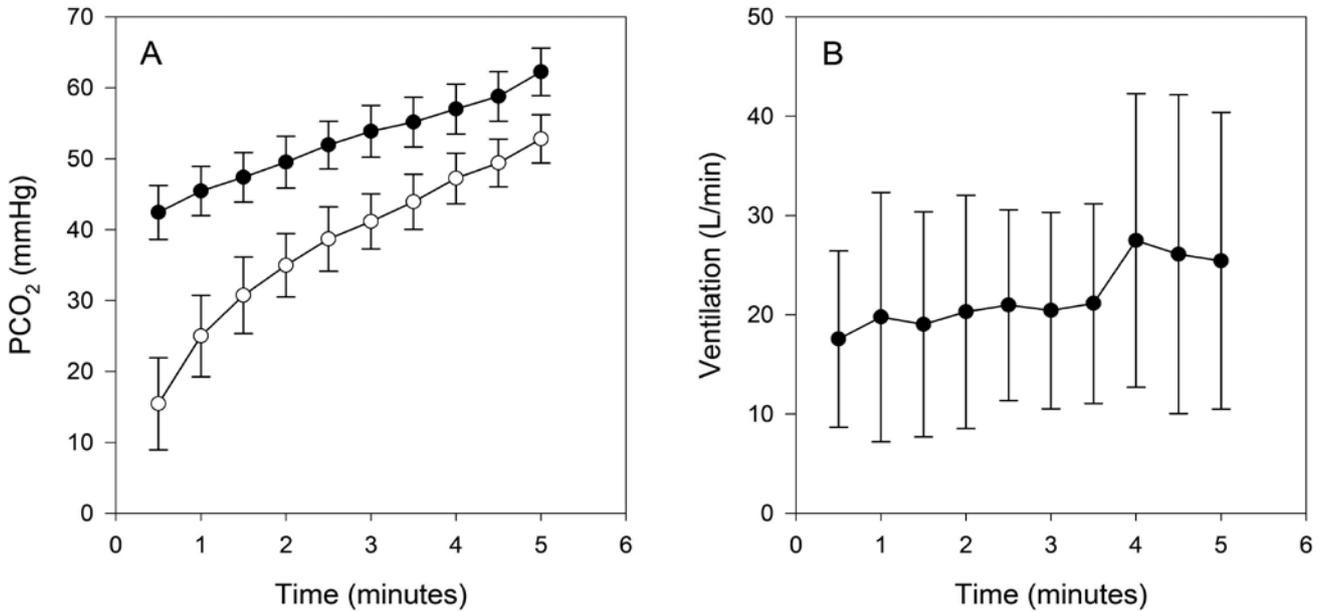
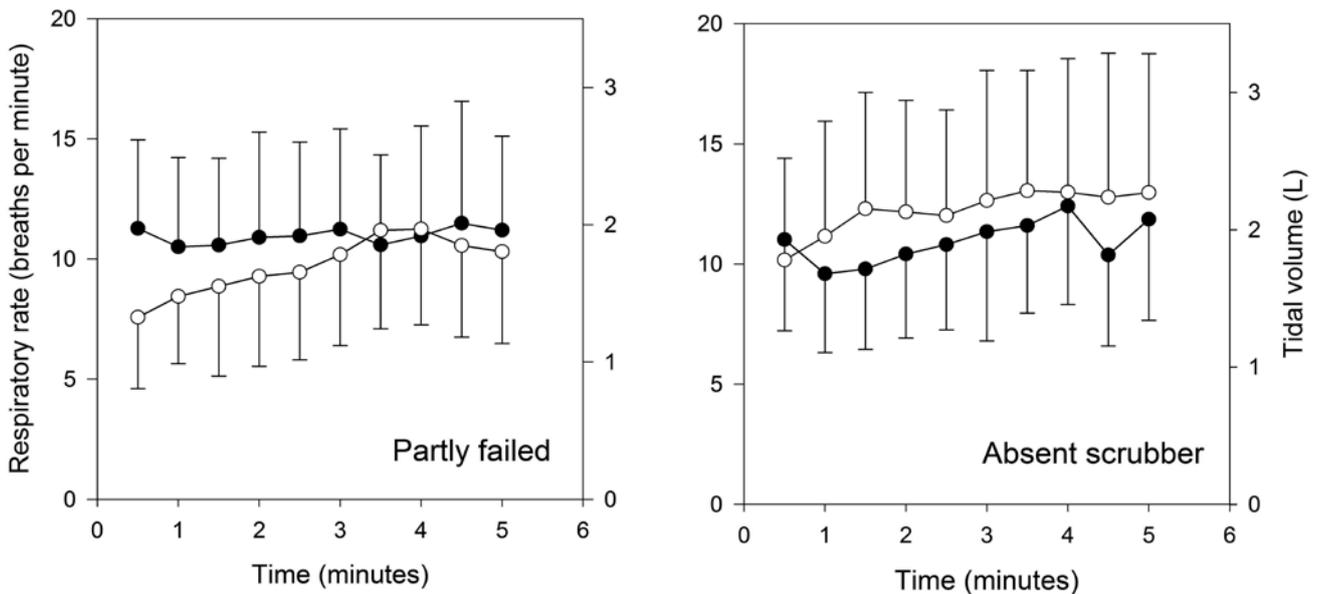


Figure 5

Effect of the partly-failed and absent scrubber conditions on respiratory rate (closed circles) and tidal volume (open circles) (mean \pm SD) during the course of a five-minute prebreathe; respiratory rate remains relatively unchanged whilst tidal volume increases in both conditions; note in both cases the first reading was made 30 s after commencement of the prebreathe, therefore, these readings are not true baseline values



‘shortness of breath’ or ‘increased work of breathing’ (16 of the 18), followed by ‘dizziness’ or ‘light-headedness’ (3/18). Cognitive changes (3/18), anxiety (2/18), visual changes (1/18) and the perception of a ‘racing pulse’ (1/18) were also reported.

There were no significant differences between the subjects who were rebreather or open-circuit divers in relation to the primary outcome. For example, in the absent scrubber condition 9 of 13 rebreather divers versus 6 of 7 open-circuit divers terminated the prebreathe ($P = 0.61$).

Figure 6

Subjects in the absent scrubber group, separated into A – those who completed the prebreathe, and B – those who terminated the prebreathe; each subject is represented by a straight line linking the $P_{ET}CO_2$ and V_E pairs at the beginning and end of the prebreathe

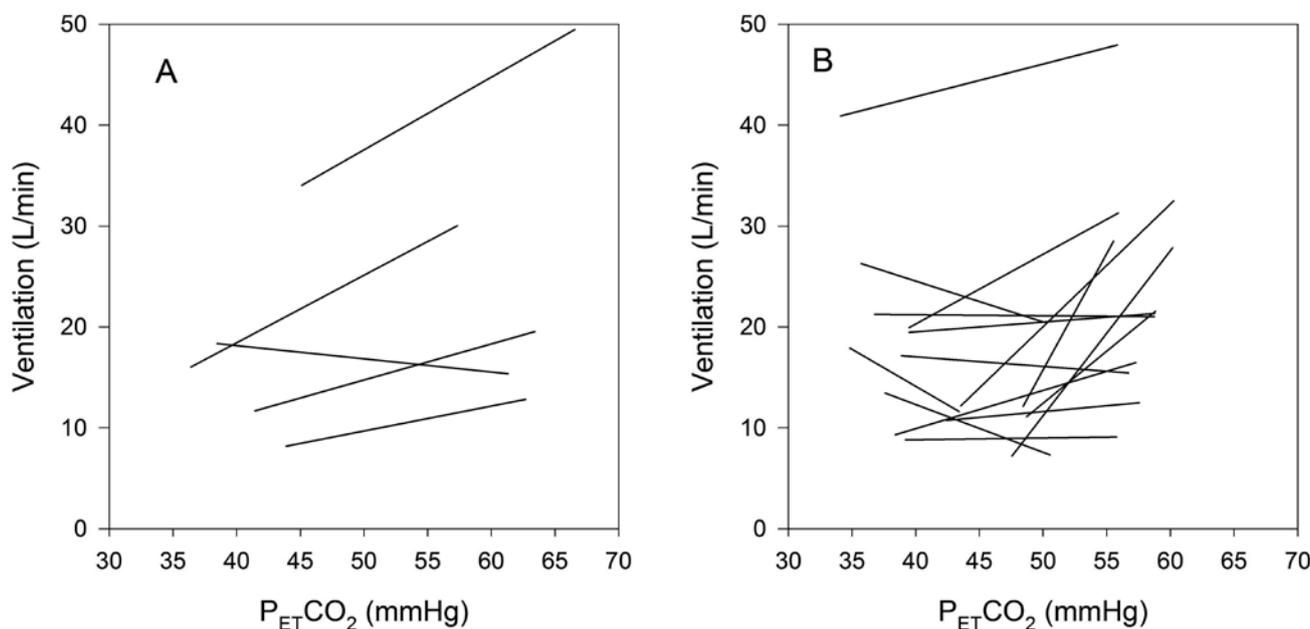


Table 3

Peak inspiratory and expiratory pressures (cm H₂O, mean (SD) shown) required for a breathing simulator to move a 1.5 L tidal volume around the rebreather circuit in the three scrubber conditions, and in the presence and absence of the mouthpiece filter; data represent the mean of 10 breaths measured over a 1-min period

| Condition | Expiratory pressure | | Inspiratory pressure | |
|---|---------------------|--------|----------------------|--------|
| Filter only | 2.56 | (0.03) | -2.42 | (0.07) |
| Rebreather + normal scrubber | 3.51 | (0.02) | -4.33 | (0.06) |
| Rebreather + partly failed | 3.49 | (0.04) | -4.14 | (0.02) |
| Rebreather + absent scrubber | 2.74 | (0.01) | -3.24 | (0.08) |
| Rebreather + filter + normal scrubber | 4.67 | (0.05) | -5.35 | (0.07) |
| Rebreather + filter + partly failed | 4.50 | (0.05) | -5.31 | (0.07) |
| Rebreather + filter + absent scrubber | 4.21 | (0.09) | -5.06 | (0.05) |
| Δ normal vs. absent scrubber, no filter | 0.77 | -1.09 | | |
| Δ normal vs. absent scrubber, with filter | 0.46 | -0.29 | | |

EFFECT OF THE THREE CONDITIONS ON PHYSIOLOGICAL PARAMETERS

The effects of the three experimental conditions on $P_I CO_2$, $P_{ET} CO_2$ and ventilation during the five-minute prebreathe period are shown in Figures 2 to 4. In the normal scrubber condition (Figure 2) these parameters did not change significantly throughout the prebreathe. A low $P_I CO_2$ (< 5 mmHg), which did not change, was detected in this condition.

In the partly-failed condition, the mean $P_I CO_2$ rose immediately and by three or four minutes into the prebreathe had plateaued near 20 mm Hg (Figure 3A). Despite this, the mean $P_{ET} CO_2$ did not change due to a small compensatory increase in mean ventilation (Figure 3B) achieved

predominantly by an increase in V_T (Figure 5).

In the absent scrubber condition, the mean $P_I CO_2$ and $P_{ET} CO_2$ rose inexorably (Figure 4A) despite an increase in mean V_E (Figure 4B); the latter once again explained primarily due to an increase in V_T rather than respiratory rate (Figure 5). There was, however, marked variability among individuals in the ventilation response to rising $P_{ET} CO_2$ (Figure 6). Some individuals tolerated increases in $P_{ET} CO_2$ to higher than 50 mm Hg with no change or even a decrease in V_E , whilst others quickly increased V_E to levels around 40–50 L·min⁻¹ very early as the $P_{ET} CO_2$ began to rise.

These observations still applied when subjects were separated into those who terminated (Figure 6B) and those who did not (Figure 6A), and into rebreather divers and open-

circuit divers (data not presented). The reported symptoms precipitating termination were often inconsistent with the obvious physiological responses. For example, all seven subjects who terminated despite no significant increase ($\leq 2 \text{ L}\cdot\text{min}^{-1}$), no change, or even a decrease in V_E still cited dyspnoea as a precipitating symptom. Heart rate did not rise as the $P_{ET}\text{CO}_2$ increased in this group (including the subject who perceived a “ *racing heart* ”); the mean (\pm SD) heart rate at minutes 1 to 5, being 73 ± 11 , 73 ± 9 , 74 ± 10 , 76 ± 12 and $72 \pm 12 \text{ beats}\cdot\text{min}^{-1}$ respectively.

MANOMETRY EXPERIMENT

Peak inspiratory and expiratory pressures recorded at the mouthpiece with the filter present and absent in each of the three experimental conditions are shown in Table 3. As anticipated, the difference in pressures between the full scrubber and absent scrubber condition was reduced (and therefore less likely to be apparent to subjects) when the filter was in place.

Discussion

Rebreathers are complex devices with many failure points and potential user errors. Errors in preparation, assembly or installation of the CO_2 scrubber may result in CO_2 rebreathing and hypercapnia. Hypercapnic events, in turn, may potentiate oxygen toxicity or precipitate other fatal accidents. As a screen to detect such errors, most divers are taught to conduct a five-minute ‘prebreathe’ on the assembled rebreather circuit prior to diving.

The validity of this prebreathe strategy has been questioned. A small, non-peer-reviewed study reported that none of 14 subjects terminated a five-minute prebreathe on a rebreather with no scrubber canister installed.⁷ Ventilation parameters were not reported, and it is not clear how the subjects were briefed. It is therefore difficult to compare the results to those we report here. Nevertheless, our study also indicates that the prebreathe strategy is insensitive to failure of the CO_2 scrubber.

Most importantly, we exposed the partly-failed group to a known assembly error that allowed a fraction of the expired gas to bypass the CO_2 scrubber canister, resulting in a $P_I\text{CO}_2$ that rose to approximately 20 mmHg over several minutes. Despite this, 18 of 20 subjects did not terminate the prebreathe in this condition. Other errors or problems encountered in the real world may result in more (or less) inspired CO_2 than in this partly-failed scenario, and these would be correspondingly more (or less) likely to be detected by a prebreathe. However, since a quarter of our subjects did not terminate even when allocated to the worst possible CO_2 rebreathing scenario (complete omission of the CO_2 scrubber canister) the prebreathe must be considered an insensitive test over the entire range of errors leading to partial failure.

An interesting physiological consideration in interpreting

these results is “*what causes subjects to terminate a prebreathe?*” Although our study was not designed specifically to answer this question we made some relevant observations. Our data suggest that an increase in ventilation is not a prerequisite for subjects to perceive dyspnoea (Figures 4B and 6). Virtually all terminating subjects, including those whose ventilation did not increase, cited shortness of breath as one of the precipitating symptoms. Thus, it is possible that in at least some subjects termination is driven biochemically; that is, by symptoms (including the perception of dyspnoea) mediated by an increasing arterial $P_a\text{CO}_2$, rather than by perception of an actual increase in ventilation. This may help to explain the very poor sensitivity of the prebreathe in the partly-failed condition. In that setting (Figure 2), a relatively small increase in ventilation, certainly below a threshold noticeable to the vast majority of our subjects, was sufficient to compensate for a $P_I\text{CO}_2$ that plateaued near 20 mm Hg. This prevented the $P_{ET}\text{CO}_2$ from increasing, and therefore the subjects in the partly-failed group were not exposed to the same biochemical stimulus (an increasing $P_a\text{CO}_2$) which seems likely to have driven termination in the absent scrubber group.

The ability to maintain normocapnia during a surface prebreathe despite partial scrubber failure should not be interpreted to indicate that minor degrees of bypass are benign. Indeed, as has been mentioned previously, commission of the assembly error we used to produce a repeatable partly-failed condition is widely reported among divers, and (anecdotally) has led to hypercapnia-induced incidents. This apparent inconsistency whereby the same partly-failed condition causes hypercapnia during diving but not during a prebreathe can be explained by the derangement of respiratory control that occurs during a dive.

Static lung loads, external resistance to gas flow, and increased respired gas density all contribute to an increase in the work of breathing during a dive.⁸ It has been known for decades that in some divers this increased work causes hypoventilation and CO_2 retention, even in the absence of an increased $P_I\text{CO}_2$.⁹ This tendency has been characterized as a propensity for the respiratory controller to sacrifice tight CO_2 homeostasis in order to avoid performing the respiratory work that homeostasis would require.¹⁰ There is evidence that the presence of inhaled CO_2 during exercise and respiratory loading further blunts respiratory drive,^{11,12} paradoxically (in the present context), at the very time that responsiveness is crucial to safety.

Not surprisingly, others have reported that a $P_I\text{CO}_2$ similar to that in our partly-failed condition is dangerous when combined with exercise and external breathing resistance similar to that imposed by a rebreather apparatus. In an experiment aiming to investigate maximum acceptable CO_2 breakthrough levels in rebreather circuits, a 2% C_IO_2 (15 mmHg) combined with relevant levels of resistance, exercise, and oxygen breathing caused dangerous levels of CO_2 retention with poor awareness in many of the subjects.¹³

It was concluded that, for diving safety when using typical underwater breathing apparatus, P_{iCO_2} must be maintained as close to zero as possible. Thus, we reiterate the point that divers should not assume partial scrubber failure and CO_2 rebreathing at levels similar to those measured in our study are benign simply because our subjects maintained a normal $P_{ET}CO_2$ in this condition. It is notable that we detected a very small amount of inhaled CO_2 (~ 3 mmHg) even in the normal scrubber condition (Figure 2). This could have been due to dead space in the mouthpiece and/or filter, trivial incompetency in the mouthpiece non-return valves, a very low level of CO_2 bypass at the scrubber or a combination of these factors. Since we only studied one rebreather, we do not know whether this is a generalized phenomenon.

A number of subjects exposed to the absent scrubber condition failed to increase or actually decreased ventilation as $P_{ET}CO_2$ increased (Figure 6). Although this is at odds with classical descriptions of the $P_{ET}CO_2/\dot{V}_E$ response,^{14,15} substantial variability in the ventilation response to rising $P_{ET}CO_2$ has been reported previously in both non-divers and divers.^{14,16-18} There is some evidence that divers are more prone to abnormal responses and that diving itself conditions participants to become 'CO₂ retainers'.¹⁹ The subjects in our study were relatively experienced divers. Moreover, some aspects of our experimental conditions may have been contributory. For example, the rebreather used in our study would have imposed greater external breathing resistance than the low resistance respiratory measurement equipment typically used in studies of CO_2 response, and greater external resistance may dampen the ventilatory response to inhaled CO_2 as discussed earlier.^{11,12} In addition, to be consistent with usual diving practice, the subjects breathed a high fraction of inspired oxygen (70%), and elevated inspired oxygen may make a further contribution to dampening the CO_2 response.¹⁶

There are several limitations to our study. First, subjects performed the prebreathe in a laboratory environment that does not faithfully simulate the distracting conditions on a dive deck before a dive. We attempted to lessen any impact of the laboratory setting by maintaining lively conversation among investigators (without directly involving the subjects) throughout each prebreathe trial.

Second, unlike a real world scenario in which there would be a low expectation of problems, and although blinded, our subjects knew there was a substantial chance of being randomised to breathe on a loop with a scrubber fault. It was reassuring that despite this, there were no false positives among 20 subjects when there was a normal scrubber in place. Nevertheless, the experiment almost certainly promoted vigilance and our results arguably represent a best possible case for prebreathe sensitivity (see also the fourth point below).

Third, due to difficulties in recruiting 60 subjects for the study, we block-randomised 30 subjects to two of three

scrubber conditions and imposed a concealed manipulation on the order of those two conditions such that the condition least likely to result in hypercapnia was tested first in all participants. This required the subjects to undertake two prebreathes at least 20 minutes apart. Since the groups had some subjects in common, they are not entirely independent. We also considered the possibility of one exposure to inhaled CO_2 somehow affecting the physiological response to a second administered in close succession, but others have shown that this does not happen.¹⁴

Fourth, the use of an antibacterial filter did impose a small increase in the manometric pressures required to move a fixed gas volume around the circuit (Table 3). This could have contributed to an increased tendency to retain CO_2 , but given subjects in the normal condition (and even the partly-failed condition) maintained a normal $P_{ET}CO_2$, there is little evidence to suggest a prominent effect in that regard. The small increase in breathing resistance imposed by the filter may also have increased sensitivity of the prebreathe to the fault conditions by increasing the likelihood of dyspnoea as the $P_{ET}CO_2$ increased. Thus, we reiterate that our results arguably represent a best possible case for prebreathe sensitivity.

Finally, the investigators were not blinded to scrubber condition. It is therefore possible that the primary outcome could have been influenced by subtle differences in the way we interacted with the subjects. However, there was little opportunity for this. Once the prebreathe started, no attempts were made to ask the subjects questions or engage them in any conversation. Discussion about the state of the rebreather or the outcomes for other subjects were explicitly avoided during experimental runs.

We also believe the study has several strengths. First, it is the only study known to address this issue with blinded subjects and careful physiological monitoring. Second, the fact that none of 20 subjects terminated when breathing with a normal scrubber suggests that expectation of problems was not excessively high, blinding was effective, and the slight increase in resistance associated with use of the antibacterial filter did not substantially increase perceptions of hypercapnic symptoms. Third, the study incorporated a repeatable partly-failed condition arising from an assembly error known to have occurred many times in real-world diving. The implications for translation of study findings to the diving community are obvious. Finally, all 30 volunteers attended the study sessions and completed their allocated experimental trials. There were no drop outs resulting in missing data.

Conclusions

The five-minute prebreathe is an insensitive test for CO_2 scrubber function in a diving rebreather, even when the scrubber canister is absent. A prebreathe is nevertheless recommended for purposes such as checking the function

of the oxygen addition system before entering the water, but a duration less than five minutes should be adequate for that purpose. Arguably the most important secondary finding of our study is that partial scrubber failure in a rebreather is a particularly insidious fault if divers rely on a prebreathe to detect it. By modestly increasing ventilation, subjects typically maintain normocapnia during a surface prebreathe in this condition, resulting in a false negative that is dangerous because normocapnia is much less likely to be maintained during the dive itself. These findings raise concerns around methods for testing and monitoring safe CO₂ elimination in rebreather circuits. Several manufacturers offer CO₂ analyzers in the inhale limb of the rebreather circuit as an option, but these are not yet mainstream features. We recommend that rebreather training courses emphasize the importance of correct packing and installation of CO₂ scrubber canisters. There is mounting evidence that divers are poor at recognizing the early symptoms of hypercapnia (during both prebreathes and diving) and strategies for avoidance of hypercapnia should be prioritized.

References

- Doolette DJ, Mitchell SJ. Recreational technical diving part 1. An introduction to technical diving. *Diving Hyperb Med.* 2013;43:86-93.
- Higuchi H, Adachi Y, Arimura S, Kanno M, Satoh T. The carbon dioxide absorption capacity of Amsorb is half that of soda lime. *Anesth Analg.* 2001;93:221-5.
- Mitchell SJ, Cronje F, Meintjes WAJ, Britz HC. Fatal respiratory failure during a technical rebreather dive at extreme pressure. *Aviat Space Environ Med.* 2007;78:81-6.
- Arieli R, Ertracht O. Latency to CNS oxygen toxicity in rats as a function of PCO₂ and PO₂. *Eur J Appl Physiol.* 1999;80:598-603.
- Arieli R, Rashkovan G, Moskovitz Y, Ertracht O. PCO₂ threshold for CNS oxygen toxicity in rats in the low range of hyperbaric PO₂. *J Appl Physiol.* 2001;91:1582-7.
- Hesser CM, Adolfson J, Fagraeus L. Role of CO₂ in compressed air narcosis. *Aerospace Med.* 1971;42:163-8.
- Graham D, Bozanic JE. Prebreathing during closed-circuit diving apparatus set-up ineffective in assessing scrubber efficacy. In: Vann RD, Denoble PJ, Pollock NW, editors. *Rebreather Forum 3 Proceedings*, Durham, NC: AAUS/DAN/PADI; 2014. p. 268-71.
- Doolette DJ, Mitchell SJ. Hyperbaric conditions. *Comprehensive Physiol.* 2011;1:163-201.
- Jarrett AS. Alveolar carbon dioxide tension at increased ambient pressures. *J Appl Physiol.* 1966;21:158-62.
- Poon CS. Ventilatory control in hypercapnia and exercise: Optimization hypothesis. *J Appl Physiol.* 1987;62:2447-59.
- Poon CS. Effects of inspiratory resistive load on respiratory control in hypercapnia and exercise. *J Appl Physiol.* 1989;66:2391-9.
- Poon CS. Effects of inspiratory elastic load on respiratory control in hypercapnia and exercise. *J Appl Physiol.* 1989;66:2400-6.
- Shykoff BE, Warkander DE. Exercise carbon dioxide (CO₂) retention with inhaled CO₂ and breathing resistance. *Undersea Hyperb Med.* 2012;39:815-28.
- Sahn SA, Zwilllich CW, Dick N, McCullough RE, Lakshminarayan S, Weil JV. Variability of ventilatory responses to hypoxia and hypercapnia. *J Appl Physiol.* 1977;43:1019-25.
- Sherrill DL, Swanson GD. On-line computer estimation of carbon dioxide response curves. *J Clin Monit.* 1986;2:198-202.
- Lanphier EH, Bookspan J. Carbon dioxide retention. In: Lundgren CEG, Miller JN, editors. *The Lung at Depth*. New York: Marcel Dekker; 1999. p. 211-36.
- Schaefer KE. Respiratory pattern and respiratory response to CO₂. *J Appl Physiol.* 1958;13:1-14.
- Davis FM, Graves M, Guy H, et al. Carbon dioxide responses and breath-hold times in underwater hockey players. *Undersea Biomedical Research.* 1987;14:527-34.
- Kerem D, Melamed Y, Moran A. Alveolar PCO₂ during rest and exercise in divers and non-divers breathing O₂ at 1 atm abs. *Undersea Biomedical Research.* 1980;7:17-26.

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An observation of venous gas emboli in divers and susceptibility to decompression sickness

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Abstract

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Introduction: Decompression sickness (DCS) results from the formation of bubbles within the tissues and blood in response to a reduction in environmental pressure. Venous gas emboli (VGE) are common after diving and are usually only present in small numbers. Greater VGE numbers are an indication of decompression stress, and can be reliably detected using ultrasound imaging.

Aim: To examine the relationship between production of VGE following a routine dive and the risk of DCS.

Methods: A matched population of divers with and without a history of DCS were monitored for the production of VGE at 15-minute intervals using ultrasound, following a 405 kPa air dive in a hyperbaric chamber using the DCIEM air decompression table. VGE production was graded using a validated grading system and the data analysed to compare maximum VGE grade and duration of VGE formation.

Results: Eleven divers with a history of DCS were compared with 13 divers with no history of DCS. Divers with a history of DCS demonstrated both a higher maximum grade ($P = 0.04$) and longer duration ($P = 0.002$) of VGE production compared to divers without a history of DCS.

Conclusion: Higher maximum VGE grades and longer durations of VGE following decompression were associated with a history of DCS and, in particular, musculoskeletal DCS. Although the exact mechanism of DCS remains poorly understood, our data suggest some individuals are inherently more prone to develop VGE, increasing the probability of DCS. Modification of diving practices in those with high VGE grades could potentially decrease DCS risk in these individuals.

Key words

Decompression sickness, Doppler, venous gas emboli, scuba diving

Introduction

Decompression sickness (DCS) arises from the formation of bubbles within the tissues and blood in response to a reduction in environmental pressure. These bubbles can be measured in the form of venous gas emboli (VGE) by ultrasound imaging. The number of VGE can be used to indicate a diver's exposure to decompression stress.^{1,2} Standardised grading systems of these VGE have been established to predict this risk.³⁻⁵

It appears that some divers are more prone to developing DCS than others. Although the grade of bubble production and subsequent risk of developing DCS has been studied widely, it is not known whether divers with a history of DCS produce higher levels of VGE after routine diving. The aim of this study was to establish whether there is an association between the production of VGE in an individual diver and the risk of developing DCS.

Methods

We performed an observational cohort study comparing a population of divers with a history of DCS to a control group of divers with no history of DCS. The study was approved by the South Metropolitan Health Service Human Research Ethics Committee (HREC), Western Australia (approval no: 13/27), and The University of Notre Dame Australia HREC,

Western Australia (approval no: 13057F). Informed, written consent was obtained for all subjects.

STUDY POPULATION

Divers with a history of DCS were recruited from the Fremantle Hyperbaric Unit database of divers treated between 2009 and 2013. The control group was a sample of volunteer contacts recruited from local diving clubs, and divers known to the researchers.

Inclusion criteria for DCS subjects included a history of mild to moderate DCS that had been medically diagnosed and treated at the Fremantle Hospital Hyperbaric Unit. All the divers had been medically cleared to dive again. Subjects in the control group were experienced recreational divers with a minimum of 50 logged dives who had not previously been medically diagnosed with DCS. Similarly the DCS subjects were all experienced recreational divers with over 50 logged dives. The age range for inclusion in the study was 18 to 60 years of age.

Divers with DCS who were excluded from the study were those who had been recommended to cease diving permanently because of severe DCS, those with a history of neurological symptoms and signs consistent with a diagnosis of cerebral artery gas embolism (CAGE) and those with a known history of DCS features that were suggestive of a

patent foramen ovale (PFO). Control divers who had no history of DCS were excluded if a PFO or other atrial septal defect was identified during echocardiography.

DIVING PROTOCOL

The simulated diving protocol involved a no-decompression bounce dive to 405 kPa with a 15-minute bottom time in a multiplace chamber. The dive profile followed the Defence and Civil Institute of Environmental Medicine (DCIEM) air table and was used due to its recognised safety profile. Groups of up to six divers were studied over four consecutive weekends out of the diving season in July 2013. None of the divers in the study had dived during the week prior to the study.

VGE MONITORING

Observations began immediately following the dive at time zero and then every 15 minutes until a minimum of at least 75 minutes had elapsed if no VGE had been detected, or for a minimum of two clear scans (30 minutes) post cessation of any detected VGE. Subjects were imaged supine in the left lateral position with a phase-array cardiac ultrasound probe (1–4 MHz) attached to a Zonare Z1 ultrasound machine. A right ventricular foreshortened apical view of the heart was performed to assess for VGE production and the left side of the heart assessed for the presence of VGE that may have ‘arterialised’. The scans were performed by a hyperbaric physician with a formal qualification in ultrasound. VGE were graded using the Eftedal and Brubakk two-dimensional echocardiographic imaging scale.³ The grading system is described as follows:

Grade 0 – No observed bubbles

Grade 1 – Occasional bubbles

Grade 2 – At least one bubble every four cardiac cycles

Grade 3 – At least one bubble every cardiac cycle

Grade 4 – At least one bubble per cm² in every image

Grade 5 – White-out, single bubbles cannot be discriminated

Subjects were imaged for up to 60 seconds at a time and the images were recorded as 10-second prospective loops and saved on to a database for review. No dynamic manoeuvres were performed prior to or during the imaging. The divers were carefully monitored and reviewed for symptoms of DCS by a hyperbaric physician.

STATISTICAL ANALYSIS

Descriptive data are described as means \pm standard deviations (SD). Test of normality was carried out using the Shapiro-Wilk test, showing normally distributed data; normal distribution was not significantly skewed. Normality was confirmed using Q-Q plots for both age and BMI. Between-group comparisons for continuous data were assessed with Student’s *t*-tests. Non-parametric data were assessed using the χ^2 comparison for independence. Effect

size was calculated using the phi coefficient. The Mann-Whitney U test was used to compare bubble formation and duration for those with and without DCS. Statistical significance was set at $P < 0.05$. Analysis was performed using SPSS version 20.

Results

Twenty-six subjects were recruited into the study with 24 included in the final data analysis. One subject was excluded for a previous episode of cutaneous DCS that had not been formally assessed for the presence of a PFO, whilst a second participant, a very thin female, from the non-DCS group was excluded due to difficulty attaining high-quality ultrasound images. The 24 subjects consisted of 18 males and six females (Table 1). From the 11 subjects in the DCS group, six had a history of musculoskeletal DCS, three lymphatic, one mild spinal and one constitutional DCS. The three patients with lymphatic DCS had undergone formal PFO testing with transthoracic bubble contrast echocardiography and no PFOs were detected.

No subjects developed symptoms or signs of DCS during the study. VGE were only observed in the right heart with no subject having an obvious PFO or other atrial septal defect.

Neither age ($P = 0.94$) nor body mass index ($P = 0.62$) were associated with a history of DCS in this study. Overall, the DCS group was more likely to produce bubbles at any grade compared with the non-DCS group: ($\chi^2 [1, n = 24] = 4.847, P = 0.04, \phi = 0.44$). Non-parametric assessment of bubble producers against DCS showed that there was a significant difference in maximum grade across DCS types (Mann-Whitney U test: Z-value -2.2, $P = 0.03$). The median bubble grade for those without a history of DCS was 0 (no bubbles produced), and 1 for those with DCS.

Because of single subjects in the groups representing mild spinal and constitutional forms of DCS post hoc, Bonferroni analysis was not possible on the group as a whole. With the removal of the two groups mentioned above, those who formed bubbles remained more likely to have had DCS than those who did not: ($\chi^2 [2, n = 22] = 9.1, P = 0.01, \phi = 0.56$). There remained a significantly higher bubble grade across the DCS types (Mann-Whitney U test: Z-value -1.8, $P = 0.04$).

Table 1

Demographic profile of divers involved in the study; means (SD) shown for age and BMI – body mass index; there were no differences between the groups

| | Male | Female | Age (years) | BMI (kg·m ⁻²) |
|----------------|------|--------|-------------|---------------------------|
| No DCS | 11 | 2 | 42 (9) | 27 (4) |
| History of DCS | 7 | 4 | 41 (9) | 26 (5) |
| Combined group | 18 | 6 | 42 (8) | 27 (4) |

Table 2
Group comparison of DCS type and VGE grade; * 15 minute intervals

| | Bubble grade | | Time points (n) with bubbles * | | Subjects (n) with bubble grade \geq |
|-----------------------------|--------------|---------|--------------------------------|---------|--|
| | median | maximum | median | maximum | |
| 1 | | | | | |
| No DCS (n = 13) | 0 | 2 | 0 | 1 | 5 |
| Musculoskeletal DCS (n = 6) | 1 | 3 | 4 | 6 | 6 |

The same assessment was performed for DCS type against VGE duration, demonstrating a significant increase in duration of VGE production among those with prior DCS: ($\chi^2 [1, n = 24] = 9.151, P = 0.002, \phi = 0.66$). As above, constitutional and mild spinal groups were removed from analysis due to single participants and the assessment performed again with duration of VGE production compared to no DCS, lymphatic DCS and musculoskeletal DCS. This again demonstrated a significant difference in distribution of duration of VGE production across the groups: ($\chi^2 [1, n = 22] = 7.84, P = 0.005, \phi = 0.66$). Table 2 shows differing DCS types with respect to the median and maximum bubble grades and detectable bubble durations.

Discussion

Previous research has suggested no direct correlation between the increased presence of VGE and the risk of DCS development; however, the absence of VGE has been strongly associated with decompression safety.^{2,6-8} This seems to suggest that there is a complex relationship between the presence of bubbles and their pathological effects. Our research suggests that divers with a history of DCS, on average, produce VGE over a longer period and at a higher grade than divers never having experienced DCS. This indicates that an individual diver's characteristics influence bubble formation following decompression even in the absence of DCS.

No single mechanism has been elicited for the formation of DCS, with a multitude of processes likely to contribute. Such processes include gas bubbles causing direct mechanical effects, gas emboli resulting in downstream ischaemia and interactions with the endothelium of blood vessels resulting in the release of inflammatory mediators.⁹⁻¹² Given the complex relationship between the grade of VGE formation and the development of DCS, the duration of bubble formation may become increasingly important. A prolonged action of VGE formation could potentially increase the risk of DCS via two mechanisms. Firstly a sustained action of bubbles could increase the degree of endothelial interaction, and the release of inflammatory mediators. Secondly given that DCS may develop in the absence of high bubble grades, longer durations of VGE formation could increase the risk of DCS occurring simply by increasing time-exposure to the abnormal intravascular milieu.

Divers with a history of DCS, specifically those with musculoskeletal manifestations, appear more prone to producing longer durations of VGE and higher grades in comparison to those divers having never experienced DCS but also possibly in those having experienced other DCS types. However, the limited numbers in our study mean no firm conclusions can be drawn in this regard. Lymphatic DCS remains poorly understood and has traditionally been grouped with other cutaneous forms of the disease. Cutaneous DCS is associated with a PFO;¹³ however, the three divers with lymphatic DCS had been formally screened for inter-atrial shunting. It is hypothesised that lymphatic DCS could be caused by local tissue compression whilst diving from the pressure effect of, for example, a buoyancy control device and, therefore, may only need small bubble loads to cause symptoms that may not be related to the degree of intravascular bubble formation.¹⁴ Further, this independent mechanism, if unrelated to intravascular VGE formation, may not be associated with as high a risk as musculoskeletal and neurological DCS.

The variability between divers identified in this study is suggestive of certain physiological catalysts that facilitate bubble production, found in differing degrees between subjects. One explanation may be the varying presence of hydrophobic surfaces within the body. It has long been suggested that large bubbles require a pre-existing gas nucleus to form around, with studies aimed at decreasing these gas nuclei being successful in reducing the observed rate of DCS in rats.^{15,16} Caveolae have been proposed as possible sites for the formation and stabilisation of bubble nuclei within the endothelium.¹⁷ These 50–100 nm cup-shaped depressions found in plasma membranes are composed of specialised lipid domains and thought to be involved in numerous processes including cell signalling, endocytosis and cell metabolism.¹⁸ Since hydroxymethyl coenzyme A reductase inhibitors (statins) have been demonstrated to decrease levels of caveolae, one intriguing possibility would be the effect of statins on bubble formation.¹⁹

Following experimental studies it has been proposed that nanobubbles may spontaneously form on flat hydrophobic surfaces from dissolved gases in solution under hyperbaric conditions.²⁰ This, in combination with the structure of caveolae and their propensity for distribution within endothelial and muscle tissues, could possibly be a factor in bubble formation.²¹ Their regulation in response to the

expression of proteins and the role that cholesterol plays in their existence could account for varying degrees of bubble formation demonstrated between participants.²²

Fremantle Hyperbaric Unit treats on average 35 to 40 patients with decompression illness (DCI) a year from across Western Australia. We hope to increase our study population in future studies. A number of additional factors also clearly play a role in the development of DCS. Previous studies have associated increasing age, gender and weight with an increased production of VGE.²³ We found no such statistical correlations but do note the mean age of our DCS group is higher. The presence of a PFO has been linked to an increased risk of developing DCI, so we attempted to exclude any patients with known PFOs or diagnostic features of PFOs, such as a history of migraines, characteristic skin rashes or neurological symptoms.^{24,25}

The low levels of VGE production seen in this study are consistent with previously published data on short bounce dives and low levels of bubbling in keeping with the DCIEM tables.²⁶ The DCIEM tables were developed with the exclusion of diver profiles that produce a greater than 50% incidence of grade 2 bubbling.²⁷ The schedule used in the study was chosen for its safety profile. It will be interesting to see if we can replicate the results in future studies over a range of diving tables and with more provocative dive profiles producing higher levels of VGE. Dynamic manoeuvres, often in the form of knee bends, can be performed during monitoring for VGE to 'squeeze' bubbles into the venous circulation. This provides showers of bubbles that can be easily detected; however, these dynamic manoeuvres are hard to standardise and were not used in this study.

Conclusions

This study has demonstrated that a higher maximum VGE grade and longer durations of VGE production following decompression from a pressure of 405 kPa were associated with a history of DCS, and in particular musculoskeletal DCS. Although the exact mechanism of DCS remains poorly understood, our data suggest that some individuals are inherently more prone to develop VGE, increasing their likelihood of DCS. We would suggest that patients who have been treated for DCS be advised to modify their diving practices as they appear to be at an increased risk. Further studies are needed to identify the exact mechanisms of VGE production, so that targeted therapies can be applied to individuals at risk of DCS.

References

- Eftedal OS, Lydersen S, Brubakk AO. The relationship between venous gas bubbles and adverse effects of decompression after air dives. *Undersea Hyperb Med.* 2007;34:99-105.
- Nishi RY, Brubakk AO, Eftedal OS. Bubble detection. *Bennett and Elliot's physiology and medicine of diving*, 5th ed. Toronto: Saunders; 2003. p. 501-30.
- Eftedal OS, Brubakk AO. Agreement between trained and untrained observers in grading intravascular bubble signals in ultrasonic images. *Undersea Hyperb Med.* 1997;24:203-9.
- Brubakk AO, Eftedal O. Comparison of three different ultrasonic methods for quantification of intravascular gas bubbles. *Undersea Hyperb Med.* 2001;28:131-6.
- Pollock NW. Use of ultrasound in decompression research. *Diving Hyperb Med.* 2007;37:68-72.
- Sawatzky KD. *The relationship between intravascular Doppler-detected gas bubbles and decompression sickness after bounce diving in humans.* MSc Thesis, Toronto, Ontario: York University; 1991.
- Möllerlökken A, Gaustad SE, Havnes MB, Gutvik CR, Hjelde A, Wisloff U, et al. Venous gas embolism as a predictive tool for improving CNS decompression safety. *Eur J Appl Physiol.* 2012;112:401-9.
- Eftedal OS, Tjelmeland H, Brubakk AO. Validation of decompression procedures based on detection of venous gas bubbles: A Bayesian approach. *Aviat Space Environ Med.* 2007;78:94-9.
- Jepson PD, Arbelo M, Deaville R, Patterson IA, Castro P, Baker JR, et al. Gas-bubble lesions in stranded cetaceans. *Nature.* 2003;425(6958):575-6.
- L'Abbate A, Kusmic C, Matteucci M, Pelosi G, Navari A, Pagliazzo A, et al. Gas embolization of the liver in a rat model of rapid decompression. *Am J Physiol Regul Integr Comp Physiol.* 2010;299:R673-82.
- Neuman TS. Arterial gas embolism and decompression sickness. *News Physiol Sci.* 2002;17:77-81.
- Vince RV, McNaughton LR, Taylor L, Midgley AW, Laden G, Madden LA. Release of VCAM-1 associated endothelial microparticles following simulated SCUBA dives. *Eur J Appl Physiol.* 2009;105:507-13.
- 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.
- Trevett AJ, Sheehan C, Forbes R. Decompression illness presenting as breast pain. *Undersea Hyperb Med.* 2004;94:270-3.
- Katsenelson K, Arieli Y, Abramovich A, Feinsod M, Arieli R. Hyperbaric oxygen pretreatment reduces the incidence of decompression sickness in rats. *Eur J Appl Physiol.* 2007;101:571-6.
- Arieli R, Boaron E, Abramovich A. Combined effect of denucleation and denitrogenation on the risk of decompression sickness in rats. *J Appl Physiol.* 2009;106:1453-8.
- Razani B, Woodman SE, Lisanti MP. Caveolae: from cell biology to animal physiology. *Pharmacol Rev.* 2002;54:431-67.
- Bastiani M, Parton RG. Caveolae at a glance. *J Cell Sci.* 2010;123(Pt 22):3831-6.
- Hailstones D, Sleur LS, Parton RG, Stanley KK. Regulation of caveolin and caveolae by cholesterol in MDCK cells. *J Lipid Res.* 1998;39:369-79.
- Arieli R, Marmur A. Decompression sickness bubbles: are gas micronuclei formed on a flat hydrophobic surface? *Respir Physiol Neurobiol.* 2011;177:19-23.
- Cohen AW, Hnasko R, Schubert W, Lisanti MP. Role of caveolae and caveolins in health and disease. *Physiol Rev.* 2004;84:1341-79.
- Li S, Song KS, Koh SS, Kikuchi A, Lisanti MP. Baculovirus-based expression of mammalian caveolin in Sf21 insect cells. A model system for the biochemical and morphological study

- of caveolae biogenesis. *J Biol Chem.* 1996;271:28647-54.
- 23 Carturan D, Boussuges A, Burnet H, Fondarai J, Vanuxem P, Gardette B. Circulating venous bubbles in recreational diving: relationships with age, weight, maximal oxygen uptake and body fat percentage. *Int J Sports Med.* 1999;20:410-4.
- 24 Wilmshurst PT, Byme JC, Webb-Peploe MM. Relation between interatrial shunts and decompression sickness in divers. *Lancet.* 1989;2(8675):1302-6.
- 25 Moon RE, Camporesi EM, Kisslo JA. Patent foramen ovale and decompression sickness in divers. *Lancet.* 1989;1(8637):513-4.
- 26 Blogg SL, Gennser M. The need for optimisation of post-dive ultrasound monitoring to properly evaluate the evolution of venous gas emboli. *Diving Hyperb Med.* 2011;41:139-46.
- 27 Nishi RY, Eatock BC. The role of bubble detection in table validation. In: Schreiner HR, Hamilton RW, editors. *Validation of decompression tables.* The 37th Undersea and Hyperbaric Medical Society Workshop. Bethesda, MA: Undersea and Hyperbaric Medicine Society; 1989. p.133-8.

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The lifetimes of small arterial gas emboli, and their possible connection to inner ear decompression sickness

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Abstract

We solved both the diffusion and Laplace equations which predicted very similar results for the problem of a dissolving small gas bubble suspended in a liquid medium. These bubbles dissolved both because of surface tension and solute concentration effects. We focused on predicting bubble lifetimes ('td'), and dissolution dynamics – radius vs time (R vs t) for these contracting bubbles. We also presented a direct comparison of the predicted results, obtained by applying either Dirichlet or Neumann boundary conditions, to the bubble/medium interface. To the best of our knowledge, this is the first direct comparison that has ever been published on the application of these different boundary conditions to a moving gas/liquid boundary. We found that the results obtained by applying either Dirichlet or Neumann boundary conditions were very similar for small, short-lived bubbles ($R_0 < 25 \mu\text{m}$; $t_d < 40 \text{ s}$), but diverged considerably for larger, longer-lived bubbles. We applied our expressions to the timely problem of inner ear decompression sickness, where we found that our predictions were consistent with much of what is known about this condition.

Key words

Models, bubbles, inner ear, decompression sickness, arterial gas embolism, reprinted from

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Hyperbaric oxygen therapy increases insulin sensitivity in overweight men with and without type 2 diabetes

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Abstract

(Wilkinson D, Nolting M, Mahadi MK, Chapman I, Heilbronn L. Hyperbaric oxygen therapy increases insulin sensitivity in overweight men with and without type 2 diabetes. *Diving and Hyperbaric Medicine*. 2015 March;45(1):30-36.)

Aims: The onset of insulin resistance is an important metabolic event in the development of type 2 diabetes. For patients with type 2 diabetes, we recently showed that peripheral insulin sensitivity was increased during hyperbaric oxygen treatment (HBOT). This study aims to investigate whether this occurs in a non-patient population with and without type 2 diabetes, along with the mechanism of this effect.

Methods: Overweight and obese male participants were recruited from the community, 11 without and eight with type 2 diabetes. Insulin sensitivity was measured by the glucose infusion rate (GIR) during a hyperinsulinaemic euglycaemic clamp ($80 \text{ mU}\cdot\text{m}^{-2}\cdot\text{min}^{-1}$) at baseline and during the third HBOT session. Monocyte chemo-attractant protein-1 (MCP-1), tumour necrosis factor- (TNF-) and interleukin-6 (IL-6) were measured in fasting serum and adipose tissue samples taken for their gene expression at baseline and immediately following four HBOT sessions. Additional fasting serum samples were collected during the first HBOT at 0, 60 and 120 minutes, and 24-hours after the last HBOT.

Results: In response to HBOT, GIR was increased by $29 \pm 32\%$ in those without ($n = 10, P = 0.01$), and by $57 \pm 66\%$ in those with type 2 diabetes ($n = 7, P = 0.04$). This increase was maintained for 30 minutes post HBOT. Reduced MCP-1 and TNF- were observed after HBOT, whereas IL-6 was increased only in individuals without diabetes and this correlated with the increase in insulin sensitivity ($r^2 = 0.72, P = 0.004$).

Conclusions: Peripheral insulin sensitivity was increased following HBOT in overweight or obese males with and without type 2 diabetes; this increase was maintained for at least 30 minutes post HBOT. Changes in inflammatory cytokines may partly explain this effect.

Key words

Endocrinology, hyperbaric oxygen, obesity, diabetes, inflammation, metabolism, hyperbaric research

Introduction

Hyperbaric oxygen treatment (HBOT) is defined as breathing 100% oxygen at a pressure greater than 101.3 kPa and is used clinically to treat a range of conditions including non-healing wounds.¹ When patients with type 2 diabetes undergo HBOT they sometimes report symptoms of hypoglycaemia, while studies have shown that fasting glucose levels are reduced by a greater amount during HBOT as compared to room air in patients with type 2 diabetes.^{2,3} In a recent pilot study of hospital patients with type 2 diabetes who were receiving a prescribed course of HBOT for a medical condition, we showed that insulin sensitivity, as measured by the hyperinsulinaemic euglycaemic clamp technique, was increased during the third and the thirtieth HBOT sessions.⁴ The mechanism was not investigated and it was unknown whether the insulin-sensitising effect was influenced by their medical conditions improving over time.

Insulin resistance is defined as a relative impairment in the ability of insulin to exert its effect on glucose metabolism in target tissues (e.g., skeletal muscle, liver) and is considered one of the best predictors of the future development of type 2 diabetes.⁵ Obesity is also associated with insulin resistance,⁶ and both obesity and type 2 diabetes are increasing in prevalence and have become major health issues globally. Obesity-related insulin resistance is closely associated with a chronic, low-grade inflammatory response within

adipose tissue, characterised by immune cell infiltration, altered cytokine production and activation of inflammatory signalling pathways.⁷ Pro-inflammatory cytokines linked to insulin resistance include tumour necrosis factor (TNF)-,⁸ monocyte chemo-attractant protein (MCP)-1,^{9,10} interleukin (IL)-6^{11,12} and members of the IL-1 family; IL-1, IL-1 receptor antagonist (IL-1ra) and IL-18.¹³⁻¹⁵

This study aims to determine whether the insulin-sensitising effect of HBOT can be demonstrated in a relatively healthy urban population including those with and without type 2 diabetes, whether the effect is still measurable after exit from the hyperbaric chamber and whether HBOT-induced changes in insulin resistance are associated with changes in pro-inflammatory cytokines in serum and adipose tissue known to be associated with insulin resistance.

Methods

The study received ethics approval from the University of Adelaide and the Royal Adelaide Hospital (approval no: 100615). All investigations were conducted in accordance with the Declaration of Helsinki and all subjects provided written informed consent.

SUBJECTS AND SCREENING

Advertisements and a web-recruitment company were

used to enlist overweight and obese male volunteers (BMI > 25kg·m⁻²) who had no other excluded medical conditions apart from the sub-group with type 2 diabetes. As insulin sensitivity can vary throughout the menstrual cycle, only male volunteers were recruited. We undertook no specific investigation of the diabetes status of the volunteers, the diagnosis of type 2 diabetes was made from their personal medical history together with the prescription of appropriate medication. Excluded medical conditions included anything that could potentially alter insulin response or the inflammatory pathways being investigated, such as: smoking; consumption of more than three standard alcoholic drinks per day; vigorous exercise more often than twice a week; conditions that might be associated with a pathological inflammatory process or could influence inflammatory markers (such as sleep apnoea, malignancy, autoimmune and inflammatory diseases) and medication that might affect angiogenesis, lipid metabolism or have anti-inflammatory properties. Each volunteer was assessed for suitability to enter the hyperbaric chamber by a hyperbaric physician according to the standard clinical criteria used at the facility; this included history, examination and audiology assessment. Body composition was measured by dual-emission X-ray absorptiometry (DXA) to calculate fat mass and fat-free mass (FFM). Nineteen male volunteers were recruited, aged 45–70 years old, with BMI in the range of 24.3 to 45 kg·m⁻².

STUDY VISITS

Volunteers attended the Hyperbaric Medicine Unit at the Royal Adelaide Hospital on six occasions following a 10-hour overnight fast (Figure 1). Testing was undertaken at approximately the same time each morning and sampling was undertaken at a similar time each visit. Baseline assessments (V0) were performed one week and the following week participants attended the facility for five consecutive days (V1 to V5). Visits V1 to V4 included a routine 2-hour HBOT exposure. This involved compression to 203 kPa while breathing 100% oxygen for 90-minutes,

followed by a linear decompression over 30 minutes and was administered in a rectangular twin-lock multiplace hyperbaric chamber (Fink Engineering/Cowan Engineering, Australia, 1994).

The 3.5-hour hyperinsulinaemic euglycaemic clamp was performed at baseline (V0) and visit V3. The baseline clamp was performed in normobaric room air, outside the hyperbaric chamber, as previously described.¹⁶ Briefly, two intravenous cannulae were inserted into veins on opposite arms. One cannula was connected to an infusion of insulin (Actrapid®, Novo Nordisk, Baulkham Hills, Australia) at a fixed rate of 80 mU·m⁻²·min⁻¹, together with a variable-rate infusion of 25% dextrose (Baxter Healthcare, Toongabbie, Australia). The other cannula allowed five to 10-minutely blood sampling to assess blood glucose levels by a hand-held glucometer (Accu-Chek Performa, Roche Diagnostics, Australia). The target blood glucose level was 6 mmol·L⁻¹. Insulin sensitivity was calculated from the glucose infusion rate (GIR) during two separate 30-minute steady-state (SS) periods at the end of the 3.5-hour clamp; SS1 corresponded with the period 2.5 to 3 hours and SS2 with 3 to 3.5 hours. The GIR was then standardized against FFM for each volunteer. The clamp was repeated during visit V3 with the two-hour HBOT session administered between the one- and the three-hour period of the clamp.

Therefore, when considering insulin sensitivity results, SS1 represented the last 30 minutes of the HBOT session while SS2 reflected the first 30 minutes immediately post-HBOT. Serum insulin was measured during both steady state periods. To avoid any physical effort that might influence glucose uptake, the volunteers remained sedentary in a chair which was wheeled in and out of the hyperbaric chamber. One non-diabetic subject was unable to adequately perform middle ear equalization during the first HBOT and took no further part in the study. Data from SS2 were not available for two volunteers.

Blood samples were taken at three time points during the first HBOT at visit V1: at time zero (pre-HBOT) and at 60 and 120-minutes relative to the 2-hour HBOT session. Further blood samples were taken at visit V4 (immediately after the fourth HBOT) and V5 (24 hours later). Blood samples were analysed for fasting glucose and insulin as well as cytokine markers of inflammation that are known to be associated with insulin resistance (TNF- α , IL-6, IL-18, IL-1ra and MCP-1). Abdominal subcutaneous adipose tissue was biopsied at baseline (V0) and visit V4 according to previously described techniques, snap frozen in liquid nitrogen and subsequently analysed for gene expression of inflammatory markers (IL-6, IL-1ra, TNF- α and MCP-1).¹⁶

LABORATORY ANALYSIS

Blood glucose samples sent to the laboratory were analysed by the hexokinase method (Olympus 4500, Beckman, USA) and insulin was measured by radioimmunoassay (Merck

Figure 1

Timeline of study visits; V1–V5 were at same time of day on consecutive days; V0 was during the preceding week

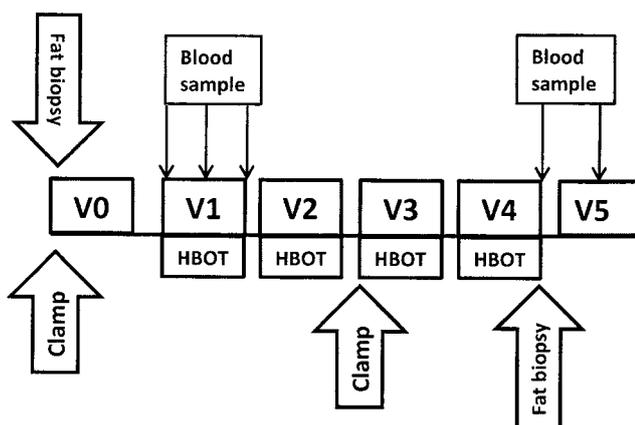


Table 1
Baseline characteristics of men, stratified by diabetes status; median (95% CI), * $P \leq 0.001$

| | Type 2 diabetes ($n = 8$) | | No diabetes ($n = 11$) | |
|---|-----------------------------|--------------|--------------------------|--------------|
| Age (years) | 53 | (49–60) | 64 | (53–66) |
| Height (m) | 1.76 | (1.69–1.79) | 1.74 | (1.69–1.80) |
| Weight (kg) | 99.1 | (87.9–111.5) | 92.8 | (80.4–108.5) |
| Body mass index (kg m^{-2}) | 30.8 | (29.8–35.5) | 30.5 | (27.5–34.6) |
| Body fat (%) | 35 | (30–40) | 32 | (29–38) |
| Glucose ($\text{mmol}\cdot\text{L}^{-1}$) | 9.8 | (8.0–12.9) * | 5.4 | (5.0–5.9) |
| HDL ($\text{mmol}\cdot\text{L}^{-1}$) | 1.2 | (0.9–1.3) | 1.2 | (0.9–1.5) |
| LDL ($\text{mmol}\cdot\text{L}^{-1}$) | 3.4 | (2.1–4.2) | 3.4 | (2.1–4.2) |
| Triglycerides ($\text{mmol}\cdot\text{L}^{-1}$) | 1.8 | (0.8–4.9) | 1.7 | (1.0–2.0) |
| Total cholesterol ($\text{mmol}\cdot\text{L}^{-1}$) | 5.6 | (4.4–6.8) | 5.3 | (4.5–5.9) |

Millipore, Billerica, MA, USA). Serum cytokine levels were determined using ELISA (R&D systems, Minneapolis, MN, USA). Total RNA was extracted from 100 mg adipose tissue using TRIzol reagent (Invitrogen, Carlsbad, CA). The integrity and concentration of RNA was assessed by spectrophotometry (Nanodrop, 2000, Thermoline). cDNA was synthesized using Omniscript RT kit (Qiagen, GmbH, Germany) and recombinant RNasin ribonuclease inhibitor (Promega, Madison, WI) according to kit instructions. For RT-PCR analyses, we used gene-specific primer probes from Taqman (MCP-1, IL-6, TNF- α , IL1- α) and Taqman universal PCR master mix (Applied Biosystems, Darmstadt, Germany). The samples were run in duplicate on an ABI Fast 7500 system (Applied Biosystems, Darmstadt, Germany) with internal negative controls and a standard curve. The cycle threshold (CT) value for each sample was normalized to the CT value of 18S ribosomal RNA to normalise for any changes in sample amplification, which was not different between V0 and V4.

STATISTICS

Statistical analysis was performed using SPSS for Windows (Version 19, SPSS Inc., Chicago, IL). Data were checked for normality by Shapiro-Wilk and log transformed prior to analysis if necessary. Differences between groups were analysed using one-way ANOVA. All other outcomes were analysed with linear mixed effects models using maximum likelihood estimation. Correlations were analysed by linear regression with coefficient of determination (r^2) and P value (Statistica v6, Statsoft, Tulsa, OK). Baseline characteristics, GIR and serum insulin were reported as median with 95% confidence intervals (CI_{95}). Significance was considered at $P < 0.05$.

Results

The baseline characteristics of groups stratified by diabetes status are shown in Table 1. Those with type 2 diabetes had higher fasting glucose ($P < 0.001$) and lower insulin sensitivity by hyperinsulinaemic clamp (Figure 2,

Figure 2

(A) Glucose infusion rate at baseline (V0) vs. HBOT (V3) during Steady State-1 (last 30 min of HBOT) in individuals with and without type 2 diabetes; (B), Glucose infusion rate at baseline vs. HBOT at Steady State-2 (first 30 min after HBOT) (mean and SEM, * $P < 0.05$, † $P < 0.01$)

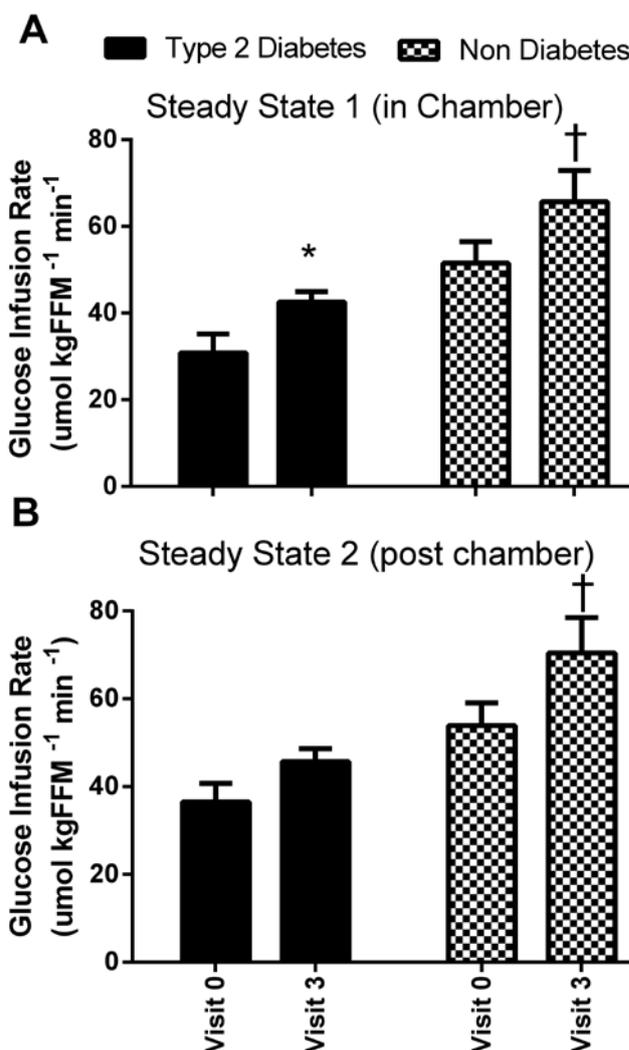
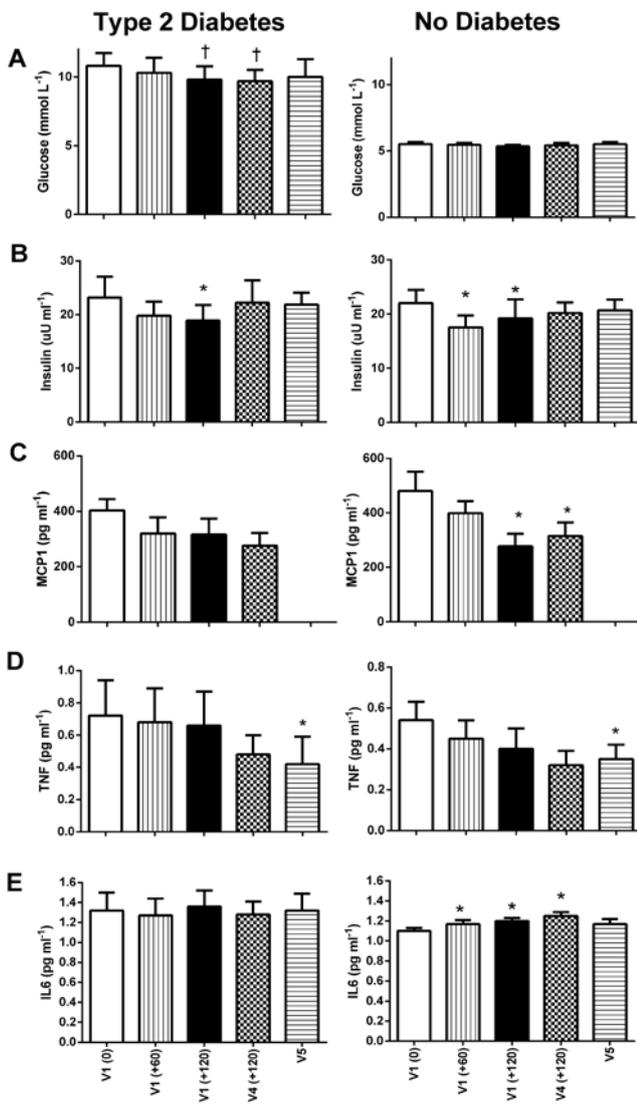


Figure 3

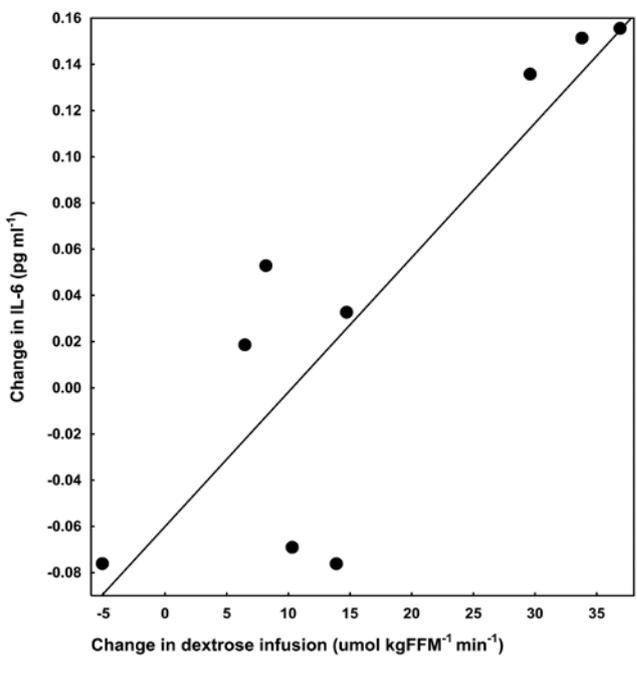
(A) Fasting glucose; (B) Insulin; (C); Monocyte chemotactic protein 1 – MCP-1; (D) Tumour necrosis factor – TNF ; (E) Interleukin–6 – IL-6 concentrations taken prior to and during the first HBOT exposure at 60 and 120 minutes, immediately following the 4th HBOT and 24 hours after the final HBOT (mean and SEM, * $P < 0.05$, † $P < 0.01$)



$P = 0.006$). A significant time effect was observed in the change in insulin sensitivity during the HBOT session (Figure 2A). For the group without diabetes, the median GIR at baseline in SS1 was $49.8 (39.6-62.7) \mu\text{mol}\cdot\text{kg}\cdot\text{FFM}^{-1}\cdot\text{min}^{-1}$. This increased during HBOT to $61.7 (49.4-82.1) \mu\text{mol}\cdot\text{kg}\cdot\text{FFM}^{-1}\cdot\text{min}^{-1}$. For the group with type 2 diabetes, baseline median GIR at SS1 was $32.6 (20.1-41.6) \mu\text{mol}\cdot\text{kg}\cdot\text{FFM}^{-1}\cdot\text{min}^{-1}$, increasing to $39.1 (36.6-48.5) \mu\text{mol}\cdot\text{kg}\cdot\text{FFM}^{-1}\cdot\text{min}^{-1}$ during HBOT. The increase in insulin sensitivity was maintained for an additional 30 minutes after exit from the hyperbaric chamber whilst breathing normobaric air in those without diabetes ($n = 9, P = 0.008$, Figure 2B), but this was not significant in the group with diabetes ($n = 6$, Figure

Figure 4

Relationship between the change in insulin sensitivity measured at visit V3 and change in serum interleukin–6 (IL-6) at visit V4 in non-diabetics ($r^2 = 0.72, P = 0.004$)



2B). During the baseline hyperinsulinaemic euglycaemic clamp, steady state serum insulin was $204.3 (182.8-229.4) \mu\text{U}\cdot\text{ml}^{-1}$ during SS1 and $199.2 (184.1-229.0) \mu\text{U}\cdot\text{ml}^{-1}$ during SS2, with no significant difference during HBOT.

We observed significant time effects for the change in glucose, insulin, MCP-1, TNF- and IL-6 with HBOT (all $P < 0.02$), with a time*group (diabetes/no diabetes) interaction observed in the change in fasting glucose only ($P = 0.03$). Further analysis by group revealed significant reductions in fasting glucose during the first and fourth HBOT sessions at 120 minutes only in those with type 2 diabetes (Figure 3A). Serum insulin was reduced during the first HBOT session in both groups (Figure 3B). MCP-1 was significantly reduced after HBOT at visits V1 and V4 in those without diabetes (Figure 3C), but this did not reach statistical significance in those with type 2 diabetes (Figure 3C). TNF- was significantly reduced 24-hours after the final HBOT in both groups (Figure 3D). In contrast, serum IL-6 was elevated in those without diabetes during and after HBOT at visits V1 and V4 (Figure 3E). The increase in IL-6 from baseline to visit 4 in the group without diabetes correlated with the increase in insulin sensitivity during SS2 ($n = 9, r^2 = 0.72, P = 0.004$, Figure 4). Neither group showed any significant changes for IL-1ra and IL-18 (data not shown). Adipose tissue was analysed for gene expression of IL-6, MCP-1, TNF- and IL-1ra; however, no significant changes were detected (data not shown).

Discussion

In this study, we have demonstrated that peripheral insulin sensitivity is increased following HBOT in a relatively healthy urban population sample. Moreover, we have demonstrated that the increase in insulin sensitivity occurs in overweight and obese males without diabetes as well as those with type 2 diabetes. Importantly, the insulin sensitising effect was maintained after exit from the hyperbaric chamber for at least 30 minutes. We also observed small changes in inflammatory cytokines following HBOT that may have partly contributed to the observed increases in insulin sensitivity.

Diabetes is a common contributing or coincidental factor in patients referred for HBOT. Within hyperbaric medicine practice, it has been recognised for some time that patients with diabetes are prone to a fall in blood glucose during HBOT.^{2,3} We also observed a significant fall in the blood glucose levels during the first HBOT in those with type 2 diabetes. Although greater decreases in fasting glucose inside versus outside the chamber have been reported,² we did not test this in our study and the changes could also be due to the prolonged length of the fast. Fasting glucose is predominantly under the control of hepatic glucose production; however, this was not specifically assessed in the current study. We also observed a fall in serum insulin during the first HBOT session in both groups; although other studies have found no effect of HBOT on insulin levels.^{2,17} Our previous study tested a patient population during clinical HBOT exposure,⁴ whilst the current study, which found a similar increase in insulin sensitivity, was in volunteers with no clinical indication for HBOT.

HBOT may induce an insulin-sensitizing effect by a number of possible mechanisms. Here, we studied circulating concentrations of pro-inflammatory cytokines since these have been observed in obesity and are closely associated with insulin resistance.⁷ TNF- is a pro-inflammatory cytokine which is overproduced from adipose tissue in human obesity,^{8,18} and infusion of TNF- induces insulin resistance in humans.¹⁹ The pro-inflammatory cytokine MCP-1 is also overproduced from adipose tissue in obesity²⁰ and impairs the insulin signalling cascade in a murine adipose tissue model independent of the associated macrophage infiltration.^{9,10} Reductions in both TNF- and MCP-1 were observed following HBOT and may partly explain the insulin-sensitizing effect, although the reduction in these cytokines did not correlate with the increase in insulin sensitivity.

IL-6 is a pleiotropic cytokine displaying both pro- and anti-inflammatory actions. Increased IL-6 is associated with human obesity and insulin resistance.^{11,21} Conversely, exercise, a known insulin sensitiser, is associated with a transient release of IL-6 from muscle,²² and acute infusion of IL-6 in humans leads to an increase in insulin sensitivity as measured by clamp studies.¹² IL-6 was not changed in those

with type 2 diabetes, but was acutely increased by HBOT in those without diabetes. Interestingly, this was positively associated with increased insulin sensitivity. However, the changes in IL-6 are clinically small and may be a chance finding. We did not observe changes in IL-6 expression in adipose tissue, but no other tissues were investigated in this study.

The literature is mixed regarding the effect of HBOT on circulating cytokines, although most studies support an anti-inflammatory action of HBOT. Animal models suggest HBOT has, in part, an anti-inflammatory action in positive outcomes to abdominal sepsis,²³ multi-organ dysfunction²⁴ and development of atherosclerosis.²⁵ Human clinical data suggest HBOT-induced immunomodulation may be behind reduced restenosis following coronary angioplasty and stenting,²⁶ better outcome following cardio-pulmonary bypass,²⁷ and following ischaemia-reperfusion-related soft-tissue crush injury.²⁸ Even HBOT in the treatment of decompression illness is recognised to include an anti-inflammatory modulation of neutrophil activity as part of the therapeutic mechanism.²⁹ However, isolated cytokine changes should be interpreted with caution since the final effect on insulin sensitivity may depend on “*a subtle balance of their relative concentrations (high or low), kinetics (acute or chronic) and targets*”.¹⁵

Alternatively, it has been proposed that insulin resistance may be induced by adipose tissue dysfunction secondary to hypoxia.³⁰ The growth of adipocytes in obesity is not matched by the blood supply, which may result in reduced oxygen delivery and regions of relative hypoxia.³⁰ Certainly, lower oxygen partial pressures have been measured in the adipose tissue of obese humans compared to lean controls.³¹ However, another study concluded that adipose tissue had low oxygen consumption and the measurement of lactate/pyruvate ratios in blood draining this tissue revealed no evidence of metabolic stress.³² The effects of hyperbaric oxygen on adipose tissue physiology have not been reported previously. However, studies investigating the reverse, using a hypoxic breathing gas mixture, have produced conflicting results. In two human studies using hyperinsulinaemic euglycaemic clamps, insulin resistance increased during acute exposure to hypoxia,³³ but decreased after a more chronic hypoxia protocol.³⁴ The substantial rise in tissue oxygen tensions associated with HBOT will also be accompanied by a transient increase in reactive oxygen species (ROS). This warrants further investigation since ROS, whilst having the potential to cause cell damage, also act as vital messengers in cell signalling,³⁵ including a positive effect on insulin signalling.³⁶

This study employed the hyperinsulinaemic euglycaemic clamp which is considered to be the gold standard technique to assess peripheral insulin sensitivity.³⁷ Performing the clamp in a hyperbaric chamber was novel and required consideration of some technical issues and physiological

responses. Our glucometer used glucose dehydrogenase as the strip reagent, found to be more accurate than glucose oxidase when exposed to increased ambient oxygen.³⁸ Microvascular alterations in blood flow can influence measurement of insulin sensitivity as a consequence of varying the glucose delivery to the tissues.³⁹ Therefore, it is relevant to consider that vasoconstriction is an expected physiological response to hyperbaric oxygenation.⁴⁰ While the effects of HBOT on the microvasculature have not been tested, the sustained increase in insulin sensitivity observed upon exit from the hyperbaric chamber suggests our results were not influenced by changes in tissue blood flow.

Insulin resistance is a pivotal early change in obesity-related type 2 diabetes. The identification of pathways that influence insulin responsiveness may potentially lead to clinical therapies that prevent the development or progression of this disease. This study introduces a pathway that has not previously been exploited. The new findings, that HBOT can also increase insulin sensitivity in those without diabetes and also that the effect is sustained for a period after HBOT, have implications beyond diabetes involving obesity and glucose metabolism broadly. Further studies are now required to describe the precise mechanisms involved and to define the time course of the insulin sensitising effect – how much HBOT is required to initiate the effect and how long it persists after leaving the hyperbaric chamber.

Conclusions

This study has demonstrated that hyperbaric oxygen leads to an increase in insulin sensitivity in an overweight and obese male population with and without type 2 diabetes mellitus. Furthermore, the increase in insulin sensitivity was still evident 30 minutes after exiting the hyperbaric chamber. We have also demonstrated a favourable modulation of inflammatory markers in response to HBOT that may partly explain this effect on insulin sensitivity.

References

- Gesell L, editor. *Hyperbaric oxygen therapy indications*. 12th ed. Durham, NC: Undersea and Hyperbaric Medical Society; 2008.
- Ekanayake L, Doolette DJ. Effects of hyperbaric oxygen treatment on blood sugar levels and insulin levels in diabetics. *SPUMS Journal*. 2001;31:16-20.
- Trytko B, Bennett MH. Blood sugar changes in diabetic patients undergoing hyperbaric oxygen therapy. *SPUMS Journal*. 2003;33:62-9.
- Wilkinson D, Chapman IM, Heilbronn LK. Hyperbaric oxygen therapy improves peripheral insulin sensitivity in humans. *Diabet Med*. 2012;29:986-9.
- Warram JH, Martin BC, Krolewski AS, Soeldner JS, Kahn CR. Slow glucose removal rate and hyperinsulinemia precede the development of type II diabetes in the offspring of diabetic parents. *Ann Intern Med*. 1990;113:909-15.
- Hotamisligil GS. Inflammation and metabolic disorders. *Nature*. 2006;444:860-7.
- Heilbronn LK, Campbell LV. Adipose tissue macrophages, low grade inflammation and insulin resistance in human obesity. *Curr Pharm Des*. 2008;14:1225-30.
- Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor- α : direct role in obesity-linked insulin resistance. *Science*. 1993;259:87-91.
- Tateya S, Tamori Y, Kawaguchi T, Kanda H, Kasuga M. An increase in the circulating concentration of monocyte chemoattractant protein-1 elicits systemic insulin resistance irrespective of adipose tissue inflammation in mice. *Endocrinology*. 2010;151:971-9.
- Kanda H, Tateya S, Tamori Y, Kotani K, Hiasa K, Kitazawa R, et al. MCP-1 contributes to macrophage infiltration into adipose tissue, insulin resistance, and hepatic steatosis in obesity. *J Clin Invest*. 2006;116:1494-505.
- Kern PA, Ranganathan S, Li C, Wood L, Ranganathan G. Adipose tissue tumor necrosis factor and interleukin-6 expression in human obesity and insulin resistance. *Am J Physiol Endocrinol Metab*. 2001;280:E745-51.
- Carey AL, Steinberg GR, Macaulay SL, Thomas WG, Holmes AG, Ramm G, et al. Interleukin-6 increases insulin-stimulated glucose disposal in humans and glucose uptake and fatty acid oxidation in vitro via AMP-activated protein kinase. *Diabetes*. 2006;55:2688-97.
- Jager J, Gremeaux T, Cormont M, Le Marchand-Brustel Y, Tanti JF. Interleukin-1 β -induced insulin resistance in adipocytes through down-regulation of insulin receptor substrate-1 expression. *Endocrinology*. 2007;148:241-51.
- Lagathu C, Yvan-Charvet L, Bastard JP, Maachi M, Quignard-Boulangé A, Capeau J, et al. Long-term treatment with interleukin-1 β induces insulin resistance in murine and human adipocytes. *Diabetologia*. 2006;49:2162-73.
- Feve B, Bastard JP. The role of interleukins in insulin resistance and type 2 diabetes mellitus. *Nature Reviews Endocrinology*. 2009;5:305-11.
- Heilbronn LK, Rood J, Janderova L, Albu JB, Kelley DE, Ravussin E, et al. Relationship between serum resistin concentrations and insulin resistance in nonobese, obese, and obese diabetic subjects. *J Clin Endocrinol Metab*. 2004;89:1844-8.
- Chen SJ, Yu CT, Cheng YL, Yu SY, Lo HC. Effects of hyperbaric oxygen therapy on circulating interleukin-8, nitric oxide, and insulin-like growth factors in patients with type 2 diabetes mellitus. *Clin Biochem*. 2007;40:30-6.
- Kern PA, Saghizadeh M, Ong JM, Bosch RJ, Deem R, Simsolo RB. The expression of tumor necrosis factor in human adipose tissue. Regulation by obesity, weight loss, and relationship to lipoprotein lipase. *J Clin Invest*. 1995;95:2111-9.
- Plomgaard P, Bouzakri K, Krogh-Madsen R, Mittendorfer B, Zierath JR, Pedersen BK. Tumor necrosis factor- α induces skeletal muscle insulin resistance in healthy human subjects via inhibition of Akt substrate 160 phosphorylation. *Diabetes*. 2005;54:2939-45.
- Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr. Obesity is associated with macrophage accumulation in adipose tissue. *J Clin Invest*. 2003;112:1796-808.
- Bastard JP, Jardel C, Bruckert E, Blondy P, Capeau J, Laville M, et al. Elevated levels of interleukin 6 are reduced in serum and subcutaneous adipose tissue of obese women after weight loss. *J Clin Endocrinol Metab*. 2000;85:3338-42.
- Febbraio MA, Pedersen BK. Muscle-derived interleukin-6: mechanisms for activation and possible biological roles. *FASEB Journal*. 2002;16:1335-47.
- Buras JA, Holt D, Orlow D, Belikoff B, Pavlides S, Reenstra

- WR. Hyperbaric oxygen protects from sepsis mortality via an interleukin-10-dependent mechanism. *Crit Care Med.* 2006;34:2624-9.
- 24 Rinaldi B, Cuzzocrea S, Donniacuo M, Capuano A, Di Palma D, Imperatore F, et al. Hyperbaric oxygen therapy reduces the toll-like receptor signaling pathway in multiple organ failures. *Intensive Care Med.* 2011;37:1110-9.
- 25 Kudchodkar B, Jones H, Simecka J, Dory L. Hyperbaric oxygen treatment attenuates the pro-inflammatory and immune responses in apolipoprotein E knockout mice. *Clin Immunol.* 2008;128:435-41.
- 26 Sharifi M, Fares W, Abdel-Karim I, Koch JM, Sopko J, Adler D. Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol.* 2004;93:1533-5.
- 27 Alex J, Laden G, Cale ARJ, Bennett S, Flowers K, Madden L, et al. Pretreatment with hyperbaric oxygen and its effect on neuropsychometric dysfunction and systemic inflammatory response after cardiopulmonary bypass: A prospective randomized double-blind trial. *J Thorac Cardiovasc Surg.* 2005;130:1623-30.
- 28 Bouachour G, Cronier P, Gouello JP, Toulemonde JL, Talha A, Alquier P. Hyperbaric oxygen therapy in the management of crush injuries: a randomized double-blind placebo-controlled clinical trial. *Journal of Trauma, Injury, Infection and Critical Care.* 1996;41:333-9.
- 29 Martin JD, Thom SR. Vascular leukocyte sequestration in decompression sickness and prophylactic hyperbaric oxygen therapy in rats. *Aviat Space Environ Med.* 2002;73:565-9.
- 30 Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr.* 2004;92:347-55.
- 31 Pesarica M, Sereda OR, Redman LM, Albarado DC, Hymel DT, Roan LE, et al. Reduced adipose tissue oxygenation in human obesity: evidence for rarefaction, macrophage chemotaxis, and inflammation without an angiogenic response. *Diabetes.* 2009;58:718-25.
- 32 Hodson L, Humphreys SM, Karpe F, Frayn KN. Metabolic signatures of human adipose tissue hypoxia in obesity. *Diabetes.* 2013;62:1417-25.
- 33 Oltmanns KM, Gehring H, Rudolf S, Schultes B, Rook S, Schweiger U, et al. Hypoxia causes glucose intolerance in humans. *Am J Respir Crit Care Med.* 2004;169:1231-7.
- 34 Lecoultre V, Peterson CM, Covington JD, Ebenezer PJ, Frost EA, Schwarz JM, et al. Ten nights of moderate hypoxia improves insulin sensitivity in obese humans. *Diabetes Care.* 2013;36:e197-8.
- 35 Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. *Plast Reconstr Surg.* 2011;127(Suppl 1):131-41.
- 36 Tiganis T. Reactive oxygen species and insulin resistance: the good, the bad and the ugly. *Trends Pharmacol Sci.* 2011;32:82-9.
- 37 Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance in vivo: advantages, limitations, and appropriate usage. *Am J Physiol Endocrinol Metab.* 2008;294:E15-26.
- 38 Tang Z, Louie RF, Lee JH, Lee DM, Miller EE, Kost GJ. Oxygen effects on glucose meter measurements with glucose dehydrogenase- and oxidase-based test strips for point-of-care testing. *Crit Care Med.* 2001;29:1062-70.
- 39 Rattigan S, Bussey CT, Ross RM, Richards SM. Obesity, insulin resistance, and capillary recruitment. *Microcirculation.* 2007;14:299-309.
- 40 Abel FL, McNamee JE, Cone DL, Clarke D, Tao J. Effects of hyperbaric oxygen on ventricular performance, pulmonary blood volume, and systemic and pulmonary vascular resistance. *Undersea Hyperb Med.* 2000;27:67-73.

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The database of randomised controlled trials in hyperbaric medicine maintained by Michael Bennett and his colleagues at the Prince of Wales Hospital Diving and Hyperbaric Medicine Unit, Sydney is at:
<<http://hboevidence.unsw.wikispaces.net/>>

Assistance from interested physicians in preparing critical appraisals is welcomed, indeed needed, as there is a considerable backlog. Guidance on completing a CAT is provided.

Contact Associate Professor Michael Bennett: <m.bennett@unsw.edu.au>

Technical report

Performance of the Baxter Infusor LV10 under hyperbaric conditions

Iestyn Lewis, David Smart, Bebe Brown and Carol Baines

Abstract

(Lewis I, Smart D, Brown B, Baine C. Performance of the Baxter Infusor LV10 under hyperbaric conditions. *Diving and Hyperbaric Medicine*. 2015 March;45(1):37-41.)

Introduction: Elastomeric drug delivery devices are a simple way to provide long-term IV therapy to patients in the outpatient setting. Patients receiving hyperbaric oxygen therapy occasionally need these devices. This study compared the performance of the Baxter infusor LV10 elastomeric device in repetitive conditions at pressures of 101.3 kPa and 243 kPa.

Methods: Ten Baxter infusor LV10 elastomeric devices were pressurised in a hyperbaric chamber to 243 kPa over a two-hour period consistent with a standard medical treatment run. This process was repeated 10 times for each device giving a total of 20 hours under pressure. The fluid delivered by each device was measured and the device weighed at the end of each pressurisation. Ten control devices containing identical drugs were tested in the same manner at 101.3 kPa over the same time period.

Results: No significant differences in output of the devices were observed between hyperbaric and control conditions. The flow rates measured in both study groups were 35% lower than the manufacturer's stated flow rate, possibly due to lower test environment temperature and outdated devices used in the tests.

Conclusion: Despite lower than expected flow rates, this study demonstrated no significant difference in the delivery rate of the Baxter infusor LV10 under 243 kPa hyperbaric conditions compared with room pressure.

Key words

Hyperbaric oxygen therapy, drugs, treatment, equipment, elastomers

Introduction

Elastomeric infusion pumps are disposable, non-electronic drug delivery devices. They provide an infusion of medication by deflation of a fluid-filled elastomeric balloon to drive solutions through intravenous (IV) tubing and into an IV catheter. Typical devices are stated to provide an infusion over 30 minutes to 12 days at +/- 10–20% of the desired flow rate.¹ Such pumps are small, lightweight, simple to use and enable ambulatory infusion therapy, particularly in the outpatient setting. They are used to deliver a wide variety of medication, such as antibiotics, analgesia and chemotherapy.

Hyperbaric oxygen treatment (HBOT) is the therapeutic use of oxygen at a pressure higher than one atmosphere absolute (101.3 kPa).² Given the nature of the conditions for which HBOT may be used, particularly infected deep wounds and osteomyelitis, patients often require long-term antimicrobial therapy, usually given orally, but IV antibiotics are sometimes required. Providing continuous infusions to a patient under hyperbaric conditions can be problematic using traditional electronic pumps.³ Pumps require modification to function in the hyperbaric environment to prevent failure or damage from the increased pressure. In addition, batteries and electronics pose a fire risk within the chamber.⁴ The majority of patients receiving HBOT are outpatients. In this setting, a cost-effective way to deliver IV antibiotics is via an elastomeric device over a 24-hour period.⁵

The Baxter LV10 infusor is the most commonly used

elastomeric device in patients who require long-term IV antibiotics at the Royal Hobart Hospital. It is a large-volume, elastomeric device containing 240 ml of fluid. It has a stated flow rate of 10 ml·h⁻¹ over a 24-hour period if the flow restrictor is kept at a temperature of 33°C.⁶ The elastomer is made of polyisoprene. Mechanical testing of this material shows that a filled device generates a decreasing flow rate while it delivered the first third of the fluid contained within it; a steady state is then reached until the flow rate increased just before the balloon empties, after which the flow rate drops precipitously.⁷ Figure 1 shows the flow rate as a function of time for a polyisoprene reservoir filled with different volumes.

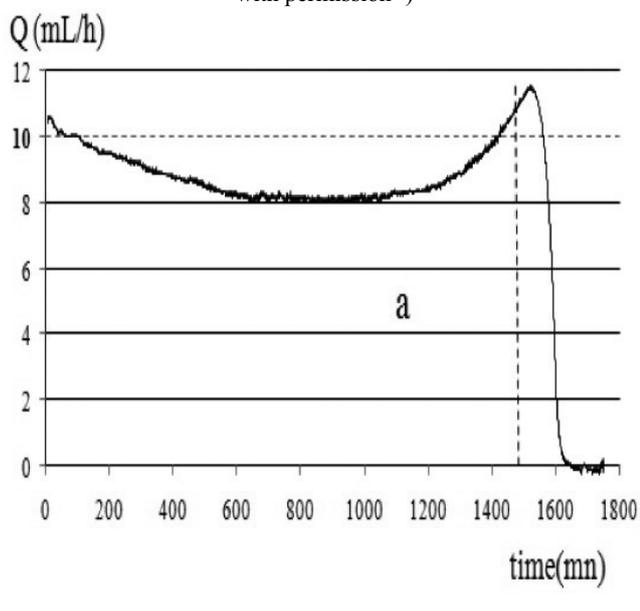
The aim of this study was to prospectively compare the performance of the Baxter Infusor LV 10 under clinically relevant hyperbaric conditions of 243 kPa to that at room pressure (101.3 kPa).

Method

The Baxter infusor LV10 elastomeric delivery devices used for this study were supplied at no cost because they had reached their expiry dates and were to be discarded by the Royal Hobart Hospital Pharmacy. Fourteen devices contained antibiotics (tazocin, vancomycin & ceftriaxone) and were one month out of date. Six devices contained dopamine and were 18 months out of date. Saline (0.9%) was the diluent for all medications in the elastomeric devices.

Figure 1

Flow rate as a function of time for a polyisoprene reservoir filled with 240 ml for a 10 ml·h⁻¹ claimed flow rate value (reproduced with permission¹¹)



The study apparatus is shown in Figure 2. The elastomeric devices were divided into two matched groups of 10 containing identical medications. Each group had four devices containing tazocin, three of dopamine, two ceftriaxone and one vancomycin. Ten elastomeric devices were placed inside the hyperbaric chamber and 10 were kept at room pressure outside the chamber. Both groups were then subject to 10 discrete two-hour sampling periods over 10 consecutive working days to a total of 20 hours of testing.

During sampling, fluid was run from the device via its infusion catheter into a 25-ml syringe. The syringe had the plunger removed and a luer-lock stopper to cover the tip, so it formed a closed collection reservoir. This was attached to the elastomeric device with an elastic band. A rubber balloon was used to cover the opening of the syringe to minimise evaporation of liquid. All the devices were weighed before the study and after every sampling period using laboratory scales. (ACB plus 600H, AE ADAM, Adam Equipment (SE Asia) PTY Ltd, Perth, Australia). These scales had been calibrated prior to the study to an accuracy of ± 10 milligrams. Sample volumes were also measured using the 1 ml graduations on the side of the syringe to the nearest millilitre. Following sampling, a luer-lock stopper was used to contain the remaining contents of the elastomeric device between sampling periods, which corresponded to each hyperbaric pressurisation.

Hyperbaric samples were pressurised to 243 kPa and the control group maintained at 101.3 kPa. A twin-lock, multiplace hyperbaric chamber was used for the study (Hydro-Electric Commission Enterprises Corporation, Hobart, 1992). The hyperbaric protocol involved pressurising

Figure 2

The Baxter Infusor LV 10 with syringe collection device and rubber syringe cover to prevent evaporation



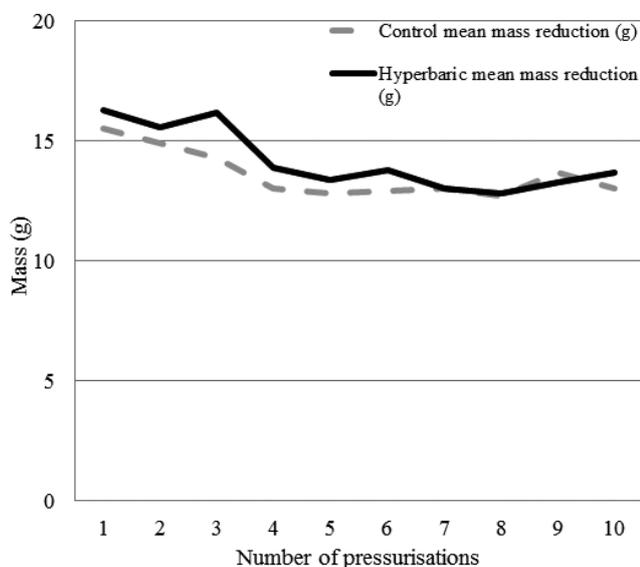
the chamber to 243 kPa over 10 minutes, remaining at pressure for 90 minutes, followed by 20 minutes of depressurisation; the standard clinical hyperbaric treatment at our facility. Ten consecutive measurements were collected from each device to assess flow rates across the devices' life cycle. This was considered clinically relevant as some patients may receive more than one treatment per day, or they may be receiving HBOT at any time across the 24-hour period of elastomeric device delivery. The control group was tested at 22°C and the hyperbaric group at 23°C; some variability in temperature was experienced in the hyperbaric group during compression and decompression.

At the start of each sampling period, the devices were unclamped and allowed to drain into the measuring syringe for two hours before being clamped off. As this was an open system there was no resistance to the discharge of fluid. At the end of each sampling period, the volume of discharged fluid was measured and the device weighed. Volumes and masses for each sampling period were then tabulated producing 10 measurements for each of the 10 devices in both groups.

Data are presented as the mean and 95% confidence intervals (95% CI). Differences in mass and volume between the hyperbaric and control groups were compared with an unpaired Student's *t*-test. A linear mixed model regression was also produced to account for the repeated results over

Figure 3

Total change in mass delivered by Baxter infusor LV10 over each two-hour sample period



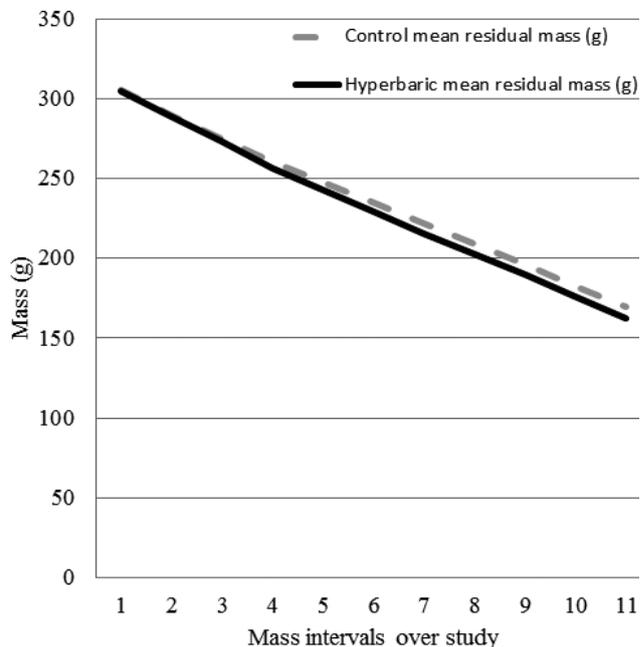
time and to allow for the variability of the different devices. Power analysis showed 20 infusion devices would have a power of 90% to predict a 15% difference in flow rate with an α -value of 0.05. Two statistics programmes were used: Graphpad Prism 6, Graphpad Software Inc. version 6.0e 2014, La Jolla CA and Stata 12, Stata Corp 2011, Stata Statistical Software Release 12, College Station TX.

Results

The hyperbaric group delivered slightly larger volumes than the control group, 13.5 ml (95% CI 12.5–14.4) vs. 12.8 ml (11.9–13.5). Mean mass reduction per pressurisation was 14.22 g (13.28–15.17) hyperbaric vs. 13.57 g (12.86–14.28) control. Neither of these results was statistically significant. Analysis of the individual treatment runs showed no statistically significant difference between the hyperbaric group and the control group at any time. The mean mass reduction was 0.65 g less (-0.97 to 2.28) in the control group (13.57) compared to the hyperbaric group (14.22). The mean volume reduction was 0.7 ml (0.9–2.3) less in the control group compared to the hyperbaric group. Over the 10 sample periods all devices in both groups progressively delivered less fluid in each two-hour sample collection period. The mean mass reduction decreased by 0.30 g (-0.34 to -0.26 g) for both groups per successive two-hour period. The mean volume reduction fell by 0.3 ml (-0.4 to -0.3) for both groups per successive two-hour interval ($P < 0.001$). The linear mixed model regression showed that neither the mean mass reduction nor the mean volume reduction differed significantly ($P = 0.43$ and $P = 0.39$ respectively) between the control and hyperbaric groups when averaged over the 10 sample periods.

Figure 4

Mean residual mass in the Baxter infusors over 11 samples and 10 sampling periods for the hyperbaric (243 kPa) and control (101.3 kPa) groups



The delivery rate was slightly higher in the first three sample periods, when the devices were full. After this, both groups of devices settled into a relative steady state (Figure 3). Charting the total residual mass of the devices over the eleven mass measurements during the study showed there was no difference between the groups (Figure 4). When hourly flow rates were calculated, neither group achieved their stated nominal flow rate of 10 ml·h⁻¹; hyperbaric group 6.6 ml·h⁻¹ (5.9–7.3) control group 6.3 ml·h⁻¹ (5.6–6.9).

Further calculations were made in an attempt to control for the actual ambient temperatures in this study compared to the manufacturer’s specified optimum temperature. Lower ambient temperatures were stated to produce lower flow rates. Using data from the manufacturer, flow rates are stated to fall by 2.3% for every 1°C below 33°C. Table 1 summarises the measured flow rates and the theoretical calculated flow rates if the ambient study temperatures of 22–23°C were converted to 33°C.

Subgroup analysis showed that the less out-of-date antibiotic devices delivered 15.2 ml (14.0–16.5) over two hours for the hyperbaric group and 14.4 ml (13.0–15.8) for the control group. The dopamine group delivered 11.9 ml (11.7–12.5) over two hours for the hyperbaric group and 11.6 ml (9.0–14.2) for the control group. There were no significant differences in flow rates between the hyperbaric and the control groups for either the antibiotic or dopamine samples, but the differences in flow rates between the newer antibiotic preparations and the older dopamine solutions

Table 1

Calculated volumes delivered over 60 min at the study temperature (22–23°C) and when converted to the manufacturer's specified optimum operating temperature of 33 °C and using their temperature change data (2.3% per 1°C)⁶; mean (95% CI)

| | Hyperbaric group | Control group |
|--|-------------------------|----------------------|
| Measured flow rate (ml·hr ⁻¹) at 22–23°C | 6.6 (5.9–7.3) | 6.3 (5.6–6.9) |
| Calculated flow rate (ml·hr ⁻¹) at 33°C | 8.3 (7.4–9.2) | 8.1 (7.2–8.9) |

were statistically significant ($P = 0.025$ in the hyperbaric group and $P = 0.005$ in the control group).

Discussion

Previous studies have shown variable performance of elastomeric devices under hyper- and hypobaric conditions.^{8–10} Nineteen On-Q pain infusion devices were tested under hyperbaric conditions against five atmospheric controls, all at room temperature. The devices in the hyperbaric group were subjected to six 104-minute treatment protocols; seven minutes to pressurise the chamber, 90 minutes at a test pressure of 101.3, 203, 243 or 304 kPa and seven minutes to depressurise. No differences in delivery performance were found at pressure, although there was a decrease in output over the 10 hours the devices were subject to testing. Initial output in the first 104-minute study period was 30% higher than the stated device output. By the sixth study period, after 10 hours of testing, the device was delivering 6% above the stated output. Testing was only carried out for 10 hours of the potential 28-hour lifespan of the device quoted by the manufacturer.⁸

The Baxter infusor LV10 device has been tested under a wide range of atmospheric conditions (81, 91, 101.3, 172 and 253 kPa for 21.5 hours at an ambient temperature of 30–32°C.⁹ No significant difference in flow rates were discerned between different atmospheric pressures if the complete unit (reservoir and restrictor) were at the same pressure. Increased flow rates have been observed in an elastomeric patient-controlled analgesia (PCA) system under hyperbaric conditions, particularly with dextrose solutions.¹⁰ These changes were more profound with higher concentration dextrose solutions, which are particularly viscous. Viscosity has an inverse relationship to flow rate and increasing concentrations of drug may affect a solution's viscosity.¹

Our data on the Baxter Infusor LV10 are consistent with the materials science data available on polyisoprene elastomers, where at full stretch (when the elastomeric balloon is full), there is greater tension on the elastomer, and a non-linear steeper tension-versus-length curve results. The effect on the clinical device is to produce greater pressure on the contents and a higher flow rate in the first quartile of the device's functional time line. In the middle two quartiles,

the tension versus length curve is relatively linear and even (Figure 1), delivering a relatively consistent flow rate, which is important clinically. In the last quartile of its functional time line, as the elastomer returns to its resting empty state, the tension falls rapidly as the volume falls and a reduced flow results.⁷

The devices were not tested until empty in our study, so we cannot comment on the performance in the last four hours of their 24-hour life. Based on our findings, each device would contain in excess of 70 ml of medication. A residual volume is clinically desirable, because it ensures some tension remains in the elastomer, thus ensuring that the flow (drug delivery) is maintained. The variability of flow rates across time was confirmed in this study, although it was not our primary aim.

We found no significant differences in flow rates between devices exposed to 243 kPa hyperbaric conditions and devices at room pressure. In the hyperbaric-exposed devices, pressure is exerted on the whole apparatus, and the elastomeric balloon was vented to the external pressure via holes in the protective casing. Hence, there are no areas of higher or lower pressure within the device.

Unlike the previous studies on the On-Q and Baxter devices,^{8–10} the delivered flows in our study were consistently lower than the flow rates claimed by the manufacturer by up to 35%, but this was independent of pressure. Some of this underperformance could be attributed to the ambient temperatures under which our study was conducted. A second study on the On-Q pain infusion device exposed to temperature changes of 15–33°C above and below room temperature found that output varied by up to 50%.¹¹

Baxter states that the ideal temperature for the use of the LV10 is 33°C, with a variability of +2.3% for every 1°C increase in temperature and -2.3% for every 1°C decrease in temperature.⁶ The flow restrictor for this device is part of the leur-lock connector which, in clinical use, will be close to skin temperature. A potential flaw in this study is that the devices were tested at room temperature. Considering this, a reduction in drug delivery of approximately 20% could have been expected. We did attempt to correct for the temperature difference from the manufacturer's ideal by undertaking a theoretical calculation of flow rates using the above data. Even with this correction, the devices still underperformed.

Whether the manufacturer's 'optimal' temperature of 33°C is actually achieved in routine clinical use is unproven and requires investigation. Because the flow restrictor for this device is part of the leur-lock connector in clinical use, it is usually taped to the underlying skin. Skin temperature varies markedly with cardiovascular and hydration status, pyrexial infections and variations in ambient conditions, etc. Therefore, if the assumption is that the device is close to skin temperature, mounting the device on the skin may result in marked

variations in delivered flow rates. This has never been studied for these devices. Therefore, we chose to test the devices at a controlled ambient temperature environment of 22–23°C.

Two additional factors may account for the lower flow rates observed in our study. These include the age of the elastomer and the viscosity of the solution. All the devices were out of date, but the oldest (dopamine, 18 months out of date) had significantly lower flow rates than the one-month out of date antibiotic-filled devices. It is likely that the aging process reduces the performance of the elastomer. Polyisoprene elastomer is similar to rubber in structure, and has similar potential to 'perish', thus reducing its elasticity. Differences in viscosity of the contents may also have affected the performance of the elastomers used in this study.^{1,9} Baxter were unable to provide the viscosity figures for the different drugs, but it must be remembered that the diluent in each bottle was 0.9% saline (Baxter Healthcare Pty Ltd, personal communication, 2014). A further possible interaction could be the direct effect of the contents on the elastomer, accelerating its breakdown. It would seem that even in new devices there are variations in flow rate due to the characteristics of the contents that are not able to be applied in the daily clinical setting.

Variations in performance and the factors that affect elastomeric performance must be taken into account when treating patients with these devices. It is a concern that if patients had received treatment from the devices used in our study, they would have received a substantially lower dose of medication than expected. However, given the freedom of mobility provided for the patient and the cost effectiveness for long-term treatment using elastomeric devices, an under-performance of 20–30% may be acceptable for delivering antibiotics to patients with chronic infections.⁵ If this is a consistent finding, drug doses could also be increased to compensate. Unfortunately, due to our use of out-dated elastomeric devices, and undertaking the study at lower than recommended temperatures, caution should be given to generalising from our data to patient populations. However, such underperformance is unlikely to be acceptable when analgesia, local anaesthesia and chemotherapy agents are being delivered. Ideally the study should be repeated with a total study period of 24 hours using in-date devices. Despite some limitations to this study, the important finding was that the devices performed the same at 243 kPa pressure in the chamber as they did at a normal atmospheric pressure of 101.3 kPa.

Conclusion

Our investigation demonstrates no significant difference in performance in the Baxter Infusor LV10 when used under clinically relevant hyperbaric conditions, providing the whole device is under pressure. On this basis we consider this device may be suitable for clinical use in the hyperbaric environment, but further validation is required.

References

- 1 Skryabina E, Dunn TS. Disposable infusion pumps. *Am J Health-Syst Pharm.* 2006;63:1260-8.
- 2 Mathieu D. *Handbook on hyperbaric medicine.* Dordrecht: Springer; 2006.
- 3 Lavon H, Shupak A, Tal D, Ziser A, Abromovich A, Yanir Y, Shoshani O, Gil A, Leiba R, Nachum Z. Performance of infusion pumps during hyperbaric conditions. *Anesthesiology.* 2002;96:849-54.
- 4 Australian Standards. *Work in compressed air and hyperbaric facilities. Part 2 Hyperbaric oxygen facilities.* AS4774.2 section 3.8, Standards Australia International Ltd 2002.
- 5 Bernard L, El-hajj, Pron B, Lotthe A, Gleizes V, Signoret F, et al. Outpatient parenteral antimicrobial therapy (OPAT) for the treatment of osteomyelitis: evaluation of efficacy, tolerance and cost. *J Clin Pharm Ther.* 2001;26:445-51.
- 6 *Baxter elastomeric pumps clinician guide.* Ontario, Canada: Baxter Corporation; 2010.
- 7 Guiffant G, Durussel JJ, Flaud P, Vigier JP, Dupont C, Bourget P, Merckx J. Mechanical performances of elastomers used in diffusers. *Med Devices (Auckl).* 2011;4:71-6.
- 8 Tobias JD, Johnson GA, Patel M. Performance of the On-Q pain infusion device during hyperbaric therapy. *Anesth Analg.* 2011;113:275-7.
- 9 Wang J, Moeller A, Ding YS. Effects of atmospheric pressure conditions on flow rate of an elastomeric infusion pump. *Am J Health-Syst Pharm.* 2012;69:587-91.
- 10 Radcliffe JJ, Spencer I. Performance of the Baxter disposable patient-controlled analgesia infusor under hyperbaric conditions. *Anaesthesia.* 1994;49:796-7.
- 11 Burnett T, Bhalla T, Sawardekar A, Tobias JD. Performance of the On-Q pain infusion device during changes in environmental temperature. *Pediatr Anesth.* 2011;21:1231-3.

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Physicians and critical care in hyperbaric chambers

Papers from the European Underwater and Baromedical Society (EUBS) special session at the 40th Annual Scientific Meeting in Wiesbaden, Germany, September 2014

The following four papers are based on previously unpublished presentations and discussions from the European Committee for Hyperbaric Medicine (ECHM) satellite symposium, Sharm El-Sheik, Egypt, in 2007 and updated at a special session of the EUBS Annual Scientific Meeting, Wiesbaden, September 2014. The session was co-chaired by Michael A Lang, OxyHeal Health Group, National City, California, USA, Karin Hasmilller, BG-Unfallklinik Murnau, Murnau-am-Staffelsee, Germany and Peter HJ Müller, Universitätsspital Basel, Basel, Switzerland and past European Editor, *Diving and Hyperbaric Medicine*.

All faculty members openly disclosed any conflict of interest that could have influenced the content of their presentations; however, there were none. In addition to the investments made by the participants, the EUBS and the ECHM are most grateful to the Organisation Committee of the EUBS 2014 Conference and the OxyHeal Health Group for their administrative efforts and generous financial support in making this session possible.

Hyperbaric oxygen therapy for intensive care patients: position statement by the European Committee for Hyperbaric Medicine

Daniel Mathieu, Beatrice Ratzenhofer-Komenda and Jacek Kot

Abstract

(Mathieu D, Ratzenhofer-Komenda B, Kot J. Hyperbaric oxygen therapy for intensive care patients: indications and risk/benefit balance. *Diving and Hyperbaric Medicine*. 2015;45 March;45(1):42-46.)

Many of the accepted indications for hyperbaric oxygen treatment (HBOT) may occur in critically ill patients. HBOT itself may cause a number of physiological changes which may further compromise the patient's state. Guidelines on the management of critically ill patients in a hyperbaric facility have been founded on the conclusions of the 2007 European Committee for Hyperbaric Medicine (ECHM) meeting. With regard to patient management, HBOT should be included in the overall care of ICU patients only after a risk/benefit assessment related to the specifics of both the hyperbaric centre and the patient's clinical condition and should not delay or interrupt their overall management. Neither patient monitoring nor treatment should be altered or stopped due to HBOT, and any HBOT effects must be strictly evaluated and appropriately mitigated. With regard to the hyperbaric facility itself, the hyperbaric chamber should be specifically designed for ICU patients and should be fully equipped to allow continuation of patient monitoring and treatment. The hyperbaric chamber ideally should be located in, or around the immediate vicinity of the ICU, and be run by a sufficiently large and well-trained team of physicians, nurses, chamber operators and technicians. All devices to be introduced into the chamber should be evaluated, tested and acknowledged as safe for use in a hyperbaric environment and all procedures (standard and emergency) should be tested and written before being implemented.

Key words

Hyperbaric oxygen treatment, intensive care medicine, standards, ECHM - European Committee for Hyperbaric Medicine, safety, hyperbaric facilities, patient monitoring, ventilators, training

Introduction

Hyperbaric oxygen treatment (HBOT) is a therapeutic modality in which oxygen (O₂) is given via the patient's respiratory system at a pressure above atmospheric pressure. The objective is to obtain an increase in tissue oxygen pressure, either to compensate for a deficiency in oxygen supply, or to recruit the effects of oxygen delivered at partial pressures above normal.

Many of the accepted indications for HBOT may occur in critically ill patients. However, HBOT causes many

physiological changes that may further compromise a patient's haemodynamic and respiratory state. Furthermore, to provide intensive care inside a hyperbaric chamber is not an easy task and many hyperbaric centres do not have the chamber, equipment and trained staff to provide such care. Finally, the hyperbaric facility is rarely in the immediate vicinity of the intensive care unit (ICU), so repeated patient transport between the ICU and the chamber may be necessary, with all its attendant, potentially adverse events.

Therefore, the decision to treat an ICU patient with HBOT is made by a careful risk/benefit analysis related to the specifics

of both the hyperbaric centre and the patient's condition. This explains the heterogeneity in practice between centres that have developed an expertise in treating ICU patients and those more orientated towards outpatient treatment.

HBOT actions and indications in ICU patients

The therapeutic mechanisms of HBOT are complex and may be summarized as follows:^{1,2}

- Reduction of the volume of gas bubbles by increasing the hydrostatic pressure;
- Correction of tissue hypoxia by increasing blood oxygen content via dissolved oxygen;
- Redistribution of blood flow to hypoxic areas due to reduction in oedema and the hyperoxic vasoconstriction in healthy regions, without inducing downstream hypoxia;
- Increased red blood cell deformability which, combined with the reduced oedema formation, enhances microcirculatory blood flow;
- Antibacterial actions through direct effects on anaerobic bacteria and indirect effects on aerobic bacteria by enhancing the microbicidal capability of polymorphonuclear leukocytes;
- Enhanced cellular metabolism, with preservation of intracellular ATP and reduced oxidative injury to cells;
- Through actions on reactive oxygen and nitrogen species, the adherence properties of neutrophils are enhanced, modulating inflammatory cytokine production and enhancing protective tissue defence mechanisms such as heme oxygenase 1, heat shock proteins and hypoxia-inducible factor 1- production.

These actions, alone or in combination, provide the rationale for HBOT. In the list of ECHM-accepted indications for HBOT, several may concern critically ill patients:

- Air or gas embolism;
- Decompression injury (especially severe neurological cases);
- Carbon monoxide poisoning (including that associated with burns, smoke inhalation or cyanide poisoning);
- Necrotising soft-tissue infections, including gas gangrene;
- Crush injury, compartment syndrome, open fracture Gustillo III b and c and other traumatic acute ischaemia;
- Selected cases of neurological disorders such as intracranial abscess;
- Compromised grafts and flaps in the immediate post-operative period;
- Acute burn injury.

Not all patients with such disorders are critically ill; it is often the most severe forms that require intensive care. All these disorders are accepted indications in Europe for HBOT currently treated in hyperbaric centres in hospitalized patients in a general ward or as an outpatient. However, if the patient requires ICU care, many hyperbaric physicians are reluctant to treat with HBOT, yet paradoxically it is these

severely ill patients who may have the most to gain from the addition of HBOT to their clinical management.³

Physiological changes induced by HBOT

This reluctance to treat ICU patients with HBOT is explained in part by the fact that, besides the usual risks of HBOT (barotrauma, oxygen toxicity, claustrophobia, fire), HBOT induces several physiological changes that may further compromise the patient's condition, especially the cardio-respiratory systems.

VENTILATION

Two main factors have to be taken into account to predict patient respiratory behaviour under HBOT. Firstly for a patient breathing spontaneously, the increase in gas density induces an increase in airway resistance which, in turn, leads to an increase in the work of breathing and in respiratory muscle oxygen consumption. The patient must be monitored carefully and assisted/controlled ventilation may need to be introduced earlier than at normal atmospheric pressure. Because assisted modes of ventilation are often based on demand regulators, the effort required to trigger inspiration and the level of pressure support have to be taken into account in considering the extra work of breathing due to the hyperbaric environment.

Secondly because of the difficulties in setting up many ventilators correctly under hyperbaric conditions and the lack of an assisted mode of ventilation in some models, fully controlled ventilation is often the preferred mode in a hyperbaric chamber. This is not without consequences, as sedation is often required to avoid patient/ventilator asynchrony and to reduce the risk of barotrauma.

Ventilation with pure oxygen induces a decrease in mucociliary clearance and the development of pulmonary micro-atelectasis, increasing intrapulmonary shunt. Hypoxic episodes after HBOT sessions have been reported and are probably explained by these mechanisms.⁴ In clinical practice, some simple measures may limit these problems; inhaled oxygen must be correctly humidified, a low level of positive end expiratory pressure (PEEP) should be applied (5–10 cm H₂O) and if hypoxia occurs after the HBOT session, recruitment manoeuvres should be used.

HAEMODYNAMICS

Haemodynamics are influenced by the same two factors as ventilation. The increase in gas density induces an increase in intrathoracic pressure, leading to an increase in right ventricular afterload and a decrease in right ventricular venous return. Thus, the right ventricle is at risk of failure. Usually, moderate intravenous volume infusion (0.5–1.0 L) is required at the beginning of the HBOT session and is sufficient to correct hypotension. However, in some patients, vasoactive drug support may be required.

The hyperoxia induced during HBOT leads to arterial vasoconstriction and an increase in systemic vascular resistance and left ventricular afterload, so the left ventricle is also at risk of failure. At best, haemodynamics should be stabilized before the HBOT session. In the case of haemodynamic instability, extensive invasive haemodynamic monitoring may be required to guide volume infusion and inotropic support. Conversely, HBOT may stabilise haemodynamics as its therapeutic effects come into play.

Patient condition may interfere with expected effects of HBOT

Another important point to consider in the risk/benefit balance of HBOT for ICU patients is organ failure, which may interfere with the expected beneficial effects of HBOT. In particular, in case of respiratory failure, the intrapulmonary shunt will impair the expected rise in arterial oxygen pressure (P_aO_2) and, therefore, compromise HBOT efficacy. Similarly, in the case of circulatory failure, decreased cardiac output and arterial vasoconstriction will impair organ blood flow and tissue oxygen delivery. Thus, in an under-resuscitated critically ill patient, HBOT may be ineffectual because the expected rise in tissue PO_2 will not occur. Therefore tissue oxygenation monitoring such as transcutaneous oxygen pressure is mandatory in order to correctly evaluate the effects of HBOT.

Aside from this potential decrease in the beneficial effects of HBOT, ICU patients may be at a higher risk of adverse events in the chamber. In respiratory failure, pulmonary heterogeneity with air trapping increases the risk of barotrauma. Trauma and surgery may create new air-filled cavities with an increased risk of barotrauma (e.g., intracranial pneumatocele). O_2 toxicity may be enhanced because cerebral trauma, sepsis and pyrexia decrease the hyperoxic convulsion level, and pulmonary injury may increase the sensitivity of the lung to hyperoxic injury.

Hyperbaric environmental constraints on patient care

Hyperbaric centres have specific characteristics in terms of location, chambers, environment and safety. However, ICU patients also require specific conditions with respect to these three characteristics and they are often far removed from those of elective hyperbaric practice. These constraints are not necessarily insurmountable, but need to be analysed and mitigated before accepting an ICU patient for treatment.⁵

LOCATION

Hyperbaric chambers are vessels designed to support pressures exceeding atmospheric pressure. The patient has to be transported from the ICU to the chamber and back after each session. Transportation of a critically ill patient may expose them to an increased risk of deterioration and requires specially equipped trolleys or beds in order to

continue patient monitoring and treatment during transfer; specially trained personnel and a specially formulated transfer management plan according to the Society of Critical Care Medicine guidelines.⁶

CHAMBER

Hyperbaric chambers are usually small compared to the recommended ICU room (26 m²). This may pose several detrimental consequences:

- Nosocomial infection may be favoured because of three factors: inter-patient distance is reduced, increasing the risk for cross-contamination; hyperbaric chambers are often cluttered with multiple valves, pipes and devices, making disinfection difficult and inefficient;
- Available free space for the attendant and patient accessibility are reduced, so cross-contamination prevention measures and care procedures are difficult to apply consistently;
- Noise, inadequate control of temperature and humidity and confinement make the working environment unpleasant. High nitrogen partial pressure may induce nitrogen narcosis, which will impair personnel's ability to deliver proper care.

All these factors contribute to increased nurse/physician stress and may lead to increased errors in patient management.

PERSONNEL

ICU patients are under constant supervision by well-trained nurses and specialized medical staff. This level of medical/nursing education and training cannot be permanently guaranteed in some hyperbaric centres. However, this is a prerequisite before acceptance of an ICU patient for treatment. The most important rules concerning HBOT personnel caring for ICU patients are:

- The patient has to be under physician/nurse control in an ICU room;
- Usually, nurses attend the patient in the hyperbaric chamber, while physicians are available if intervention is necessary (personnel lock required);
- All personnel have to be medically fit and educated to work under pressure;
- All personnel have to be educated and trained to be able to care for intensive care patients.

PATIENT MONITORING

All of the monitoring devices used in ICU should be adapted for use in the hyperbaric environment.⁷⁻⁹ These include:

Haemodynamics

- Electrocardiogram (ECG);
- Arterial pressure (non-invasive, invasive);
- Central venous pressure (CVP);
- PA catheter;
- Cardiac output (thermodilution, transthoracic bio-impedance, transoesophageal echocardiography);
- Mixed venous oxygen saturation (S_{vO_2}).

Ventilation

- Respiratory rate;
- Airway pressure;
- Tidal volume (V_T) (rotameter, pneumotachograph);
- Pulse oxymetry;
- Arterial blood gases;
 - Of little value when measurement is done outside the chamber;
 - Good value when measurement is done inside the chamber;
 - Easy when continuously measured by an intra-arterial probe;
 - Indirect evaluation by transcutaneous oxygen measurements;
- Expired gas measurements;
 - Measurement of end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$) by standard mainstream methods is subject to errors; sidestream capnometry is reliable for measurement if performed outside the chamber at room pressure on a decompressed gas sample;
 - Measurements are best performed by mass spectrometer (requires special, expensive installation).

Neurological

- Intracranial pressure (ICP);
- Electroencephalography (EEG);
- Bi-spectral EEG analysis;
- Jugular venous oxygen saturation (S_jO_2);

Other

- Temperature;
- Urine output;
- Intra-abdominal pressure;
- Intra-compartmental pressure.

Tissue oxygenation

Evaluation is mandatory in ICU patients to check if the rise in PO_2 expected under HBOT is reached:

- Transcutaneous oxygen pressure (TCOM)
- Continuous arterial oxygen pressure (P_aO_2)
- Tissue oxygen partial pressure (P_tO_2)
- For the future:
 - Tissue oxygen saturations (S_tO_2) and Cyto aa3 redox state by near-infrared spectroscopy (NIRS)
 - Lactate/pyruvate by microdialysis

TREATMENT DEVICES

The same rules apply to all therapeutic devices used in ICU:

Ventilation

- Mask and head hood may be easily used for non-invasive ventilation (NIV);
- Mechanical PEEP valve is preferred for continuous positive airway pressure (CPAP);
- Tracheal tube cuff must be water-filled; a foam cuff is a convenient alternative;
- Breathing gas must be correctly humidified;
- Tracheal aspiration must be accurately pressure-limited to avoid any mucosal injury.

Cardiac support

- Defibrillation is still a matter of debate due to safety

reasons.¹⁰ It is probably safe if the self-adhesive pads are placed and secured before the session and the defibrillator device is located outside the chamber. However, the clinical advantages of defibrillation inside the chamber under pressure, versus the traditional procedure (cardiac resuscitation, quick decompression and defibrillation at atmospheric pressure) are not established.

- External pacing (transthoracic and by intra-ventricular catheter) is safe if the device is placed outside, but should be validated after a risk analysis if the device is inside;
- Implantable pacemakers and defibrillators are safe up to 304 kPa;
- Artificial hearts are safe up to 405 kPa (at least on one patient!).

Infusion therapy

- Fluid administration by gravity: there is a risk of a decreased infusion rate and blood aspiration during compression, and uncontrolled infusion and gas embolism during decompression, related to the Boyle-Mariotte Law.
- Syringe pumps are safe if the soft key pad is open to ambient pressure (a cautionary note: some syringes have an air-filled space between the piston and the plastic tip).
- The infusion rate may be impaired during compression and decompression in infusion controllers, patient-controlled analgesic devices and insulin infusion pumps.
- Unplanned drug or device needs require an equipment lock to be permanently available.

Drainage and suctioning

- Intensive care patients often have multiple drainage systems. Most of these (e.g., pleural, mediastinal, pericardial and abdominal drains) require accurate, regulated negative-pressure drainage. High negative pressures may occur inadvertently during compression, with the consequent risk of organ injury and rupture. Conversely, low negative pressures or even overpressurisation may occur during decompression, with risks of barotrauma, gas embolism and/or retrograde fluid flow.
- The aspiration pressure has to be set before the HBOT session and remain constant throughout.
- Manual adjustment is difficult and may expose the patient to inadvertent over- or under-pressurisation.
- To use the pressure difference between the chamber and ambient pressure, even with a vacuum regulator, may be dangerous.
- The best system involves creating a vacuum with a Venturi device and using a second stage regulator.

SAFETY ASPECTS

Any medical device introduced into a hyperbaric chamber may be associated with increased risk to patients and attendants, as the function of the device may be altered and compromise patient care and/or safety, integrity of the device may be altered (exposing occupants to the risks of

fire, explosion and gas toxicity) and improper use of the device may occur.

The high partial pressure and any increase in the fraction of oxygen in the chamber atmosphere combined with a combustible product and a source of ignition (e.g., electrostatic sparks or an overheated surface) constitute the classic “*Triangle of Fire*”.

A major problem is the fact that manufacturers have to get prior approval to market any medical devices (in Europe: CE marking, in USA: FDA approval). All these approval processes require financial investments that may not be profitable as the market for medical devices to be used in a hyperbaric environment is small. As a consequence, many manufacturers do not apply for hyperbaric approval and thus, the responsibility for using such a device in a hyperbaric chamber is entirely that of the physician-in-charge.

Prior to installing a medical device in a hyperbaric chamber, the following rules must be followed:

- Make certain that it does not contain any closed compartments under atmospheric pressure and that the pressure in all compartments of the device is equivalent with that of the environment or that it is pressure-resistant to the working pressure of the chamber;
- Ensure, by conducting hyperbaric tests, that:
 - Controls, e.g., the keyboard pads, do not become distorted and function blocked;
 - Performance of the device probes do not deteriorate due to changes in pressure or this can be rectified;
 - Operation of the built-in electronics of the device is not compromised;
 - Display is not compromised;
 - Flow rates, pressures and frequencies with which the device dispenses any medical products are not compromised or, at least, are accurately evaluated;
 - In case of doubt, do not install the medical device in the chamber.

Conclusions

In the context of the ECHM-accepted indications for HBOT, ICU patients represent a specific group for which the risk/benefit analysis should be based both on the individual patient’s condition and the hyperbaric centre capability.

ICU PATIENT MANAGEMENT

HBOT shall be included in the overall management of ICU patients so long as its benefit outweighs any perceived risks and does not delay or interrupt the overall management of the patient. Neither patient monitoring nor treatment should be altered or stopped during HBOT, but the physiological effects of HBOT must be all the more strictly evaluated because of the severe condition of the patient.

THE HYPERBARIC FACILITY

The hyperbaric chamber should be specifically designed for critically ill patients and fully equipped to allow continuation of patient monitoring and treatment. The hyperbaric chamber should be located in or around the immediate vicinity of the ICU and be run by a sufficiently large and well-trained team of physicians, nurses, chamber operators and technicians. All devices to be introduced into the chamber should be evaluated, tested and certified as safe in a hyperbaric environment and all procedures (standard and emergency) should be tested and written before being implemented.

References

- 1 Mathieu D, editor. *Handbook on hyperbaric medicine*. Doordrecht: Springer; 2006.
- 2 Neuman TS, Thom SR, editors *Physiology and medicine of hyperbaric oxygen therapy*. Philadelphia: Saunders; 2008.
- 3 Weaver LK. Hyperbaric oxygen in the critically ill. *Crit Care Med*. 2011;39:1784-91.
- 4 Ratzenhofer-Komenda B, Offner A, Quehenberger F, Klemen H, Berger J, Fadai JH, et al. Hemodynamic and oxygenation profiles in the early period after hyperbaric oxygen: an observational study of intensive-care patients. *Acta Anaesthesiol Scand*. 2003;47:554-8.
- 5 Kot J, Desola J, Simao AG, Gough-Allen R, Houman R, Meliet JL, et al. A European code of good practice for hyperbaric oxygen therapy. *Int Marit Health*. 2004;55:121-30.
- 6 Warren J, Fromm RE, Orr RA, Rotello LC, Horst HM. Guidelines for the inter- and intra-hospital transport of critically ill patients *Crit Care Med*. 2004;32:256-62.
- 7 Kot J. Medical equipment for multiplace hyperbaric chambers, part 1. *European Journal of Underwater and Hyperbaric Medicine*. 2005;6:115-20.
- 8 Kot J. Medical equipment for multiplace hyperbaric chambers, part 2. *European Journal of Underwater and Hyperbaric Medicine*, 2006;7:9-12.
- 9 Kot J. Medical Equipment for multiplace hyperbaric chambers, part 3. *European Journal of Underwater and Hyperbaric Medicine*. 2006;7:29-31.
- 10 Kot J. Medical devices and procedures in the hyperbaric chamber. *Diving Hyperb Med*. 2014;44:223-7.

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Staffing and training issues in critical care hyperbaric medicine

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Abstract

(Kot J. Staffing and training issues in critical care hyperbaric medicine. *Diving and Hyperbaric Medicine*. 2015 March;45(1):47-50.)

The integrated chain of treatment of the most severe clinical cases that require hyperbaric oxygen therapy (HBOT) assumes that intensive care is continued while inside the hyperbaric chamber. Such an approach needs to take into account all the risks associated with transportation of the critically ill patient from the ICU to the chamber and back, changing of ventilator circuits and intravascular lines, using different medical devices in a hyperbaric environment, advanced invasive physiological monitoring as well as medical procedures (infusions, drainage, etc) during long or frequently repeated HBOT sessions. Any medical staff who take care of critically ill patients during HBOT should be certified and trained according to both emergency/intensive care and hyperbaric requirements. For any HBOT session, the number of staff needed for any HBOT session depends on both the type of chamber and the patient's status – stable, demanding or critically ill. For a critically ill patient, the standard procedure is a one-to-one patient-staff ratio inside the chamber; however, the final decision whether this is enough is taken after careful risk assessment based on the patient's condition, clinical indication for HBOT, experience of the personnel involved in that treatment and the available equipment.

Key words

Hyperbaric oxygen treatment, intensive care medicine, education, training, qualifications, safety, review article

Introduction

Conducting a hyperbaric oxygen treatment (HBOT) in intensive care (IC) mode is a basic requirement for ensuring the continuation of the treatment of the most severe cases. When taking into account the time burden related to HBOT for at least some indications, patients may spend up to 30–40% of a day away from the intensive care unit (ICU) in the chamber or being transported to and fro (Table 1).

Treating ICU patients in a hyperbaric chamber is a clinical challenge that needs to take into account the risks associated with transportation of the critically ill patient from the ICU to the chamber and back (intra- or inter-hospital transportation), changing of ventilator circuits and intravascular lines, using medical devices in a hyperbaric environment, advanced invasive physiological monitoring, as well as continuation of intensive treatment (drugs, fluid therapy, drains, etc.) during long or frequently repeated HBOT sessions. This is a fairly straightforward therapeutic routine for those hospital-based hyperbaric centres which have frequent experience conducting such sessions. For example, of all

ICU patients referred for HBOT, 80% would receive about six intensive care HBOT sessions (e.g., necrotizing soft-tissue infections) and 20% would have had two sessions (e.g., carbon monoxide (CO) poisoning, decompression illness), the weighted mean per ICU patient would be approximately five sessions. There are no hard data but, to be recognised as well-experienced, a hyperbaric centre should treat about 70 ICU patients for approximately 350 HBOT per year. However, if the hyperbaric staff are ICU-trained and keep working in an ICU, about 20 ICU patients for 100 sessions per year should be sufficient to maintain competence. For others, including stand-alone hyperbaric centres, that treat mostly elective, chronic and stable patients, an IC HBOT session, either for severe emergency patients or standard intensive care patients, can be a clinical nightmare.

The risks associated with inter-hospital transportation of critically ill patients have been identified as those related to equipment (technical factors), the transport team (human factors), indications for and organization of the transport (collective factors) and the patients themselves (including clinical stability).¹ Preventive measures for increasing

Table 1

Time of a day spent during HBOT for intensive care patients for different clinical indications: COP – carbon monoxide poisoning; NSTI – necrotising soft-tissue infections; DCI – decompression illness

| Condition | Sessions per 24 h | Duration of HBOT session (h) | Transportation for hospital-based facility (h) | Transportation for stand-alone facility (h) | HBOT total time per 24 h (h) |
|-----------|-------------------|------------------------------|--|---|------------------------------|
| COP | 2 | 2 | 2 x 0.5 | 2 x 1 | 5–7 |
| NSTI | 3 | 2 | 2 x 0.5 | 2 x 1 | 7–8 |
| DCI | 1 | 5–8 | 2 x 0.5 | 2 x 1 | 5–10 |
| Other | 1 | 2 | 2 x 0.5 | 2 x 1 | 3–4 |

safety of the transportation of the critically ill have been proposed, including: the competence and experience of the teams, efficiency (indications and risk-benefit analysis), stabilization and preparation of the patient prior to transportation, anticipation, organization and planning, dedicated transport equipment, standardization of procedures and protocols, including the use of check lists.

During a one-month prospective observation of 3,444 HBOT sessions conducted in eight European hyperbaric centres, the overall incident rate during HBOT sessions, including transport to and from the referring unit, was approximately ten times greater for sessions with IC modalities compared to elective HBOT sessions (18.6% versus 1.5%). This was not related predominantly to patient problems (55.6% vs. 86.3% respectively), but more to device problems (33.3% vs. 5.9% respectively).² Fortunately these incidents led to interruption of treatment in only a small proportion of incidents (5.6% vs. 7.8% respectively), and there was no statistically significant difference in the rates of clinical consequences (27.8% vs. 13.7%).

Standardized checklists for IC HBOT have been proposed recently.³ To accept intensive care patients and assess their risk-benefit and clinical indication for HBOT, the necessity for either inter- or intra-hospital transportation must be taken into account, as well as the technical capabilities of the facility (e.g., mono- or multiplace chamber), its medical equipment, and the experience of the hyperbaric staff.

The two most important questions concerning medical, nursing and technical staff and their training are the numbers needed for an IC HBOT and how they should be trained?

Training

The first consideration is how the medical staff who take care of critically ill patients during HBOT should be trained. In Europe at present, there are only two documents referring to this issue. One is ECHM-EDTC Educational and Training Standards (ETS) published in 2011⁴ and the other is the EBAss-ECHM Resources Manual (RM) on Education of Nurses, Operators and Technicians in Hyperbaric Facilities in Europe published in 2008.⁵

In the ECHM-EDTC ETS document, which refers to physicians only, there is a requirement that the Hyperbaric Medicine Physician (so called Level 2H) should have appropriate experience in anaesthesia and intensive care in order to manage the HBOT patient, but there is no requirement to be a certified specialist in either to be in compliance with the standards. The appropriate experience is defined as at least six months' work as a medical intern in an intensive/critical care unit. In fact, this clinical experience is enforced by the additional requirement of at least six months' work as medical intern in an approved hyperbaric centre, where this term includes the requirement of having the capability to treat all clinical indications according to

the ECHM list of indications in all patients, including those needing intensive care. In the list of theory modules for the hyperbaric medicine course, there is no specific module related exclusively to ICU patients. However, in several modules there are training objectives requiring that the hyperbaric medicine physician should know the treatment hazards for ICU patients and have the ability to transfer an ICU patient into the chamber with all necessary monitoring and therapeutic equipment.

However, in at least some European countries, the physician providing hyperbaric intensive care must be a registered specialist in this field or at least be able to clinically support such patients during transportation, e.g., a specialist in emergency medicine. This requirement, which is stricter than the ECHM-EDTC guidelines for hyperbaric medicine, can easily be met by hospital-based hyperbaric medicine facilities. However for stand-alone centres, this requirement can be a limiting factor, even if they are functionally linked to general hospital services. In such situations, hyperbaric staff certification and training could be a determining factor in referring a patient to the hyperbaric facility.

In the EBAss-ECHM Resources Manual for non-physician staff, there is a specific module – Hyperbaric Nursing for Intensive Care – dedicated exclusively to registered nurses, who are allowed by national regulations to take care of intensive care patients. This module lasts 40 hours with eight hours of theory and 32 hours of practical training and covers all aspects of conducting IC HBOT sessions. There is no specific module for operators for IC HBOT sessions.

Staffing

There are no prospective studies validating guidelines for the number of patients that can be managed by a single attendant in a multiplace chamber or for the number of monoplace chambers being operated by one hyperbaric operator at the same time. A general guideline can be proposed, depending on both the type of chamber and the patients' status – stable, demanding or critically ill (Table 2). The standard procedure is for a one-to-one patient-staff ratio for a critically ill patient inside the chamber for both multiplace and monoplace chambers.

If the patient's condition has been assessed and stabilized before starting the HBOT session, the clinical burden during a 243–284 kPa for 60–90 min, or an extended schedules up to 608 kPa for 5–8 hours can be fully met by one person. This fulfills the European criteria of having continuous, one-to-one nursing care for the sickest patients (so-called Level 3, Intensive Care Society levels of care).^{6,7} The decision as to whether the attendant is a nurse or a physician depends on the current patient's status, previous HBOT sessions, if any, the skill of the attendant and local policy for attendants. If the attendant is a nurse, there must be a trained physician capable of entering the chamber immediately in case of an emergency.

Table 2

Required number of personnel (chamber operators, internal medical attendants and hyperbaric physicians) for hyperbaric sessions

| Type of chamber | Staffing requirements | Patient condition | | |
|-----------------|-----------------------------------|-------------------|-----------|----------------|
| | | Stable | Demanding | Critically ill |
| Monoplace | Chamber operators per chambers | 1:3 | 1:2 | 1:1 |
| Monoplace | Hyperbaric physician per facility | 1 | 1 | 1 |
| Multiplace | Chamber operators per chambers | 1:1 | 1:1 | 1:1 |
| Multiplace | Internal attendants per patients | 1:12 | 1:5 | 1:1 or 2:1 |
| Multiplace | Hyperbaric physician per facility | 1 | 1 | 1 or 2 * |

* Second physician in the facility can be requested if the first must enter the chamber and stay for any length of time (see text for explanation)

On rare occasions the patient may need to be attended inside the hyperbaric chamber by at least two staff members, a physician and a nurse. Such situations include those sessions during which the clinical burden is overwhelming for one person. This can happen for example during emergency indications for HBOT, like carbon monoxide intoxication, when time to start the session matters and the patient's status quickly improves during HBOT. Because this improvement in general status can coexist with a transient period of confusion concerning time and place or even a delirious state, heavy sedation or conversion to general anesthesia while under pressure may be necessary. Alternatively, but generally not desirable, could be partial discontinuation of intensive therapy, including extubation, during the HBOT session. In both situations one staff member may find it difficult to control the patient's behaviour within the confined space of the hyperbaric chamber. If there is any need for the hyperbaric physician to enter the chamber for any emergency situation and stay there for an extended time, another hyperbaric physician should be summoned to supervise the session. Whatever the local policy for such cases, it should be clearly stated in the standard operating procedures. In some countries, there is also a requirement that artificial ventilation must be directly supervised by a respiratory therapist (or equivalent), which means additional personnel inside the hyperbaric chamber.

In some hyperbaric facilities there are also operating procedures that allow remote attendance of the intensive care patient inside the hyperbaric chamber by medical personnel outside the chamber. The intent is to decrease the decompression burden of the medical personnel and is based on the similarity to those medical procedures that preclude direct presence of medical personnel, e.g., MRI scanning. Because of lack of direct supervision and the inability to perform an immediate action in case of need, this is not a preferred method.

Theoretically, in certain circumstances when ordered by a specialist experienced in both intensive care and hyperbaric medicine, it could work after fulfilling several requirements. First, compression and decompression are conducted in direct attendance mode, which means that the patient attendant leaves the chamber only once the

treatment pressure has been reached and after control of respiratory and haemodynamic parameters; this should not be the first HBOT session for the patient, so that ventilator settings have been correctly established and the patient's condition was stable during previous sessions and before this particular session. Second, the patient is fully sedated, anesthetized or sometimes even paralyzed in order to avoid any unexpected movement leading to disconnection either of the ventilator circuit or intravenous/intra-arterial lines. Third, full monitoring of physiological parameters, including oxygenation and carbon dioxide levels, must be available. Finally, there is a staff member present who is able to immediately enter the hyperbaric chamber. The term 'immediate' means equivalent to the time required within the ICU. From this list of requirements, it is clear that, in practice, it is virtually impossible for most hyperbaric centres to ensure the safety of an intensive care patient left alone in a multiplace chamber. Even the advantage of decreased decompression burden for one medical attendant will be lost by necessity of ensuring several fast compressions for other staff members.

In all cases of critically ill patients being treated with HBOT, the decision on number and position of the hyperbaric staff member taking care of the patient while they are in the chamber is left to the physician's discretion after careful risk assessment that takes into account the patient's condition, clinical indication for HBOT, experience of the personnel involved in that treatment and the available equipment. In order to make decisions simpler, every HBOT centre that treats critically ill patients must develop their own local policies for conducting such sessions.

Conclusion

The number of available trained hyperbaric staff and their experience is an important factor in estimating the risk/benefit balance for the intensive care patient and their clinical indication for HBOT. Mono- or multiplace hyperbaric centres that treat emergency and critically ill patients should have at least one physician certified either in emergency medicine or intensive care and trained in hyperbaric medicine.

References

- 1 Fanara BI, Manzon C, Barbot O, Desmettre T, Capellier G. Recommendations for the intra-hospital transport of critically ill patients. *Crit Care*. 2010;14(3):R87. doi: 10.1186/cc9018
- 2 Kot J, Hajek M, Houman R, Klemen H, Kemmer A, Kirchner K, et al. COST B14 Action Working Group “*HBO and Intensive Care*”. Comparison of incident rates during intensive care versus non-intensive care HBO sessions – a prospective one month observational study in eight European centres. *International conference on diving and hyperbaric medicine*; 2005 Sept 7–9, Barcelona, Spain. p. 70.
- 3 Preininger A. Prearrangements for ICU patients undergoing HBO therapy [abstract]. *40th Annual Scientific Meeting of the European Underwater and Baromedical Society*; 2014 Sept 24–27. p. 100.
- 4 ECHM-EDTC. *Educational and Training Standards* (2011). [cited 2014 Aug 30]. Available from: <http://www.echm.org/ECHM-Documents.htm>
- 5 EBAss/ECHM. *Resources manual on education of nurses, operators and technicians in hyperbaric facilities in Europe* (September 2008). [cited 2014 Aug 30]. Available from: <http://www.echm.org/ECHM-Documents.htm>
- 6 Intensive Care Society. *Core standards for ICU 2013*. Edition 1. [cited 2014 Aug 30]. Available from: <http://www.ics.ac.uk/ics-homepage/guidelines-and-standards/>
- 7 Intensive Care Society. *Levels of critical care for adult patients* (revised 2009). [cited 2014 Aug 30]. Available from: <http://www.ics.ac.uk/ics-homepage/guidelines-and-standards/>

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Hyperbaric intensive care technology and equipment

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Abstract

(Millar IL. Hyperbaric intensive care technology and equipment. *Diving and Hyperbaric Medicine*. 2015;45 March:50-56.) In an emergency, life support can be provided during recompression or hyperbaric oxygen therapy using very basic equipment, provided the equipment is hyperbaric-compatible and the clinicians have appropriate experience. For hyperbaric critical care to be provided safely on a routine basis, however, a great deal of preparation and specific equipment is needed, and relatively few facilities have optimal capabilities at present. The type, size and location of the chamber are very influential factors. Although monoplace chamber critical care is possible, it involves special adaptations and inherent limitations that make it inappropriate for all but specifically experienced teams. A large, purpose-designed chamber co-located with an intensive care unit is ideal. Keeping the critically ill patient on their normal bed significantly improves quality of care where this is possible. The latest hyperbaric ventilators have resolved many of the issues normally associated with hyperbaric ventilation, but at significant cost. Multi-parameter monitoring is relatively simple with advanced portable monitors, or preferably installed units that are of the same type as used elsewhere in the hospital. Whilst end-tidal CO₂ readings are changed by pressure and require interpretation, most other parameters display normally. All normal infusions can be continued, with several examples of syringe drivers and infusion pumps shown to function essentially normally at pressure. Techniques exist for continuous suction drainage and most other aspects of standard critical care. At present, the most complex life support technologies such as haemofiltration, cardiac assist devices and extra-corporeal membrane oxygenation remain incompatible with the hyperbaric environment.

Key words

Hyperbaric oxygen therapy, intensive care medicine, hyperbaric facilities, safety, equipment, patient monitoring, ventilators, review article

Introduction

Although relatively few intensive care units have the capability to provide hyperbaric oxygen treatment (HBOT) to their patients, it is clear that hyperbaric intensive care is feasible and that it can be delivered safely to appropriate

patients by experienced teams who have suitable technology. All critical care interventions should be subject to risk-benefit evaluations at multiple levels, including on a policy-making basis as to whether the intervention is used at all and when the technology and skills are available, whether to use the therapy in any particular patient at a particular time.

These principles apply equally to HBOT, and it is highly undesirable to embark upon HBOT for critically ill patients using 'makeshift' or 'minimalist' arrangements.

Whilst the potential benefits of HBOT should be independent of where and how HBOT is delivered, it is clear that the risk of treating critically ill patients depends heavily upon the type of hyperbaric chamber, its location, the experience of the clinical teams involved, and the equipment available. The critical care capability of some units is sufficiently good for HBOT to be used for sub-acute indications such as the promotion of wound healing or ischaemic tissue salvage in ventilated patients. More commonly, hyperbaric critical care will be reserved for situations where there is imminent threat of death from highly oxygen-responsive conditions such as gas gangrene. A recent review of hyperbaric critical care, as well as a series of four papers on medical equipment for multiplace chambers are particularly useful.¹⁻⁵ This paper builds upon these sources.

Monoplace chamber intensive care

Although monoplace chambers are generally regarded as unsuitable for critical care in Europe, there are some centres that have achieved high capabilities as a result of local expertise, ingenuity in creating custom adaptations and many years of clinical experience. The hyperbaric medicine facility at Salt Lake City, USA has developed what is probably the premier example of this, with capabilities to routinely ventilate, monitor invasive blood pressures, take blood gases and much more. This capacity has taken many years to develop and the expertise and equipment that make high-level monoplace critical care possible in Salt Lake City would be difficult to reproduce elsewhere. Conceptually, monoplace chamber critical care shares similarities with anaesthesia for neurosurgery or ENT surgical cases where the anaesthetist must remotely control all monitoring and the delivery of physiological and drug therapies. In some cases, monoplace chambers are taken to the intensive care unit (ICU) so as to avoid patient transport away from the critical care environment. Transfer from the ICU bed to a monoplace stretcher is still required, however, as is a change of ventilator and re-routing of fluid and monitoring connections through the chamber penetrators. This is all very time consuming and potentially disruptive of optimal critical care. The ventilators presently available for monoplace chambers are very basic units that have significant functional limitations. Most critically, the models of intravenous fluid pumps that were capable of pushing fluid into the chamber from outside have been discontinued, creating a potential crisis for all hospital patient care in locations that have only monoplace chambers. Further detail on the techniques used in monoplace critical care can be found in various papers and textbook chapters on the subject.¹

An alternative monoplace critical care configuration under development is the use of a large, air filled monoplace

chamber within which is located remotely controlled ventilation and infusion equipment, as well as the patient. This arrangement has the potential to allow more sophisticated ventilators to be used, along with a wider variety of infusion pumps, but any further development of this concept will be inherently tied to the availability of remotely controllable, hyperbaric-compatible ventilators and infusion equipment.

Multiplace chamber intensive care: the location of the chamber

The ideal hyperbaric chamber for critical care would be physically integrated into the ICU, or at least immediately adjacent, such that transport requirements are minimised. Ideally the clinicians looking after the patient in the ICU would continue to look after the patient in the hyperbaric chamber, or at least be close by, such that continuity of care direction can be ensured, with expert clinical back up immediately available should there be any problems.

More commonly, the hyperbaric chamber will be located at some distance, and there will need to be a 'philosophical' choice with respect to staffing. Hyperbaric oxygen sessions can be delivered using the staffing model usually used for transports to investigations like MRI or angiography where the intensive care team travels with the patient and provides continuity of care. Alternatively, the intensive care team can hand over care to a separate but appropriately qualified team. This care model mirrors transfers to the operating theatre team for surgery, with subsequent post-procedure transfer back to intensive care.

The chamber location and staffing arrangements will determine whether the hyperbaric unit can be supported by the existing critical care infrastructure such as blood gas analysers, resuscitation and 'difficult airway' equipment, etc., or whether dedicated support equipment will be necessary in the chamber vicinity.

The type of chamber

Hyperbaric intensive care is easiest if the floor space and features of the chamber closely resemble a normal intensive care cubicle. A number of the leading centres have achieved this through large rectangular chambers with doorways up to 1.4–1.5 m wide, and a critical care compartment floor area close to that of a small to medium-sized intensive care cubicle: 18–21 m². The optimal facility will also have lighting, temperature control, noise levels and internal equipment similar to an ICU, with hand wash basins in all relevant compartments. All of this is now demonstrably feasible, albeit at a cost, for new facilities. Existing facilities will not be able to change the basic size and shape of their chamber, but other features may possibly be retrofitted during an upgrade.

Medical gas services

Many items of critical care equipment require medical gas supplies in order to function. Hyperbaric chambers designed to facilitate high-level critical patient care should have medical gas outlets for oxygen and air that have the same connection types used in the rest of the hospital. These should be installed in a manner that ensures that the pressures and flows available meet the national hospital systems requirements both at the surface and under pressure, so that gas-utilising equipment such as ventilators can operate as normally as possible under pressure.

The performance of suction systems should also, ideally, match normobaric hospital standards, corrected for pressure. This has proven more technically difficult to achieve, however, and test methods have not been published or validated for medical suction at pressure. Whilst most systems are probably functionally adequate, it seems likely that variable and technically non-compliant flows and/or vacuum levels are unknowingly generated in many cases, especially during pressure changes.

A number of different approaches can be taken to provide in-chamber suction. The simplest approach is to use commercially available air-powered venturi suction units. Such systems can provide adequate suction of fluids but should not be used to scavenge ventilator gas exhausts as oxygen-enriched gas will be dumped into the chamber. Permanently installed suction systems generally use the differential pressure between the chamber interior and exterior to provide suction, which will only work when the chamber is at pressure unless the system is externally connected to the hospital suction system or a locally installed suction pump. In all such configurations, regulation is required to prevent excessive suction when the chamber is at pressure. It is also important to be aware that relatively small leaks of chamber air into the suction system can quickly overload the capacity of hospital suction pumps. Suction systems design needs to allow for system cleaning including disassembly if blockage occurs. Any filters need to be readily accessible for removal and cleaning or replacement when necessary. It is highly desirable for multiple suction outlets to be available for patients with multiple suction drains or intercostal catheters. At least some outlets should be fitted with a hyperbaric-tested vacuum regulator to provide continuation of low-level suction. Many commercially available low-suction regulators have been successfully used for this purpose without modification.

Electrical power

Although some chambers have standard alternating current power outlets as used in the country where the chamber is located (e.g., 220V, 50Hz or 110V, 60Hz), this is generally considered an excessive hazard. Most hyperbaric chamber safety codes and guidelines recommend only low voltage power installations or batteries, and a maximum power may

be cited. The relevant European standard, EN14931, includes some general recommendations on this subject and the NFPA 99 Healthcare Facilities Code used in the United States has some valuable detail that is very worthy of consideration in jurisdictions where this Code is not mandated.⁶

Unless a local design standard requires otherwise, it is recommended that electrical connectors be selected that cannot be confused or interconnected with other systems and that are screw-connected or otherwise protected against accidental disconnection under pressure. These should be supplied from dedicated medical-grade power supplies with battery or uninterruptable power supplies (UPS) back-up separate from other services such as lighting or entertainment. Attention needs to be paid to critically selecting which electrical systems are automatically disconnected in case of fire deluge operation. It may be necessary to supply multiple different voltages to meet the requirements of different items of critical care equipment.

Electrical safety rating

The patient care areas of an optimal hyperbaric critical care facility will be certified to the same electrical safety standards that apply to the hospital's ICUs. The chamber should also meet the same levels of electrical design, construction, protection systems and testing, although some of the special requirements for safe chamber installations may create barriers to certification according to normobaric hospital standards. It is arguable whether the highest level of 'cardiac protection' is needed as it is unlikely that invasive intracardiac pacing would be initiated or that electrocardiac mapping studies or open chest procedures would be undertaken in the chamber. The highest levels of electrical protection require completely conductive and grounded floor coverings and specially bonded earthing conductors for every metal item in the chamber, including all plumbing and metal panels. This is costly and may create maintenance difficulties. There are certain elements of electrical and electromagnetic radiation safety inherent in the metal construction of a chamber, provided there are only suitable low voltage electrical installations and suitable battery-powered devices. A critical design point for direct current (DC) power systems is that they should be ungrounded and therefore not capable of 'shorting' to the chamber steel.

There are high levels of electrical safety built into modern, proprietary intensive care monitors, whether they are operating off battery power, or installed outside the chamber with connections inside, and electrical supply coming from circuits fitted with low threshold residual current devices and circuit breakers that meet hospital electrical standards. In some cases, core balance transformers and/or line isolation monitoring may be used. Medical device standards generally require electrical equipment to 'fail safe' and not risk delivering a dangerous shock to the patient but the applicability of this in hyperbaric conditions should be assessed for each type of device. Continuity of electrical

grounding and circuit protection must be considered when designing battery back-up or UPS for medical devices in the chamber as many standard UPS installations can bypass or invalidate medical grade electrical protection systems.

Batteries

Many items of critical care equipment have rechargeable batteries that are primarily designed for patient transport and to ensure continuity of care during short duration power failures or accidental mains power disconnection. Provided the battery duration is sufficient and the battery type is tested and agreed to be safe for hyperbaric use, such battery-powered devices can be a good option for hyperbaric critical care. It should be noted that battery capacity tends to decrease with age and in some battery types, capacity decreases with frequent partial discharge as is a common usage pattern for much of the equipment routinely used in critical care. Unless the device has a long duration battery, regular 'run time' testing should be scheduled in addition to ensuring the best charging practices that are practical. A periodic battery replacement programme is highly desirable.

Batteries should not be charged under pressure as charging is the most common trigger for high-temperature battery failures. In addition, some battery types release hydrogen when charging – a very potent fire hazard. The chemistry of nickel metal hydride batteries is inherently safer in this regard. In some devices, charging when external power is connected cannot be disabled and, if so, robust systems will need to be put in place to prevent power connection in the chamber unless batteries are removed.

Lead acid batteries can be sealed or unsealed, with the electrolyte in liquid, gel or adsorbed form. Unsealed and liquid electrolyte type lead acid batteries risk acid spillage and are unsuitable as a result. Most authorities have great concerns about the hazard inherent in lithium chemistry batteries in the hyperbaric environment, given that pressure exposure may increase failure risk and many lithium battery types are capable of failing in a high-temperature 'melt down' mode. This can be a source of fire ignition that could in some cases continue even when immersed in fire-fighting water. With ageing, it is not uncommon for the lithium polymer batteries commonly used in mobile telephones, tablets and personal music players to swell before failing after a few years of heavy use. If any types of lithium batteries were to be assessed and approved as safe for hyperbaric use, it would be important to specify a number of usage cycles and an age at which to retire such batteries, well before the normally estimated end of useful battery life. It should be noted that repeated pressurisations anecdotally seem to reduce battery life at least in some cases.

Most electronic devices will also have one or more small long-life internal batteries to maintain timeclock and BIOS functions and memory of settings. Non-rechargeable lithium 'button cell' or circuit board-installed batteries are often

used for this function and these will require risk assessment when evaluating the safety of any individual device but most authorities consider the failure and fire risk of these small, sealed, single-use cells to be very much lower than larger and/or rechargeable batteries.

Beds and trolleys

Some smaller chambers will require patients to be transferred to a fixed chamber bunk for treatment, which involves undesirable patient handling but does have the benefit of minimising the risk of 'contraband' entering the chamber. For chambers that allow entry of a trolley, it is preferable for any patient transfers to the hyperbaric trolley to occur in the intensive care unit so as to minimise patient transfer risks and optimise care if instability results from physical handling. Ideally, the standard intensive care bed should be capable of being taken into the chamber. This has proven possible in recently constructed critical care chambers, subject to risk assessment of the bed components, and generally with the requirement to remove or disable high capacity battery powered bed-positioning systems. In these cases, the bed must have manual systems to enable emergency repositioning of the patient, for instance to the flat position for resuscitation or head down if required. Opinions vary with respect to the risk presented by grease in wheel bearings or actuators and hydraulic fluid, where relevant. The author's institution has exposed a range of standard critical care and general hospital beds to repetitive pressure cycles, and to saturation pressurisations followed by rapid decompression, in order to evaluate whether leakage of greases or fluids can be triggered. We have not experienced any such problems in 15 years. The bearings on most bed wheels are now either lubricant free or 'maintenance free', implying that any lubricants used are not volatile. Nevertheless, a good system of preventive maintenance and inspection prior to each hyperbaric session seems prudent.

Physiological monitoring

A primary component of critical care is continuous monitoring of a range of physiological variables, especially electrocardiogram, pulse oximetry, invasive or non-invasive blood pressures, end-tidal CO₂ and temperature. This is all possible, with varying degrees of sophistication and integration with the parent ICU systems. An optimal system will allow continuity of monitoring from the intensive care unit, during transport and throughout hyperbaric treatment with similar or identical equipment. All data should be viewable from across the intensive care network, with storage of monitoring and trend data as is available for all other patients; this subject has been detailed previously.⁷

Fluid infusion

In multiplace chambers, simple gravity-fed intravenous fluid infusions work as normal, provided attention is paid to the fluid level in the drip chamber and to venting of any non-

flexible containers. However, modern critical care practice requires multiple infusions to be controlled by infusion pumps and syringe drivers so that dose-critical agents such as inotropes can be delivered accurately and multiple infusions can be delivered without the need for continuous visual monitoring of multiple infusions to the detriment of attending to other matters. A range of infusion pumps and devices have been utilised in multiplace hyperbaric chambers with varying degrees of rigour of testing. Most are used in battery-powered mode but a few utilise a wired continuous power supply, including the CE-marked Fresenius Pilot(e) hyperbaric syringe driver. Unfortunately, manufacture of this infusion pump appears to have been discontinued recently.

There are significant clinical advantages if the same type of infusor can be used in the critical care unit, during transport, and in the hyperbaric chamber, as this removes the need for interruption of dose-critical infusions and reduces the risk of change-over errors. In addition to the list of devices published to date, the Alfred Hospital has rigorously evaluated the B-Braun Infusor Space syringe driver and the Carefusion Alaris System's Point of Care Unit and Pump Module. Both appear safe and have proved capable of working according to specifications when used on battery power in the hyperbaric chambers (publications pending) with some safety precautions noted for the Carefusion modular system and with a syringe preference for accurate performance of the B-Braun device at low flows. It is understood that several other infusors are presently in development or under evaluation at other centres, including some examples of infusors connected to remote controls which allow device control from outside the chamber.

There are also several brands of non-electrical fluid infusion systems available which use an elastomeric fluid bag inside a protective container to generate flow through a critical orifice. Some of these are known to be in use in monoplace and multiplace hyperbaric chambers and formal testing results for one such device are published in this issue.⁸

Passive drainage systems (wound, urinary, nasogastric)

Most passive drain tubes and bags can be accommodated provided attention is paid to the gas-containing patient anatomy as well as to the drain bag to ensure that excess pressure does not lead to expansion barotraumas of the patient or equipment, with the potential for dangerous or at least very unpleasant spillages during decompression.

Intercostal drainage

The dynamics of pleural drainage differ depending upon whether suction is important or not and, in particular, whether the patient has a pleural leak. Many hyperbaric units use simple 'Heimlich' one-way valves during HBOT with or without connection to an underwater seal drain and/or suction. A more sophisticated option is to utilise proprietary pleural drain units but some variations in function do occur

especially during pressurisation when a pressure differential arises between the increasing pressure of the ambient chamber air and the interior gas spaces of the device. Manual or automatic venting will be needed in most cases and it may be necessary to limit the rate of pressurisation.

Suction drainage systems

Proprietary suction drainage systems are commonly used as both sterile dressings and active therapy for surgical wounds (negative pressure wound therapy). Therefore, these can be in place on patients prescribed HBOT. These systems use proprietary electrical pumps that provide regulated and in some cases pulsed suction into closed containers. None of these pumps appear to have been validated as safe for hyperbaric use to date and many are mains power operated only. It is possible, however, to fabricate adapters to enable the connection of regulated low-pressure suction so that wound suction can be continued during hyperbaric exposure. This approach has been extensively used in the author's institution with a range of different suction containers being used inside the chamber. The efficacy and tolerability of in-chamber vacuum therapy, along with practical details of one simple but practical method of connection, have been published in this journal.⁹

Airway management

The need to manage the volume of the sealing cuff of endotracheal tubes is well known, with most units using water or saline replacement of the cuff air during HBOT. The compliance of a fluid-filled cuff is not as good as an air-filled cuff, however, increasing the risk of tracheal necrosis if fluid is left in situ. Therefore, most would recommend removal of the fluid and refilling with air after each hyperbaric session. Even with meticulous technique and adequate pharyngeal suction this does risk repeated small-volume aspiration into the lungs, which is undesirable, and as a result, automatic air-volume compensation systems are worth considering.

Ventilation

There are well-known challenges involved in selecting a ventilator for hyperbaric critical care. Unfortunately, some of the most successful hyperbaric ventilators are no longer manufactured or supported. The Oxford Penlon was an early pneumatically powered bellows ventilator with a design that enabled it to operate satisfactorily even with helium-oxygen gas mixtures in high-pressure saturation diving chambers at 20–30 bar. The Multivent version is also discontinued. The Siemens Servo 900C was one of the first and most successful of the modern-style, electronically controlled intensive care ventilators and it has proved capable of operating satisfactorily in clinical hyperbaric chambers in a range of installation configurations with the controls being operated either internally or externally depending upon the installation. Many of these remain in service but parts are becoming difficult to source.

A portable, hyperbaric-specific ventilator manufactured by Siare has been in service for some years, but this unit still has a number of limitations compared to what would be considered ideal. It is understood that a new, and much more sophisticated Siare model should be released in coming months and that this unit will offer multiple ventilation modes and an advanced graphic display/control interface.

An alternative, advanced, CE-marked hyperbaric critical care ventilator has recently been released, the Maquet Servo-i Hyperbaric. This unit is based upon Maquet's standard critical care Servo-I ventilator, and thus has the same dimensions, controls and displays as its 'parent' model which is widely used internationally. It is relatively large which may be a disadvantage for smaller hyperbaric chambers. The hyperbaric Servo-i has proved very serviceable and does not require any significant adjustments for pressurisation regardless of ventilation mode. In many ways, it meets the goals of optimal hyperbaric critical care in being a standard critical care device that is hyperbaric compatible. It is, however, presently marketed with only three ventilation modes available, which will limit the ability for this relatively expensive ventilator to be used in non-hyperbaric settings. It is understood that Maquet may offer upgraded capabilities for this ventilator via software update in the future, once the proposed additional modes and features are validated.

Many other, but not all ventilators are capable of being used in hyperbaric conditions. In general, the simpler anaesthesia and transport ventilators are more likely to function, albeit with some limitations and modifications of settings. Most 'full-feature' critical care ventilators will either not be electrically safe for hyperbaric use or will fail due to limitations of the pressure sensors or software systems intrinsic to the device.

Defibrillation

A stand-alone CE-marked portable hyperbaric defibrillator is now available (Corpuls). It is understood another should be available shortly (Haux). As an alternative arrangement a number of chambers have cables installed to allow an external defibrillator to be connected to internal adhesive pads, in some cases with safety interlocked switches to require two persons to activate a shock. However, the most common arrangement is to not have defibrillation available inside the chamber at all, on the basis that a 'shockable rhythm problem' is most unlikely during HBOT and the degree of oxygen dissolved in tissues provides for adequate time for a safe, urgent decompression for defibrillation at surface pressure in a 'doors-open' state. The issue of defibrillation is further explored in a recent publication.⁵

Blood gas analysis and biochemistry

Very few chambers have the capacity for blood-gas analysis and/or any biochemical testing at pressure. In most cases, arterial or venous blood samples will be transferred out for

external testing. This is generally satisfactory, although it is hoped that, in the future, some 'Point of Care' systems may prove hyperbaric compatible. Blood glucose will usually be ascertained as a by-product of blood gas testing but simple glucometers selected as hyperbaric-compatible have proved useful. It should be noted that not all glucometers designed for bedside and ambulatory use are hyperbaric compatible and the chemistry or electronics involved can deliver false results under pressure.

The medical device regulatory problem

A major issue for all who wish to provide critical care in the hyperbaric environment is the relevant national medical device regulatory system and its interpretation by the individual hospital. If local law or policies require all devices to be 'CE-marked' specifically for hyperbaric use, this will very much limit the choice of what is available for use. In other cases, the Medical Director of the hyperbaric unit may be able to choose to take responsibility for using medical devices 'off label' in an environmental sense – that is, to use a device that is approved for normobaric use for standard purposes but in a non-standard environment, the hyperbaric chamber. The formal legal situation will vary from country to country. This subject was addressed in some detail at the 2012 ECHM Consensus Conference in Belgrade, Serbia.^{10,11}

References

- 1 Weaver LK. Hyperbaric oxygen in the critically ill. *Crit Care Med.* 2011;39:1784-91.
- 2 Kot J. Medical equipment for multiplace hyperbaric chambers, part 1. *European Journal of Underwater and Hyperbaric Medicine.* 2005; 6(4):115-20.
- 3 Kot J. Medical equipment for multiplace hyperbaric chambers, part 2. *European Journal of Underwater and Hyperbaric Medicine.* 2006; 7(1):9-12.
- 4 Kot J. Medical equipment for multiplace hyperbaric chambers, part 3. *European Journal of Underwater and Hyperbaric Medicine.* 2006;7(2):29-31.
- 5 Kot J. Medical devices and procedures in the hyperbaric chamber. *Diving Hyperb Med.* 2014;44:223-7.
- 6 Bielen R, Lathrop J, editors. *Health care facilities code handbook*, 9th Ed, Chapter 14, Hyperbaric Facilities. Quincy, USA: National Fire Protection Association; 2012.
- 7 Millar IL. Monitoring the intensive care patient in the hyperbaric environment. In: *Proceedings of the ECHM satellite symposium, 2007: HBO for patients in critical conditions.* Sharm el Sheik, Egypt. European Committee for Hyperbaric Medicine; 2007. (Out of print but available from the author or downloadable from the ResearchGate website at: http://www.researchgate.net/publication/251875503_Monitoring_the_intensive_care_patient_in_the_hyperbaric_environment)
- 8 Lewis I, Smart D, Brown B, Baine C. Performance of the Baxter Infusor LV10 under hyperbaric conditions. *Diving Hyperb Med.* 2015;45:37-41.
- 9 Chong SJ, Tan MK, Liang w, KimSJ, Soh CR. Maintenance of negative-pressure wound therapy while undergoing hyperbaric oxygen therapy. *Diving Hyperb Med.* 2011;41:147-50.
- 10 Millar IL. Medical equipment inside hyperbaric chamber. *Proceedings of the 9th ECHM Consensus Conference:*

Organisation of a clinical hyperbaric therapy centre and related health management issues, Belgrade, Serbia, September 2012. European Committee for Hyperbaric Medicine; 2012. p. 206-22.

- 11 Burman F. Quality assurance. *Proceedings of the 9th ECHM Consensus Conference: Organisation of a clinical hyperbaric therapy centre and related health management issues*, Belgrade, Serbia, September 2012. European Committee for Hyperbaric Medicine; 2012. p. 225-237.

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A pro/con review comparing the use of mono- and multiplace hyperbaric chambers for critical care

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Abstract

(Lind F. A pro/con review comparing the use of mono- and multiplace hyperbaric chambers for critical care. *Diving and Hyperbaric Medicine*. 2015 March;45(1):56-60.)

Hyperbaric oxygen treatment (HBOT) of critically ill patients requires special technology and appropriately trained medical team staffing for '24/7' emergency services. Regardless of the chamber system used it is essential that the attending nurse and critical care specialist understand the physics and physiology of hyperbaric oxygen for safe treatment and compression/decompression procedures. Mechanical ventilation through endotracheal tube or tracheotomy is hampered by the increased gas density and flow resistance with risks of hypoventilation, carbon dioxide retention and oxygen seizures. Ventilation should be controlled and arterial and end-tidal carbon dioxide levels monitored. Haemodynamically unstable patients require careful risk-benefit evaluation, invasive monitoring and close supervision of inotropes, vasopressors and sedative drug infusions to avoid blood pressure swings and risk of awareness. Two distinctly different chambers are used for critical care. Small cost-efficient and easy-to-install acrylic monoplace chambers require less staffing and no inside attendant. Major disadvantages include patient isolation with difficulties to maintain standard organ support and invasive monitoring. Monoplace ventilators are less advanced and require the use of muscle relaxants and excessive sedation. Intravenous lines must be changed to specially designed IV pumps located outside the chamber with chamber pass-through and risk of inaccurate drug delivery. The multiplace chamber is better suited for HBOT of critically ill patients with failing vital functions and organ systems, primarily because it permits appropriate ICU equipment to be used inside the chamber by accompanying staff. Normal 'hands-on' intensive care continues during HBOT with close attention to all aspects of critical patient care. A regional trauma hospital-based rectangular chamber system immediately bordering critical care and emergency ward facilities is the best solution for safe HBOT in the critically ill. Disadvantages include long-term commitment, larger space requirements and higher capitalization, technical and staffing costs.

Key words

Hyperbaric oxygen therapy, intensive care medicine, pressure chambers, safety, review article

Introduction

This review is influenced by 25 years of clinical hyperbaric work by the author as a specialist in anaesthesia and intensive care medicine, with research and development of hyperbaric medicine in a hyperbaric oxygen treatment (HBOT) facility with multiplace ICU capability and 24-hour emergency services in the academic university trauma hospital setting. Since 2006, the Karolinska University Hospital has used a large four-lock rectangular chamber immediately bordering the ICU, staffed and equipped for simultaneous full

intensive care of up to four critically ill adult or paediatric patients with failing vital functions.¹ In cooperation with manufacturers, Germanischer Lloyd and the Karolinska Biomedical Engineering Department, many of the medical devices like infusion pumps, patient monitors, the patient data management system, defibrillator and ventilator have received CE approval for use within the hyperbaric chamber.²

Since 1992, the Karolinska has also had monoplace chambers in daily clinical practice, introduced for daily elective treatments in spontaneously breathing patients.

Monoplace chambers have been found valuable for emergencies, traumatic ischaemic conditions, neurosurgical infections and also in spontaneously breathing intensive care patients. This experience of monoplace practice has been augmented by repeated visits to hyperbaric units in Salt Lake City, Long Beach, San Pablo and other reputable American centres, generally run by specialists in pulmonary critical care or emergency medicine, where monoplace chambers are used extensively.

A large number of experienced and dedicated nurses, technicians and colleagues at the Karolinska have helped to develop our multiplace and monoplace programmes to ensure that HBOT can be performed safely in patients of all ages. With appropriate monoplace chamber pass-throughs and infusion pumps, drugs can be administered continuously intravenously and through an epidural catheter during HBOT. This makes it possible to combat pain, anxiety and nausea effectively. The monoplace has also been used to treat many newly extubated intensive care patients, especially in small children who will not easily be persuaded to breathe through a mask or a hood in the multiplace chamber. An intensive care nurse can accompany the child in the monoplace chamber and deliver all drugs manually for constant drug delivery and to keep lines from clotting. However, we have not used the monoplace in intubated patients nor in unstable patients or 'when in doubt', e.g., worries over pulmonary oedema or immediately after a central line has been inserted (with risk of pneumothorax), when we have taken the option to use the multiplace chamber.

With this background of personal experience and having never treated an intubated, unstable patient in a monoplace chamber, this pro/con review contrasts mono- and multiplace hyperbaric chambers for critical care. My views on how to design a new hospital-based hyperbaric facility with ICU capabilities were presented at the 2012 European Committee for Hyperbaric Medicine Consensus Conference in Belgrade; and again at the 2013 Conference on Diving Physiology and Hyperbaric Medicine in Japan.^{3,4}

Background

HBOT has been used clinically for critically ill patients for over 60 years,^{1,5-11} and the two distinctly different types of chambers contrasted in this review have also been available since the 1960s. In treating the critically ill patient safely with HBOT, like with many other medical interventions, it is important to do a risk/benefit assessment. This requires unique competence both in the complex pathophysiology of the conditions treated as well as knowledge of HBOT physics and physiology to avoid possible complications unique to HBOT exposure. Ventilation, whether spontaneous or ventilator-assisted, is hampered by the increased gas density at depth. This does not affect oxygen (O₂) uptake but can lead to hypoventilation. At 283 kPa pressure, the three-fold density causes a doubling of flow resistance with a need for change in ventilator settings to avoid harmful

high pressure, hypoventilation and carbon dioxide (CO₂) retention which, in turn, increases cerebral blood flow and the risk of O₂ seizures. Ventilation should be well controlled including careful monitoring of arterial blood gases and end-tidal CO₂.¹²

Haemodynamically unstable patients require careful risk-benefit evaluation and close supervision due to, for example, O₂-induced systemic vasoconstriction with changes in preload and afterload. During HBOT, patients with hypervolaemia and/or reduced left ventricular function are in danger of acute cardiogenic pulmonary oedema, especially if treated supine. Patients in septic shock risk hypovolaemia after HBOT when vasoconstriction and thoracic blood pooling cease. Short-term, reversible hypoxaemia is frequently seen immediately after HBOT due to atelectasis and changes in central haemodynamics.¹³

Time to treatment is crucial for acute HBOT indications, for example, cerebral arterial gas embolism in a comatose diver after free ascent or in the anaesthetized patient not waking up after open heart surgery; the burns victim with carbon dioxide (CO) and cyanide poisoning and inhalation injuries; the unstable, septic fasciitis patient with multi-organ failure or the motorcyclist with multiple trauma with crush injuries, arterial damage with ischaemia or with reperfusion injury after vascular reconstruction. In general, the earlier these patients are treated, the better the outcome.

Critical care HBOT 24/7 is often not available in hospital-based HBOT centres due to lack of funding, experience, specialized equipment, intensive care unit cooperation, trust between specialties, staffing, etc. The political and historical background of each hospital, region, country and continent has influenced the location and critical care capabilities of available HBOT facilities. The design of a HBOT facility often depends on the individual physician in charge, accepted indications and how sick the patients are, i.e., whether emergency care is required. We therefore have a multitude of different solutions globally regarding the availability of HBOT and the use of mono- or multiplace hyperbaric chambers for critical care.

MULTIPLACE CHAMBERS

Multiplace steel chambers are designed with two or more independent compartments (locks) to accommodate patients and hyperbaric staff who may enter and exit the chamber via an adjacent lock during therapy. The multiplace chamber is compressed with air. Patients are provided with oxygen via an individualized built-in breathing system, usually a mask or head hood or by mechanical ventilation via an endotracheal or tracheostomy tube. Dedicated air compressors and large low- or high-pressure receivers provide the chamber air supply. A specialized fire suppression system with water tanks for each lock is necessary. A multiplace chamber allows appropriate ICU equipment to be used bedside/inside the chamber by the accompanying staff.

MONOPLACE CHAMBERS

Monoplace chambers are designed for single occupancy, usually constructed of see-through acrylic with a pressure capability of 304 kPa and pressurized with 100% O₂, which allows the patient to breathe comfortably without a mask or hood. The high-flow O₂ requirement is ideally supplied via a hospital's existing liquid O₂ system. Operators and medical staff maintain communication with the patient via intercom. Technical inventions and modifications of the medical equipment allow critically ill and ventilator-dependent patients to undergo HBOT without accompanying staff.

Multiplace chamber advantages

- Hands-on patient attendance and bedside medical and nursing supervision of all aspects of evaluation and treatment;
- Immediate medical interventions by the inside attendant, including endotracheal suctioning, resolving acute airway obstruction, defibrillation or a chest tube insertion; additional staff can be locked in during medical emergencies;
- Not having to change bed or monitoring in modern chambers with spacious design and wide doors;
- Uninterrupted mechanical ventilation via a battery-powered, modern, state-of-the-art ICU ventilator that does not have to be disconnected throughout transport and HBOT;
- Uninterrupted, continuous and reliable infusions via battery-powered infusion pumps approved for hyperbaric use that do not have to be disconnected during transport or HBOT; septic or otherwise haemodynamically unstable patients, in particular, require accurate haemodynamic monitoring, uninterrupted vasoactive drug infusions and continuous blood, fluid and electrolyte therapy during treatment; there is a particular need for close attention of inotrope and vasopressor infusions during pressurization of the chamber when remaining gas in a syringe and/or tubing may reduce or even cease drug delivery which is not detected by the syringe pump but can be corrected manually by accompanying staff;¹⁴
- Less risk of barotrauma and iatrogenic air embolism during decompression than in a monoplace, as volume changes in an air-filled endotracheal cuff or in IV containers can be corrected immediately;
- Defibrillation if need be with battery-powered defibrillator;
- Catastrophes: a trauma centre will normally be best prepared and equipped to take care of several critically ill patients simultaneously, e.g., a family with CO poisoning and smoke inhalation injuries found comatose inside a burning apartment;
- There are more options regarding tables with choice of pressure and treatment gas; it is also possible to conduct a neurological examination to help guide treatment in severe cases of decompression illness.

Multiplace chamber disadvantages

- High capitalization, technical and staffing costs;
- Large space requirements, difficult to install close to the ICU in old hospitals, and a long-term commitment; once installed it is difficult and expensive to change facility and location due to weight, dimensions and associated compressor, fire extinguishing and other systems;
- Limited availability of multiplace HBOT facilities with ICU capability and 24-hour emergency services;
- Many multiplace chambers in use today are not located in regional centres; often they are in a less specialized hospital without intensive care resources and not accustomed to multidisciplinary treatment programmes; competence will limit referrals;
- Critical care and emergency patients 'disturb' regular planned HBOT practice in the multiplace; depending upon configuration and size there will be a conflict of interest to immediately prepare for an emergency treatment and stop an ongoing elective treatment;
- Risk of decompression sickness (DCS) in the attending staff; more staff are needed with repeat sessions with the risk of not having staff available;
- Risk of barotrauma and iatrogenic air embolism; e.g., during pressurization and decompression the endotracheal cuff can harm the trachea due to overpressure or leak; during decompression, expanding gas in a plastic or glass bottle can give rise to venous air embolism;
- Increased risk of nosocomial infection; special cleanliness considerations, hygiene procedures and technical solutions are needed.

Monoplace chamber advantages

- Cost-efficient delivery of HBOT (capitalization and operating costs) with less financial risk so that more hospitals in less densely populated areas can deliver HBOT in a timely fashion;
- Flexibility, they can be installed within an existing ICU if sufficient space is available;
- Require less staffing and no inside attendant, i.e., no risk for DCS;
- Better hygiene and less risk of nosocomial infection;
- Excellent delivery tool in awake spontaneously breathing children; after extubation, children can be treated together with accompanying nurse who can manually deliver most IV drugs, epidural pain relief, etc.

Monoplace chamber disadvantages

- Patient isolation
- Use of muscle relaxants and/or restraints to prevent the patient from pulling out tubes, lines, catheters, etc;
- Risk of awareness from inadequate sedation and analgesia whilst being unable to move or communicate their anxiety, pain and discomfort;
- Hypotension if too much sedation, especially in

comatose patients from CO/cyanide poisoning or cerebral arterial gas embolism and in the unstable patient with necrotizing infection coming directly from the operating room;

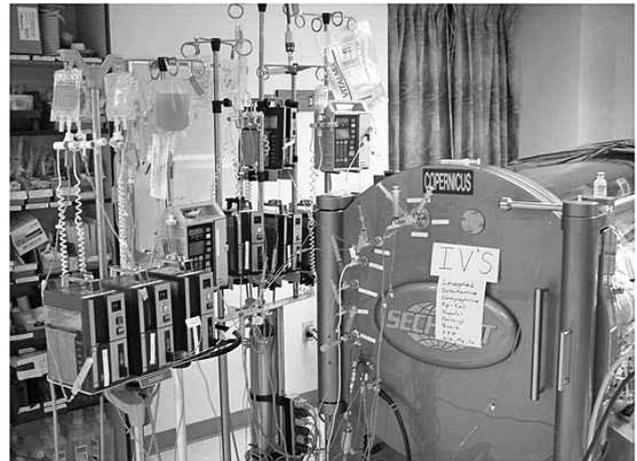
- Pneumothorax is difficult to treat and diagnose; chest tubes with negative pleural suction or a one-way Heimlich valve can be used, but a pneumothorax under pressure becomes a tension pneumothorax and medical emergency during decompression with major impairment of respiration and/or blood circulation;
- Acute airway obstruction; the mechanically ventilated, intubated patient often requires frequent endotracheal suctioning which is very difficult in a monoplace;
- Difficult to monitor and correct the patient's vital functions throughout the HBOT session, e.g., diuresis, fluid and electrolyte status, arterial blood gases and end-tidal CO₂;
- Change of ICU bed to an uncomfortable mattress on stretcher with risk of pressure ulcers;
- Risk of acute cardiogenic pulmonary oedema, especially if treated supine;
- The oxygen environment and fire hazard limits the use of a variety of specialized critical care equipment inside the chamber;
- Mechanical monoplace ventilators located inside the chamber lack modern control, modes and settings;
- Infusion pumps are located outside the chamber; inaccurate drug delivery especially with low delivery rates becomes a real problem in unstable patients; tubing compliance during compression and decompression may affect fluid volumes delivered by the pump since it has to overcome the chamber overpressure;¹⁵
- Limited number of pass-through tubes for conveying IV fluid to a patient under pressure;
- Bolus doses of drugs are difficult unless the IV line is dedicated to that drug;
- Suction can only be accomplished by specially adapting existing hospital equipment;^{16,17}
- Time-consuming changes of lines before and after treatment, with consequent risk of contamination.

Discussion

Regardless of chamber system, HBOT of critically ill patients should be regionalized to maintain quality and cost effectiveness with good helicopter and other emergency transportation services.^{3,4} Hyperbaric intensive care should be performed within a hospital and be supervised by properly trained and experienced medical staff with intensive care skills. Out-patient hyperbaric chambers are not recommended even though many emergencies are still being treated in such facilities because of lack of alternatives. The chamber should preferably be located in close proximity to the ICU to minimize the risk of transport-, equipment-, staff- or patient-related problems. It should be operated and maintained according to written guidelines and regulations. In Europe, a "European code of good practice for HBO

Figure 1

Critical care in a monoplace chamber; intensive care requires modifications of chamber and equipment (courtesy of Lindell K Weaver, Salt Lake City, USA)



therapy"¹⁸ (to be revised 2015, <www.ECHM.org>) should be followed. If appropriate safety precautions are not strictly adhered to, catastrophic accidents may continue to occur regardless of chamber type!

A regional trauma hospital-based, large, three to four lock, multiplace, rectangular chamber immediately bordering the ICU, staffed and equipped for full intensive care is the ideal (see front cover photo of the Karolinska facility). In reality, this is uncommon and it is evident that appropriately medically-equipped monoplace and smaller multiplace chambers in less ideal locations are being used to treat critically ill and ventilator-dependent patients. Critically ill patients can be managed in many different settings providing the facility is staffed with physicians, nurses and therapists skilled in their care and possessing a thorough understanding of hyperbaric physiology and the medical techniques unique to HBOT. Several modifications of chamber and equipment have to be implemented, which requires technical competence.^{16,17}

The monoplace chamber, although less well suited for intensive care can be used to treat critically ill patients and permit clinical research (Figure 1). The safe treatment of severe, traumatic brain injury patients, including monitoring of cardiovascular and ventilatory parameters as well as intracranial pressure, brain tissue oxygen levels, brain temperature and cerebral microdialysis, provides an example of what is possible using a monoplace chamber.¹⁹ This required specially modified equipment for ventilation, monitoring and management of the patient. Ventilator-dependent neonatal patients with acute hypoxic ischaemic encephalopathy and necrotizing enterocolitis have also been treated in the monoplace chamber, given bag-valve-mask ventilation by an accompanying neonatologist during the treatment.²⁰

A hyperbaric critical care patient data management system should be in place in order to provide continuous bedside and remote clinical patient documentation and information.²⁻⁴ At the Karolinska, data are fed into a central clinical information management system to monitor, display trends and record data of vital parameters, ventilator settings and drugs. This has improved the quality of care during HBOT and facilitated research and development in hyperbaric medicine.

Conclusion

The multiplace chamber is better suited than a monoplace chamber for HBOT of critically ill patients with failing vital functions and organ systems, primarily because it permits appropriate ICU equipment to be used inside the chamber by bedside staff accompanying the patient in the chamber.

References

- Lind F, Öhlen G, Lindén V, Eriksson B, Frostell C. *Treatment with hyperbaric oxygen (HBO) at the Karolinska University Hospital; A Stockholm County Council report on the clinical practice and evidence basis of hyperbaric medicine*. Stockholm: Stockholms Läns Landsting; 2011. Available from: <http://www.hyperbaricoxygen.se>
- Kronlund P, Olsson D, Lind F. Hyperbaric critical care patient data management system. *Diving Hyperb Med*, 2012;42:85-7.
- Lind F. How I would design my HBO facility. In: *The Proceedings Book of the 9th ECHM Consensus Conference on Organisation of a Clinical Hyperbaric Therapy Centre and Related Health Management Issues*. Belgrade, Serbia: European Committee for Hyperbaric Medicine; 2012. p. 3-10.
- Lind F. The design of a therapeutic hyperbaric facility for emergencies. In: Mano Y, editor. *Proceedings of the 4th Conference on Diving Physiology, Technology and Hyperbaric Medicine*. Tokyo: The Japanese Society of Hyperbaric and Undersea Medicine; 2013.
- Brummelkamp WH, Hoogendijk J, Boerema I. Treatment of anaerobic infections (clostridial myositis) by drenching the tissues with oxygen under high atmospheric pressure. *Surgery*. 1961;49:299-302.
- Keenan HT, Bratton SL, Norkool DM, Brogan TV, Hampson NB. Delivery of hyperbaric oxygen therapy to critically ill, mechanically ventilated children. *J Crit Care*. 1998;13:7-12.
- Marroni A, Mathieu D, Wattel F, editors. *ECHM 2004 Consensus Conference, Lille. The ECHM Collection*. Flagstaff, AZ: Best Publishing Company; 2007. Also available from: <http://www.echm.org>
- Bitterman H. Bench-to-bedside review: oxygen as a drug. *Critical Care*. 2009;13:205-12.
- Moon RE, Camporesi EM. Clinical care in extreme environments. In: Miller RD, Editor. *Miller's Anesthesia*, Philadelphia, PA: Saunders, 2015. p. 2674-704.
- Weaver LK. Hyperbaric oxygen in the critically ill. *Crit Care Med*. 2011;39:1784-91.
- Frawley G, Bennett M, Thistlethwaite K, Banham N. Australian paediatric hyperbaric oxygen therapy 1998–2011. *Anaesth Intensive Care*. 2013;41:74-81.
- Handell S, Ansjön R, Castor R, Lind F. Respiratory CO₂ monitoring of the critically ill patient in the multiplace chamber. In: Schutz J and Wendling J editors. *Proceedings of the 18th Annual Meeting of the European Underwater and Baromedical Society*. Basel: European Underwater and Baromedical Society; 1992. p. 59-61.
- Ratzenhofer-Komenda B, Offner A, Quehenberger F, Klemen. H, Berger J, Fadaei JH, et al. Hemodynamic and oxygenation profiles in the early period after hyperbaric oxygen: an observational study of intensive-care patients. *Acta Anaesthesiol Scand*. 2003;47:554-8.
- Hopson ASM, Greenstein A. Intravenous infusions in hyperbaric chambers: effect of compression on syringe function. *Anaesthesia*. 2007;62:602-4.
- Bell J, Weaver LK, Deru K. Performance of the Hospira Plum A+ (HB) hyperbaric infusion pump. *Undersea Hyperb Med*, 2014;41:235-43.
- Weaver, LK. Monoplace hyperbaric chambers. In: Thom SR, Neuman T, editors. *The physiology and medicine of hyperbaric oxygen therapy*. Philadelphia: Saunders/Elsevier; 2008. p. 27-35.
- Weaver, LK. Critical care of patients needing hyperbaric oxygen. In: Thom SR, Neuman T, editors. *The physiology and medicine of hyperbaric oxygen therapy*. Philadelphia: Saunders/Elsevier, 2008. p. 117-29.
- Kot J, Desola J, Simao AG, Gough-Allen R, Houman R, Meliet JL, et al. A European code of good practice for hyperbaric oxygen therapy. *Int Marit Health*, 2004;55:121-30.
- Gossett WA, Rockswold GL, Rockswold SB, Adkinson CD, Bergman TA, Quickel RR. The safe treatment, monitoring and management of severe traumatic brain injury patients in a monoplace chamber. *Undersea Hyperb Med*. 2010;37:35-48.
- Sánchez EC. Use of hyperbaric oxygenation in neonatal patients: a pilot study of 8 patients. *Crit Care Nurs Q*. 2013;36:280-9.

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Front cover photo (courtesy Dr Lind, with permission) shows hands-on critical care in the Karolinska multiplace chamber. The four-lock rectangular chamber immediately borders the ICU and is staffed and equipped for simultaneous full intensive care of up to four critically ill patients with failing vital functions, also in children. In cooperation with manufacturers, technical supervisory organization and classification society Germanischer Lloyd and the Karolinska Biomedical Engineering Department many of the medical devices used have received CE approval for use within the hyperbaric chamber.

Letters to the Editor

Diving injuries are (usually) no accident

When recently submitting a manuscript to DHM, I noticed that three of our keywords contain the word accident, namely ‘accidents’, ‘diving accidents’ and ‘scuba accidents’. ‘Accident’ is most strictly defined in the legal sense thus: “... the word accident is used only for events that occur without the intervention of a human being. This kind of accident also may be called an act of God. It is an event that no person caused or could have prevented – such as a tornado, a tidal wave, or an ice storm.”¹

In a review of cave diving fatalities, the medical examiner’s cause of death in each case ($n = 368$) was considered and, from these and their extensive case files, case histories were traced back through the disabling injury to the triggering event.² In the majority of cases there was a clear breach of established safe procedures. The number of ‘accidents’ where, for example, a cave unexpectedly collapsed was rare, by far the exception.

Including these words in our approved list is at odds with the stable of British Medical Journal publications, (e.g., *Injury Prevention*) which have dissuaded use of the word ‘accident’ since 1993 and banned the word since 2001.³ Since 2004, at considerable expense, many former NHS hospital accident and emergency wards in the UK have steadily been re-named emergency departments.⁴ The *Journal of Accident and Emergency Medicine* has been renamed *Emergency Medicine Journal* and, as recently as last year, the New York Police Department changed the name of their *Accident Investigation Squad* to *Collision Investigation Squad*. They also no longer use the word ‘accident’ in their reports, following the lead of the US Department of Transportation’s National Highway Traffic Safety Administration which stopped using the word in all its printed material in 1997, claiming it “...promotes the concept that these events are outside of human influence or control.”(p.1).⁵

There are many such examples of this subtle yet important change that is overtaking both western medicine and, in particular, public health. Rather than ‘accident’ the current trend is to accurately describe the cause of an injury.⁶ To illustrate, a submission formerly entitled ‘Hot water accidents in Welsh children’ would now more likely be titled ‘Hot water burns in Welsh children’. The difference should be obvious; hot water burns in children are largely avoidable, (as are diving injuries). Therefore, I respectfully request we remove these key words from our journal’s list.

Hopefully this would not inconvenience some of our European colleagues for whom English is a second language, and this should be considered. In France, for example, decompression sickness (DCS) is known as an “*accident de desaturation*” and decompression illness (DCI, including

arterial gas embolism), is initially described in French as an *accident de decompression* (ADD). After all signs and symptoms are identified, commonly at around 24 h, then the injury is termed a “*maladie de decompression*” (MDD). The Canadian Government department responsible for aviation, Transports Canada, also refer to DCS/DCI as MDD.

The BMJ makes exceptions, e.g., if the word appears in a formal title such as *Child Accident Prevention Trust*. Regarding ADD however, may I respectfully suggest to my French colleagues they consider adopting “*blesure de décompression*” (BDD)? In diving research at least, the leading hypothesis is that DCS may be prevented through better understanding of the mechanisms of this protean disease. That DCS is an ‘accident’ is the null hypothesis.

References

- 1 Farlex. *The free dictionary: legal dictionary*. 2014. [cited 17 October 2014]. Available from: <http://legal-dictionary.thefreedictionary.com/accident>
- 2 Buzzacott P, Zeigler E, Denoble P, Vann R. American cave diving fatalities 1969–2007. *International Journal of Aquatic Research and Education*. 2009;3:162-77.
- 3 Davis RM. BMJ bans “accidents”: Accidents are not unpredictable. *BMJ*. 2001;322:1320.
- 4 Walker E. Fetch a doctor! *The Guardian*. Published 14 January 2003. [cited 17 October 2014]. Available from: <http://www.theguardian.com/society/2003/jan/14/NHS.lifeandhealth>
- 5 National Highway Traffic Safety Administration. “Crashes aren’t accidents” campaign. *NHTSA Now*. 1997;3(11):1-2.
- 6 Reid C, Chan L. Emergency medicine terminology in the United Kingdom – time to follow the trend? *Emerg Med J*. 2001;18:79-80.

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Key words

Diving incidents, injuries, diving deaths, writing – medical, letters (to the Editor)

Editor’s note: In New Zealand, the Accident Compensation Corporation (ACC) is a publicly-funded insurance compensation scheme for acute at-work, sporting and other injuries. Over recent years, ACC has increasingly focused on injury prevention as well as paying for treatment and compensation, but the term ‘accident’ continues to pervade our language when dealing with these issues. DHM will adopt the change in usage encouraged by Dr Buzzacott. Nevertheless, the accident terms need to remain (unused from here on) in our key-word list, otherwise many older articles might be missed in literature searches of the SPUMS Journal and earlier DHM articles.

Don't dive cold when you don't have to

The San Diego Center of Excellence in Diving at UC San Diego aims to help divers be effective consumers of scientific information through its “*Healthy Divers in Healthy Oceans*” mission. A 2007 research report from the Navy Experimental Diving Unit (NEDU) entitled “*the influence of thermal exposure on diver susceptibility to decompression sickness*”¹ is leading some divers to think they should be cold if they want to reduce decompression risk. That is a misinterpretation of the report, and may be causing divers to miss some of the joy of diving. There is no substitute for comfort and safety on a dive. Gerth et al questioned the conventional wisdom that cold at depth increases the risk of decompression sickness (DCS). After conducting a carefully designed experiment, they were surprised to find that exactly the opposite was true. Some degree of cooling was beneficial, as long as the diver was warm during ascent.

There are some important caveats for the non-Navy diver to consider. First of all, it was anticipated that a diver would have a system for carefully controlling their temperature during the separate phases of bottom time and decompression. Most non-Navy divers do not have that sort of surface support. Secondly, the ‘cold’ water in the NEDU study was 80°F (27°C). For most of us, this is an ideal swimming pool temperature, not exactly what you are going to find in non-tropical oceans and lakes. The warm water was 97°F (36°C), also a temperature not likely to be available to recreational and technical divers.

When testing the effect of anything on decompression results, the Navy uses their extensive mathematical expertise to select the one dive profile that, in their estimation, is the most likely to identify a difference in decompression risk, if that difference exists. A 37 metres’ sea water (msw) dive with 25 to 70 min bottom time, decompressed on a USN Standard Air table for 37 msw and 70 min bottom time was selected.

A total of 400 carefully controlled dives yielded 21 diagnosed cases of DCS. Overwhelmingly, the lowest risk of decompression was found when divers were kept warm during decompression. The effect of a 9°C increase in water temperature during decompression was comparable to the effects of halving bottom time. That is, of course, a remarkable result, apparently remarkable enough to cause civilian divers to alter their behavior when performing decompression dives. However, before you decide to chill yourself on the bottom or increase your risk of becoming hypothermic, consider these facts:

- Do you have a way of keeping yourself warm, for instance with a hot water suit, during decompression? If not, the study results do not apply to you.
- Of many possible decompression schedules, the Navy tested only one, considered the best for showing a thermal influence on decompression risk. Although this result might possibly be extrapolated to other dive profiles, such extrapolation is always risky, especially if

the planned dive is deeper and longer than that tested.

- Most commercial decompression computers do not adhere to the US Navy Air Tables; few recreational dives are square profiles. Furthermore, additional conservatism is usually added to commercial algorithms. NEDU is not able to test the effects of diver skin temperature on all proprietary decompression tables, nor should they. That is not their mission.
- The scientific method requires research to be replicated before test results can be proven or generalized. However, owing to the labour and expense involved in the NEDU dive series, it seems unlikely that any experiments that would determine the relevance of these results to recreational or technical diving will ever be performed. As such, it may raise as many questions as it answers. For instance, the original question remains; if you become chilled on a dive, how does that affect your overall risk of DCS compared to remaining comfortably warm? Unfortunately, that question may never be answered fully.
- Thermoneutral temperatures for swim-suited divers are reported to be 93–97°F (34–36°C) for divers at rest and 90°F (32°C) during light to moderate work.² So a skin temperature of 80°F (27°C) is indeed cold for long-duration dives. If your skin temperature is less than this, then you are venturing into the unknown; NEDU’s results may not apply.

In summary, beer and some wines are best chilled; arguably, divers are not. Diving physicians should be aware of this inappropriate practice.

References

- 1 Gerth WA, Ruterbusch VL, Long ET. *The influence of thermal exposure on diver susceptibility to decompression sickness*. NEDU Technical Report 06-07. Panama City: Navy Experimental Diving Unit; 2007.
- 2 Sterba JA. Thermal problems: prevention and treatment. In: Bennett PB, Elliott DH, editors. *The physiology and medicine of diving*, 4th ed. London: Saunders; 1993. p. 301-41.

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In April 2014, the Undersea and Hyperbaric Medical Society (UHMS) published the thirteenth edition of their list of hyperbaric oxygen therapy (HBOT) indications. The twelfth edition was published in 2008 so, after six years, there is no doubt that some new findings and developments may have an impact on the currently recommended indications for HBOT.

Whilst my expectations were not great, awaiting an update on the reference list but no substantial changes, the first impression of receiving the 13th edition was that this edition is something completely new. In fact, the new edition has grown considerably compared to previous editions and now is closer to a text book on HBOT than to plain recommendations of a scientific society on a specific topic. The publisher himself announces that the page count has doubled to approximately 450 pages compared to the previous edition, whilst the eBook runs to 625 pages – a discrepancy which I will explain later.

Taking a closer look, this new edition consists of introductory and two main sections. Section I is the well-known list of indications, including a new indication since the 12th edition – idiopathic sudden sensorineural hearing loss. Section II is completely new with five additional chapters, a new appendix and two new indexes. The additional chapters are: mechanisms of action of HBOT; a chapter on pre-treatment and pre-conditioning prior to HBOT; a review on randomized controlled trials of diving and hyperbaric medicine; regulatory considerations for traumatic brain injury (TBI) and a product summary on hyperbaric medicine for post-concussive syndrome.

The first part provides a short introduction to the UHMS, a short definition of what hyperbaric oxygen is, followed by a statement on the acceptance of new indications for HBOT as well as a list of abbreviations, which is useful. This part ends with brief biographies of the authors who contributed to this edition. It has to be stated that the authors, as listed here, are indeed recognized experts in the fields they report on.

To those familiar with the previous editions of the list of indications, Section I is what these readers are used to: it contains the recommended indications for HBOT as approved by the UHMS. Each of these fourteen indications has a chapter and each chapter is a review on the specific topic with a brief explanation for the specific background, the rationale for the treatment, patient selection criteria, clinical management, evidence-based review and a statement on the cost impact. Each chapter also contains a reference list of its own and in most chapters the references are really up-to-date with even very recent publications. The chapters appear in alphabetical order of the indications, starting with *air or gas embolism*, ending with *thermal burns*.

Some of these chapters, such as that on air embolism, are succinct whilst others, such as that on arterial insufficiency, are more extensive. In most cases, this is of value for the reader, as some of these indications are less common, so it is helpful to get additional explanations on the pathophysiology of the specific problem. Also very helpful are tables that summarize either important facts or give a short overview on controlled studies, as well as some figures, as in the chapters on central retinal artery occlusion, crush injuries, refractory osteomyelitis and thermal burns.

Altogether, Section I is very informative and gives an excellent and up-to-date overview of the UHMS recommendations. This part of the publication is well in line with previous editions.

Section II is the really ‘new part’. It is informative, yes, but reminds one a little of a quilt put together from different pieces that do not necessarily belong together. The first chapter of this section is on the mechanisms of action of hyperbaric oxygen. This chapter, although quite short, gives a very good introduction to what is triggered by HBOT and, again, is up to date. I think it is an excellent idea to include it, but it could find a better place at the beginning of the book. In addition, I would hope that it will be expanded in the next edition.

I also think that the chapter on randomized controlled trials in diving and hyperbaric medicine could be placed better in the introductory section of the book. This chapter helps the reader to understand why HBOT sometimes is considered to be ‘weak’ in terms of evidence and why randomized controlled trials (RCTs) are of such importance. With respect to this, the tables that list RCTs in specific indications and that are part of some of the chapters in Section I are even more valuable.

The short chapter on side effects is placed well here whereas the following chapter, on pre-treatment and preconditioning, is very interesting to read but seems misplaced. It is still a highly experimental area and I have some problems in understanding why it is embedded between side effects and RCTs.

I have bigger problems with the next two chapters because it is difficult for me to see why these topics are published in this context and not as separate statements of the society or as a review paper in a scientific journal. The chapter on regulatory considerations for TBI indications gives little to no information on the mechanism of action of HBOT in TBI, but tells about the problems new indications have in the regulatory processes of public health, etc. However, this chapter refers to the next chapter (20), where HBOT for post concussive syndrome and chronic TBI is discussed extensively. I do not doubt that chronic TBI is a problem and I am interested to learn if (and if so, how) HBOT can lead to an improvement, but, again, this is still experimental and, therefore, the publication in this book seems to be somewhat premature. Furthermore, this whole chapter is quite extensive, but to a major degree repeats what has been come in other sections. Therefore, much of this information is redundant. The chapter itself is well written no doubt, but it appears like a foreign body within the rest, so it seems that originally it was written for a totally different purpose and then was inserted here. Nevertheless, it will be interesting to see if in one of the next editions TBI will be listed as indication number 15 by the UHMS.

The text ends at page 483 and is then followed by some useful appendices with tables on a summary of the literature and on the currently approved indications for HBOT. From page 492 to 609, all references from all chapters are listed again in alphabetical order, which makes the book thicker but is

not really necessary, as each chapter is followed by a specific reference list, although these lists are sorted according to their appearance in the text rather than alphabetically. The rest of the book is filled with a very useful index and in the eBook version the key-words here are hyperlinked with the text.

The new edition of the official list of hyperbaric oxygen therapy indications of the UHMS, is a valuable publication for all those working in hyperbaric medicine. The main part, the approved indication list itself, is updated and provides good information. The new parts are interesting, but seem somewhat cobbled together. No doubt one would get used to the Section I / Section II solution in the future, particularly if it can be sorted better. The new edition cannot replace totally a textbook on HBOT, but, nevertheless, it is a very good source of information and a must-have for a hyperbaric physician.

Claus-Martin Muth

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Key words

Hyperbaric oxygen therapy, medical conditions and problems, medical society, textbook, book reviews

Continuing professional development

Drink, drugs and diving

Christine Penny

Accreditation statement

INTENDED AUDIENCE

The intended audience consists of all physicians subscribing to *Diving and Hyperbaric Medicine* (DHM), including anaesthetists and other specialists who are members of the Australia and New Zealand College of Anaesthetists (ANZCA) Diving and Hyperbaric Medicine Special Interest Group (DHM SIG). However, all subscribers to DHM may apply to their respective CPD programme coordinator or specialty college for approval of participation. This activity, published in association with DHM, is accredited by the ANZCA Continuing Professional Development Programme for members of the ANZCA DHM SIG under Learning Projects: Category 2 / Level 2: 2 credits per hour.

OBJECTIVES

The questions are designed to affirm the takers' knowledge of the topics covered, and participants should be able to

evaluate the appropriateness of the clinical information as it applies to the provision of patient care.

FACULTY DISCLOSURE

Authors of these activities are required to disclose activities and relationships that, if known to others, might be viewed as a conflict of interest. Any such author disclosures will be published with each relevant CPD activity.

DO I HAVE TO PAY?

All activities are free to subscribers.

Key words

Diving, scuba, alcohol, drugs, fitness to dive, epilepsy, MOPS (maintenance of professional standards)

Recommended background reading

Practitioners are referred to the following background references and reading.

- 1 Smart D, Lippman J. Epilepsy, scuba diving and its risk assessment. Near misses and the need for ongoing vigilance. *Diving Hyperb Med.* 2013;43:37-41.

- 2 UK Sport Diving Medical Committee Medical Standards – *Epilepsy*. [cited 2014 Feb 11]. Available from: http://www.uksdmc.co.uk/index.php?option=com_content&view=article&id=10:epilepsy&catid=3:neurological&Itemid=2
- 3 Verster JC, Kienhorst EAM, van Hulst RA. Alcohol, drugs and diving: implications for health and fitness to dive. *Current Drug Abuse Reviews*. 2012;5:85-6. Available from: <http://eurekaselect.com/97813>
- 4 St Leger Dowse M, Cridge C, Shaw S, Smerdon G. Alcohol and UK recreational divers: consumption and attitudes. *Diving Hyperb Med*. 2012;42:201-7.
- 5 St Leger Dowse M, Shaw S, Cridge C, Smerdon G. The use of drugs by UK recreational divers: illicit drugs. *Diving Hyperb Med*. 2011;41:9-15.
- 6 St Leger Dowse M, Shaw S, Cridge C, Smerdon G. The use of drugs by UK recreational divers: prescribed and over-the-counter medications. *Diving Hyperb Med*. 2011;41:16-21.
- 7 Sheldrake SJ, Pollock NW, editors. *Alcohol and diving*. Proceedings of the American Academy of Underwater Sciences 31st Symposium; 2012. [cited DATE]. Available from: http://archive.rubicon-foundation.org/xmlui/bitstream/handle/123456789/10162/AAUS_alcohol_and_diving_2012.pdf?sequence=1

How to answer the questions

Please answer all responses (A to E) as True or False, except for question 5, which requires a brief text answer as well. Answers should be posted by e-mail to the nominated CPD co-ordinator.

For EUBS members, this will be Lesley Blogg, **E-mail:** <euroeditor@dhmjournal.com>

For ANZCA DHM SIG and SPUMS members, this will be Neil Banham, **E-mail:** <N.Banham@health.wa.gov.au>.

If you would like to discuss any aspects with the author, contact her at **E-mail:** <Christine.Penny@ddrc.org>.

On submission of your answers, you will receive a set of correct answers with a brief explanation of why each response is correct or incorrect. A correct response rate of 80% or more is required to successfully undertake the activity. Each task will expire within 24 months of its publication to ensure that additional, more recent data has not superseded the activity.

Question 1. Alcohol and diving:

- A. Safe blood alcohol concentrations for diving in the UK are aligned with the UK government permitted blood alcohol concentrations for driving.
- B. The recommended abstinence from alcohol before diving of 12 hours is well established and simple to monitor.
- C. Less than 40% of respondents in a survey of UK recreational divers felt their dive clubs demonstrated a responsible attitude to alcohol.
- D. The physiological effects of alcohol include action as a CNS stimulant, vasoconstriction and reduced narcosis.
- E. Random testing of working divers for alcohol is commonly used by many USA institutions.

Question 2. Regarding epilepsy and medication used in its treatment:

- A. Medication used to control epilepsy may cause side effects which compound nitrogen narcosis;
- B. Consensus exists internationally regarding fitness to undertake diving for an individual fit-free and off medication for six years;
- C. Factors that increase risk of seizure activity whilst diving include hypercapnia, stress and hyperoxia;
- D. A petit mal seizure occurring seven years ago, according to UK Sport Diving Medical Committee guidelines, may be compatible with safe diving;
- E. Some studies have shown that approximately one third of individuals with a history of epilepsy who are fit-free may relapse once they stop medication.

Question 3. Recreational or illicit drugs:

- A. Will be detected on a urinary drug screen if undertaken within two weeks of drug use.
- B. UK divers in one study were found to use illicit drugs less than the background level of use in the British population.
- C. Ecstasy is the most commonly used illicit drug in UK divers.
- D. Amphetamines will have on-going effects that could impact on diving eight hours after ingestion.
- E. The effects of illicit drugs under pressure is well established.

Question 4. Medication and illicit drugs:

- A. Recommendations regarding the use of various medications and compatibility with safe diving is evidence-based.
- B. Potential problems with self-certified medical questionnaires are that divers may forget, omit or not realise the importance of medications they are taking.
- C. Some medications may be permissible in individuals in a hyperbaric chamber but not for in-water diving.
- D. A higher prevalence of anxiety and depression has been reported in divers who use illicit drugs.
- E. Decongestants were the most commonly reported medication sourced from over the counter in a study on UK divers.

Question 5. Using the suggested framework in one of the papers, decide whether the following medication are compatible with safe diving activity and consider why:

- A. Mefloquine
- B. Citalopram
- C. Methotrexate
- D. Pseudoephedrine
- E. Nicorandil

Obituary



George B Hart, MD, FACS
29 January 1930 – 27 September 2014

George B ('Babe') Hart was born in Lamesa, Texas and educated at Abilene Christian College before graduating from Texas Christian University in 1952. He went on to the University of Texas Medical Branch, Galveston, and an internship at Rochester General Hospital before joining the US Navy. Retiring as a Captain after 20 years, in 1977 he became Medical Director of the Baromedical Department, Long Beach Memorial Medical Center until his retirement in 1992.

George Hart was a 'giant' in the field of hyperbaric medicine. The triumvirate of Jefferson Davis, Eric Kindwall and George Hart in the USA was the keystone in making hyperbaric medicine in America what it is today. Dr Hart was a great innovator, and it is a challenge to summarise his many achievements, some of which are listed here.

- He was the 'brains' behind modernizing the monoplace hyperbaric chamber from the cumbersome two-part chamber and console complex that required wrenches to secure the hatch to our current generation of easy-to-operate, single-unit monoplace chambers.
- He was instrumental in formulating the approved clinical uses of HBO₂ promulgated by the Undersea and Hyperbaric Medical Society.
- Dr Hart served as the American College of Surgeons advisor to the NFPA (National Fire Protection Association) and helped establish fire safety regulations for multiplace and monoplace chambers.
- He initiated the 'Annual Conferences on Clinical Application of Hyperbaric Oxygen' in 1976 which was eventually amalgamated with the annual Undersea Medical Society meetings, and which, with a 'gentleman's agreement' resulted in adding "*Hyperbaric*" to the society's name in 1987.
- In 1977 the 'Introduction to Hyperbaric Medicine' course was initiated at Long Beach Memorial Medical and has continued semi-annually since then.

- Under his auspices the first hyperbaric medicine fellowship was established in 1985, with Stephen Thom as the first Fellow.
- In 1987, Dr Hart served as President of the UHMS. Under his leadership he brought the society's finances into the black and established the first pre-course during the meeting in New Orleans.
- He authored multiple publications on the use of hyperbaric oxygen, including for burns, acute blood loss anaemia, central retinal artery occlusion, gas gangrene, radiation injury, osteomyelitis, cyanide poisoning, spinal cord injury, gas embolism, crush injury, compartment syndrome and acute myocardial infarction.
- He intensively researched the tissue oxygenation effects of HBO₂ and determined the duration that oxygen levels remain elevated in tissues as well as stating the juxta-wound transcutaneous oxygen tensions needed for wounds to heal with HBO₂.
- Not to be overlooked is his contribution to diving medicine. He formulated oxygen treatment tables for treating decompression sickness in a monoplace chamber and the value of repetitive treatments when residual symptoms and signs persist after the first treatment. This approach was also extended to carbon monoxide poisoning. For these he was initially severely criticized, but now these practices are fully accepted.
- Finally, Dr Hart had remarkable observational and intuitive abilities. As early as 1997, he postulated that radiation injury of tissues and refractory osteomyelitis were ischaemic disorders. This is now contemporary thinking and the basis for the science to justify the use of HBO₂ for these problems. In addition, he appreciated that 'hard' scar formed in ischaemic tissues while the desirable 'soft' scar formed in well-oxygenated tissues. These observations have recently been substantiated with recognition of the inducers of fibroblast functions.

George Hart had the ability to captivate his audiences with his folksy remembrances, his keen acumen and his incredible clinical experience. He was not diverted by the disdain and disapproval of skeptics and cynics and had strong feelings about the roles of HBO₂ for acute life- and limb-threatening conditions and the need for hyperbaric medicine facilities to be able to provide these services.

Synopsed with minor editing from the 'In Memoriam' in *Pressure*, The Membership Newsletter of the Undersea and Hyperbaric Medical Society, November/December 2014 written by Dr Hart's long-time colleague, Michael B Strauss, Medical Director, Hyperbaric Medicine Program, Long Beach Memorial Medical Center, Long Beach, California. Dr Strauss and UHMS are thanked for their kind permission.

Key words

Obituary, hyperbaric medicine, diving, medicine, general interest



Notices and news

SPUMS 44th Annual Scientific Meeting 2015
Palau Royal Resort, Malakai, Palau, Micronesia, 16–23 May 2015

Guest Speaker

Neal Pollock, PhD, Duke University and Director of Research DAN International

Topics

Diabetes and diving; the older diver; breath-hold diving

Convenor: Dr Catherine Meehan, Cairns

Preferred travel from Australia will be with China Airlines ex Brisbane. This avoids lengthy layovers and awkward connections. Several packages with significant cost savings are likely to be available.

The link to the conference booking site is open at: <www.spums.org.au>

Register now, bookings still being accepted

For further information e-mail: <cmeehan@mcleodstmed.com.au>

SPUMS notices and news and all other society information is now to be found on the society website: <www.spums.org.au>

The

website is at
<www.spums.org.au>

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

Notice of SPUMS Annual General Meeting
Palau Royal Resort, Koror, Republic of Palau 1700 h
Thursday 21 May, 2015

Agenda

- (i) Apologies;
 - (ii) Submission of proxy forms in accordance with rule 36;
 - (iii) Reading and confirmation of minutes from previous Annual General Meeting or any Special General Meeting; minutes of the Annual General Meeting of SPUMS held on 27 May, 2014 will be posted on the notice board at Palau Royal Resort and were published on the SPUMS website <www.spums.org.au>.
 - (iv) Matters arising from minutes;
 - (v) Annual reports of Officers of the Society;
 - (vi) Committee performance indicator reports;
 - (vii) Annual financial statement, audit and certificate signed by two Committee members;
 - (viii) Fix the subscription for the coming year;
 - (ix) Announcement of the newly elected Committee and the holding of any ballots necessary under Rule 56;
 - Election of office bearers:
Secretary; one Committee Member
 - (x) Appointment of Auditor;
 - (xi) Acceptance of new members;
 - (xii) Any business of which notice has been given.
- Nominations for office bearers and expressions of interest for the Committee positions are to be forwarded to the Secretary by 20 May, 2015.

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Photo by Christopher Ross

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:

- 1 (S)he must be medically qualified, and remain a current financial member of the Society at least until they have completed all requirements of the Diploma.
- 2 (S)he must 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 (S)he must 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 (S)he must submit a written proposal for research in a relevant area of underwater or hyperbaric medicine, in a standard format, for approval before commencing their research project.
- 5 (S)he must 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 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 Education Officer 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 or clinical research is acceptable. Case series reports may be acceptable if thoroughly documented, subject to quantitative analysis and if the subject is extensively researched and discussed 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 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 project is approved prior to commencing research.

As of 01 June 2014, projects will be deemed to have lapsed if

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

With respect to 1 above, for unforeseen delays where the project will exceed three years, candidates must advise the Education Officer in writing if they wish their diploma project to remain active, and an additional three-year extension will be granted.

With respect to 2 above, if there are extenuating circumstances that a candidate is unable to maintain financial membership, then these must be advised in writing to the Education Officer 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 June 2014, the SPUMS Academic Board consists of:

- Dr David Wilkinson, Education Officer;
- Associate Professor Simon Mitchell;
- Associate Professor (retired) Mike Davis;
- Dr Denise Blake.

All enquiries and applications should be addressed to:

David Wilkinson

Fax: +61-(0)8-8232-4207

E-mail: <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 on the society website: <www.eubs.org>

41st EUBS Annual Scientific Meeting 2015

Second Announcement

Dates: 19–22 August

Venue: The Academic Medical Center (AMC), Amsterdam

The AMC was one of the founders of hyperbaric medicine in the last century owing to the work of Professor Boerema and his colleagues. His work, in close cooperation with the Royal Netherlands Navy, is often quoted in textbooks on diving and hyperbaric medicine. AMC continues to be highly active.

Call for Abstracts

Please submit your Abstract by 31 March 2015 via the website: <www.eubs2015.org>

There will be an excellent mixture of science in diving and hyperbaric medicine.

The annual EUBS meeting coincides with SAIL 2015 – the world-famous, 5-yearly event with Tall Ships and other sailing ships referring to the maritime history and heritage of The Netherlands. The maritime sail event and the numerous cultural aspects of Amsterdam, combined with the renewal of scientific ideas and social contacts, will inspire you!

Looking forward to seeing you in Amsterdam, on behalf of the organizing committee.

Albert van den Brink, General Secretary

Robert van Hulst, Chairman of the Scientific Committee

For more information and to submit an Abstract: <www.eubs2015.org>

Zetterström and Patrick Musimu Awards 2014

Zetterström Award for the best poster presentation:

Dror Ofir, Yehuda Arieli, Michael Mullokandov, Ben Aviner, Alexander Liboff, Yoav Yanir

Quantifying the risk of acute neuronal injury after a 'Yo-Yo' dive in swine by histopathological evaluation of the spinal cord

Patrick Musimu Award for the best presentation (oral or poster) on breath-hold diving:

Danilo Cialoni, Massimo Pieri, Nicola Sponsiello, Vittorio Lucchini, Alessandro Marroni

Genetic predisposition to breath-hold diving induced pulmonary oedema - update



The
website is at
<www.eubs.org>

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

The
Diving and Hyperbaric Medicine Journal
website is at

<www.dhmjournal.com>

Hyperbaric Oxygen, Karolinska

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

This site, supported by the Karolinska University Hospital, Stockholm, Sweden, offers publications and free, high-quality video lectures from leading authorities and principal investigators in the field of hyperbaric medicine. You need to register to obtain a password via e-mail. Once registered, watch the lectures online, or download them to your iPhone, iPad or computer for later viewing.

For further information contact:

Folke Lind, MD PhD

E-mail: <folke.lind@karolinska.se>

Website: <www.hyperbaricoxygen.se>

British Hyperbaric Association Annual Scientific Meeting 2015

Dates: 22–24 October

Venue: National Exhibition Centre, Birmingham

Jointly with the UK Sport Diving Medical Committee (UKSDMC) and chosen to coincide with DIVE 2015.

The content of 22–23 October will be aligned to the requirements of refresher training for Health and Safety Executive-approved Medical Examiners of Divers.

22 Oct: Fitness to dive – primarily of interest to UKSDMC

23 Oct: Diving – of interest to UKSDMC and BHA

24 Oct: Hyperbaric therapy – primarily of interest to BHA

Further information in next issue or contact:

<<http://www.hyperbaric.org.uk/>>

Undersea and Hyperbaric Medical Society Annual Scientific Meeting 2015

Dates: 18–20 June

Venue: Hilton Montréal Bonaventure, Montréal, Canada

Pre-Courses: 17 June

Pre-course 1: Hyperbaric oxygen safety

Pre-course 2: Patent foramen ovale

Pre-Course 3: Preparing for accreditation

For further information and to register for the meeting:

<www.uhms.org>

Capita Selecta Duikgeneeskunde 'De duikkeuring'

Dates: 18–25 April; Bonaire

Diving pathophysiology and cases, with special attention to dehydration, dysthermia and the cardiopulmonary system.

Lecturers: Jacques Regnard (France) and Adel Taher, diving & hyperbaric physician (Egypt).

For further information: <www.diverresearch.org>

Advanced Professional Diving Medicine 1st course to EDTC Training Standards

Dates: 03–10 October

Venue: Institut National de la Plongée Professionnelle (INPP), Marseille (France)

This is a top-up course for diving medicine physicians (Level 2d), with hands-on training in all kinds of advanced professional diving including saturation and bell diving, on-site recompression treatment and risk analysis.

The course is recognised for the EDTC certificate of competence in Diving Medicine.

Approval pending for CME and ETCS (50 contact hours + 50 hours web-based study).

Speakers/Faculty: Alf Brubakk, Norway; Alain Barthélemy, France; Marc Borgnetta, France (Course director); Michel Hugon, France; Pasquale Longobardi, Italy; Jack Meintjes, South Africa; Roland van den Eede, Belgium; Jürg Wendling, Switzerland and others.

For further information and applications:

<www.edtcmcd.ch>

German Society for Diving and Hyperbaric Medicine

An overview of basic and refresher courses in diving and hyperbaric medicine, accredited by the German Society for Diving and Hyperbaric Medicine (GTÜeM) according to EDTC/ECHM curricula, can be found on the website:

<http://www.gtuem.org/212/Kurse/_/Termine/Kurse.html>

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 – EUBS and SPUMS – appears on the journal website: <www.dhmjournal.com>

For advertising rates and formatting requirements contact: <editorialassist@dhmjournal.com>

International Meeting on Ultrasound for Diving Research – Ultrasound 2015

Dates: 25–26 August

Venue: The Swedish Armed Forces Diving and Naval Medical Centre (DNC), Karlskrona, Sweden

This inaugural meeting will bring together experts in diving and decompression physiology to discuss and educate on the use of ultrasound in assessing the stress caused by decompression and the associated risks of decompression sickness. The meeting will include a methodology consensus discussion and hands-on workshops.

Speakers include: Ron Nishi, Alf Brubakk, Neal Pollock, Jay Buckley and Mikael Gennser

Convenors: Lesley Blogg and Andreas Møllerlökken

For more information, please visit:

<ultrasound2015.wix.com/ultrasound2015>

Facebook: <www.facebook.com/Ultrasound2015>

E-mail: <ultrasound2015@yahoo.co.uk>

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Dates: 03–10 October

Venue: Institut National de la Plongée Professionnelle (INPP), Marseille (France)

This is a top-up course for diving medicine physicians (Level 2d), with hands-on training in all kinds of advanced professional diving including saturation and bell diving, on-site recompression treatment and risk analysis. The course is recognised for the EDTC certificate of competence in Diving Medicine. Approval pending for CME and ETCS (50 contact hours + 50 hours web-based study).

Speakers/Faculty: Alf Brubakk, Norway; Alain Barthélemy, France; Marc Borgnetta, France (Course director); Michel Hugon, France; Pasquale Longobardi, Italy; Jack Meintjes, South Africa; Roland van den Eede, Belgium; Jürg Wendling, Switzerland and others.

For further information and applications:

<www.edtcmcd.ch>

Scott Haldane Foundation

The Scott Haldane Foundation is dedicated to education in diving medicine, and has organized more than 180 courses over the past 20 years. In 2015 SHF will organize more courses than ever, targeting an international audience. The courses Medical Examiner The courses Medical Examiner of Diver (parts I and II) and the modules of the Diving Medicine Physician course comply fully with the ECHM/EDTC curriculum for Level 1 and 2d respectively and are accredited by the European College of Baromedicine.



SHF courses for 2015

11 & 17 April: Basic course diving medicine (level 1 part 1); Loosdrecht, Netherlands

18, 24 & 25 April: Basic course diving medicine (level 1 part 2); Amsterdam, Netherlands

13, 14 May: Basic course diving medicine (level 1 part 1); Oman

16–23 May: Basic course diving medicine (level 1 part 2); Oman

12 & 13 June: In-depth course diving medicine in case studies; Loosdrecht, Netherlands

25–26 August: International Meeting on Ultrasound for Diving Research; Karlskrona, Sweden

3 October: ENT and diving refresher course; Rotterdam, Netherlands

7–14 November: Basic course diving medicine (level 1 part 1); Palau

14–21 November: 23rd SHF In-depth course diving medicine; Palau

21–28 November: 23rd SHF In-depth course diving medicine; Palau

For further information: <www.scotthaldane.org>

The 5th Arthur-Bornstein Workshop Diving in offshore wind farms

Unfortunately this meeting had to be postponed as a satellite meeting of the 40th EUBS ASM 2014 in Wiesbaden. It is intended to hold the meeting during 2015 in Germany.

For more information contact Karl-Peter Faesecke: <faesecke@schlaichpartner.de>

Back articles from *Diving and Hyperbaric Medicine*

After a one-year embargo, articles from *Diving and Hyperbaric Medicine* are placed on the Rubicon Foundation website <<http://www.rubicon-foundation.org/>>, an open-access database, available free of charge and containing many other publications, some otherwise unobtainable. At present, this task is not fully up to date for DHM but articles to the September 2012 issue are now available. Rubicon seeks donations to continue its work to document the hyperbaric scientific literature.

More recent articles or other enquiries about articles should be sent to: <editorialassist@dhmjournal.com>

Embargoed articles will be charged for; details on application.

Royal Australian Navy Medical Officers' Underwater Medicine Course 2015

Dates: 14–25 September 2015 (TBC)
Venue: HMAS PENGUIN, Sydney

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

Cost: AUD1,355 without accommodation (AUD2,300 approx with accommodation and meals at HMAS Penguin)

For information and application forms contact:

Rajeev Karekar, for Officer in Charge,
 Submarine and Underwater Medicine Unit
 HMAS PENGUIN

Middle Head Rd, Mosman
 NSW 2088, Australia

Phone: +61-(0)2-9647-5572

Fax: +61-(0)2-9647-5117

E-mail: <Rajeev.Karekar@defence.gov.au>

Royal Adelaide Hospital Hyperbaric Medicine Unit Courses 2015

Medical Officers' Courses

30 November – 04 December: Basic
 07–11 December: Advanced

DMT Refresher Courses

20–24 April
 27 April – 01 May
 14–18 September
 21–25 September

All enquiries to:

Lorna Mirabelli, Course Administrator

Phone: +61-(0)8-8222-5116

Fax: +61-(0)8-8232-4207

E-mail: <Lorna.Mirabelli@health.sa.gov.au>

Certificate in Diving and Hyperbaric Medicine of the Australian and New Zealand College of Anaesthetists

Eligible candidates are invited to present for the examination for the Certificate in Diving and Hyperbaric Medicine of the Australian and New Zealand College of Anaesthetists.

All details are available on the ANZCA website at:

<<http://anzca.edu.au/edutaining/DHM/index.htm>>

Suzy Szekely, FANZCA, Chair, ANZCA/ASA Special Interest Group in Diving and Hyperbaric Medicine.

E-mail: <Suzy.Szekely@health.sa.gov.au>



DIVING HISTORICAL SOCIETY AUSTRALIA, SE ASIA

P O Box 347, Dingley Village
 Victoria, 3172, Australia

E-mail: <hdsaustraliapacific@hotmail.com.au>

Website:

<www.classicdiver.org>

DAN Europe

DAN Europe has a fresh, multilingual selection of recent news, articles and events featuring DAN and its staff.

Go to the website: <<http://www.daneurope.org/web/guest/>>

Instructions to authors

A downloadable pdf of the 'Instructions to Authors' (revised January 2015) is to be found on the *Diving and Hyperbaric Medicine* website: <www.dhmjournal.com>. Authors must read and follow these instructions. As of January 2015, submissions to *Diving and Hyperbaric Medicine* should be made using the portal at <<http://www.manuscriptmanager.com/dhm>>. Before submitting, authors are also advised to view video 5 on how to prepare a submission on the main Manuscript Manager web site <<http://www.manuscriptmanager.com>>. In case of difficulty, please contact the Editorial Assistant by e-mail at <editorialassist@dhmjournal.com>.

DIVER EMERGENCY SERVICES PHONE NUMBERS

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1800-088200 (in Australia, toll-free)
+61-8-8212-9242 (International)

SOUTHERN AFRICA

0800-020111 (in South Africa, toll-free)
+27-10-209-8112 (International, call collect)

NEW ZEALAND

0800-4DES-111 (in New Zealand, toll-free)
+64-9-445-8454 (International)

EUROPE

+39-6-4211-8685 (24-hour hotline)

ASIA

+10-4500-9113 (Korea)
+81-3-3812-4999 (Japan)

UNITED KINGDOM

07831-151523 (England)
0845-408-6008 (Scotland)

USA

+1-919-684-9111

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

DAN ASIA-PACIFIC DIVE ACCIDENT REPORTING PROJECT

This project is an ongoing investigation seeking to document all types and severities of diving-related accidents. All information is treated confidentially with regard to identifying details when utilised in reports on fatal and non-fatal cases. Such reports may be used by interested parties to increase diving safety through better awareness of critical factors.

Information may be sent (in confidence unless otherwise agreed) to:

DAN Research
Divers Alert Network Asia Pacific
PO Box 384, Ashburton VIC 3147, Australia
Enquiries to: <research@danasiapacific.org>

DAN Asia-Pacific NON-FATAL DIVING INCIDENTS REPORTING (NFDIR)

NFDIR is an ongoing study of diving incidents, formerly known as the Diving Incident Monitoring Study (DIMS). An incident is any error or occurrence which could, or did, reduce the safety margin for a diver on a particular dive. Please report anonymously any incident occurring in your dive party. Most incidents cause no harm but reporting them will give valuable information about which incidents are common and which tend to lead to diver injury. Using this information to alter diver behaviour will make diving safer.

The NFDIR reporting form can be accessed on line at the DAN AP website:
<www.danasiapacific.org/main/accident/nfdir.php>

DISCLAIMER

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

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