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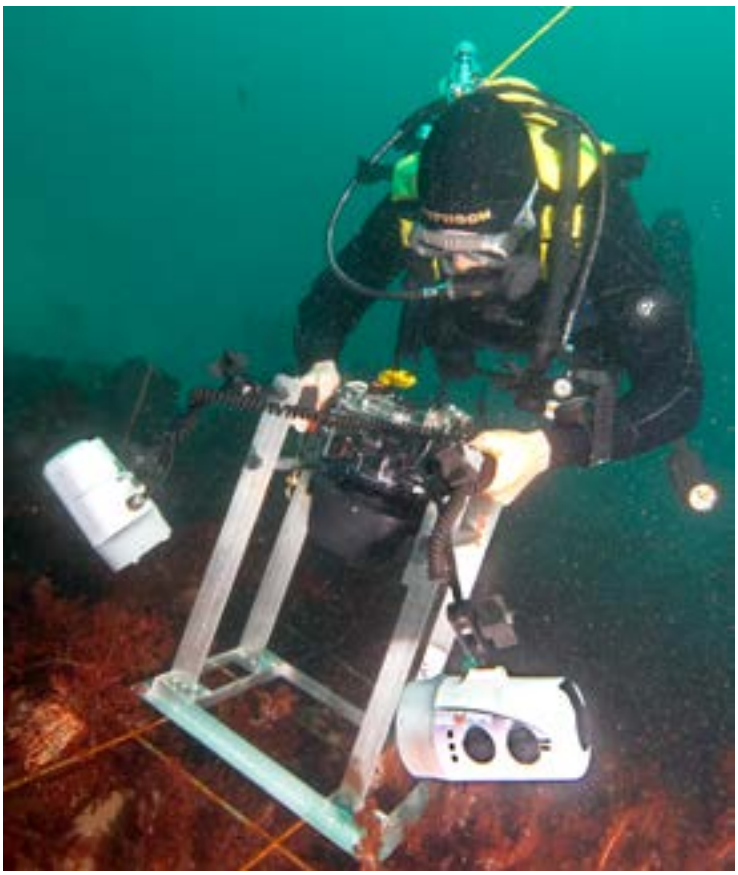

Venous gas emboli and decompression sickness

Concensus guidelines for ultrasound in diving research

Iatrogenic cerebral gas embolism

Scuba diving affects peak expiratory flow

Effect of blood-thinning drugs on middle ear barotrauma

Measuring Eustachian tube function

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PURPOSES OF THE SOCIETIES

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

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Diving and Hyperbaric Medicine **is published jointly by the South Pacific Underwater Medicine Society and the European Underwater and Baromedical Society (ISSN 1833-3516, ABN 29 299 823 713)**

The Editor's offering

In 2015, a workshop on ultrasound in diving research was held in Sweden, at which 27 participants from 12 countries hammered out guidelines to provide better standardisation of methods for both Doppler and echocardiography bubble counts. These guidelines and two papers from the meeting are published in this issue. The guidelines complement those developed in 2014 for the echocardiographic investigation of persistent foramen ovale in divers. Both guidelines are available on the journal website <www.dhmjournal.com>.

Publication of *Diving and Hyperbaric Medicine* (DHM)

There has been a lot of discussion recently about improving access to the diving and hyperbaric medicine literature generally and articles in this journal in particular. There is an increasing call for DHM to be available in a usable electronic form, though many members do not wish to lose the print copy. Since the renaming of the *SPUMS Journal* as DHM in 2006 and the amalgamation of our two societies' resources into the Journal in 2008, our publishing policy has been that DHM is a print journal. This policy is now under serious review by the ExComs. The Journal Governance Committee (JGC) and I have recommended that a fully electronic version of DHM be made available to subscribers from March 2018. This cannot be done immediately as there are many decisions to make in the process in a structured, professional manner. Members' thoughts on what they would like to see in an electronic journal are most welcome.

At its 2015 General Assembly, the EUBS voted to provide a pdf-only membership (at a reduced subscription) for full members who did not want a print copy and for Associate and Student members. As I mentioned in December, this decision was taken without consultation with EUBS's co-publishers, SPUMS. After protracted discussions between the Presidents and the Editor a compromise has been reached. The pdfs will continue to appear on the society websites, but clearly marked for personal use only. All members are reminded that articles have a one-year embargo, and distribution in the public domain before that time breaches copyright.

HBOEvidence

HBOEvidence <http://hboevidence.unsw.wikispaces.net/> is a database of 'Critical Appraisals' (CATs) of randomised, prospective trials in diving and hyperbaric medicine. It was created and is maintained by Professor Michael Bennett and his colleagues at the Prince of Wales Hospital Diving and Hyperbaric Medicine Unit, Sydney. The critical appraisals in this site have been written using CATmaker, developed by Douglas Badenoch at the Oxford Centre for Evidence-Based Medicine (CEBM). This software is highly recommended and may be ordered on the CEBM website < http://www.cebm.net/>. This site has a wealth of information and resources for anyone interested in evidence based medicine. The appraisals present critical information about each trial to enable a quick appreciation of the methodology and results. *They are an introduction to each trial and should not be viewed as a substitute for a careful appraisal of the whole article.* The structure and aims of the CAT approach are discussed more fully on the CEBM site and I recommend a visit there. Please note that the views expressed in the CATs are those of the individual authors concerned. DHM publishes CATs from *HBOevidence* from time to time.

Assistance from interested physicians in preparing critical appraisals is welcomed, indeed needed, as there is a considerable backlog (the latest posting is from 2014). There are resources available on the site on how to create a CAT, plus Mike will personally mentor anyone who wants to learn how to go about these things; please contact Mike Bennett at <m.bennett@unsw.edu.au>. For those simply wishing to use and search the site, there is no need to join as an actual member; there are no advantages, only drawbacks! Mike is very keen to hear from people who want to learn. We sincerely hope that at least a few of our 900-odd subscribers will show some enthusiasm for helping grow this potentially very valuable resource to support and legitimise our small specialty. Hyperbaric medicine is under threat in many countries; the most recent example being the ill-informed, misrepresentational report in Australia on which David Smart commented in his column in the last issue.[1]

Manuscript Manager

DHM has been using an electronic submission process called *Manuscript Manager* since the start of 2015. This has proved a boon for our office processes in managing individual papers through the submission and peer review processes. Unfortunately a large minority of authors still fail to follow the journal's *Instructions to Authors* or the submission process correctly. Since many authors do it perfectly, there is no excuse for such carelessness. We have been patient about this for the first year, but manuscripts not submitted in the correct format and using the proper processes will be rejected automatically, to be resubmitted properly.

Reference

1 Smart D. The Presidents' pages. *Diving and Hyperbaric Medicine*. 2015;45:220.

Michael Davis

Front page photo, taken by Dr Martin Sayer, is of a diver from the UK National Facility for Scientific Diving using a photoquadrat technique to generate quantitative information of hard-substrata communities. *Aquatic Conservation Marine and Freshwater Ecosystems*. 2011;21:676-89.

The Presidents' pages

David Smart, President SPUMS

We are entering a new era in journal production, but as with all change, high quality communication and step-wise implementation is required. The SPUMS Executive voted in October to move to a full electronic version of the Journal by first issue 2018, and we now look forward to working with EUBS to achieve this goal.

SPUMS and EUBS have in place a verbal agreement to jointly publish *Diving and Hyperbaric Medicine*. The venture is, however, lacking a formal governance structure which clearly defines the relationship, the responsibilities of each organisation, and how the governance of the Journal should occur. Recent events demonstrated the fragility of such a relationship. A clear memorandum of understanding (MOU) and publishing agreement between the societies regarding the journal is urgently required. Maintaining a database of subscribers is also essential for Journal reporting internationally and for its Impact Factor.

Both Societies have a passion for the field of diving and hyperbaric medicine. Processes of scientific and clinical governance are natural parts of our daily work. Administrative (including financial) governance not infrequently assumes lower priority. To ensure a healthy maturation of the SPUMS–EUBS relationship, *now* is the time to cement this administrative governance structure so we have a clear set of guidelines in achieving a common purpose – elevating *Diving and Hyperbaric Medicine* to the status of premier journal in the field. The events alluded to above highlight an urgent need for written governance. I will be working with my colleague, EUBS President Jacek Kot, to create this essential structure before I complete my term as SPUMS President. I am pleased to report that the Journal Governance Committee (members Mike Bennett and John Lippmann for SPUMS and Peter Müller and Joerg Schmutz for EUBS) has become fully operational.

It is with great pleasure that I announce the achievements of two SPUMS members:

Dr Michael Bennett has been appointed as a full professor with the University of New South Wales. Congratulations, Professor Mike – an appointment richly deserved. Your contributions to the science and teaching of diving and hyperbaric medicine continue to be enormous.

Dr Brian Spain was named in the Australia Day honours list as a Member (AM), in the general division for significant service to medicine in the discipline of anaesthesia as a clinician, to healthcare standards and to professional bodies. Congratulations Brian, and thank you so much for your ongoing contributions.

SPUMS 2016 in Fiji is shaping up to be another terrific event. The theme "*Diver resuscitation in and out of the water*" is so consistent with the fundamental philosophy of SPUMS. Janine Gregson has kicked things off with great energy, handing over the convener role to Douglas Falconer as she goes on Defence leave. Mike Bennett is scientific convener. Thank you team, the Annual Scientific Meeting is one of SPUMS' key reasons for existence, and the voluntary efforts of everyone to produce a world class event every year are greatly appreciated. Planning for 2017 is well underway.

I would like to advise SPUMS members that the InterContinental says they fortunately were not hit too badly by Cyclone Winston and that the SPUMS ASM will not be affected by this catastrophic event. A Cyclone Relief Fund has been set up to allow you to contribute towards rebuilding Fiji and getting their beautiful country back on track. To make a contribution towards this fund, go to: <www.generosity.com/community-fundraising/fiji-cyclone-winston-disaster-relief-fund>.

Key words
Medical society; general interest

The SPUMS website is at **<www.spums.org.au>**

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

Jacek Kot, President EUBS

Have you ever thought why you need a scientific society? Why pay a membership? If you are already a long-standing EUBS member, you already know the answer. So there is no need for you to bother reading this message. In such case, just pass it on to a colleague who is not yet a member of EUBS but is interested in the baromedical sciences.

From the very beginning of our professional medical or scientific career, we are obliged to join scientific societies that match our professional interests. At first, this mainly serves to stimulate our educational process, listening to lectures and attending seminars. For this purpose, it is usually sufficient to join a national society, if one exists for such an 'exotic' speciality as diving and hyperbaric medicine. This allows knowledge to be imparted in one's native language, and reflects the local standards for organisation, working practices, reporting systems, reimbursement procedures, etc. No wonder, then, this is sufficient for many physicians and researchers, and is mostly the case in the European Union, a confederation of 28 member states with 24 official languages!

However, we must recognize that, in the modern world, professionals need to be open to different viewpoints. Agreed local standards are useful in practice, but can restrict one's scientific perspective. Therefore, I am convinced that active exchange between different cultures, nations or systems is both refreshing and important. In practice, this means that one must seriously consider being a member of several scientific societies or organisations actively participating in one's chosen field.

That is the reason why, a few years ago, the EUBS started a programme of cooperation with various national diving and hyperbaric societies to attract their members to also join the EUBS at a discounted membership rate, if there was a group of people wanting to be members of both. Sometimes it works in reverse; for example, EUBS members can apply for Undersea and Hyperbaric Medical Society (UHMS) membership at a discounted rate. As a Society, we will continue our efforts in establishing international connections. Such approaches mean treating different scientific societies as partners or, at least, as complementing our endeavours, rather than as competitors.

For two examples in the near future, the EUBS will support the European Committee for Hyperbaric Medicine in the preparation of the updated list of clinical indications for hyperbaric oxygen treatment (HBOT) to be finalised during the Consensus Conference to be held in April 2016 in Lille, France. Secondly, the EUBS will contribute to the position document on the use of oxygen therapies, including HBOT, in wound healing which is to be concluded during the European Wound Management Association Conference in May 2017 in Amsterdam, The Netherlands. We are also developing plans for the Tri-Continental Conference of the EUBS, SPUMS and Southern African Undersea and Hyperbaric Medical Association to be organised cooperatively somewhere in the World in 2018.

What is equally important from the viewpoint of new EUBS members is that Full Membership provides access to the 'members only' pages of our website, which include access to the German Society for Diving and Underwater Medicine database. This database includes both peer-reviewed and other literature (including all the Proceedings of previous EUBS Annual Meetings) not presented anywhere else.

From the financial viewpoint, EUBS members also benefit from a reduced registration rate at our Annual Scientific Meeting, the forum for presentation of scientific research and for exchange of practical information and opinions between medical professionals, both formally and informally. In fact, the reduced registration rate covers nearly half of the membership fee so, if you plan to participate in the EUBS conference, it is always better to do this as an EUBS member, not as our guest. Register now for the next EUBS scientific meeting this September in Geneva, Switzerland, <www.EUBS2016.com>.

In the EUBS, we are in a fortunate position that our members also receive *Diving and Hyperbaric Medicine*, the Journal published jointly with the SPUMS. In my personal opinion, this is the best journal in the field, not only taking into account the original scientific papers and excellent reviews but also because of the additional texts, including technical reports, consensus statements, opinion pieces and the notices and news carefully selected by the Editors. Those additional texts cannot always be found through any of the existing literature indexes like PubMed, so they are available exclusively for members.

These arguments convince me every year to renew my EUBS membership. If you share any of them, join the Society and stay connected through our website <www.eubs.org>.

Key words
Medical society; general interest

The

website is at
<www.eubs.org>

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

Original articles

Venous gas emboli detected by two-dimensional echocardiography are an imperfect surrogate endpoint for decompression sickness

David J Doolette

Abstract

(Doolette DJ. Venous gas emboli detected by two-dimensional echocardiography are an imperfect surrogate endpoint for decompression sickness. *Diving and Hyperbaric Medicine*. 2016 March;46(1):4-10.)

Introduction: In studies of decompression procedures, ultrasonically detected venous gas emboli (VGE) are commonly used as a surrogate endpoint for decompression sickness (DCS). However, VGE have not been rigorously validated as a surrogate endpoint for DCS.

Methods: A data set for validation of VGE as a surrogate endpoint for DCS was retrospectively assembled comprising maximum VGE grades measured using two-dimensional echocardiography and DCS outcome following 868 laboratory man-dives. Dives were conducted according to only ten different experimental interventions such that the ten cumulative incidences of DCS (0–22%) provide relatively precise point estimates of the probability of DCS, *P(DCS)*. Logistic models relating the *P(DCS)* to VGE grade and intervention were fitted to these validation data. Assessment of the models was used to evaluate the Prentice criteria for validating a surrogate endpoint.

Results: The *P(DCS)*) increased with increasing VGE grade. However, the difference in the *P(DCS)* between interventions was larger than explained by differences in VGE grades. Therefore, VGE grades did not largely capture the intervention effect on the true endpoint (DCS) in accord with the Prentice definition of a surrogate endpoint.

Conclusions: VGE can be used for comparisons of decompression procedures in samples of subjects but must be interpreted cautiously. A significant difference in VGE grade probably indicates a difference in the *P(DCS)*. However, failure to find a significant difference in VGE grades does not necessarily indicate no difference in *P(DCS)*.

Key words

Venous gas emboli; echocardiography; decompression sickness; decompression; diving; research; statistics

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Introduction

A reduction in ambient pressure (decompression) can result in decompression sickness (DCS). The conventional approach to evaluating the efficacy of a new decompression procedure aimed at reducing the risk of DCS is to conduct a trial of the procedure with DCS as the endpoint. The incidence of DCS is necessarily kept low to protect subjects and so that the tested procedure is operationally relevant, and such trials require many man-dives. As with any clinical trial in which the true endpoint is rare, replacement of the true endpoint with a more frequently occurring surrogate endpoint has the potential to reduce the trial sample size.

DCS is thought to be caused by intracorporeal bubble formation.[1] Venous bubbles (venous gas emboli, VGE) can be detected by ultrasonic methods after dives, whether the dive results in DCS or not. The number of VGE is usually represented by an ordinal grade. The VGE grade in the mixed venous blood is presumed to be correlated with the risk of bubbles forming at, or impacting, sites where they will cause DCS.[1] The cumulative incidence of DCS does increase with increasing VGE grade in large compilations of data from decompression trials.[1,2] On the bases of these presumed and actual correlations, VGE grades are sometimes used as a surrogate endpoint for DCS in studies of decompression procedures.

Using inappropriate surrogate endpoints can lead to misleading results and prescription of improper interventions. Consequently, criteria have been developed for validating surrogate endpoints for clinical trials.[3,4] VGE have not been rigorously validated as a surrogate endpoint for DCS. This paper reviews the operational definition of a surrogate endpoint and examines whether VGE meet the criteria for a surrogate endpoint for DCS.

Methods

OPERATIONAL DEFINITION OF A SURROGATE ENDPOINT

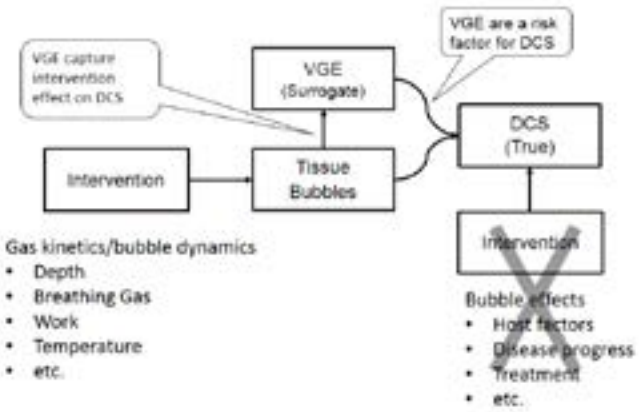
Prentice defined surrogate endpoints with respect to the effect of a particular intervention on the surrogate and true endpoints: for a specified intervention, the test of a null hypothesis on a surrogate endpoint is a valid test of the corresponding null hypothesis on the true endpoint.[3] This operational definition requires that a surrogate endpoint meet the following 'Prentice' criteria: 1) the surrogate endpoint captures the intervention effect on the true endpoint; and 2) the surrogate endpoint is prognostic for the true endpoint. These two Prentice criteria are expressed formally as:

$$P(DCS|VGE_i, X_j) = P(DCS|VGE_i) \quad [1]$$

and

$$P(DCS|VGE_i) \neq P(DCS) \quad [2]$$

Figure 1
Model of intervention, VGE as a surrogate endpoint, and DCS as the true endpoint; for interventions that act via tissue bubbles and result in a corresponding effect on both VGE and DCS, VGE may meet the operational definition for a surrogate for DCS; for interventions that do not act on tissue bubbles, illustrated with the large X, VGE do not meet the operational definition for a surrogate for DCS



respectively.[3] In the equations, *DCS* is the true endpoint which is binary (0,1); VGE_i is the surrogate endpoint which can be one of $i = 1...m$ ordinal VGE grades, and X_j is the j^{th} intervention.[3] This operational definition of a surrogate endpoint for the particular case of VGE as a surrogate endpoint for DCS is illustrated in Figure 1 which shows the intervention must have a corresponding effect on both VGE and DCS, and VGE must be prognostic for DCS.

Mechanistically, relevant interventions act via effects on tissue gas kinetics and bubble dynamics; VGE arise from tissue bubbles and centrally detected VGE numbers are presumed proportional to tissue bubble numbers; both VGE and tissue bubbles can cause manifestations of DCS. Interventions for which VGE would not meet the operational definition for a surrogate for DCS are interventions acting on processes 'downstream' of centrally-detected VGE, for instance on bubble-tissue complexes at DCS sites.

Equation [1] provides a link between the null hypothesis that the intervention has no effect on the true endpoint (DCS) and the null hypothesis that the intervention has no effect on the surrogate endpoint (VGE). Proof of this relationship has been given for failure rates and binary true endpoints.[3,4] This proof is reprised here for the specific case of a binary true endpoint (DCS) and an ordinal surrogate endpoint (VGE). Since the $i = 1...m$ *VGE* grades partition the sample space for *DCS*, a link between *DCS* and *VGE*, conditional on the intervention (X_j), can be obtained from the Law of Total Probability.

$$P(DCS|X_j) = \sum_{i=1}^{m} P(DCS|X_j, VGE_i)\, P(VGE_i|X_j) \quad [3]$$

The null hypotheses that the intervention has no effect on VGE is:

$$P(VGE_i|X_j) = P(VGE_i). \quad [4]$$

Substitution of Equations (1) and (4) into Equation (3) gives:

$$P(DCS|X_j) = \sum_{i=1}^{k} P(DCS|VGE_i)\, P(VGE_i) = P(DCS) \quad [5]$$

which is the null hypothesis that the intervention has no effect on DCS.

Equation [2] ensures that rejection of the null hypothesis on VGE (Eq. [4]) implies a rejection of the null hypothesis on DCS (Eq. [5]). Equations [1] and [2] provide guidelines for validating potential surrogate endpoints.

VALIDATION DATA

The data required to validate a surrogate endpoint are large numbers of observations with both the surrogate and true endpoints for any specified intervention. The Navy Experimental Diving Unit (NEDU) has measured VGE using two-dimensional (2-D) echocardiography as a secondary outcome measure following experimental dives in which DCS was used as the primary endpoint. Among these data are two decompression trials of single, air, decompression bounce dives that will be used as validation data.[5,6]

VGE were measured and graded in the same manner in two decompression trials.[5,6] With subjects in the left decubital position, the heart chambers were imaged (apical long-axis four-chamber view) using a 2-D echocardiograph (Siemens Medical Solutions® Acuson Cypress Portable Colorflow Ultrasound System). VGE in the right heart chambers were graded according to the ordinal scale defined in Table 1.

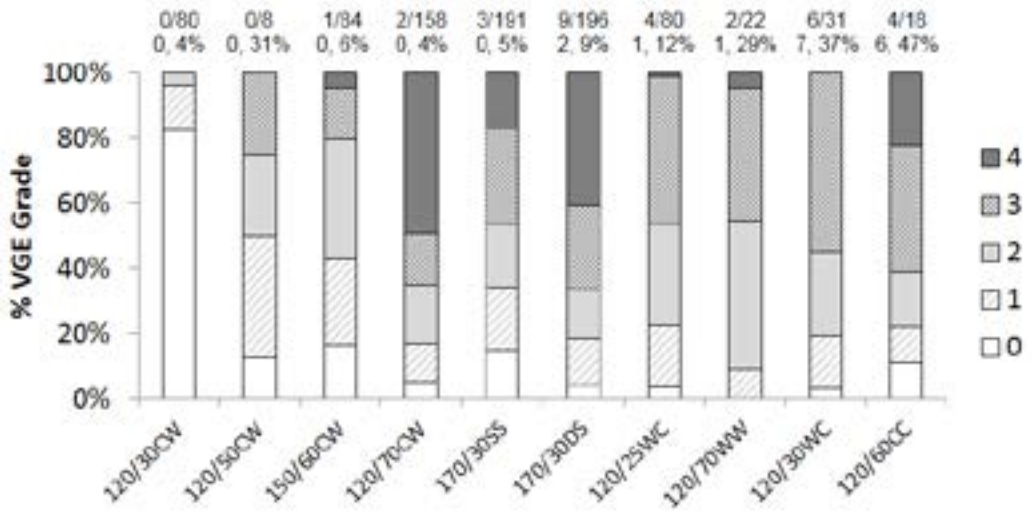
At each examination, VGE were measured five times: after the subject had been at rest for approximately one minute and then after forceful limb flexions around each elbow and knee. VGE were examined at about 30 minutes and two hours post dive in both trials. VGE were additionally examined at four hours post dive in the trial of diver thermal status (profiles with 'C' and 'W' labels in Figure 2). Only the maximum VGE grade observed at any time (rest or limb flexion, any examination) were used in this report, and will be referred to as 'VGE grade' without qualification. Maximum observed VGE grades have previously been shown to have the strongest relationship with cumulative incidence of DCS.[2] DCS was diagnosed by the duty Diving Medical Officer.

Table 1
NEDU 2-D Echocardiography VGE scale

Grade	Description
0	No bubble seen
1	Rare (< 1 per 5 heart beats), individual bubble seen
2	Several discrete bubbles visible in the same image
3	Multiple bubbles in most cardiac cycles, but not obscuring image
4	Bubbles in all cardiac cycles, bubbles dominate image and may blur chamber outlines

Figure 2

Summary of VGE grades and DCS for individual dive profiles (interventions); the stacked bars illustrate the percentage of man-dives in each dive profile that resulted in each VGE grade; the labels above the bars give the number of DCS cases / number of man dives and the 95% binomial confidence limits of the resulting estimate of *P(DCS)* as per cent; the labels along the horizontal axis identify the individual dive profiles in the original technical reports (see text for more details)



Individual VGE grades and descriptions of each DCS case are given in the original reports.[5,6]

Table 2 summarizes these data for single air decompression bounce dives.[5,6] These data are a unique resource for validating VGE as a surrogate endpoint for DCS because enough dives have been conducted on most dive profiles that the observed cumulative incidences of DCS provide credible point estimates of the probability of DCS, *P(DCS)*, for those dive profiles (Figure 2). Each distinct dive profile can be considered a distinct intervention (X) that modifies gas kinetics or bubble dynamics, as illustrated in Figure 1. All dive profiles were air decompression dives. The labels along the horizontal axis in Figure 2 identify the individual dive profiles in the original technical reports. For each dive profile the first part of the label gives the bottom depth in feet' sea water / bottom time in minutes. The two dives to 170/30 had 174 minutes of decompression stops in a shallow stops (SS) or deep stops (DS) distribution.[6]

The remaining dive profiles are all from a trial in which diver thermal status was manipulated independently for the bottom time and decompression.[5] For instance divers might be cold (C) on the bottom and warm (W) during decompression, indicated by 'CW'. All dives to 120 feet' sea water had 87 minutes of decompression stops. The dive to 150/60 had 110 minutes of decompression stops. These data exclude six man-dives for which VGE measurements were not available. Five of these were man-dives that resulted in onset of symptoms of DCS before VGE measurements were made. Two of these missing DCS cases are from 170/30DS, two from 120/70WW, and one from 120/30WC, resulting in cumulative incidences of DCS of 5.6%, 17%, and 22%, respectively. VGE data were lost for one man-dive which did not result in DCS from dive profile 170/30SS; this had little effect on the cumulative incidence of DCS.

Table 2

NEDU 2-D echocardiography VGE data for single bounce dives; DCS - decompression sickness; CL - confidence limits

Grade	# Dives	# DCS	% DCS	95% CL
0	134	0	0	(0, 2)
1	141	2	1	(0, 5)
2	178	4	2	(1, 6)
3	215	15	7	(4, 11)
4	200	10	5	(2, 9)
Total	868	31	4	(2, 5)

Validation

The two Prentice criteria, Equations [1] and [2], are assessed by first fitting the following nested logistic regressions models to these validation data.[4]

$$\ln\left(\frac{P(DCS)}{1-P(DCS)}\right) = \beta_0 + \beta_1 VGE_i + \beta_2 X_j + \beta_3 VGE_i \times X_j \quad [6]$$

$$\ln\left(\frac{P(DCS)}{1-P(DCS)}\right) = \beta_0 + \beta_1 VGE_i + \beta_2 X_j \quad [7]$$

$$\ln\left(\frac{P(DCS)}{1-P(DCS)}\right) = \beta_0 + \beta_1 VGE_i \quad [8]$$

If VGE contributes significantly to the fit of these models to the validation data, Eq. [2] is satisfied. If the intervention factor X or the interaction of X with VGE contribute significantly to the fit of models [6] or [7] to the validation data, Eq. [1] is not satisfied. Failure to find a significant contribution of X does not prove that Eq. [1], which is a

null hypothesis, is satisfied. Equation [1] implies that the surrogate fully captures the intervention effect on the true endpoint. Realistically, a surrogate endpoint will capture a proportion of the intervention effect on the true endpoint. This proportion can be assessed by fitting the model [9], which has the intervention as the only independent variable,

$$\ln\left(\frac{P(DCS)}{1-P(DCS)}\right) = \alpha_0 + \alpha_2 X_j \qquad [9]$$

and model [7], which includes the intervention and the surrogate, to the same validation data. The proportion of the intervention effect explained by including the surrogate endpoint in the model is assessed as the proportional decrease in the estimated coefficient for the intervention, $(\alpha_2 - ß_2)/\alpha_2$, where α_2 is the unadjusted coefficient for the intervention in model [9] and β_2 is the coefficient for the intervention factor adjusted for the effect of VGE in model [7].[4]

The coefficient vectors ($\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$) of the logistic models [6], [7], [8], and [9], as well as a null model in which *logit(DCS)* equals a constant (β_0), were estimated by fit to the data illustrated in Figure 2. The X_j were dummy coded and VGE grades were treated as interval data. Similar results, which are not presented, were obtained if VGE grades were grouped into zero, low (grades 1 and 2) and high (3 and 4) grades, or if the five VGE grades were linearized to values of 0, 0.1, 0.4, 2, and 10.[1] The contributions of the variables *VGE* and *X* to the fit were assessed by comparing the log-likelihood of nested models. The log-likelihood of the full model (LL_f) with p_f adjustable coefficients and the log-likelihood of the reduced model (LL_r) with p_r adjustable coefficients were compared by using the likelihood ratio test with goodness-of-fit statistic $G = -2(LL_r, -LL_f)$. If $P(\chi^2 > G) \leq 0.05$, $df = p_f - p_r$, the extra factors in the full model were considered to contribute significantly to the fit. Models were fitted to different subsets of the data.

Results

The logistic models were fitted to several subsets of the data, starting first with the eight dive profiles with non-zero cumulative incidence of DCS. All data from the two dive profiles with zero cumulative incidence of DCS were excluded to avoid the numerical problems that arise with fitting to data with covariate patterns (e.g., dive profiles) that have zero or 100% occurrence of a binary outcome (e.g., DCS). The likelihood ratio tests are shown in Table 3. The interaction of *X* with *VGE* did not contribute significantly to the fit of this model to this data subset or any subsequent data subsets investigated, as indicated by no significant difference between model [6] with the interaction term and model [7] without the term. The intervention factor *X* did contribute significantly to the model fit to this data subset as indicated by the significantly improved fit of model [7] with this factor over model [8] without this factor. This is evidence that Eq. [1] is not satisfied for this data subset. VGE grades contributed significantly to explaining the *P(DCS)* as indicated by the significant improvement of model [8] over the null model; therefore, Eq. [2] is satisfied for this data subset.

Table 3
Likelihood ratio tests of logistic models fit to data subsets; a,b; b,c; c,d – models compared

Model	LL		df	$P(\chi^2>G)$	
X_j: all dive profiles with DCS >0					
[6]	-105	a	16	0.1877	a,b
[7]	-110	b	9	< 0.0001	b,c
[8]	-126	c	2	0.0040	c,d
Null	-130	d	1		
X_j: 150/60CW, 120/70CW,170/30SS, 170/30DS, 120/25WC,120/70WW					
[6]	-82	a	12	0.0869	a,b
[7]	-86	b	7	0.0813	b,c
[8]	-91	c	2	0.0047	c,d
Null	-95	d	1		
X_j: LR: (150/60CW, 120/70CW,170/30SS); HR: (170/30DS, 120/25WC,120/70WW)					
[6]	-88	a	4	0.4540	a,b
[7]	-88	b	3	0.0055	b,c
[8]	-91	c	2	0.0007	c,d
Null	-95	d	1		
X_j: 170/30SS, 170/30DS					
[6]	-50	a	4	0.2618	a,b
[7]	-51	b	3	0.1947	b,c
[8]	-52	c	2	0.0572	c,d
Null	-53	d	1		

The fit of model [7] to the eight dive profiles with non-zero cumulative incidence of DCS produced significant Wald statistics, (not shown), for the X_j corresponding to 120/30WC and 120/60CC, the two dive profiles with the highest observed cumulative incidences of DCS. This finding indicates that the VGE grade alone does not explain the cumulative incidence of DCS on these dive profiles. The reason for this is apparent by examining the fitted *P(DCS)* from model [8] in which VGE are the only independent variable. These fitted values of the *P(DCS)* range from 1.1% for VGE grade 0 to 6.8% for VGE grade 4. Thus, the highest possible cumulative incidence of DCS estimated by model [8] is 6.8%, for a dive profile that results in grade 4 VGE after every dive. This latter value is a ceiling imposed by the data, and is obvious from inspection of Table 2 in which 7% is the highest cumulative incidence of DCS associated with any VGE grade. Dive profiles 120/30WC and 120/60CC have observed cumulative incidence of DCS much higher than can be predicted by any model based on VGE grade alone.

The logistic models were next fitted to a data subset that omitted dive profiles 120/30WC and 120/60CC, as well as the two dive profiles with zero cumulative incidence of DCS. In this case, the intervention factor (*X*) did not contribute

Table 4
Model coefficient estimates and proportion of intervention effect explained for two data subsets

Model	Variable	Coeff.	Estimate	S.E.	$(\alpha_2 - \beta_2)\ \alpha_2$
[7]	Intercept	β_0	-5.7703	0.8289	
	VGE	β_1	0.5457	0.2292	
	X: HR	β_2	1.2359	0.4912	
[9]	Intercept	α_0	-4.2650	0.4111	
	X: HR	α_2	1.3276	0.4891	0.0690
[7]	Intercept	β_0	-5.1030	0.9734	
	VGE	β_1	0.3940	0.2846	
	X: 170/30DS	β_2	0.8551	0.6941	
[9]	Intercept	α_0	-4.1431	0.5819	
	X: 170/30DS	α_2	1.1093	0.6746	0.2291

significantly to the model fit to this data subset (Table 3). Therefore, there is insufficient evidence to reject Eq. [1] for this data subset. However, because the *P*-value of the likelihood ratio test was only 0.0813, it was investigated if the lack of significance was due to the number of degrees of freedom associated with the six levels of the intervention factor. The six X_j were recoded into two levels, LR and HR, indicating all dive profiles with cumulative incidence of DCS less than 2% and greater than 2%, respectively. The cumulative incidences of DCS in the resulting LR and HR groups were 1.4% and 5.0%, respectively. The recoded intervention factor (*X*) did contribute significantly to the model fit to these data, indicating Eq. [1] is not satisfied for this recoded data subset.

Finally, the logistic models were fitted to a data subset comprising only dive profiles 170/30SS and 170/30DS. These dive profiles have the most precise estimated *P(DCS)* and the same ultrasound operator graded the VGE on all the dives. The intervention factor did not contribute significantly to the fit of model [7] to this data subset; however, model [8] just failed to reach significance compared to the null model.

The proportion of the intervention effect on the *P(DCS)* explained by VGE grade was assessed in the two data subsets in which the factor *X* has only two levels. Table 4 shows the estimates of the coefficients for models [7] and [9] and the proportion of the intervention effect explained by VGE. These proportions were quite small even for the data set for which there was insufficient evidence to reject the first Prentice criterion. The reference level of the intervention factor *X* was the group with the lower cumulative incidence of DCS, so the estimated coefficient is the effect of being in the group with higher cumulative incidence of DCS. In model [7], the estimated coefficients for *X*, adjusted for VGE, are positive for both data subsets, indicating a greater increase in *P(DCS)* than can be explained by the increase in VGE grade.

Discussion

The 'gold standard' data showing increasing cumulative incidence of DCS with increasing VGE grades following diving is the compilation of data arising from the development of the DCIEM decompression tables.[1,2] Those VGE data are Kisman-Masurel grades determined from the bubble noises in ultrasonic Doppler flow transducer signals. The present NEDU data are the first to show a similar association between cumulative incidence of DCS and VGE grades measured using 2-D echocardiography following diving. The present NEDU data are the only published data suitable for assessing the first Prentice criterion, and therefore validating VGE as a surrogate for DCS. In most of the subsets of the data examined the first Prentice criterion was rejected because differences in VGE grades only explained a small proportion of the differences in *P(DCS)* between dive profiles. This has implications for the interpretation of experimental findings arising from using VGE as a surrogate endpoint for DCS.

Inspection of Table 2 shows that detecting no VGE is strongly negatively predictive of DCS, but there is no VGE grade that has both good sensitivity and specificity for DCS, and it is well known that VGE are not a surrogate for DCS in the individual diver.[5,7] Nevertheless, the increasing cumulative incidence of DCS with increasing VGE grades, consistent with the second Prentice criterion, can allow comparison of decompression procedures in sufficiently large samples of divers.[8]

If a significant difference in the distribution of VGE grades is found between decompression procedures, this likely indicates a difference in the *P(DCS)* between the procedures. This is particularly true if there is a difference in the distribution of VGE grades among zero, low (grades 1 and 2) and high (3 and 4) grades, since there are substantive differences in cumulative incidences of DCS between these groups of VGE grades.[8] However, the difference in the *P(DCS)* may be greater than indicated by differences in VGE grades. Therefore, difference in VGE grades can be used to rank decompression procedures in order of relative *P(DCS)* but not to reliably quantify the difference in *P(DCS)*. The range of *P(DCS)* that can be estimated from VGE grades is the range of cumulative incidences of DCS associated with those grades, as illustrated here and described previously.[9] Therefore all *P(DCS)* estimated from the present VGE data must be compressed into the range 0–7% shown in Table 2.

For several reasons, failure to detected difference in VGE grades between decompression procedures is insufficient evidence to retain the null hypothesis of no difference in *P(DCS)*. First, VGE data cannot be used to distinguish differences between procedures which have *P(DCS)* outside the range of cumulative incidence of DCS associated with those grades. The maximum cumulative incidence of DCS associated with any 2-D echocardiographic VGE grade in the present data is 7%, and the maximum cumulative incidence

of DCS associated with any Doppler-detected VGE grade in the DCIEM air diving data set is about 10%.[1,2] Therefore it is not possible to distinguish between decompression procedures with actual *P(DCS)* above about 10%. This ceiling may be of little consequence for normal exposure diving; however *P(DCS)* at or above 7–10% is associated with higher risk, but operationally relevant, military, exceptional-exposure diving or DISSUB procedures.[10,11]

Second, it has been shown that for decompression procedures with *P(DCS)* in the range that is potentially distinguishable by VGE, 80% power to detect one-grade differences in VGE requires a paired comparison of about 50 subjects.[8] Smaller sample sizes may fail to detect a one-grade differences in VGE grades that can indicate a difference in *P(DCS)*. Finally, because VGE grades only capture a small proportion of the intervention effect, even between decompression procedures with *P(DCS)* less than 7–10%, an operationally relevant difference in *P(DCS)* may exist between procedures that does not manifest as a difference in VGE grades.

The implications of the present analysis are relevant to the other commonly used methods to detect and grade VGE because 1) there is good agreement between VGE scores measured using 2-D echocardiography and Doppler[12], and 2) the present analysis is based on the NEDU VGE scale that is broadly similar to other VGE scales. With respect to this latter point, the five NEDU VGE grades (0–4) were designed to be similar to the five grades in the Spencer and Kisman-Masurel Doppler scales.[1,5,11] The NEDU VGE grades differ slightly from those of the more widely used Eftedal-Brubakk scale for grading VGE in 2-D echocardiography images.[1,12] The principal difference is that the NEDU grade 4 covers what is described as grades 4b, 4c, and 5 in the recently proposed expanded version of the Eftedal-Brubakk scale.[13]

A strength of the Eftedal-Brubakk scale is that the grades are unambiguously defined, which facilitates inter-rater reliability. However, it is worth noting that a Medline search for studies that graded VGE in 2-D echocardiographic images after diving in humans found 13 papers reporting 12 dive trials identifying a total of 384 man-dives. All these trials use the original or expanded Eftedal-Brubakk scale. Thus, fewer man-dives have been evaluated using alternative 2-D echocardiography VGE scales than the number of man-dives reported here and evaluated using the NEDU VGE scale.

The present findings should be relatively broadly applicable to studies using VGE as an endpoint, but caution should be used when extrapolating findings from one set of experimental conditions to another, First, the present dives had higher *P(DCS)* than studies that use VGE to evaluate decompression procedures intended not to result in DCS. The present data are from experiments which used DCS as the primary endpoint and the tested decompression procedures were designed to have a measurable DCS incidence. The procedures were designed with predicted *P(DCS)* approaching the maximum for normal exposure military diving, and the actual observed incidences occasionally exceeded those predicted. However, the present data show a similar distribution of cumulative incidence of DCS among VGE grades as the larger DCIEM data set for air decompression dives, a data set which has an overall cumulative incidence of DCS half that of the present data.[1,2] This suggests that the present analysis is relevant to evaluation of decompression procedures with lower *P(DCS)* than are in the present data set.

Second, the present data are exclusively from wet working dives, but show a similar distribution of cumulative incidence of DCS among VGE grades as the DCIEM data set which includes both wet, working, and dry, resting dives.[1,2] This suggests the present findings are applicable to a range of diving conditions.

Finally, many of the decompression procedures in the present data involved manipulation of diver thermal status.[5] These manipulations presumably modified the *P*(*DCS*) by modifying tissue blood flow and, consequently, tissue gas kinetics and bubble dynamics. Therefore, manipulation of thermal status is a suitable intervention for using VGE as a surrogate endpoint, in accord with the model illustrated in Figure 1. The present data should be relevant to interventions that manipulate gas kinetics and bubble dynamics by other methods.

The present data have some limitations. First, these data were assembled from dive trials not designed for the present analysis, and any such retrospective analysis must acknowledge the possibility of confounding factors. Second, five dives which resulted in DCS (14% of the total DCS cases) were excluded because of the onset of DCS symptoms before VGE measurements could be made. This may have influenced the distribution of DCS with VGE grades in Table 2. Such data loss is inevitable in decompression trials.

Finally, although VGE measurements were made throughout the period during which the maximum VGE grade typically occurs following long bounce dives, the measurements were made relatively infrequently following each dive, and it is possible that maximum VGE grade was not always captured.[14] It is uncertain that this influenced the overall distribution of DCS with VGE grades and interventions, since, presumably, the likelihood of missing the maximum VGE grade was no different for any intervention or outcome in this large data set.

Conclusions

VGE grades are in imperfect surrogate endpoint for DCS and data using VGE must be interpreted cautiously. VGE cannot be used to diagnose DCS but can be used for comparisons of decompression procedures in samples of subjects. Whereas a significant difference in VGE grade probably indicates a difference in the *P(DCS)*, failure to find a significant

difference in VGE grades does not necessarily indicate no difference in *P(DCS)*.

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The effect of scuba diving on airflow obstruction in divers with asthma

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Abstract

Lawrence CHD, Chen IYD. The effect of scuba diving on airflow obstruction in divers with asthma. *Diving and Hyperbaric Medicine*. 2016 March;46(1):11-14.)

Background: People with asthma are an under-represented group amongst scuba divers. Many may avoid or are advised against diving due to the potential risks, including bronchoconstriction, pulmonary barotrauma and arterial gas embolism. The aim of this study was to establish whether divers with asthma were more likely to experience reversible airways obstruction following typical scuba diving than divers without asthma.

Method: All divers with a history of asthma attending *Operation Wallacea* in Honduras were identified and peak expiratory flow rates (PEF) were measured pre and immediately post dive. All dives were boat dives in tropical sea water. Scuba dives were defined as those lasting between 40 and 55 minutes to a depth of between 10 and 18 metres. Of the 356 divers attending, 22 were identified as having asthma, of whom 19 were suitable for testing. They were classified by treatment regimen: five on no treatment, 11 on salbutamol only and three on regular preventative treatment. Twenty-four divers without a history of asthma acted as a control group.

Results: Open-water scuba diving caused a small decrease in PEF in all populations (median decrease 4.4%, $P < 0.001$). Percentage decrease in PEF was significantly more in divers with asthma on regular preventative medication than in the control group (mean 9.3%, median decrease 6% vs. mean 3.1%, median 4.3%; $P = 0.039$).

Conclusion: These findings support the view that asthmatics are more susceptible to airway changes following scuba diving. Differences to previous studies are likely due to environmental conditions, including dive depth.

Key words

Lung function; respiratory; diving research

Introduction

The prevalence of asthma amongst recreational scuba divers is around 6%, compared to a UK population prevalence of 8.4% and prevalence among UK 15 to 44-year-olds of 23%.[1–3] This lower prevalence suggests that many asthmatics avoid or are advised against scuba diving, while for some divers their asthma does not prevent them from diving.

Asthma was previously considered a contraindication to scuba diving owing to the danger of bronchoconstriction,[4,5] although this view has since progressed such that asthmatics with little airways hyper-reactivity are cleared for diving.[6,7] The British Thoracic Society's and other's guidelines now recommend that asthmatic individuals who are well controlled with normal pulmonary function tests (e.g., peak expiratory flow rate, PEF, within 10% of predicted) may dive if they have a negative exercise test.[7–9] Those with wheeze precipitated by exercise, cold or emotion are advised against diving.[10] The evidence to guide this view is largely based on case studies rather than bronchial provocation testing.[7]

There have been concerns over the potential for bronchoconstriction during diving to result in gas trapping and an increased risk of pulmonary barotrauma, as well as asthma being implicated as a risk factor for arterial gas embolism.[4,7] The various triggers to airways obstruction unique to diving include cold water, dry compressed air, salt water inhalation, exercise and anxiety.

PEF in healthy divers has been shown to decrease following scuba,[10] but whether scuba provokes increased airflow obstruction in an asthmatic population has not been established, as current evidence relies on swimming pool dives not open-water diving.[11,12] The aim of this study was to test the null hypothesis that people with asthma are no more likely to develop airway obstruction following scuba diving in typical recreational diving conditions than those without asthma.

Methods

SUBJECTS

All non-smoking recreational scuba divers joining *Operation Wallacea*[13] in Honduras, who had a history of asthma and had been passed fit to dive by their personal medical practitioner prior to arrival, were consented. Divers were identified from their submitted medical records and by interview on arrival at the diving site; smokers were excluded. Minimum requirements were that all participants had confirmed and had signed with their ordinary medical practitioner the Professional Association of Dive Instructors (PADI) Medical Statement, which requires normal spirometry pre- and post-exercise.[14] Informed research consent was obtained from each individual diver and ethical approval was granted by the supervising research organisation *Operation Wallacea*. Participants completed a short questionnaire regarding relevant health history, including current medications and personal demographic data. This was repeated with age- and

Table 1
Change in peak expiratory flow (PEF) after a scuba air dive between divers with or without asthma; A1 – no medication; A2 – short-acting beta agonists only; A3 – regular preventative medication

Groups	Divers (*n*)	Total dives (*n*)	Mean / median decrease PEF (%)	*P*-value
Non-asthmatic controls	23	51	3.1 / 4.3	0.004
Asthma				
A1	5	17	2.3 / 0.0	0.108
A2	11	44	3.6 / 5.1	< 0.001
A3	3	13	9.3 / 6.0	0.002
Total	42	125	3.8 / 4.4	< 0.001

sex-matched controls with no history of respiratory illness attending the same dives as the divers with asthma.

STUDY DIVE PROFILES

All dives were boat dives in tropical sea water, lasting for 40–55 min to a depth of 10–18 metres' sea water (msw). Water temperature was measured with each dive. Night dives and deep dives (over 18 msw) were excluded to avoid complicating environmental influences. In all cases, compressed, purified air was used. Dives took place during the morning (0900 h) and afternoon (1400 h).

PEAK EXPIRATORY FLOW

All participants received training in the correct use of a peak flow meter prior to providing measurements. Readings were all taken sitting in the upright position while in a wetsuit or swimming attire, not while wearing scuba equipment. PEF measurements were taken following the European Respiratory Society protocol[15] using a MediHealth Adult Peak Flow Meter with standard EU scale at 0–5 minutes pre dive and 0–5 min post dive, with the best-of-three PEF being chosen for analysis. The mean number of readings per person in the divers with asthma was 3.9 (median 5) and in the control group 2.2 (median 2).

The percentage change in PEF after each dive compared to the pre-dive value was then calculated. This process was repeated over multiple separate dives up to a maximum of five sets of measurements in any one individual. Results were grouped according to asthma severity as determined by treatment level as follows:

- Control group (C): divers with no history of asthma;
- Asthma group 1 (A1): no treatment, history of asthma;
- Asthma group 2 (A2): short-acting beta agonist only; history of asthma;
- Asthma group 3 (A3): regular preventative treatment, inhaled corticosteroid and long-acting beta agonists.

DATA ANALYSIS

Data were entered into SPSS® version 17 for analysis using descriptive statistics. Data significantly deviated from normal distribution (Kolmogorov-Smirnov and the Shapiro-Wilk tests). Consequently we compared the control group with each of the three asthma groups using a non-parametric one-way ANOVA (Kruskal Wallis). Change in PEF in each group was compared against no change using the Wilcoxon signed ranks test.

Results

DEMOGRAPHICS AND EXCLUSIONS

Of the 356 divers attending, 22 were identified as having asthma. Two of these 22 divers were considered unfit to dive due to co-morbidity and recent asthma exacerbation and another declined to take part in the study, leaving 19 divers (six female and 13 male) with a total number of changes in PEF readings (TR) of 73; five (TR 16) in group A1, 11 (TR 43) in group A2 and three (TR 14) in group A3. No divers were using pre-dive salbutamol. One of the 24 control group divers was excluded owing to a co-morbidity, leaving 23 (six female and 17 male; TR 51). Diving experience varied from five to over 400 dives in the control group and five to 100 dives in the asthmatic group.

The age range of the sample group was from 16 to 27 years (median 20 years). Complications due to rough seas and seasickness affected divers' ability to perform post-dive PEF in certain circumstances and this limited total data collection. Water temperature was 28–30ºC for all dives. No diver reported symptomatic airflow obstruction during or post dive.

PEAK EXPIRATORY FLOW

Pre-dive PEF was significantly lower in groups A1 (P = 0.003) and A3 (P = 0.022) compared with group C (Figure 1). The percentage decrease in PEF (and median values for each group) for all recorded dives (total 125) are plotted in Figure 2. Comparison between Group C and the combined asthma groups showed no significant difference. There was a significant difference in the decrease in PEF in group C compared to the A3 group (4.3% vs. 6%; P = 0.039; Figure 2) but not to groups A1 and A2 (P = 0.398 and P = 0.82, respectively). The mean and median decreases in PEF from pre dive in the four groups are shown in Table 1; except for Group A1 these decreases were statistically significant.

Figure 1
Pre-dive peak expiratory flow (PEF) measurements in all groups with medians; C – control group; A1 – no medication; A2 – short-acting beta agonists only; A3 – regular preventative medication

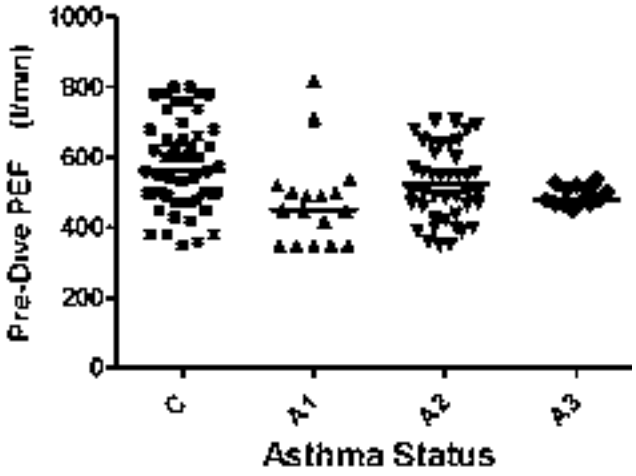
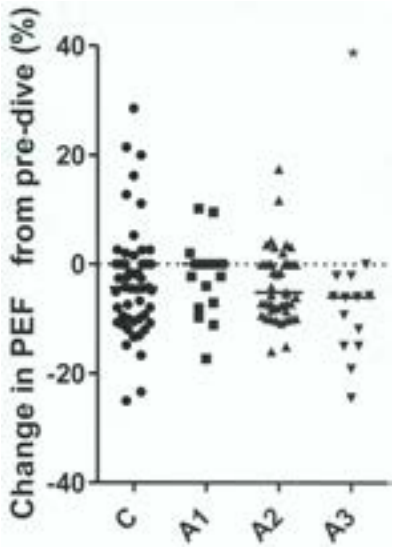


Figure 2
Percentage change in peak expiratory flow (PEF) following a scuba dive on each recorded occasion, sorted by asthma type, with medians; C – control group; A1 – no medication; A2 – short-acting beta agonists only; A3 – regular preventative medication; * $P < 0.05$, non-asthmatic controls vs. Group A3 asthmatics, horizontal lines represent medians



Discussion

In a swimming pool study to a depth of five metres looking at the effect of scuba on divers with and without asthma, no significant changes in PEF were seen pre and post dive.[11] In contrast, our study shows that tropical, open-water scuba diving is associated with a post-dive increase in airflow limitation as measured by PEF in divers both with and without asthma. This is likely to represent increased airflow obstruction, as recorded in previous studies.[16] Based on current medication usage, those divers at greater risk of increased post-dive airflow obstruction were those taking regular preventative medication (inhaled corticosteroids +/- long-acting beta agonists). This is particularly relevant because we investigated typical recreational scuba dives to a depth of 18 msw, to which a PADI Open Water certified diver, the most commonly attained registered recreational scuba diving level, may reach.[17]

This decrease may be a consequence of increased depth and the increased hydrostatic pressure leading to an increase in thoracic blood flow during diving[18] and to decreased lung elasticity. A depth-dependent response would be in keeping with findings from a study of healthy divers, comparing dives of 10- and 50-metre depths, in which a significantly reduced forced expiratory volume in one sec (FEV_1) was found post 50-metre dives but not post 10-metre dives.[7]

In asthma, this is relevant due to the increased bronchial mucosal blood flow present in this condition.[19] This, in combination with the effect of increased hydrostatic pressure, may compound the decreased pulmonary elasticity and increase the stress on the peribronchial alveolar tissue,[20] thus increasing the risk of alveolar damage and potentially provoking bronchoconstriction.

We had the advantage of being able to collect data in tropical diving conditions where temperature and diving technique were stable. However, this does not allow us to comment on the cause of the identified airflow obstruction. We suspect that certain features specific to diving such as breathing of dry compressed air, salt water, dive depth and duration and exposure to other toxins such as boat fumes may be causally linked to bronchial hyper-responsiveness.

Diving, compared to other more vigorous exercise, is thought to be low risk for exercise-induced asthma;[21] however, the cool, dry air used in scuba is in keeping with the identified triggers for bronchospasm in asthma.[22] A fall in FEV_1 was seen in subjects with exercise-induced bronchoconstriction after breathing compressed air via a regulator, which supports the notion that the cool, dry air was the key trigger for this. However, these tests took place after a treadmill test, which the authors acknowledged represented a higher exercise intensity than that of a typical scuba dive.[23]

There are several limitations to our study, especially the small number of divers with a history of asthma joining *Operation Wallacea*.[1] Also, the highest risk group for airflow obstruction was limited to only three out of the 19 divers studied; actively recruiting more divers to this group for further studies may present an ethical dilemma. Use of a peak flow meter has the advantage of cost and portability over a spirometer; however, its use can be unreliable in people with poor technique.[24] Nevertheless, our subjects were instructed in correct technique. In addition, we did not control for the diurnal variation in PEF which may confound results as dives

took place in both the morning and afternoon.[25] Height data were not collected, so we were unable to calculate exact predicted PEF values.

We hope that these data will provide practitioners assessing and risk stratifying people with asthma prior to diving with a modest evidence basis on which to advise them of their relative risk of airflow obstruction compared to the normal population. We aim to repeat this study with portable spirometry to allow more detailed interpretation. The effect of depth on airway obstruction needs further investigation. Additionally, previous studies have demonstrated a decrease in forced vital capacity (FVC) following diving,[7,16] but PEF is probably independent of FVC in this population, and these changes in PEF, although small, do represent a separate effect on airways.

Conclusions

Open-water scuba diving causes a small decrease in PEF in divers with and without asthma. This appears to be greater in divers with asthma who are taking regular preventative medication. However, our asthma sub-groups were small. Differences to previous studies are likely due to environmental conditions, including dive depth. These findings support the view that people with asthma are more susceptible to airway changes following scuba diving.

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Iatrogenic cerebral gas embolism: analysis of the presentation, management and outcomes of patients referred to The Alfred Hospital Hyperbaric Unit

Harriet Beevor and Geoff Frawley

Abstract

(Beevor H, Frawley G. Iatrogenic cerebral gas embolism: analysis of the presentation, management and outcomes of patients referred to the Alfred Hospital Hyperbaric Unit. *Diving and Hyperbaric Medicine*. 2016 March; 46(1):15-21.)

Introduction: The aim of this study was to review patients with iatrogenic cerebral gas embolism (CGE) referred to The Alfred Hospital hyperbaric unit to determine whether hyperbaric oxygen treatment (HBOT) reduced morbidity and mortality.

Methods: This is a retrospective cohort study with a contemporaneous comparison group of patients referred between January 1998 and December 2014. The primary end point was good neurological outcome at the time of discharge from hospital or rehabilitation facility as assessed by the Glasgow Outcome Scale (GOS-E).

Results: Thirty-six patients were treated with HBOT for CGE and nine patients were diagnosed with CGE but did not receive HBOT. Thirty-two patients developed CGE from an arterial source and 13 from a venous source. The mean time from recognition of the event to institution of HBOT was 15 hours. Four of 45 patients (8.9%) died. Good neurological outcomes (defined as GOS-E 7 or 8) occurred in 27 patients and moderate disability in 13. The only independent factor that was associated with good neurological outcome was time to first HBOT (OR 0.94, 0.89–0.99; $P = 0.05$). Hemiplegia as the first presenting sign, however, was associated with poor outcome (OR 0.27, 0.06–1.08; $P = 0.05$). The source of embolus (arterial versus venous), hyperbaric treatment table used and patient age did not affect outcome.

Conclusion: Appropriate treatment of CGE with hyperbaric oxygen was found to be impeded by delays in diagnosis and subsequent transfer of patients. Better neurological outcome was associated with HBOT within eight hours of CGE.

Key words

Cerebral arterial gas embolism (CAGE); venous gas embolism; hyperbaric oxygen therapy; outcome; clinical audit

Introduction

Iatrogenic venous gas embolism (VGE) and arterial gas embolism (AGE) can occur as a result of many hospital-related procedures. This complication has been reported in almost all areas of clinical and surgical practice including cardiopulmonary bypass surgery,[1,2] angiography,[3] laparoscopy,[4] neurosurgery, caesarian delivery,[5] irrigation with hydrogen peroxide,[6] mechanical ventilation, central venous catheter placement and haemodialysis.[7] In most cases the embolised gas is air, but other medical gases such as helium[8] and carbon dioxide[9] have been described. AGE can occur as a result of direct injection into the arterial system or if there is cross-over from the venous system. VGE can move from the venous into the arterial system (paradoxical air embolism) through a right-to-left intra-cardiac shunt (persistent foramen ovale), through the pulmonary vasculature[10] or as a result of barotrauma. Bothma recently described a third generic mechanism called retrograde cerebral venous gas embolism (CVGE). This process depends on flow dynamics, buoyancy, bubble size and patient positioning.[11,12] Cerebral gas embolism (CGE) is a general term used in this article to encompass all three of these phenomena.

The pathophysiology of gas embolism is complex. Small-sized bubbles that enter either the venous or arterial circulation have both mechanical and inflammatory consequences. Gas bubbles that enter the venous system can make their way into the pulmonary circulation and impair right ventricular function. Furthermore, they can cross into the arterial circulation in the presence of an atrial or ventricular septal defect. Gas bubbles which enter the arterial circulation eventually lodge in small vessels and obstruct flow of oxygenated blood to cells causing end-organ ischaemia and endothelial injury with subsequent cell oedema and death. When gas lodges in coronary and cerebral arterioles, it can have devastating effects such as myocardial infarction, dysrhythmias, seizures and stroke phenomena. Imaging modalities, including CT and MRI scanning, may support a diagnosis but are not particularly sensitive. There is no relationship between volume of embolised gas and severity of symptoms.[13]

Furthermore, these ischaemic and local inflammatory processes activate leucocytes, platelets, complement and the clotting cascade which can result in endothelial injury and thrombus formation. Granulocyte-mediated reperfusion injuries may also occur.

In accordance with Boyle's law, hyperbaric oxygen (HBO) reduces the volume of the gas bubbles in the vessel so that blood flow can be re-established. Exposing the bubbles to hyperbaric oxygen accelerates denitrogenation by creating a gradient between the partial pressure of nitrogen in the gas bubbles and the blood (Henry's Law). This results in rapid reabsorption of nitrogen back into the blood with subsequent reduction and removal of air emboli. Therefore, in the case

of CGE, the potential benefits of HBO are thought to be reduction in the size of the penumbra and ischaemic insult, reduction in cerebral oedema by limiting cerebral vascular permeability, reduction in intracranial pressure due to oxygen-driven cerebral vasoconstriction and, finally, limiting endothelial injury by ameliorating leucocyte activation and adherence.[13–17]

Hyperbaric oxygen treatment (HBOT) is the standard treatment for diving-related decompression sickness (DCS) and gas embolism; however, there are currently no randomised controlled trials to guide best practice. Using standardised HBOT tables, recompression promotes the most rapid and complete removal of gas bubbles and, therefore, should enhance neurological outcome. Based on the pathophysiology of gas embolism, the earliest possible commencement of HBOT would seem optimal to prevent neurological sequelae by reducing ischaemic time. The efficacy of HBOT in this setting has been validated by extensive clinical experience and scientific studies.[18]

In contrast, there are few series describing iatrogenic CGE and even fewer guidelines regarding the optimal hyperbaric management. This is partly due to its infrequent occurrence. To date, most Australian literature pertains to scuba diving-related CGE, with the Prince of Wales hyperbaric unit reporting 26 cases that presented over a decade.[19] The intention of our study was to focus on presentation, management and outcome patterns of non-diving-related venous and arterial cerebral gas embolism that occurred as a result of medical procedures and were subsequently referred to The Alfred Hyperbaric Unit in Melbourne.

Methods

PATIENT SELECTION

This was a retrospective cohort study with a contemporaneous comparison group. The study examined patients admitted to the Alfred Hospital with a diagnosis of CGE between 01 January 1998 and 31 December 2014. The research proposal was approved by the Alfred Ethics Committee (AH 55/14). Using the established database at the Alfred Hyperbaric Unit, all patients were sought who had been referred to the unit from within The Alfred or from other peripheral hospitals following witnessed or suspected gas embolism. A search of The Alfred Hospital clinical coding system for air embolism (ICD9 958.0 and ICD-10 code T79.0), and air emboli from infusion, transfusion, therapeutic injection (ICD 9 999.1 and ICD-10 T80) was then performed. This provided an indication of the capture rate of all patients with air emboli during the study period and also generated a comparator group totalling nine patients who did not receive HBOT. Gas embolism was confirmed if the clinical notes reported visible gas, cardiovascular and/or central nervous system instability in the setting of an invasive procedure or if gas was visualised on CT or MRI. Exclusion criteria included patients in whom the aetiology was likely to be mixed gaseous or thromboembolic, patients in whom hyperbaric treatment could not be completed owing to cardiovascular instability and patients with CGE as a result of scuba diving.

Further examination of the hyperbaric unit's database revealed the number of treatments administered, the treatment tables used and whether other ancillary treatments were instituted, such as a lignocaine infusion. Individual medical records were then scrutinized for details pertaining to basic patient demographics, the nature of the initiating iatrogenic insult, time delay to presentation and eventual neurological outcome.

NEUROLOGICAL OUTCOME

An assessment of neurological outcome was made after the first hyperbaric treatment and at hospital discharge using the Extended Glasgow Outcome Scale (GOS-E) structured questionnaire.[20,21] The GOS-E is a practical index of social and functional outcome following head injury designed to complement the Glasgow Coma Scale (GCS) as the basis of a predictive system. Patients are assigned to one of five possible outcome categories: death, persistent vegetative state, severe disability, moderate disability, and good outcome. Using the GOS-E, each of the three categories applicable to conscious patients are subdivided into upper and lower bands that results in eight possible categories. A good neurological outcome was defined as a GOS-E of 7 or 8 (independent). The secondary outcomes included relationship between eventual neurological status and timing of hyperbaric treatment, recompression table used and the total number of treatments administered.

STATISTICS

Parametric data are presented as mean (SD), non-parametric as median (IQR), and categorical as proportions. A two sample *t*-test was used to compare the ages and weights of the HBOT and non-HBOT groups. The Pearson chi squared test was used to establish if there was an association between the confounders (gender, admission source, site of CGE, aetiology of CGE), the outcomes (mortality and complications) and predictors (HBOT versus no HBOT). Multivariate logistic regression was used for all independent variables found to be associated with mortality on univariate logistic regression with a two-tailed significance set at a P-value < 0.05. Results were expressed as odds ratio (OR) with 95% confidence intervals (CI). Data from patients with missing values were not analysed.

Results

Over the 17-year period, 61 patients were identified with an initial diagnosis of a CGE using the ICD search. A total of 36 patients were treated by the Alfred Hyperbaric Service

Table 1

Demographics of patients with cerebral gas embolism; good neurological outcome was defined as Glasgow Outcome Scale (GOS-E) 7 or 8; * $P = 0.01$; all other factors not significant; CVAD – central venous access device; $ETCO_2$ – end-tidal carbon dioxide; CVA – cerebrovascular accident

	Neurological outcome	
	Good (*n* = 27)	**Poor (*n* = 18)**
Patients		
Age (mean, 95% CI)	56.2 (44.9–63.6)	56.4 (48.4–65.7)
Gender (M:F)	16:11	9:9
Referral base		
Inpatient	19	10
Other hospital	8	8
Predisposing factors		
Cardiac surgery	16	8
Other surgery	4	0
Trauma	2	3
Interventional radiology	3	1
CVAD	2	6
Source		
Arterial	20	12
Venous	7	6
Presenting symptoms		
ET CO_2	4	0
Observed embolus	12	6
Seizure	2	1
Blindness	2	2
CVA*	2	7
Arrhythmia	2	1
Cardiac arrest	2	0
Respiratory arrest	1	1

Table 2

Interventions instituted after diagnosis of iatrogenic cerebral gas embolism; good neurological outcome was defined as Glasgow Outcome Scale (GOS-E) of 7 or 8; * $P = 0.05$; † $P = 0.002$ CT – computerised tomography; MRI – magnetic resonance imaging; HBOT – hyperbaric oxygen treatment, including RN 62 – Royal Navy treatment table 62; RN 61 – Royal Navy treatment table 61; 18:90:30 – a 284 kPa treatment table and Comex 30 – 406 kPa treatment table using a helium/oxygen mix (HeO_2)

	Neurological outcome	
	Good (*n* = 27)	**Poor (*n* = 18)**
Imaging		
CT	9	11
MRI	2	3
Both CT and MRI	3	1
Nil	13	3
Ancillary therapy		
Trendelenburg	5	0
Lignocaine	9	5
Prednisolone	2	0
Nil	16	13
Hyperbaric oxygen		
Time to HBOT (h)*	8.8 (4.7–12.8)	16.5 (9.0–24.1)
Treatments† (median, range)	1 (0.8–1.5)	3 (1.7–4.2)
RN 62	5	7
RN 61	13	7
18:90:30	2	1
Comex	1	0

and 25 did not receive HBOT. The authors reviewed the medical records of these 25 patients and determined that 16 patients had received the wrong ICD code and the other nine had been correctly diagnosed with CGE but not referred to the hyperbaric unit.

Table 1 details the characteristics of the cohort. The source of embolus was arterial in 32 patients and venous in 13 patients. The overall mortality was four of 45 patients (8.7%) (three treated with HBOT and one in the non-treated group). The most common precipitating events were cardiac surgery (24 patients) or manipulation of central venous access devices (eight patients). The most frequent presenting signs were non-haemorrhagic hemiplegia on awakening from cardiac surgery (nine patients), cardiac arrest (two patients) or respiratory arrest (two patients). An air embolus was witnessed in the cardiopulmonary bypass circuit in 18 patients and four had presumed CGE with sudden loss of their end-tidal capnography trace.

Apart from standard resuscitation drugs, 14 patients received lignocaine infusions, two received steroids and five were placed in Trendelenburg positioning. Diagnostic imaging was performed in 29 patients (20 patients had CT, five patients had MRI, four had both CT and MRI) and 16 patients had no scanning (Table 2). HBOT was offered to 36 patients. The tables frequently used were the Royal Navy Treatment Table 62 (RN 62), RN 61, an 18 msw (284 kPa) treatment table and a Comex 30 (405 kPa). The initial treatment table selected varied depending on the source of embolus, the time delay to treatment and the neurological deficit observed.

Of the patients who did receive HBOT, the majority were male, were usually younger (52.5, IQR 31–75 years old versus 64.0, IQR 29–67) and had witnessed events. The mean time from recognition of CGE to institution of HBOT was 15.0 (12.9) hours with no significant difference between the Alfred patients and those referred from other hospitals (16 (12.3) h vs. 12.8 (13.7) h; $P = 0.47$). Twenty-nine patients were referred from within the Alfred and 16 were transferred from another hospital.

The GOS-E of 30 patients could not be assessed at the end of the first HBOT as they were still sedated or intubated. The mean GOS-E at discharge was 6.5 (2.1). Good neurological outcomes (defined as GOS-E 7 or 8) occurred in 27 patients,

Table 3
Univariate regression analysis of factors associated with favourable neurological outcome; * $P = 0.05$; CAGE – cerebral arterial gas embolism; CVA – cerebral vascular accident; CVGE – cerebral venous gas embolism; HBOT – hyperbaric oxygen treatment, including RN 62 – Royal Navy treatment table 62. For factors with a binary outcome (cardiac surgery, CVGE, CAGE, HBOT) the odds ratio represents the presence or absence of the factor; for continuous data the estimate is the odds ratio for a unit increase for the factor (e.g., per year).

	Odds ratio	Std error	95% CI
Patient factors			
Age	0.99	0.01	0.96–1.02
Transfer	2.18	1.48	0.54–8.76
Aetiology			
CAGE:CVGE	1.16	0.20	0.25–5.33
Cardiac surgery	2.28	2.01	0.68–2.51
Presentation			
CVA	0.27	0.19	0.06–1.08
Cardiac	4.38	5.05	0.45–42.1
Hyperbaric oxygen			
HBOT:no HBOT	0.47	0.42	0.08–2.71
Time to first HBOT*	0.94	0.03	0.89–0.99
Early HBOT (< 8hrs)	3.25	2.30	0.81–13.03
Late HBOT (> 24hrs)	0.27	0.20	0.06–1.14
RN 62:Other table	0.46	0.32	0.11–1.83

20 in the HBOT group and seven in the non-HBOT group. Patients with good neurological outcome were treated with HBOT earlier (8.8 (1.9) hours vs. 16.5 (3.6) h; $P = 0.05$), received fewer treatments (1, IQR 1–2) vs. 1.5, IQR 1–5; $P = 0.002$) and were mainly treated with a shorter table (13 RN 61 and five RN 62 vs. seven RN 61and seven RN 62). The association between the number of HBOT and outcome was influenced by the clinicians involved. Prompt resolution of symptoms was associated with one or two HBOT treatments. In contrast, incomplete resolution after the first treatment initiated further treatment until lack of ongoing improvement or stable persistent neurological impairment.

Table 3 summarises the univariate analysis for the 11 variables considered. On univariate analysis the only independent factor associated with good neurological outcome was time to first HBOT treatment (OR 0.94, 0.89–0.99; $P = 0.05$). Those patients with poor neurological outcome were more often referred from other hospitals (8 of 18 vs. 10 of 27), had a CVAD as the source of embolus (6 of 18 vs 2 of 27) and had longer delays to initial treatment (16.5 (3.6) h vs. 8.8 (1.9) h; $P = 0.05$). Hemiplegia, as the first presenting sign, was associated with poor outcome (OR 0.2, 0.06–1.08; $P = 0.05$). No association between outcome and cardiac surgery (OR 0.99, 0.96–1.02; $P = 0.54$) or arterial source of CGE (OR 1.32, 0.36–4.81; $P = 0.36$) could be established. Although patients who were transferred had poorer neurological outcomes, there were some who had complete recovery.

Discussion

This is the largest Australian retrospective case series of iatrogenic gas embolism to date. It includes 45 cases of both arterial and venous gas embolism over a 17-year period. Whilst the incidence of CGE in this series was low, it was comparable to the incidence reported by Bessereau of a confirmed CGE rate of 2.65 per 100,000 hospital admissions.[22]

The obvious interpretation of our series is that there are a number of preventable measures which could impact on recovery from CGE. In particular earlier recognition, greater compliance with gas embolism treatment protocols and earlier referral to a hyperbaric unit are recommended.[23,24] Despite the presence of a hyperbaric medical unit on site, the mortality rate was 8.7% and complete neurological recovery only occurred in 27 of the 45 cases.

The effects of gas embolism on cerebral blood flow and subsequent ischaemia have been demonstrated by a number of authors.[25–27] The need for urgent definitive treatment has also been stressed by many.[13,19,28] Most authors agree that early HBOT treatment (certainly within eight hours) is associated with improved outcome.[22,28–30] In this series, early institution of HBOT was associated with better neurological outcome. Previous reports suggest that the diagnosis of CGE is often not made in cardiothoracic surgery until post-bypass stroke has occurred. Delayed presentation does not preclude HBOT and this series demonstrated significant improvement is possible even when hyperbaric treatment is more than 24 hours post insult.[2,32] In reality, delays inevitably occur if the patient is transferred from another hospital. This makes treatment within the optimal time frame difficult to achieve.

One retrospective study reported a good recovery in 80% of patients when HBOT was carried out within three hours, and only 48% if the delay exceeded three hours.[28,30] HBOT after a significant delay should still be considered, as some case reports suggest good neurological outcome is possible.[32,33] In one case where there was sudden onset of unresponsiveness followed by seizure activity during a diagnostic bronchoscopy, the clinical diagnosis was unclear and HBOT was not instituted until 52 hours after the initiating event, followed by two additional HBOT sessions and the patient made a full neurological recovery.[32]

Currently a number of HBOT regimes exist. The choice of HBOT table depends on multiple factors. For example the decision can be based on whether the patient with CGE is referred in the acute phase (less than eight hours after the event) or the delayed phase (greater than 24 hours after the event). In other published series, the choice of treatment table is driven by the cause of the CGE (Table 4).

Traditionally CGE related to scuba diving was treated with a US Navy Treatment Table 6A, which involves a 30-minute

Table 4

Previous case series of ≥ 10 patients with cerebral gas embolism with details of treatment tables, delay to therapy and outcome
CAGE – cerebral arterial gas embolism; CNS – central nervous system; CVC – central venous catheter; CVGE – cerebral venous gas embolism; HBOT – hyperbaric oxygen treatment; RN 62 – Royal Navy treatment table 62; USN 6 – United States Navy treatment table 6; VAE – venous air embolism; other hyperbaric treatment tables specific to the treating unit with maximum pressures of 304, 406 and 608 kPa.

Author	Patients	HBOT table	Delay to treatment (h)	Neurological outcome	Mortality	Comments
Boussuges[30]	113	608 kPa with neurology; 203 kPa without	Not recorded	69% (78) recovery	6 (5%)	71% (80) venous origin (CVC or dialysis)
Bacha[34]	Not reported	608 kPa then 304 kPa	< 12	21% sequelae	14%	Lower mortality with < 12 h delay to treatment
Ziser[35]	17	USN 6A	9.6 (mean)	8 recovery	3	Good outcome if Rx< 4 h
Blanc[28]	86	608 kPa 10 min then 203 kPa 60 min	3–8	58% (50) recovery	7	63 CVGE
Benson[36]	19	USN 6A or USN 6	8.9 (mean)	5 resolved 11 improved	5	9 CVGE
Trytko[19]	26	280 kPa	Divers 2–44; Non divers 0.75–14	2 severely affected	0	18 diving-related
Bessereau[22]	125	406 kPa then 253 kPa then 203 kPa	6 (mean)	43% (54) CNS sequelae	15 (12%)	32% (40) CVGE
Gibson[2]	12	RN 62	18 (4–48)	1 CNS sequelae	1	6 treated > 24 h post event
Tekle[29]	36	USN 6	19 patients < 6	26 "*favourable*"	1	24 VAE

period at 609 kPa breathing air. This deep air spike was designed to rapidly compress bubbles.[37] Most clinical and animal studies, however, have found no objective advantage in starting recompression at levels greater than 2.8 ATA.[15,37,38] Iatrogenic CGE generally involves smaller bubble and dissolved nitrogen loads compared to diving injuries. Therefore, the increased health and safety risks for in-chamber attendants[39] and limited evidence of increased efficacy[40] means that these deeper tables cannot be justified and they have been replaced largely by either the standard DCI treatment table (RN 62) or a shorter 284 kPa table (RN 61).

Cardiothoracic surgery has a relatively high incidence of CGE compared to other surgical specialties. It is for this reason that most centres have developed air embolism protocols which include rapid detection, placing the patient in steep head-down position,[41] commencing a lignocaine infusion,[42,43] contacting a hyperbaric service and considering retrograde cerebral perfusion. This and other studies suggest that protocols may not be adopted even when the hospital has a hyperbaric unit onsite. Potential explanations include either lack of detection at the time of gas entrainment, visualisation of gas in the bypass circuit being deemed small and clinically insignificant and uncertainty around the diagnosis prompting subsequent imaging and further time delay to starting HBOT.

Sometimes the first indication of CGE is hemiplegia or blindness on awakening from sedation or anaesthesia many hours after the precipitating event.[2] Efforts should be made to increase awareness of this significant complication to aid early detection. Familiarity with local gas embolism protocols, including the institution of ancillary treatments, should be gained and mandated in the event of CGE detection regardless of gas volume or perceived clinical significance.

Imaging with MRI or CT may support a diagnosis of CAGE but is rarely conclusive.[44] Therefore it is generally unwise to delay HBOT for the sake of image procedures unless the results will dramatically alter the immediate care.

This study has a number of limitations. Firstly, as with many retrospective studies, it is not possible to adequately generate matched comparator groups of patients with similar disease severity. If the diagnosis is obvious, the decision to refer to a hyperbaric unit largely depends on the proceduralist involved. Considerations include familiarity and previous experiences with hyperbaric units, the size and perceived clinical consequences of the gas and the logistics of inter-hospital transfer if the event had occurred outside The Alfred Hospital.

Transferring a potentially unstable patient over large distances would be a deterrent for many doctors and this introduces both selection and treatment bias. As nearly two-thirds were Alfred in-patients, it is possible that only those non-Alfred patients stable enough to be transported have been studied. Therefore, the overall mortality from gas embolism in our hospital community could be higher than reported. Since it is believed that the size of the gas

embolism has no correlation with neurological insult, all patients with known or suspected CGE should be referred for consideration of HBOT and transferred if safe to do so. [13]

Secondly, patient inclusion in this study was dependent on ICD coding at discharge or death. CGE is a clinical diagnosis and so depends on the treating surgeon or interventional radiologist to diagnose it and document the incident. It also relies on the correct interpretation of medical records and operation reports by clerical staff so that the relevant ICD codes can be applied to the patient.

Thirdly, the GOS-E provides an overall assessment of neurological outcome but does not provide detailed information pertaining to specific disabilities or level of independence. Categories are crude and subject to interpretation. The scale does not reflect subtle improvements in functional status of the individual so that a considerable improvement in ability still may not change outcome category.[20] The GOS-E was primarily intended to provide an overall summary of outcome and facilitate comparison rather than describe specific areas of dysfunction.[20] Furthermore, outcome categories are expressed as a dichotomy: poor/unfavourable outcome versus independence/favourable outcome. This results in a loss of information and decreased sensitivity.[21] In addition, there is no current way of assessing a patient's neurological injury at the time of diagnosis. One can only rely on clinical impressions such as haemodynamic instability to infer the degree of neurological insult.

Conclusion

Hyperbaric oxygen therapy is the mainstay of treatment for CGE. This study suggests that early recognition and treatment does improve neurological outcome. In some instances, benefits of treating with HBOT may extend up to 24 hours or more after the precipitating event. If CGE is recognised or even suspected, CGE protocols should be activated and adhered to, including early referral to a hyperbaric unit. This should occur irrespective of gas load or perceived clinical significance.

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Tympanic membrane bleeding complications during hyperbaric oxygen treatment in patients with or without antiplatelet and anticoagulant drug treatment

Valerie A Fijen, Peter E Westerweel, Pieter Jan AM van Ooij and Rob A van Hulst

Abstract

(Fijen VA, Westerweel PE, van Ooij PJAM, van Hulst RA. Evaluation of tympanic membrane bleeding complications during HBOT in patients with or without antiplatelet and anticoagulant drug treatment. *Diving and Hyperbaric Medicine*. 2016 March;46(1):22-25.)

Introduction: Middle ear barotrauma (MEBt) is a frequently occurring complication of hyperbaric oxygen treatment (HBOT). High-grade MEBt may involve tympanic membrane (TM) haemorrhaging. Although many patients undergoing HBOT use antiplatelet or anticoagulant drugs, it is unknown whether these drugs increase the risk of MEBt and particularly TM bleeding complications.

Methods: This multicentre, prospective cohort study investigates the prevalence of MEBt and TM bleeding during HBOT in patients using antiplatelet/anticoagulant drugs, compared with control patients not on such medications. MEBt was assessed by video otoscopy of the TM pre and post HBOT and scored according to the modified Teed score. Any complications from previous HBOT sessions were retrospectively documented.

Results: Of 73 patients receiving HBOT, 34 used antiplatelet/anticoagulant drugs. Mild MEBt (Teed score 1 or 2) occurred in 23 of these 34 patients and in 31 of the 39 controls. Teed score 3 MEBt occurred in only two of the control-group patients and none of the patients using antiplatelet/anticoagulant drugs. Two patients using anticoagulant drugs reported epistaxis during a previous HBOT session; epistaxis was not reported by any control patients.

Conclusion: Low-grade MEBt is common during HBOT; however, high-grade barotrauma is rare with current chamber operating procedures. Patients using antiplatelet/anticoagulant drugs potentially may be prone to MEBt-associated haemorrhagic complications, but we did not observe any such increase in this cohort. Only mild epistaxis occurred in patients using anticoagulant drugs.

Key words

Middle ear; barotrauma; hyperbaric oxygen therapy; medication; cardiovascular; haematology; risk factors

Introduction

There are various well-established indications for the use of hyperbaric oxygen treatment (HBOT).[1] Although generally a safe procedure, the most prevalent adverse event associated with HBOT is middle ear barotrauma (MEBt).[2] Many indications for HBOT relate to macro- and/or microvascular ischaemic injury, such as non-healing skin ulcers. In these patients with vascular disease, the use of prophylactic antiplatelet or anticoagulant medication is common. It is possible that individuals using antiplatelet/anticoagulant drugs are at increased risk of developing bleeding complications during hyperbaric exposure. In cases of MEBt, the mucosal lining is distended and blood vessels may rupture, possibly leading to haemotympanum and tympanic membrane (TM) rupture causing pain, hearing loss, and anxiety.[3]

There are no data on the influence of the use of antiplatelet/anticoagulant drugs on the prevalence of bleeding complications from MEBt during HBOT. In the present study, otological effects of hyperbaric exposure were assessed in patients undergoing HBOT and using antiplatelet/anticoagulant medication compared with control patients not using such medication.

Methods

STUDY DESIGN

This prospective, multicentre, observational cohort study included 73 patients from four hyperbaric centres in the Netherlands. The study protocol was approved by the Medical Ethical Committee of the Amsterdam Medical Center (approval W13_079 # 13.17.0099). A sample size of 30 patients per group was calculated to detect a substantial increase in the incidence of MEBt (Teed grade ≥ 3, see below) to 20% or more from an estimated 4% in controls with 80% power and an α-level of 5% using one-sided testing and accounting for 20% loss to follow-up.

A total of 93 consecutive patients treated with HBOT were evaluated of whom 73 met the inclusion/exclusion criteria. All participants provided written informed consent. All participants had to have been previously evaluated and found fit for HBOT by their hyperbaric physician. During this evaluation, routine otoscopy was performed to exclude pre-existing pathology. All patients were informed about HBOT and had been taught various middle ear equalizing manoeuvres.

For the present study, individuals were excluded in case of incomplete video-otoscopic examination during pre- and/or post-treatment evaluation, defined as the inability to assess > 50% of the tympanic membrane (TM) on the digital image. Exclusions occurred mostly due to the presence of cerumen that could not be immediately removed. For the final analysis, 34 participants using antiplatelet/anticoagulant drugs were compared with 39 control patients not using antiplatelet/anticoagulant drugs, thus meeting the predetermined sample size to reach sufficient statistical power.

VIDEO OTOSCOPY AND MEBt GRADING

Bilateral video otoscopy was performed before and within 15 min after a HBOT session. In all participants, otoscopy was carried out by a trained staff member using a Welch Allyn™ Digital Macroview Otoscope 719 series. Both TMs of each patient were examined and photographed before and after HBOT. Photographs were blinded and independently assessed by two investigators (RAvH and VAF) for grading MEBt according to the modified Teed classification:[4]

Grade 0 – Symptoms without signs;
Grade 1 – Injection of TM, especially along the handle of the malleus;
Grade 2 – Injection plus slight haemorrhage within the substance of the TM;
Grade 3 – Gross haemorrhage within the substance of the TM;
Grade 4 – Free blood in the middle ear, as evidenced by blueness and bulging;
Grade 5 – Perforation of the TM.

Photographs were taken in the standard mode with a resolution of 1280 x 1024 megapixels in jpg format. A Teed score of ≥ 3 was considered to be a significant MEBt.

QUESTIONNAIRE

Patients were asked to complete a 10-min questionnaire in which treatment indication, comorbid diseases, ENT disorders, medication use and bleeding symptoms were evaluated. The questionnaires enquired about bleeding symptoms, both in daily life and in relation to any of their previous HBOT sessions. For quantification of the general occurrence of bleeding symptoms unrelated to HBOT (e.g., the occurrence of spontaneous bruising and epistaxis, etc), the ISTH/Tosetto bleeding score was used in a slightly abbreviated form.[5,6] This score ranges from 0 (no symptoms) to 22 points, and is widely used to characterize bleeding propensity; however, it was developed to diagnose congenital bleeding disorders and has not been specifically validated to investigate the haemorrhagic effects of antiplatelet or anticoagulant drugs.

HBOT PROTOCOL

All HBOT was done in multiplace chambers with audio and camera observation. During most sessions, a trained staff member was physically present inside the chamber to assist patients when required. In the case of any patient indicating difficulty clearing their ears, compression was immediately interrupted. Compression rates ranged from 1.0–1.5 metres' sea water (msw) equivalent depth per minute for a total of 10–15 min to reach the treatment pressure of 14–15 msw (approximately 243 kPa). Patients received three intervals of HBOT of 20–30 min each with a 5–10 min break between each session. The chamber was decompressed at a rate of 1.0–1.5 msw·min^{-1}. The total treatment duration ranged from 100–130 min.

STATISTICAL ANALYSIS

Data are presented as the number of patients (*n*), mean or median (range) where appropriate. Analyses were performed with SPSS version 21. The primary research question regarding the proportion of MEBt in participants using antiplatelet/anticoagulant drugs vs. controls was tested with the Chi-square test. For secondary analyses, normality of the quantitative variables was checked with the Shapiro-Wilk test. Normally distributed continuous variables were compared with a Student's *t*-test. Non-normally distributed numerical variables were analysed with the Kruskall-Wallis test, and nominal and ordinal variables were analysed with the Chi-square test. Fisher's exact test was used when expected cell counts were low and comprised ≥ 25% of a table. The *P*-value was one-tailed for the primary research question investigating whether there would be an increase in tympanic bleeding complications associated with the use of antiplatelet/anticoagulant drugs; for other statistical comparisons, *P*-values were calculated based on a two-tailed level of significance defined at 0.05.

Results

BASELINE CHARACTERISTICS

Of the 73 patients included in the study, 34 used antiplatelet or anticoagulant drugs. The types of antiplatelet/anticoagulant drugs used were acetylsalicylic acid (*n* = 26), vitamin K antagonists (*n* = 7), dipyridamole (*n* = 3), clopidogrel (*n* = 2), low-molecular-weight heparin (*n* = 1) and, in some patients, a combination of these (*n* = 6).

Table 1 presents the baseline characteristics of the two study groups. As expected, the Tosetto bleeding score was higher in participants using antiplatelet/anticoagulant drugs, reflecting a noticeably higher bleeding tendency in daily life. Patients using these agents were more often male and had a higher average age, probably owing to the higher incidence of cardiovascular disease in males of increasing age. One patient using antiplatelet drugs and one control patient reported having experienced a MEBt with TM haemorrhage during a HBOT session prior to participating in the present study. Two patients using anticoagulant drugs, but none of the controls, reported having experienced epistaxis during a previous HBOT sessions.

Table 1
Characteristics of the study patients, AP/AC - antiplatelet/anticoagulant; NA - not available

	AP/AC patients (n = 34)	Controls (n = 39)
Sex (M/F)	25/9	19/20
Age (y; mean, range)	64 (34–82)	58 (29–77)
HBO sessions (median, range)	20 (0–152)	18 (0–44)
Tosetto bleeding score (n)		
0–3	20	29
4–5	8	8
≥ 6	4	2
NA	2	0
Bleeding incidents during previous HBOT		
Yes	3	1
No	29	38
NA	2	0

A clinically significant proportion of the patients (55 of 73) had signs of MEBt from the previous HBOT sessions (Table 2). One control patient had a TM injury (Teed score 3) from the HBO treatments prior to participating in our study sessions. The median number of previous sessions was 28 (range 0–157) in the patients using antiplatelet/anticoagulant drugs versus 19 (range 0–44) in controls. A maximum of 40 sessions is provided per HBOT cycle, whereupon in exceptional cases a repeat cycle may be provided after at least a three-month interval.

MEBt POST HBOT

In the control group, two of 71 TMs satisfactorily visualized in the 39 patients had a Teed score of ≥ 3, whilst none of 66 TMs from the 34 antiplatelet/anticoagulant patients had a Teed score > 2. There was no observed increase in haemorrhagic TM complications during HBOT in either group (Table 2). Six patients in the control group and seven in the antiplatelet/anticoagulant group showed a higher Teed score post HBOT than pre HBOT in one or both TMs. A history of aural symptoms during HBOT was associated with a higher Teed score after the treatment. There was no association of Teed scores with age or sex or the number of previous HBOT sessions. The two patients experiencing a Teed grade 3 MEBt were on their ninth and tenth sessions respectively.

Also, no non-MEBt-related bleeding complications, such as epistaxis or sinus squeeze, occurred during the study sessions.

Discussion

The present study confirms previous reports that mild forms of MEBt (modified Teed grades 1 and 2) occur frequently during HBOT.[7–9] For example, in a study evaluating the efficacy of topical decongestants on MEBt in HBOT, approximately 45% of patients had a Teed score greater than zero.[8] In another study, 17% of 782 HBOT patients reported clinically apparent middle ear symptoms consistent with MEBt occurrence.[2] Of note, the incidence of MEBt reported here is based on TM assessment, irrespective of the presence of MEBt symptoms. Patients who are unable to auto-inflate the middle ear, or who have positive pathological findings on otoscopy, are considered to be at higher risk to develop MEBt, with a reported incidence of MEBt ranging from 37 to 94%.[10–12] For this reason, as part of standard care at our hyperbaric facilities, all patients are extensively assessed for ENT comorbidity prior to the initiation of HBOT, and receive detailed instructions about middle ear equalization. The incidence of MEBt may depend on the compression rate, with a slow rate resulting in a significantly lower incidence of MEBt in one study.[13] In the present study, a slow compression rate of 1.0–1.5 msw·min^{-1} was used, which may explain the low incidence of serious MEBt.

This is the first study specifically designed to investigate the occurrence of TM haemorrhage in patients using antiplatelet or anticoagulant medication undergoing HBOT. Although bleeding phenomena during daily life occur more frequently in individuals using these agents, we found no evidence in our study that TM bleeding complications are increased in such patients. This is of importance, since aggravation of MEBt sequelae by TM haemorrhaging could cause anxiety and/or panic during the HBOT session and create a risk for aggravated middle ear injury.

The occurrence of epistaxis reported by two patients during one of their previous HBOT sessions, suggests that epistaxis might be a recurrent symptom in patients using anticoagulant drugs and undergoing HBOT. The epistaxis that occurred was easily managed by application of local pressure and, therefore, represented only a minor complication.

In a recent study investigating risk factors for MEBt with the aim of identifing patients requiring tympanostomy tubes, the use of anticoagulant therapy correlated with the incidence of MEBt in the bivariate, but not in the multivariate analysis.[8] However, because that study was not designed to investigate the influence of anticoagulant drugs, few details were provided.

The present study has several limitations. The investigation included patients who had undergone a substantial number of previous HBOT sessions and, generally, had signs of MEBt prior to the studied HBOT session. However, as no patient had a Teed score of ≥ 3, we believe that this did not affect our primary research question. Also, by including a baseline analysis, we were able to differentiate between pre-existing and new tympanic aberrancies. However, we cannot exclude that patients who were intolerant of HBOT, possibly owing to MEBt occurrence, had previously stopped their HBOT

Table 2
TEED scores for MEBt before and after the HBOT study session; Teed scores, ranging from 0 to 5, with number of subjects before session and immediately after the session. The highest Teed score from right and left tympanic membranes from each subject was used to calculate this table; there were no statisically signifcant difference between the two groups

	Patients using AP/AC drugs (n = 34)		Control patients (n = 39)	
Teed score	**Before**	**After**	**Before**	**After**
0	10	9	8	8
1	19	18	20	15
2	5	7	10	14
3	0	0	1	2
4/5	0	0	0	0

and this might have led to some selection bias. Also, we powered the study to compare any patient using any type of antiplatelet/anticoagulant drug with a control group not using these drugs. However, there may be differences between the adverse effects of the various individual subtypes of drugs or combinations thereof. The present study was underpowered to allow any meaningful sub-group analyses for different medications. Our study was too small to detect rare, but possibly more severe, complications from the use of antiplatelet/anticoagulant drugs.

Conclusions

Mild (modified Teed score 1 to 2) MEBt was common in our patients. We found no evidence that TM bleeding complications from HBOT were increased in subjects using antiplatelet/anticoagulant drugs. Therefore, these drugs should not be considered to be a contraindication to HBOT. However, every effort should be made to prevent MEBt in all patients undergoing HBOT.

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Consensus Development Conference

Consensus guidelines for the use of ultrasound for diving research

Andreas Møllerløkken, S Lesley Blogg, David J Doolette, Ronald Y Nishi and Neal W Pollock

Abstract

(Møllerløkken A, Blogg SL, Doolette DJ, Nishi RY, Pollock NW. Consensus guidelines for the use of ultrasound for diving research. *Diving and Hyperbaric Medicine*. 2016 March;46(1):26-32.)
The International Meeting on Ultrasound for Diving Research produced expert consensus recommendations for ultrasound detection of vascular gas bubbles and the analysis, interpretation and reporting of such data. Recommendations for standardization of techniques to allow comparison between studies included bubble monitoring site selection, frequency and duration of monitoring, and use of the Spencer, Kisman-Masurel or Eftedal-Brubakk scales. Recommendations for reporting of results included description of subject posture and provocation manoeuvres during monitoring, reporting of untransformed data and the appropriate use of statistics. These guidelines are available from <www.dhmjournal.com/>.

Key words
Doppler; echocardiography; bubbles; cardiovascular; right-to-left shunt; decompression illness; diving research; meetings; review article

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Introduction

The International Meeting on Ultrasound for Diving Research was held on 25–26 August 2015 in Karlskrona, Sweden. It brought together an international group of 27 physicians and scientists from 12 countries with the goal of developing consensus guidelines to aid investigators in designing research protocols and reviewers who may evaluate submitted reports. Topics addressed both Doppler ultrasound and newer two-dimensional imaging modalities. Discussion areas included the strengths and limitations of different techniques, technician training, monitoring and grading protocols, data handling and reporting. The following consensus guidelines were agreed upon through discussions during the meeting and during a post-meeting period when draft documents were circulated to the delegates. The guidelines produced by the panel are not exhaustive, but may aid in standardizing and, in some cases, improving experimental techniques. Future efforts can refine these guidelines and incorporate new and emerging technologies and procedures.

Bubbles and decompression stress

Some of the bubbles which form as a consequence of decompression can be detected by ultrasonic methods. Although technology is evolving, the most common technique is the detection of intravascular bubbles using either a Doppler flow transducer or two-dimensional echocardiography. The detection of bubbles in any individual is not diagnostic for decompression sickness (DCS). However, the bubble load detected in large systemic veins and, in particular, in the mixed venous blood is considered to be correlated with the probability of DCS. In large compilations of data, the number of venous bubbles is correlated with the observed incidence of DCS.[1,2] Therefore, ultrasonically-detected bubbles can be a useful outcome measure for some research questions.

The ability of bubble measurements to answer specific research questions should be considered carefully. If bubble studies are appropriate, they must be designed and conducted such as to produce useful results and should be reported in a manner that can be compared meaningfully to the rest of the scientific literature. A wide variety of monitoring protocols and data analyses can be found in the literature and in manuscripts submitted for publication. Whilst some variants are well founded, others reflect weaknesses in methodology that would best not be perpetuated. Ideally, well established protocols should be employed for ultrasonic monitoring. Variations should be clearly justified, should be based on scientific merit and with consideration of the value of comparison with other studies. Investigators who are new to ultrasonic detection of bubbles are encouraged to seek assistance from experienced peers to develop effective protocols.

The purpose of these guidelines is to present recommendations for best practice and standardization of protocols for ultrasonic detection of bubbles for diving research. The goal is not to stifle scientific creativity or thoughtful differences; protocols are expected to continue to be refined, or new ones developed, to improve utility or take advantage of new technological capabilities and developments. These are designed to help investigators develop and implement useful protocols. Journal editors and reviewers may also find this information useful to consider when evaluating manuscripts submitted with bubble data.

Table 1

The Spencer Scale[4] is an ordinal scale developed to facilitate semi-quantitative grading of intravascular bubble signals identified with aural Doppler ultrasound technology; Roman numerals are used to remind users that these are non-parametric data

Grade	
0	No bubble signals;
I	Occasional bubble signals; great majority of cardiac cycles signal free;
II	Many, but less than half, of the cardiac cycles contain bubble signals;
III	Most cardiac cycles contain bubble signals, but not obscuring signals of cardiac motion;
IV	Bubble signals sounding continuously throughout systole and diastole, obscuring normal cardiac signals.

Table 2

The Kisman-Masurel scale[7] was developed to allow bubble signals identified with aural Doppler ultrasound technology to be evaluated on multiple parameters; the individual parameter codes (scored with Arabic numerals) and then combined and converted to yield a single semi-quantitative ordinal, non-parametric grade (Roman numerals)

Code	Frequency (f), bubbles/cardiac period
0	0
1	1–2
2	several, 3–8
3	rolling drumbeat, 9–40
4	continuous sound

Code	Rest % (p)	Movement duration (d)
0	0	0
1	1–10	1–2
2	10–50	3–5
3	50–99	6–10
4	100	> 10

Code	Amplitude (A)
0	No bubbles discernable
1	Barely perceptible, $A_b << A_c$
2	Moderate amplitude, $A_b < A_c$
3	Loud, $A_b \approx A_c$
4	Maximal, $A_b > A_c$

Technician training

There is no credentialing standard for certifying the competency of ultrasonography technicians involved with decompression research. Obtaining interpretable ultrasound bubble signals requires practice, and grading of these signals is subjective. The reliability of research data can be enhanced by documentation of technical skill and assurance of inter-rater reliability between laboratories. Researchers who are new to ultrasonic detection of bubbles should seek training with an established laboratory or undertake an independent, blinded review of their data.[3] It is expected that 10% of the total recordings from a study, or at least 30 recordings, would constitute a minimum review effort. An independent data reviewer should be able to request and evaluate any recording reported in a study; an inability to provide the requested recordings would be cause for concern and could prompt the call for a more comprehensive review.

RECOMMENDATION 1

Ultrasound technician training and/or level of experience should be described in research reports. It is to be encouraged that research teams without established records with these techniques include the results of independent, blind reviews of their data by established investigators. These should identify the reviewer, the absolute number of records reviewed, the percentage of total measures reviewed, and the agreement between researcher and reviewer scores.

Signal grading – Doppler

While many Doppler grading scales have been described in the literature, the two most widely accepted are the Spencer and Kisman-Masurel (KM) ordinal grading scales.[4–7] Both have been used sufficiently over several decades to warrant recognition as standards of practice. The KM scale does offer the advantage that KM grades can be converted to Spencer grades. Spencer grades cannot be converted to KM values. The Spencer scale consists of five grades (0–IV) representing increasing numbers of bubbles in the Doppler signal (Table 1). The KM scale has 12 grades (0, I-, I, I+, II-, II, II+, III-, III, III+, IV-, IV), and grading is a two-step procedure. First, the Doppler signal is assigned a three-digit code, *fpA* for at rest and *fdA* for movement conditions (Table 2), where *f* (frequency) is the number of bubbles per cardiac period; *p* is the percentage of cardiac periods with specified bubble frequency at rest or *d* is the number of cardiac cycles with elevated bubble sounds after movement and *A* is the amplitude of bubble sounds (A_b) in comparison to normal blood flow/cardiac sounds (A_c).[7,8] Next, the three-digit code is converted to its corresponding KM grade (Table 3).

Signal grading – two-dimensional echocardiography

Two-dimensional imaging is gaining popularity over aural Doppler scanning. The grading scales are still evolving, as is appropriate for advances in the technology. Again, while a number of scales have been published, the original and expanded forms of the Eftedal-Brubakk (EB) scale are most widely used (Tables 4 and 5).[9–11] There are published data showing the association of Spencer and KM grades with the incidence of DCS[1,2] and demonstrating the correspondence between the EB scale and the Spencer and KM scales.[2,12]

Modifications that subdivide existing grades within well-established grading scales are potentially useful to take advantage of future, improved detection methodologies. Such expanded scales can be collapsed back to the original grades for comparison with previous studies and validation data.

Table 3
Conversion of KM codes (fpA/fdA) to KM Bubble Grades

fpA fdA	Bubble grade	fpA fdA	Bubble grade	fpA fdA	Bubble grade	fpA fdA	Bubble grade
111	I-	211	I-	311	I	411	II-
112	I	212	I	312	II-	412	II
113	I	213	I+	313	II	413	II+
114	I	214	II-	314	II	414	III-
121	I+	221	II-	321	II	421	III-
122	II	222	II	322	II+	422	III
123	II	223	II+	323	III-	423	III
124	II	224	II+	324	III	424	III+
131	II	231	II	331	III-	431	III
132	II	232	III-	332	III	432	III+
133	III-	233	III	333	III	433	IV-
134	III-	234	III	334	III+	434	IV
141	II	241	III-	341	III	441	III+
142	III-	242	III	342	III+	442	IV
143	III	243	III	343	III+	443	IV
144	III	244	III+	344	IV-	444	IV

Table 4
Eftedal-Brubakk scale[10]

Grade
- 0 – no observable bubbles
- I – occasional bubbles
- II – at least one bubble every four cardiac cycles
- III – at least one bubble every cardiac cycle
- IV – at least one bubble·cm^{-2} in every image
- V – whiteout; single bubbles cannot be discriminated

Table 5
Expanded Eftedal-Brubakk scale (fairly widely published [11,12])

Grade
- 0 – no observable bubbles
- I – occasional bubbles
- II – at least one new bubble every four cardiac cycles
- III – at least one new bubble every cardiac cycle
- IV a – at least one bubble·cm^{-2} in every image
- b – at least three bubbles·cm^{-2} in every image
- c – near whiteout; individual bubbles still discerned
- V – whiteout; individual bubbles cannot be discerned

RECOMMENDATION 2

Doppler signal grading should employ either the Spencer or KM scales. When the KM scale is used, ideally the KM grades converted to Spencer grades should also be reported. Two-dimensional imaging should use an original or expanded EB scale. Modifications of these scales or alternative scales should be clearly explained and validated to justify use.

Subject selection

There is a high degree of inter-subject variability in intravascular bubble development; some individuals bubble readily while others are relatively resistant to bubbling.[13,14] This reality is best handled by study designs in which individuals serve as their own controls. With this approach, the relative risk of different exposures can be more effectively assessed. Bubble data are far less appropriate to establish absolute risk.

RECOMMENDATION 3

Employ repeated measures designs, with subjects serving as their own controls to improve the assessment of relative risk.

Monitoring site selection

The standard site for Doppler monitoring of venous gas bubbles in decompression studies is the precordium, as this captures the entire systemic venous return. Subclavian monitoring is sometimes used for additional information. The standard for two-dimensional echocardiographic imaging of the heart is the apical long-axis view, which allows assessment of bubbles in the entire systemic venous return and any subsequent systemic arterialization of bubbles. Subcostal monitoring may be appropriate for smaller individuals. Parasternal views do not provide comparable fields to the apical or subcostal views for bubble grading. Optimal windows for ultrasonic measures can vary on an individual basis, requiring technicians to adjust their approach on a case-by-case basis.

RECOMMENDATION 4

The precordial site should be used as the standard for Doppler monitoring. Subclavian monitoring may be useful in providing additional information. The apical window should be used as the standard for two-dimensional imaging.

Body position

Numerous scanning positions have been reported: standing, seated, supine, and left lateral decubitus. Variation does make cross-study comparison more difficult.

RECOMMENDATION 5

Body position during monitoring should be standardized where practical and fully described in reports.

Provocation

Bubble measurements can be made at the end of a period during which subjects remain at rest or following active provocations that can promote showers of detectable bubbles. These provocations include intentional coughing, deep knee bends, and single, paired, or sequential limb movements. Separate measurements may be made after different provocations, particularly separate upper and lower limb movements, which can produce distinctly different results. Resting bubble measurements and provocation bubble measurements have different associations with the probability of DCS; ideally, measurements should be made following both rest and provocation.[1,2]

RECOMMENDATION 6

Resting measurements should always be made. The minimum period of rest prior to the measurement should be standardized and reported. When measurements following provocation are collected, the provocation should be standardized and clearly described. Irrespective of whether the analysis focuses on rest or provocation measurements, both should be reported.

Monitoring duration

The period following decompression during which bubble measurements are made should be designed to ensure capture of maximum bubble grade and other metrics of interest. These other metrics may include times of onset and disappearance of detectable bubbles (the latter often demonstrated by two consecutive grade zero scans). The duration of monitoring can vary appreciably as a function of the exposure variables, including: the dive profile; physical exercise; thermal stress and breathing gases. The time course for bubble onset, maximum grade and waning is not always predictable.[15]

RECOMMENDATION 7

As a standard rule, measurements should be conducted for 120 minutes from the completion of the decompression period. Shorter monitoring periods should be clearly justified. Consideration should be given to extending monitoring periods if bubbles persist at the end of the planned period. Pilot trials may be warranted to establish appropriate monitoring endpoints for exposure profiles known or expected to produce bubbles beyond 120 minutes.

Frequency of measurements

The frequency of measurements during the monitoring period is important to establish confidence that a meaningful assessment has been made.[15] The substantial variability of frequency of measurements between published reports has been problematic. Infrequent measurements are operationally easier but increase the likelihood of missing periods of active bubbling and maximum grade. Frequent measurements are more operationally demanding but much more likely to capture maximum grade and temporal patterns of detectable bubbles.

RECOMMENDATION 8

The first measurements should be made within 15 minutes following decompression. During the first 120 minutes following decompression, measurement intervals should be no greater than 20 minutes. Sampling frequency may be reduced after 120 minutes following decompression. Shorter or longer sampling intervals may be warranted for some exposures and depending on the objective of the study.

Data pooling

Grade pooling may be appropriate for analyzing and reporting bubble data. A wide range of data handling practices have been employed and they are often idiosyncratic. The pooling of bubble grades should reflect meaningful clusters.[1] Grade

'zero' has a high negative predictive value for DCS and should not be pooled with other grades.[2]

RECOMMENDATION 9

Given evidence of an increased association between DCS and the highest Spencer/KM grades, pooling grades I–II and III–IV may be appropriate. Zero grades should be reported but not pooled with other grades. Wherever possible, unpooled data should be included to allow reanalysis.

Data reporting

A variety of parameters can be reported from ultrasonic imaging. Reporting multiple parameters and raw data facilitates reanalysis and potentially comparison between studies.

RECOMMENDATION 10

Standard parameters to report include time to onset of non-zero grades, time to maximum grade reached, and maximum grade for individual subjects. In addition, median grade, grade range and mode can be reported; all measured zero grades should be included in calculated summary statistics. Wherever feasible, raw data should be reported. If deemed appropriate, data transformation may be used to allow time integration of non-zero grades to be computed. Otherwise, data transformations should be used judiciously with clear justification and, in all cases, the untransformed data should also be reported.

Statistics

Bubble grades represent nonlinear ordinal data for which nonparametric analysis is appropriate. Roman numerals are frequently employed with grading scales as a reminder that computation of means and associated measures of variability are not valid with ordinal data. Transformations purported to linearize bubble data do not make the data suitable for parametric hypothesis testing. Such transformations may be useful to compute time integrals,[13,16] or for some forms of linear modelling. There is substantial inter- and intra-individual variability in maximum bubble grade produced after identical exposures, so comparative studies should be designed with enough subjects to ensure appropriate power to detect a difference of interest. One analysis of two-dimensional echocardiographic data indicated a paired sample size of 50 subjects was required for 80% power to detect a one-grade difference in VGE (two-sided $\alpha = 0.05$). [17]

RECOMMENDATION 11

Bubble grade data are most appropriately analyzed non-parametrically. Attempts to linearize bubble data should be employed cautiously. Consideration should also be given to ensure that studies are powered appropriately.

Fair interpretation

Interpretation of bubble data should be appropriately constrained, for a number of reasons:

- bubbles do not equal DCS;
- the intravascular focus of current technology provides an incomplete picture of conditions in the body;
- the standard techniques of aural Doppler and two-dimensional cardiac imaging do not allow bubble sizing;
- Doppler technology captures only a limited three-dimensional space and two-dimensional images only a slice of the three-dimension field.

Most measures are made intermittently, capturing a small percentage of total time.

While recognition of limitations is the responsibility of authors, peer reviewers should critically evaluate manuscripts for shortcomings.

RECOMMENDATION 12

The limitations of bubble data should be considered as part of any interpretation of study results. Peer reviewers must ensure that a reasonable standard has been met to justify publication.

Data preservation

Research standards typically require preservation of raw data.

RECOMMENDATION 13

Ideally, measurements conducted for research publication should be recorded and preserved for future review. This includes audio and visual files, as appropriate for the technology employed.

Evolving technology

Evolving technology is increasing instrument sensitivity, particularly with two-dimensional imaging.[18] Caution is required in pooling data between studies or in single studies employing different instruments or when comparing data taken with earlier-generation instruments.

RECOMMENDATION 14

The validity of comparing or pooling data collected by different machines must be considered cautiously. Both equipment and protocols used should be clearly described.

Ultrasound safety/influence

Clinical ultrasound is generally well tolerated by subjects/patients but the potential impact should be considered when directing ultrasound energy into any person.[19]

RECOMMENDATION 15

The intensity of sound energy introduced during ultrasonic monitoring should be kept as low as reasonably achievable (ALARA) during ultrasonic scanning. Both the mechanical and thermal indices should be considered. Scan duration should be as short as necessary.

Conclusions

The International Meeting on Ultrasound for Diving Research brought together representatives from around the world to discuss procedures used to study the effects of diving decompression. Integration of the recommendations is expected to help researchers improve the robustness of their data, improving standardization and utility. Those reviewing relevant research that uses ultrasound procedures may also benefit, recognizing issues identified as being of concern to the meeting participants. In the future, the guidelines may be refined and perhaps new methodologies developed for new and emerging technologies.

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Nicklas Oscarsson, Christine Penny, Massimo Pieri, Roswitha Prohaska, Celine Quinsac, Anders Rosen, Olle Sandelin, Göran Sandström, Fiona Seddon, Milan Sevaljevic, David Smart, Julian Thacker, Corry Van den Broek, Claire Walsh, Wilhelm Welslau, Jurg Wendling, Peter Wilmshurst and Tomi Wuorimaa.

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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 reports

The measurement of Eustachian tube function in a hyperbaric chamber using an ear canal microphone

Hans-Georg Fischer, Andreas Koch, Wataru Kähler, Michael Pohl, Hans-Wilhelm Pau and Thorsten Zehlicke

Abstract

(Fischer H-G, Koch A, Kähler W, Pohl M, Pau H-W, Zehlicke T. The measurement of Eustachian tube function in a hyperbaric chamber using an ear canal microphone. *Diving and Hyperbaric Medicine*. 2016 March;46(1):33-37.)

Objective: The purpose of this study was to further the understanding of the opening of the Eustachian tube in relation to changes in barometric pressure.

Design: An ear canal microphone was used to measure the specific sounds related to tube opening and possible eardrum movements. Five subjects with normal tube function were examined in a hyperbaric chamber (up to 304 kPa). All active and passive equalization events were recorded and correlated with the subjectively perceived pressure regulation in the measured ear.

Results: The signals recorded were clear and reproducible. The acoustic analysis distinguished between the different kinds of equalization. Subjective impressions were confirmed by the recorded frequency of acoustic phenomena (clicks). During compression, the sequence of active equalization manoeuvres was in a more regular and steady pattern than during decompression, when the click sounds varied.

Conclusion: The study established a simple technical method for analyzing the function of the Eustachian tube and provided new information about barometric pressure regulation of the middle ear.

Key words

ENT; ear; barotrauma; Valsalva manoeuvre; middle ear; physiology

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Introduction

The Eustachian tube (ET) plays an important role in the functioning of the middle ear. It is essential for pressure regulation and for the drainage of middle ear secretions by means of the ciliated epithelium and the ET muscles.[1] Previous direct or indirect measuring methods (tympanometry, tubomanometry, sonotubometry) have proven inadequate to assess tube function, either because they are unphysiological, causing obstruction of the ear canal, or because they allow no other conclusion than to confirm tube opening during testing.[2,3] Moreover, these methods only provide a snapshot of tube ventilation. Existing methods cannot be used to examine tube function over longer periods of time and during exposure to changing pressure conditions as encountered when diving or during flight.

Knowledge about long-term tubal function would help to better understand inflammatory diseases of the middle ear, as many of these diseases are a direct or indirect consequence of chronically impaired ventilation. In addition, ET dysfunction may negatively affect the postoperative outcome of tympanoplasty or balloon Eustachian tuboplasty.[4–6] Reliable information about ventilation dysfunction could allow for more targeted planning of ear surgery. However, even examinations for professional groups exposed to pressure, such as pilots or divers, currently lack a method that provides long-term measurements in support of tube function diagnostics. In the German Armed Forces, assessment of Eustachian tube function in hyperbaric chamber tests is based entirely on clinical aspects, i.e., occurrence of ear pain during compression.

A practical, physiological, long-term measuring method would help to obtain much needed data and potentially improve diagnostics. The new assessment method presented here works by recording and analyzing acoustic signals in the ear canal. The method is based on the phenomenon that specific sounds ('clicks') can be registered along with openings of the ET. There are different explanations in terms of the origin of such sounds. On the one hand, these sounds were considered as related to movements of the tympanic membrane (TM) during pressure equalization. On the other hand, there are strong indications that the clicks correlate with the action of the tube-opening muscles (*m. tensor* and *m. levator veli palatini*).

This phenomenon served as the starting point for our study, which aimed to record the movements of the TM with an ear canal microphone (ECM) and establish this method as a practical way of obtaining long-term measurements.

Methods

SUBJECTS

Informed consent of the subjects was obtained in accordance with the Helsinki declaration. Before the tests inside the pressure chamber were conducted, the reproducibility of the method was validated in 14 subjects with normal ET function (three women, 11 men; median age 38, range 30 years) at standard atmospheric pressure while these subjects performed two methods of active equalization. Active equalization by means of the Valsalva manoeuvre was performed by closing the mouth and pinching the nose closed while trying to exhale. The subjects stopped exhalation when they perceived a popping sound of the TM. Active equalization by moving their soft palates was performed using a movement similar to yawning. Seven subjects who were unable to clear their ears acted as a control group.

For the pressure studies, five healthy volunteers (all male, median age 26, range 22 years) with normal ET function were compressed in the Hydra 2000 hyperbaric chamber (Haux-Life-Support, Karlsbad, Germany) These five subjects were experienced pressure chamber personnel and met the previously described prerequisites. Experienced pressure chamber personnel were chosen because they are familiar with the increasing feeling of pressure in the middle ear and know how to perform various techniques of pressure equalization. They were familiar with the test situation and the test environment.

EAR CANAL MICROPHONE (ECM)

A lavalier microphone (Sennheiser, Wennebostel, Germany) was used as the ECM. The lavalier was connected to a tubular earpiece that was tightly plugged into the ear canal in a fixed position to ensure consistent placement (Figure 1). The tube system of the earpiece had an additional perforation to allow for changes in ambient pressure. The microphone was brought as close as possible to the eardrum. The distance between microphone and TM was less than 2 cm. The ECM recorded the sounds that were created in the ear canal by pressure equalization as acoustic signals and transformed them into electrical signals using the built-in audio amplifier of the computer and audio-processing software (Ableton Suite 8.2.1).

To examine the effect of different distances between the microphone and the TM, we compared two acoustic tubes with lengths of 1.5 and 3.0 cm respectively. To analyze the potential effect of patient movements or movement of the ECM inside the ear canal on acoustic signals, we asked the subjects to move their heads from left to right and back ten times.

Perforated, commercially available ear defenders were placed over the ears and the ECM to block out background noise caused by the pressurization of the chamber. The electrical signals of the ECM were transmitted through the hull of the chamber via a flange connection and then amplified outside by a computer-integrated amplifier. The measurements were limited to the examination of one ear only (signal 1). By means of a hand-held switch, the subject transmitted a second signal to provide information on subjectively perceived pressure regulation in the measured ear (signal 2). At the same time, a piezoresistive, absolute pressure sensor (type 4005B) inside the pressure chamber transmitted the actual chamber pressure to an external amplifier (type 4618A0, Kistler, Winterthur, Switzerland) (signal 3) (Figure 1). All three recorded signals were converted into digital information by a digital oscilloscope using an analogue-to-digital converter (PowerLab 8/35, ADInstruments, Castle Hill, Australia). They were simultaneously analyzed using a suitable data processing programme (LabChart version 7.0.2). The oscilloscope displayed the voltage change (in mV or V) over time (in ms). During the pressurization cycle, the subject and their equalization behaviour were monitored by an inside observer and recorded by a video camera.

Voltage and time data are reported as mean ± SD, rounded to the nearest whole numbers.

HYPERBARIC PROTOCOL

The pressure chamber protocol started with the compression of the subject to 304 kPa with a duration of descent of 3 minutes. The participant then spent 3 min at this pressure level, before ascending to a normobaric environment during the subsequent decompression phase (duration of ascent: 6 min). To compensate for the volume changes during compression, pressure was actively (voluntarily) equalized only by moving the soft palate whenever the subject felt the need to equalize the pressure. In the decompression phase, the necessary equalization of the middle ear occurred passively (involuntarily) via the tube.

Results

Both the ECM and the pressurization cycle were well tolerated by all subjects. The subjects were able to insert the earpiece themselves and it remained in the desired position for the duration of the measurement in all cases. The signals recorded by the ECM during the pre-tests were clear and reproducible. The recorded sounds always coincided with the performed manoeuvre.

Differences in tube length caused only minor changes in the recorded voltage peaks but no changes in duration of the acoustic signal recordings. Head movements were found to cause no errant signals, although the subjects did not move their heads during measurements in the hyperbaric chamber.

During acoustic analysis in the control group at normobaria, no acoustic signals could be registered during the attempted

Figure 1
Schematic drawing of the test assembly; image of seated subject inside the hyperbaric chamber of the Naval Institute of Maritime Medicine

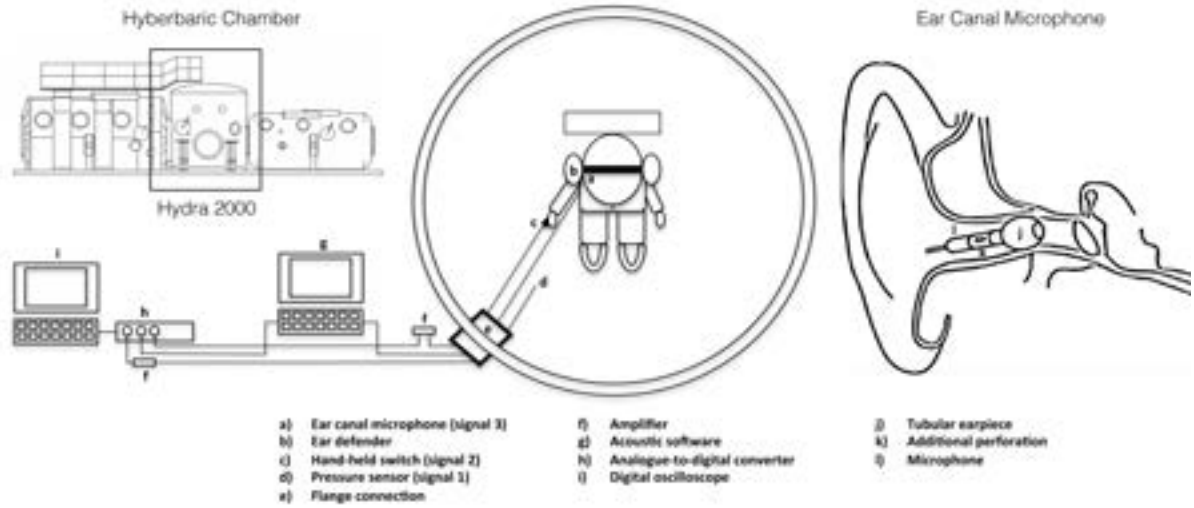


Figure 2
Voltage change caused by eardrum movements as a result of soft palate movement

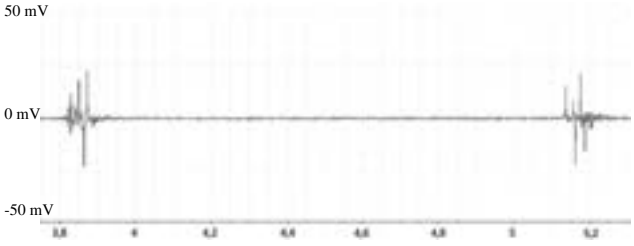


Figure 3
Voltage change caused by eardrum movements as a result of a Valsalva manoeuvre

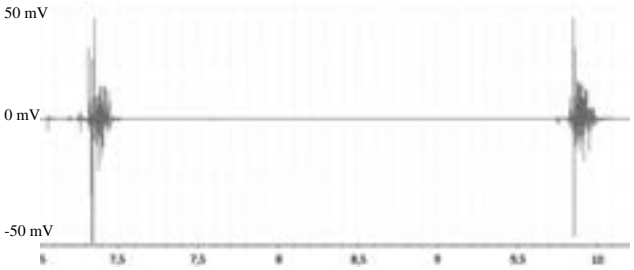
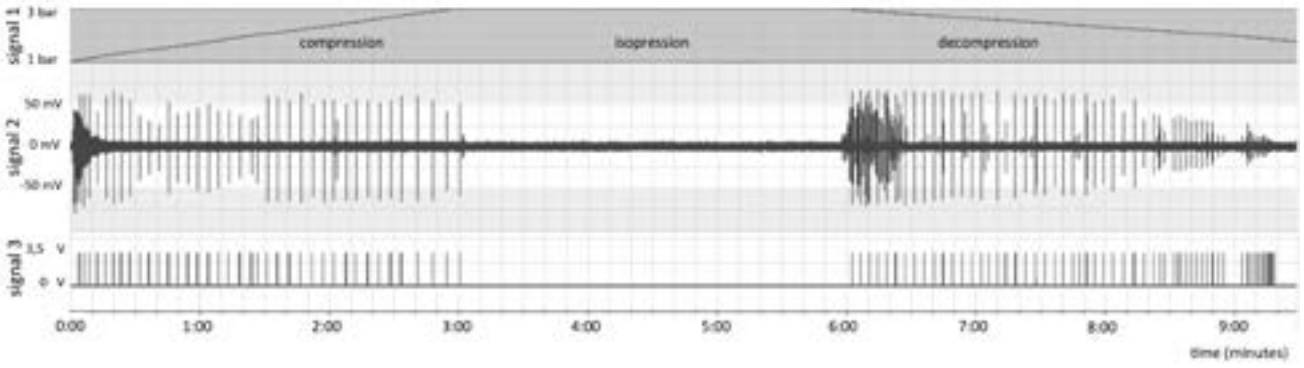


Figure 4
The captured signals during the pressurization cycle of a single individual; the voltage amplitude of passive equalization is similar to the voltage amplitude of active equalization; however, the amplitude and interval length decreases towards the end of the decompression phase; the diagram also shows the distorting effect of background noise during the early compression and decompression phase as well as a constant residual noise level



Valsalva or moving their soft palates. In subjects with normal ET function, we were able to differentiate between pressure equalization achieved by performing a Valsalva or by movements of the lower jaw. This difference could also be seen in the typical voltage configuration. The oscilloscopic representation of the characteristic popping sound caused by movements of the soft palate consistently showed a cluster with a mean value for amplitudes of 85 ± 45 mV and a

duration of 71 ± 32 ms (Figure 2). In comparison, the signals produced when the Valsalva manoeuvre was performed had a voltage amplitude that was about twice as high (180 ± 62 mV) and lasted twice as long (192 ± 60 ms) (Figure 3). The sound pattern showed a multi-peak configuration, with maximum displacements at the beginning of the cluster and subsequent peaks only one third of the magnitude of the first displacements.

The signals collected during the pressurization cycle showed the same characteristics. The recorded sounds coincided with the subjective signals the participant transmitted with the hand-held switch (more than 95%) as well as with the pressure equalization behaviour as recorded on video. During the three-minute descent, the tube opened 39 ± 6 times on average. The intervals between tube openings were regular and lasted 3–5 seconds.

The patterns obtained from the captured signals during decompression varied between subjects. The average number of passive equalization events was 76 ± 18. Amplitude size and interval length decreased continuously after the first third of the ascent phase (Figure 4). In one subject, one ear exhibited a considerably higher frequency of passive pressure equalization with time intervals as short as 100 ms. Owing to the high frequency of events (>> 150), the subject was unable to give clear push-button signals. The subject perceived the events as an intermittent, soft bubbling sound. The differences in passive equalization between different subjects as described above were also found when comparing the left and right ear of individual subjects. As background noise was considerable, especially during initial compression and decompression, we were unable to completely avoid distortions of the captured acoustic signals despite using ear defenders.

Discussion

The idea of utilizing the sounds related to openings of the Eustachian tube during middle ear ventilation, e.g., as induced by a Valsalva manoeuvre, is not new. The Toynbee tube is widely known in ENT medicine and allows the medical professional to hear the characteristic sounds when the tube opens. These acoustic phenomena may be partially related to inward/outward movements of the TM. However, studies on the acoustic phenomena occurring during myoclonic contractions of the soft-palate muscles give a different explanation. This is explained as a sudden breakdown of the surface tension of the ET during its opening.[7,8] From personal experience and our measurements we strongly support this theory. The ECM presented in this study builds on this idea and makes use of modern technological possibilities for acoustic detection and recording.

Similar approaches have used other methods such as sonotubometry. However, even recent improvements in sonotubometry using perfect sequences only provide an average concordance with ET opening of 74%.[4] In contrast, the described technique offers considerably more reliable information on successfully performed pressure equalization.

The method represents an indirect approach to measuring ET tube function but meets two important prerequisites to qualify for experimental testing as a dynamic, long-term measuring method. Firstly, pressure equalization was physiologically provoked by using a hyperbaric chamber. Secondly, using the ECM leaves the ear canal unobstructed and thus allows for continuous pressure equalization and therefore natural movement of the TM. In another study, similar conditions were met using a differential manometer in the external ear canal that registered rapid pressure changes caused by movements of the TM.[9] In contrast to our study, a hypobaric chamber was used, with smaller volume changes (decompression to 88 kPa, volume expansion of 15%). Other methods have been based on mechanical and optical measurements of TM movement.[10–12] These, however, encountered problems owing to difficulties in placing the sensors. Our study allowed the ECM to be positioned by the subjects themselves and we encountered no sensor displacements.

Another method using TM displacement measured with a loudspeaker and microphone has also been described.[13] During two one-minute measurements, only comparatively small pressure changes were simulated and passive pressure equalization was shown in a schematic representation (± 2 kPa, ± 25% volume difference). In our study, we were able to show active and passive equalization under greater ambient pressure changes. It was also possible to differentiate consistently and clearly between two types of ear clearing. The passive equalization variant with very short and frequent ET opening seen in our study may indicate that the ET in divers functions exceptionally well.

Furthermore, the decreases in amplitude and interval of the recordings of ET opening after the first third of decompression might be explained by more frequent movements of the TM due to the increase in volume changes near the surface, according to Boyle's law. Our findings also support the statement that opening of the ET is similar to a reflex mechanism with relatively constant duration.[14] That study concluded that, in order to equalize higher pressure gradients, a series of ET openings is needed, rather than the tube opening for an extended period of time.

Conclusion

An ear canal microphone provided objective, quantitative and reproducible recordings related to ear clearing manoeuvres at ambient pressure and during chamber compressions to 304 kPa.pressure. Although there is room for some technical improvements, the results achieved so far have

demonstrated the feasibility of the method. This new method allows for new ways of evaluating ET function, e.g., in long-term measurements, during pressure equalization tests or during compression chamber examinations. The method is suitable not only for aviation and diving medicine but could conceivably be applicable in otology in general. For this purpose, the method requires further development. Similar to long-term ECG or blood pressure measurement, this method could eventually be used for actual long-term measurement to record if and how often a patient's Eustachian tube opens under normal and changing pressure conditions.

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Footnote: Supplementary audio material can be provided by the authors on request.

A modified device for continuous non-invasive blood pressure measurements in humans under hyperbaric and/or oxygen-enriched conditions

René van der Bel, Bart C Sliggers, Marc J van Houwelingen, Johannes J van Lieshout, John R Halliwill, Robert A van Hulst and C T Paul Krediet

Abstract

(van der Bel R, Sliggers BC, van Houwelingen MJ, van Lieshout JJ, Halliwill JR, van Hulst RA, Krediet CTP. *Diving and Hyperbaric Medicine*. 2016 March;46(1):38-42.)

Background: It would be desirable to safely and continuously measure blood pressure noninvasively under hyperbaric and/or hyperoxic conditions, in order to explore haemodynamic responses in humans under these conditions.

Methods: A systematic analysis according to 'failure mode and effects analysis' principles of a commercially available beat-by-beat non-invasive blood pressure monitoring device was performed using specifications provided by the manufacturer. Possible failure modes related to pressure resistance and fire hazard in hyperbaric and oxygen-enriched environments were identified and the device modified accordingly to mitigate these risks. The modified device was compared to an unaltered device in five healthy volunteers under normobaric conditions. Measurements were then performed under hyperbaric conditions (243 kPa) in five healthy subjects.

Results: Modifications required included: 1) replacement of the carbon brush motorized pump by pressurized air connected through a balanced pressure valve; 2) modification of the 12V power supply connection in the multiplace hyperbaric chamber, and 3) replacement of gas-filled electrolytic capacitors by solid equivalents. There was concurrence between measurements under normobaric conditions, with no significant differences in blood pressure. Measurements under pressure were achieved without problems and matched intermittent measurement of brachial arterial pressure.

Conclusion: The modified system provides safe, stable, continuous non-invasive blood pressure trends under both normobaric and hyperbaric conditions.

Key words

Patient monitoring; hyperbaric facilities; cardiovascular; physiology

Introduction

Arterial pressure is a highly controlled variable, and its responses to environmental stresses can provide insights into both normal physiological adaptations to these environments, and identify pathophysiological responses.[1–3] Thus, in basic and applied human research and in clinical settings there is a need for a safe, non-invasive, continuous blood pressure measurement system which can be used under hyperbaric and/or hyperoxic conditions including for haemodynamic monitoring in remote situations, where invasive measurements are unavailable (e.g., in the off-shore industry). Devices used under hyperbaric and/or hyperoxic conditions must meet strict safety requirements to avoid pressure failure and spark formation.[4,5] At present, devices used to monitor critically-ill patients are not designed to withstand hyperbaric pressurization and are associated with an increased risk of fire in a pressure chamber.[4,6,7]

Several blood pressure monitoring options are available for use in hyperbaric chambers.[6,7] However, these are either invasive or measure only intermittently; there is no system available that enables continuous, non-invasive monitoring. Our aim was to perform a systematic analysis of a commercially available, beat-by-beat, non-invasive blood pressure monitor according to 'failure mode and effects analysis' (FMEA) principles,[8] and determine whether and how it could be modified to safely and accurately operate under hyperbaric and/or hyperoxic conditions.

Methods

The Portapres™ (Finapres Medical Systems, Amsterdam, The Netherlands) is a commercially available, ambulatory blood pressure monitoring system based on Peñáz-Wesseling finger arterial photo-volume plethysmography.[9] The system has been validated for use under various conditions such as during exercise, high altitude, and in space, and is used in a variety of clinical settings.[10–12] The system records finger arterial blood pressure from which the waveform can be passed through pulse-wave analysis algorithms to estimate changes in stroke volume, cardiac output, and peripheral resistance.[13] It is because of these unique characteristics that we considered the Portapres™ a suitable candidate for adaptation to the hyperbaric environment.

The Portapres™ system consists of a main unit weighing approximately 1.5 kg, which is typically worn on a waist belt that contains a 12-V battery pack. The front-end unit connecting the finger cuff with the main unit is worn on the wrist. The system records continuous finger arterial blood pressure at 100 Hz for up to 60 h. Recordings can

retrieved afterwards via a serial port. Also, an analogue output is available for real-time visualization of the pressure waveform. The system self-calibrates during a so-called 'physiocal'.

A 'physiocal' occurs over two consecutive beats (arterial pulse waves) during which the cuff pressure is fixed at mean pressure during the first of the two beats and a quarter of the pulse pressure lower during the second beat. Based on the plethysmograms of these two beats, the cuff pressure set point is determined.[14] At the start of each measurement a physiocal is automatically performed every ten beats and when the set point deviations between consecutive physiocals are within the accepted range, then the physiocal interval is automatically increased by ten beats up to a maximum of 70 beats. Disturbances from external factors or internal errors (as relevant to our testing) that interfere with the plethysmogram will automatically reduce the physical interval. Attainment of the maximum physiocal interval of 70 beats is, therefore, an excellent indicator that the measurement of the arterial pulse wave signal is stable and reliable.

RISK ASSESSMENT

Based on the specifications provided by the manufacturer, the Portapres™ system (Model 1, Finapres Medical Systems, Amsterdam, The Netherlands) was systematically analysed according to FMEA principles.[8] In the FMEA analysis, in case of a malfunction in the chamber, we identified the following potential failure modes related to pressure resistance and fire hazard in a hyperbaric and potentially oxygen-enriched environment:

- Spark formation: from various electric components, such as the carbon brush motorized pump and connections to the battery power supply;
- Overheating: due to increased power consumption at increasing gas densities;
- Hyperbaric implosion hazard of the gas-filled electrolytic capacitors.

A standard Portapres™ device was modified to mitigate these risks and then tested under normobaric and hyperbaric conditions.

RELIABILITY ASSESSMENT

After the necessary modifications (see Results) were made, the modified device was certified for electrical safety by our institutional Technical Safety Board and approved for research use in humans. The system was then applied in an on-going research protocol approved by the institution's Medical Ethics Committee (NL49531.018.14). All subjects gave written informed consent.

First, the modified device was exposed to a series of 15 hyperbaric challenges up to 283 kPa, while it was not connected to a human subject. Compression was achieved over fifteen minutes. The device was then kept at pressure for 90 minutes, before decompression over ten minutes. Thereafter, normal functioning of the device was verified by comparing the blood pressure readings to measurements with a standard non-portable version of the Portapres™ in five healthy volunteers (two male, three female, median age 27 (range 21–29) years) under normobaric conditions.

After correct functioning of the modified system was verified, hyperbaric measurements were performed in five subjects (four male, one female, median age 63 (range 61–68) years) and compared to intermittent brachial artery pressure using an Infinity Delta patient® monitor (Dräger AG, Germany). Measurements were considered stable and reliable when a physiocal interval of 70 beats was reached. Only after the maximal physical interval was reached, was brachial artery blood pressure measured.

STATISTICAL ANALYSIS

Data are presented as mean ± SD. Agreement between the modified and unmodified systems was assessed by Bland-Altman analysis.

Results

TECHNICAL MODIFICATIONS

To prevent failures as identified in the risk-assessment, we applied the following modifications (Figure 1):

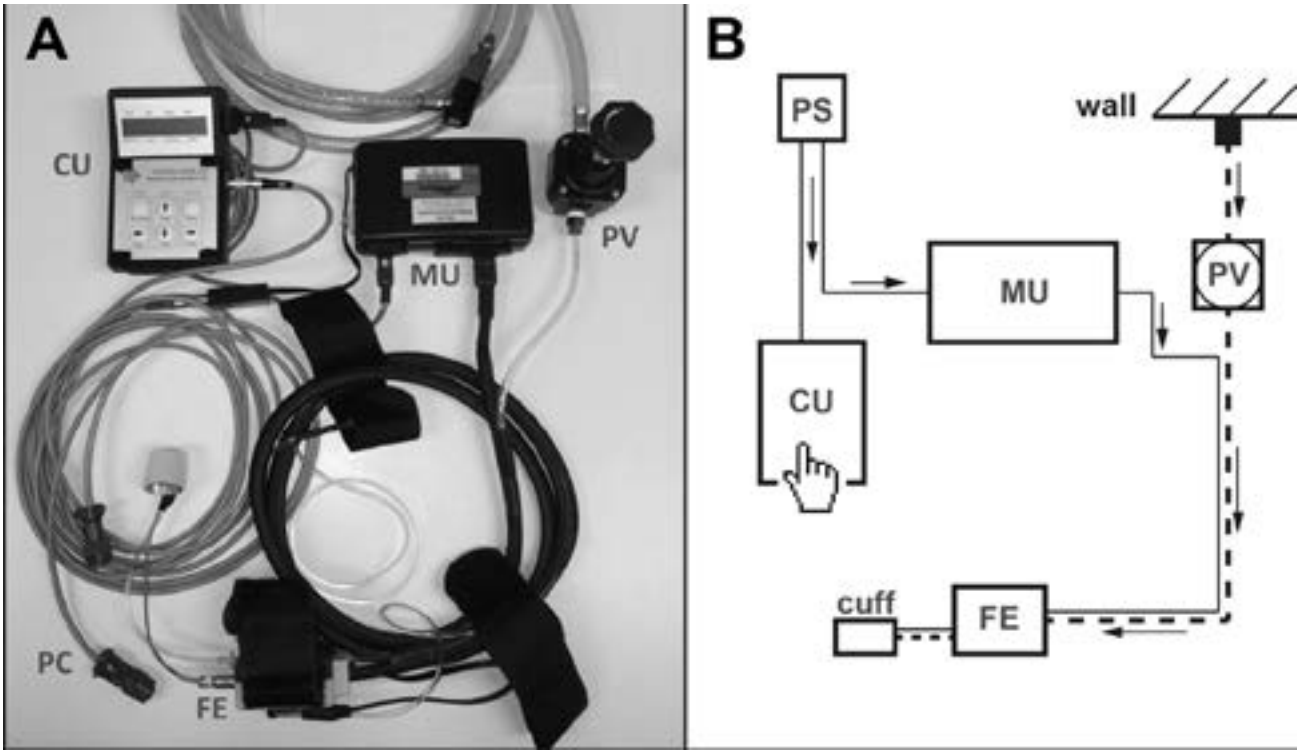
- *Spark formation*: 1) The carbon brush motorized pump was replaced by a connection to a pressurized air supply via a manually adjustable balanced pressure valve. The valve was set to 325 mbar, providing air at ≥ 60 L·min^{-1}, verified on a BP Pump 2 (Fluke Biomedical, Everett, USA) and sealed in that position. 2) The battery pack was replaced by 12-volt DC power adapters supplied by the manufacturer. These provided power through a chamber wall penetrator to a maximum rating of 2.74 A. Maximum power consumption by the device is 0.4 A.
- *Overheating*: Replacement with the air supply also eliminated this risk.
- *Hyperbaric implosion*: hazard of the gas-filled electrolytic capacitors: all gas-filled capacitors were replaced by solid-state equivalents.

Replacement of the motorized pump also reduced the power consumption of the device, meaning that power consumption would remain well below the listed 0.4 A.

Completion of these modifications by an experienced technician took approximately 15 man-hours. Applying them voided the manufacturer's warranty and CE certifications on the device; however, the modifications adhere to the EU

Figure 1

The Portapres™ system and modification; **(A)** modified Portapres™ system with main and control unit (MU, CU), front-end with cuff (FE), power cables (PC) for hyperbaric chamber power supply, and pressure valve (PV) connection to the air supply; **(B)** schematic overview with power supply (PS) and electrical current (solid lines) and air flow (dashed lines) indicated from wall to each subunit



guideline for medical devices 93/42/EEC, which allows the use of aftermarket-adapted devices to be used for research purposes. Clinical application can only be implemented after the CE certification of the device is extended to include its use under hyperbaric conditions.

DEVICE RELIABILITY

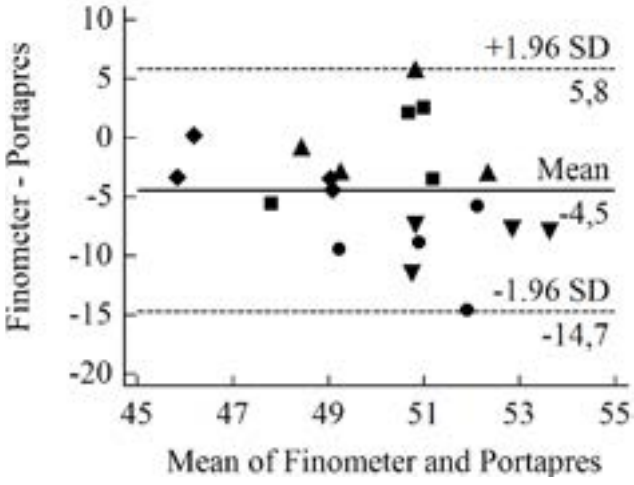
Under normobaric conditions, systolic/diastolic blood pressure was 116 ± 9/64 ± 10 mmHg, measured by the modified device, compared to 117 ± 8/69 ± 7 mmHg systolic/diastolic blood pressure using the unmodified control device, a mean difference of 1.0/4.9 mmHg systolic/diastolic blood pressure (Figure 2).

At 243 kPa in five subjects, average systolic/diastolic blood pressure was 137 ± 12/88 ± 7 mmHg compared to brachial artery measurements of 143 ± 16/93 ± 7 mmHg systolic/diastolic blood pressure, a mean difference of 6.5/4.9 mmHg systolic/diastolic pressure.

During all recordings the maximum physiocal interval of 70 beats was reached. Data were successfully stored on the device and off-loaded after the subjects had left the hyperbaric chamber.

Figure 2

Bland-Altman analyses of repeated measures, comparing consecutive continuous blood pressure readings from the modified Portapres™ system and an unmodified Finometer™ in five healthy subjects; pulse pressure was determined in four evenly distributed 'physiocal' intervals consisting of 70 beats in each recording; shapes indicate sets of repeated measurements per subject recording

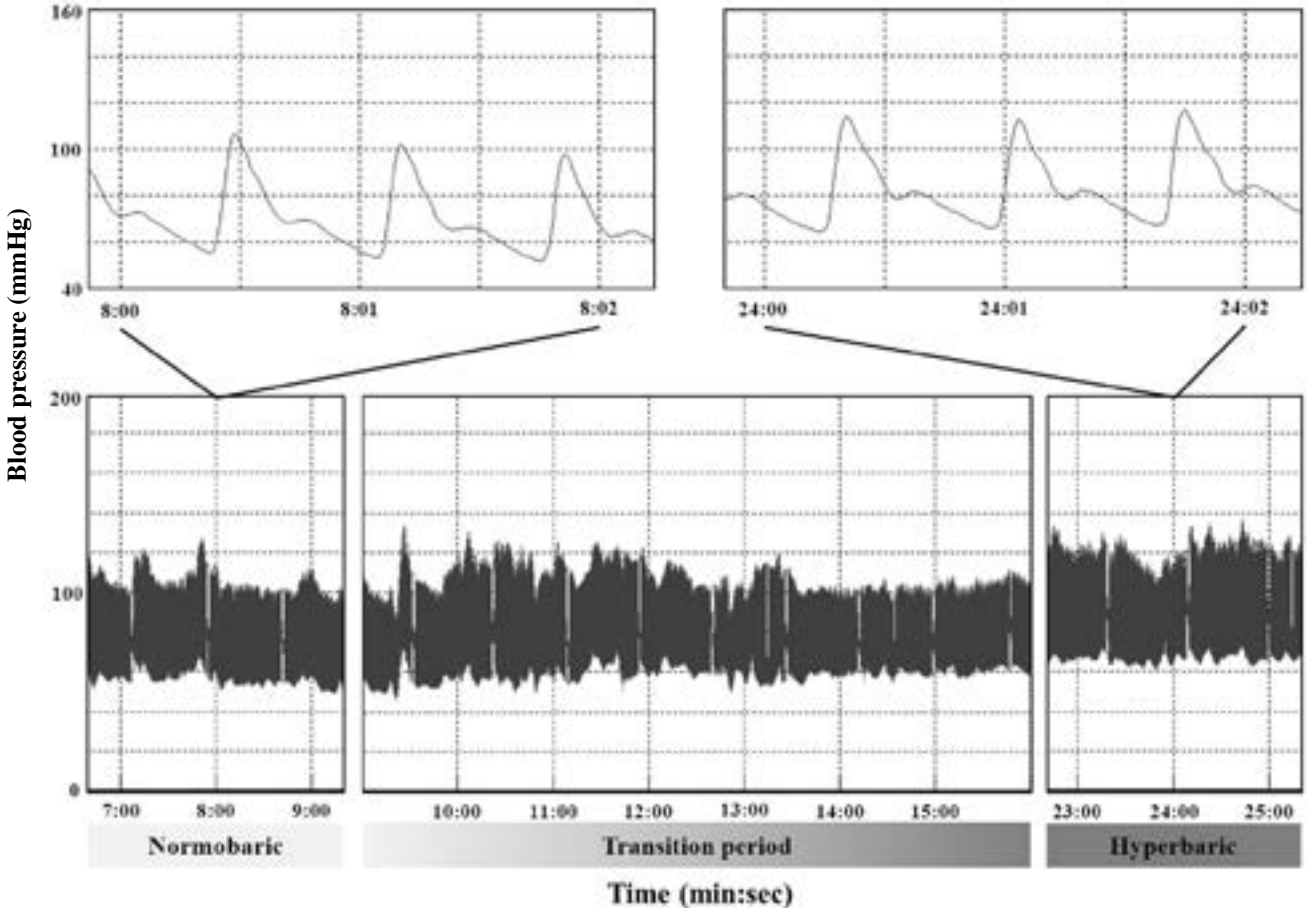


Discussion

Devices used under hyperbaric and/or hyperoxic conditions must meet strict requirements to avoid pressure failure, spark formation and overheating.[1,2] Previously continuous, non-invasive blood pressure monitoring has not been available under hyperbaric, hyperoxic conditions. A modified Portapres™ system can be used safely in a hyperbaric

Figure 3

Blood pressure recording under normo- and hyperbaric conditions; raw data from one continuous Portapres™ blood pressure recording during a normobaric (left upper and lower panels) and hyperbaric period (right upper and lower panels) in a healthy subject; included is the transitional phase during pressurization of the hyperbaric chamber from 101.3 kPa to 243 kPa in 6 minutes (middle lower panel); the upper panels depict detailed visualizations of the recorded pulse wave



chamber to provide continuous, non-invasive blood pressure monitoring. Tests in a small number of subjects demonstrate that the modified system functions normally and provides stable blood pressure readings under hyperbaric conditions at 243 kPa. Minor differences found all fall within the expected short-term physiologic variance in blood pressure as reported previously.[15]

Our aim was to perform a systematic analysis of a commercially available monitoring device according to FMEA principles to determine whether and how it could be modified to safely and accurately operate under hyperbaric and hyperoxic conditions. In all cases, once identified, components 'at risk of failure' were readily replaced with 'low risk of failure' alternatives that did not impact the overall function of the device. A FMEA approach could be applied to solve similar problems of adapting existing systems to the study of humans in technologically adverse environments. Because of the modifications, the Portapres™ device is no longer truly a portable system since both electrical power and pressurized air are no longer on board the device but, instead, are provide via chamber penetrators (or in the case of the pressurized air supply, from a gas cylinder). We did not consider preservation of portability as an important redesign constraint as our goal was to enable measurements within a hyperbaric chamber.

Limitations of this study include the absence of validation against invasive arterial monitoring in the hyperbaric chamber. The reason for this is that few patients with an intra-arterial line undergo hyperbaric treatment in this centre.

Conclusion

We have modified and tested a beat-by-beat non-invasive blood pressure monitoring device (Portapres™) for safe use in hyperbaric and/or oxygen-enriched environments. This provides new opportunities for exploring cardiovascular and respiratory regulation and their possible interactions in health and disease associated with these environments. It may also allow patients who require more advanced monitoring to undergo hyperbaric oxygen therapy without the necessity for invasive arterial pressure monitoring.

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Conflict of interest

MJvH is employed at Finapres Medical Systems.

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World as it is

The use of hyperbaric oxygen treatment for sudden sensorineural hearing loss in Europe

Günalp Uzun, Mesut Mutluoglu and Suleyman Metin

Abstract

(Uzun G, Mutluoglu M, Metin S. The use of hyperbaric oxygen treatment for sudden sensorineural hearing loss in Europe. *Diving and Hyperbaric Medicine*. 2016 March;46(1):43-46.)

Background: The aim of this study was to identify the practice differences in the use of hyperbaric oxygen treatment (HBOT) for sudden sensorineural hearing loss (SSNHL) in Europe.

Materials and methods: A questionnaire comprising nine questions was built using the surveymonkey.com website. The medical directors of hyperbaric centres in Europe were invited by e-mail to complete the survey.

Results: A total of 192 centres were invited to participate, of which 80 (41.6%) from 25 countries responded. Of these, 70 were using HBOT for SSNHL. The number of patients with SSNHL treated in these centres over a 12-month period ranged from 2 to 150 (mean 34, median 18). The majority of these centres (44 of 60) were accepting patients if they applied within 30 days of SSNHL diagnosis; 26 of these 60 centres were also treating patients presenting with tinnitus in isolation. The number of treatments ranged from five to 40 (mean 19, median 20). Forty-three of 56 centres used one session a day, whilst 13 reported using twice daily sessions for at least part of the HBOT course. Treatment duration varied between 60 and 140 minutes, and treatment pressure between 151 and 253 kPa.

Conclusion: This study has documented a wide range of approaches to the treatment of SSNHL with HBOT across Europe.

Key words

Hearing; hyperbaric oxygen therapy; hyperbaric facilities; survey

Introduction

Sudden sensorineural hearing loss (SSNHL) is characterized by a hearing loss of at least 30 dB in three sequential frequencies in the standard pure-tone audiogram developing over three days or less.[1] Hyperbaric oxygen treatment (HBOT) has been recommended in the management of SSNHL.[2–4] Although the application of HBOT appears to significantly improve hearing loss for people with early presentation of idiopathic SSNHL, the clinical significance of the level of improvement remains unclear, and a specific treatment for SSNHL is missing.[1–3] The European Committee for Hyperbaric Medicine (ECHM) and the Undersea and Hyperbaric Medicine Society (UHMS) both recognize SSNHL as an indication for HBOT and, accordingly, have released recommendations on various aspects of its utilization.[5,6] The aim of this study was to identify the practice differences in the treatment of SSNHL with HBOT amongst European hyperbaric centres.

Methods

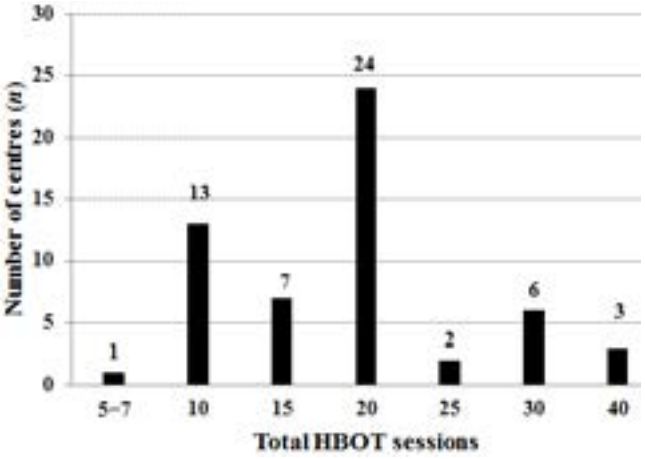
This study was conducted between 01 September and 30 November, 2014. Using a commercial online survey website,[7] we created a questionnaire* consisting of a total of nine questions. Whilst some of the questions were mandatory, others were not and response rates varied among the questions. To define our target list of facilities, we accepted inclusion in the directory of European HBOT centres on the oxynet.org website.[8] We excluded centres that did not have an e-mail address in the directory. The directors were invited to participate in this study by an e-mail containing a link directing the responders to the survey website. Non-responders were re-invited to participate in the survey at weeks two and four after study onset and the survey was closed one month after the last invitation. An Excel® spreadsheet of the answers was created and the results analyzed using basic descriptive statistics.

Results

A total of 192 centres were invited to participate, of which 80 (41.6%) from 25 different countries responded. Of these, 70 were using HBOT for SSNHL. The number of patients treated with SSNHL in the past year in each centre ranged from 2 to 150 (mean 34, median 18). Almost half of the centres responding to this specific question (26 of 60) also reported treating patients presenting with tinnitus in isolation. Twenty-six out of 56 centres noted that the treatment of SSNHL with HBOT was not covered by their national health care services. While the maximum permissible delay time to HBOT varied among centres, the majority (44 of 60) limited treatment to patients presenting within 30 days (19 within 14 days or less) of disease onset, whilst ten accepted patients even after a delay to treatment of ≥ 90 days.

*** Footnote:** Survey questionaire available on request from authors.

Figure 1
Total number of hyperbaric oxygen treatment (HBOT) sessions given for sudden sensorineural hearing loss at 56 European hyperbaric centres



The frequency of HBOT delivery varied between centres; 43 of 56 were giving one session a day whilst 13 used twice daily HBOT. Of these, ten were using twice daily HBOT only in the first three to five days, then switching to once-daily treatments thereafter. The total number of HBOT sessions delivered per patient ranged from five to 40 sessions (mean 19, median 20; Figure 1).

Treatment duration and pressure differed amongst the centres, ranging between 60 and 140 minutes and between 151 and 253 kPa, respectively. The majority of centres (48/56) were using a treatment pressure of 243/253 kPa, four were using 202 kPa, two 182 kPa and two others 151 kPa. Twenty-nine of 56 centres reported using between 90 and 105 minutes of HBOT, 20 between 120 and 140 minutes and seven 60 to 75 minutes of HBOT. The most frequently used treatment protocol was 90 minutes at 243/253 kPa by 19 of 56 centres. Forty-four of 55 centres expressed interest in participating in studies that would compare the effectiveness of different HBOT protocols in SSNHL.

Discussion

Although HBOT is now recognized as a treatment option for SSNHL by a number of national and international medical societies,[3,5,6] this study demonstrates that there are still hyperbaric centres in Europe (10 of 80 responders) that do not treat SSNHL. Given that centres that do not treat SSNHL would be less likely to respond to this survey, this proportion is almost certainly a considerable underestimate. It is possible that lack of coverage of this indication by the health care services in several countries may, in part, account for this situation.

Whilst SSNHL has been an accepted indication for HBOT (Type 2 recommendation) by the ECHM since 1994, no specific recommendations have been released concerning the maximum permissible delay duration or the treatment protocol.[5] On the other hand, the UHMS recommends its use in patients with a hearing loss greater than 40 dB who present within 14 days of disease onset.[6] Additionally, the UHMS suggests daily treatment at 202–253 kPa for 90 minutes for a total of 10 to 20 sessions.[6] In the current study, only 17 of 56 of responders were complying with both parameters of these UHMS recommendations.

Delay to HBOT is known to negatively affect treatment outcomes in patients with SSNHL.[9–11] HBOT started two weeks after the onset of the hearing loss significantly reduced the likelihood of healing.[12] In prospective randomized trials that showed beneficial effects for HBOT in SSNHL, delay to HBOT was between 48 hours and 14 days.[13–17] While current evidence, in accordance with the UHMS recommendations, indicates a benefit in the first two weeks of disease onset,[2,6] some patients presenting after this time may also experience improvement with HBOT.[18] One of the pivotal papers in this regard demonstrated that, if the onset of hearing loss was more than two but no longer than six weeks, half the cases showed a marked improvement in their hearing of more than 20 dB in at least three frequencies.[19] However, this conclusion is based on the review of observational studies rather than randomized prospective evidence.[19] The American Academy of Otolaryngology Head and Neck Foundation guideline recommends HBOT as a treatment option up to three months from symptom onset.[3]

The fact that some ENT specialists refer patients to HBOT after initial medical therapy fails, may in part account for delayed referrals. An initiative of the ECHM, the COST B14 project, has revealed that optimal cooperation between the referring ENT and the HBOT centre was crucial to minimize treatment delays.[20]

An interesting finding was the number of centres treating patients with tinnitus alone. The effectiveness of HBOT in these patents is controversial, with a Cochrane review finding no evidence to support the use of HBOT in tinnitus.[2] In addition, neither the ECHM nor the UHMS recommends the use of HBOT for tinnitus.[5,6]

The published literature on HBOT for SSNHL includes studies that utilised various treatment pressures ranging from 151 kPa to 303 kPa.[2,11–18] To our best knowledge, there has been only one study that compared the effectiveness of HBOT at different treatment pressures.[21] In this retrospective study, mean hearing gain levels in patients who received no HBOT or HBOT at 151 kPa were similar (2.6 ± 15 dB and 3.1 ± 9 dB respectively), but was significantly better with HBOT at 253 kPa (19.7 ± 23 dB). Because the baseline pure tone audiometry levels (no HBOT 32.5 ± 26.3dB; HBOT at 151 kPa 32.3 ± 27.8dB; HBOT at 253 kPa 76 ± 27.5dB) differed significantly between the groups, a firm conclusion could not be deduced from this study.

Also of note is the difference in treatment duration amongst the centres. Although we asked respondents for the 'total duration of oxygen breathing', rather than the 'total duration of the complete treatment', it is possible some centres actually reported the latter (particularly those who reported that their treatment duration with oxygen was over 120 min). The longer times in this survey may include air breaks and compression and decompression periods.

Another variation in the reported HBOT protocols was in the frequency of treatments. Whilst most centres used one session a day, some used twice-daily regimens, especially in the early part of the HBOT course. In one study of patients with SSNHL, those referred within 36 hours of exposure received twice daily HBOT for three days and once daily for an additional seven days, combined with intravenous steroid therapy followed by oral steroid therapy.[22] Patients who were referred after 36 hours received HBOT once a day for ten days combined with oral steroid therapy. While patients in both HBOT groups had better healing rates than those in a control group of patients who received oral medication only, average hearing gain and average residual hearing loss levels were similar.[22]

Our study has limitations. Although we invited non-responders to participate to the survey three times in total, the response rate remained at 41.6%. The fact that we invited centres by e-mail and not by phone, as well as language barriers, may together account for the low participation rate. Nevertheless, it was higher than a recent survey which achieved a 30% response rate from European hyperbaric centres.[23] Additionally, the rate of participation in the survey differed among countries and this may have biased our estimates of the true practice across Europe as a whole.

Conclusions

Our results showed that both the criteria for acceptance of patients with SSNHL for HBOT and the protocols used at European hyperbaric centres for this condition varied significantly. Questions remain to be answered: "*When, how and for how long should we use HBOT in the treatment of SSNHL?*" Further prospective, randomised studies are warranted.

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Practice guideline

Detection of a persistent foramen ovale using echocardiography

Peter Wilmshurst

Abstract

(Wilmshurst P. Detection of a persistent foramen ovale using echocardiography. *Diving and Hyperbaric Medicine*. 2016 March;46(1):47-49.)

Right-to-left shunts can result in decompression illness in divers and lead to a number of other conditions. Transthoracic echocardiography with intravenous injection of bubble contrast, when performed according to a well-tested protocol by trained personnel, enables the safe, simple, rapid and inexpensive detection of right-to-left shunts, the assessment of the size of the shunts and the differentiation of atrial shunts from pulmonary shunts. This article summarises the author's views on the techniques available and his preferred protocol for transthoracic echocardiography.

Key words

Bubbles; decompression; patent foramen ovale; lung; right-to-left shunt; investigations

Introduction

Right-to-left shunting of blood from the venous to arterial circulations can be the result of complex cyanotic heart diseases (such as Tetralogy of Fallot), atrial shunts that rarely cause cyanosis (i.e., an atrial septal defect, ASD, or a persistent foramen ovale (PFO) also called patent foramen ovale) and pulmonary arteriovenous shunts, which only cause cyanosis when large. The type of shunt and its size are important. It is not unusual for small pulmonary shunts to be misdiagnosed as atrial shunts. Right-to-left shunts are associated with arterial hypoxaemia when very large; paradoxical thromboembolism and cryptogenic stroke; paradoxical gas embolism and decompression illness (DCI) (particularly neurological, cutaneous and cardio-respiratory manifestations), and migraine with aura.[1–5]

In divers, venous bubbles form during decompression from many dives. In the absence of a right-to-left shunt, venous bubbles return to the right side of the heart and pulmonary arteries. During passage of the bubbles through the alveolar capillaries, gas diffuses out of the bubble down the concentration gradient so that bubbles do not get to the arterial circulation unless it was a highly provocative dive that liberated so many bubbles that the pulmonary filter is overwhelmed. When there is a right-to-left shunt, venous bubbles can circumvent the pulmonary capillary filter to reach the systemic arterial circulation and be carried to the tissues. It is postulated that if the tissues are still supersaturated with dissolved nitrogen (or other inert gas), the embolic bubbles will be amplified as nitrogen diffuses out of the tissue down the concentration gradient and, depending on the tissue, the enlarging bubbles produce the local effects that cause some forms of DCI.

PFOs are numerically the most frequent cause of right-to-left shunts. The foramen ovale is an important part of the foetal circulation in which it has the function of diverting the oxygenated blood returning from the placenta via the ductus venosus and the right atrium across the atrial septum into the left atrium and hence mainly to the developing brain. Everybody has a foramen ovale at birth. It closes during childhood and adolescence in three quarters of the population. Observational data from a large series of post-mortem examinations reported that the foramen ovale persists into adulthood in approximately one quarter of the population with a median diameter of 5 mm.[6] In divers who have a shunt-related DCI the median PFO diameter is 10 mm, which equates to a defect area four times as large.[7] Compared with half the divers who have shunt-related decompression illness, only 1.3% of the general population have a PFO with a diameter of 10 mm or larger.[7]

Paradoxical thromboembolism is the usual cardiac indication to investigate a patient for the presence of a right-to-left shunt and in those patients the great majority of shunts detected are atrial (i.e., large PFO or ASD). Pulmonary shunts account for far less than 1% of episodes of paradoxical thromboemboli. As a result, some cardiologists lack experience of detecting pulmonary right-to-left shunts and may misdiagnose a pulmonary shunt on the rare occasion that one is present. Misdiagnosis exposes patients to unnecessary risk if procedures are performed to close non-existent PFOs. Some other shunt-related illnesses are more commonly associated with pulmonary shunts. In people with shunt-related DCI and migraine with aura, 5–10% of right-to-left shunts are pulmonary.[7,8] In these conditions, pulmonary shunts are often misdiagnosed as atrial.

Investigating right-to-left shunts – what technique is optimal?

An ideal test for a right-to-left shunt should have the following features:

- It should detect all clinically significant shunts.
- It should distinguish between different types of right-

Table 1
Comparison of the qualities of different ultrasonic techniques for detecting and assessing right-to-left shunts

	Transthoracic echocardiography	Transcranial Doppler	Transoesophageal echocardiography
Sedation usually used	No	No	Yes
Views of the atria	Yes	Never	Best
Ability to quantify shunt	Good	Best	Poor
Determination of shunt site	Best	Poor	Variable

to-left shunts.
- It should be safe, simple, easy, quick and inexpensive.

The presence of a right-to-left shunt is confirmed by detection of a marker in the systemic circulation that should not pass through the alveolar capillary filter. Three ultrasonic techniques are routinely used (Table 1) – transcranial Doppler, transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE), and all are coupled with intravenous injection of a contrast medium. The best contrast consists of large numbers of microbubbles of air. Some artificial colloidal contrast media will pass through the pulmonary capillaries and produce false positive tests.

The bubble contrast is produced by pushing approximately 8 ml of sterile saline, 1 ml of air and 1 ml of the patient's blood back and forth from one 10 ml luer-lock syringe connected via a three-way tap to another syringe, until no large bubbles remain visible. It is important to use some of the patient's blood, because it stabilises the microbubbles produced, so that one gets much better contrast filling the right heart.

The three ultrasonic techniques are operator-dependent and, therefore, individual investigators have their own preferences, but the best results are obtained by strict adherence to a tested protocol. My preference is TTE with injection of bubble contrast into a left antecubital vein, as described below.

It is commonly claimed that TOE is the gold standard test for detecting a PFO and that it detects all PFOs irrespective of their size. If this were true, it would be rare for a large PFO to be missed on TOE but found using a different technique. I have closed many large PFOs when cardiologists had reassured patients that they did not have a PFO because a TOE was negative and the patient had a further event, after which my TTE with bubble contrast showed a large atrial right-to-left shunt.[9] The reasons that TOE misses some large PFOs is that the sedation used and the presence of a large probe in the oesophagus prevent patients performing manoeuvres to accentuate right-to-left shunting, such as Valsalva manoeuvres and sniffing.

TTE protocol

TTE should be performed with imaging of the heart using the apical four-chamber view. That view minimises overlap of the right and left sides of the heart and hence avoids any contrast in the left heart being obscured by a higher density of bubble contrast in the right heart. One must inject a large amount of bubble contrast into an antecubital vein. Ideally one should use a left arm vein because that is better able to detect the rare instances when there is partial anomalous systemic venous drainage to the left atrium, such as via a left superior vena cava. Contrast should be injected with the arm elevated above the level of the heart to ensure rapid drainage to the right atrium. Injection of contrast into a vein in the back of the hand should be avoided because it does not make the blood in the right atrium adequately opaque. If there are no suitable antecubital veins, the contrast should be injected into a femoral vein. But if one can get the right atrial cavity totally opaque with injection into an antecubital vein as described, my experience is that femoral vein injection has no advantage for detection and is more uncomfortable for patients.

My current protocol is to give up to six injections of contrast. The first injection is with the patient at rest and breathing normally. If no significant shunt is demonstrated at rest, the next two injections are with release of a Valsalva manoeuvre. If they are also negative, I then give injections with the patient performing a short, sharp sniff when the right atrial cavity is totally opaque. The technique should be practiced because a deep sniff will cause the left lung to come between the imaging probe and the left heart, so that the heart will be obscured. It is important that contrast is seen adjacent to the atrial septum: false negative results can be obtained if blood containing no bubbles is streaming from the inferior vena cava to prevent the area adjacent to the interatrial septum being filled with contrast. A sniff will often rectify that.

With an atrial shunt, shunting occurs in 'boluses' of bubbles crossing the atrial septum when right atrial pressure and flow are greater than left atrial. Typically that occurs when a patient or subject breathes in, releases a Valsalva manoeuvre or sniffs. This results in a 'jerky' appearance of contrast in the left heart. Pulmonary shunting builds up beat by beat in a smoother manner and also declines more gradually. Contrary to common belief, the timing of shunting after contrast fills the right atrium is not an accurate way to determine whether shunting is atrial or pulmonary. When there is a large pulmonary shunt or cardiac output is high, shunting of contrast to the left heart via a pulmonary shunt can occur within two heartbeats and very occasionally one heartbeat after the right heart has filled with contrast. Conversely atrial

shunting may not occur for several heartbeats after the right heart is opaque until the patient takes a deep breath. When there is uncertainty whether there is a pulmonary shunt, a long imaging run should be recorded to see whether bubbles are still entering the left heart when the right heart contains fewer bubbles than the left heart. Obviously that appearance can never be the result of an atrial shunt.[10]

I find that only 1–2% of patients have image quality that is inadequate for shunt demonstration and in those cases other techniques must be used. The simplest of these is to use the stand-alone continuous wave Doppler probe on the echocardiogram machine to record over a carotid artery when bubble contrast is injected intravenously.[11] If a shunt is present, this produces displays rather like transcranial Doppler with bubble contrast. If bubble contrast is injected into a left antecubital vein, it is best to image the right carotid artery to reduce the chance of interference with the carotid images as a result of reflux of contrast from the subclavian vein into the internal jugular vein. Doing that test at the time of echocardiography means that the patient does not need to come back for another investigation on another occasion if the test is negative. If the test is positive, further tests will be required to distinguish an atrial shunt from a pulmonary shunt. One can also use TOE with bubble contrast, but a negative test does not exclude a PFO.[9] Other techniques are very rarely required to detect a right-to-left shunt.

I believe that the technique we use for detecting shunts is the most accurate for a number of reasons:

- In control populations, in which about one-quarter of individuals would be anticipated to have a PFO, and in most cases they would be expected to be small in size, we have consistently found that between 24 and 28% of individuals have right-to-left shunts consistent with a PFO, and the majority of the shunts are small.[4,12]
- In populations in which we would expect there to be a high prevalence of right-to-left atrial shunts, we find such high rates. For example, in individuals with cutaneous DCI we find that 75–80% of divers have a significant right-to-left shunt.[12] In the remaining divers who have no significant shunt, their dive profiles prior to their cutaneous DCI were much more provocative, in keeping with a mechanism different from paradoxical gas embolism.[12]
- We are frequently asked to investigate divers with a history consistent with shunt-related DCI, but in whom other cardiologists have found no shunt using TOE. In them, we consistently demonstrate the presence of an atrial shunt using our technique and confirm the presence of a large atrial shunt during transcatheter closure.[9]

In conclusion, I believe that transthoracic echocardiography with intravenous injection of bubble contrast, as described, is the method of choice for investigation of patients for possible right-to-left shunts.

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Case report

Hyperbaric oxygen for the treatment of the rare combination of central retinal vein occlusion and cilioretinal artery occlusion

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Abstract

(Celebi ARC, Kilavuzoglu AE, Altiparmak UE, Cosar CB, Ozkiris A. Hyperbaric oxygen for the treatment of the rare combination of central retinal vein occlusion and cilioretinal artery occlusion. *Diving and Hyperbaric Medicine*. 2016 March;46(1):50-53.)

A 43-year-old male presented with sudden onset of painless, blurred vision in his left eye. Dilated fundoscopic examination showed signs consistent with the diagnosis of a combination of central retinal vein occlusion (CRVO) and cilioretinal artery occlusion (CLRAO). He received daily 2-h sessions of hyperbaric oxygen treatment (HBOT), 253 kPa for 14 days. At the end of the HBOT course, the patient's left visual acuity had improved from 20/200 to 20/20. Dilated fundoscopic examination showed that the intra-retinal haemorrhages in the entire retina and the retinal whitening along the course of the CLRA seen at presentation had completely resolved. The combination of CLRAO and CRVO comprises a discrete clinical entity. Even though there are many hypotheses concerning this condition, it is most likely the result of elevated intraluminal pressure in the retinal capillaries due to CRVO that exceeds the pressure in the CLRA. HBOT may be an effective treatment for CRVO-associated CLRAO.

Key words

Vision; sudden blindness; hyperbaric oxygen therapy; case report

Introduction

The cilioretinal artery (CLRA) arises from the short posterior ciliary arteries and can be seen in about 32% of eyes.[1] The number, size and distribution of these arteries vary widely. In approximately 19% of eyes, the CLRA contributes to the macular blood supply.[1] Veno-occlusive retinal disorders are a common visual-impairing condition and central retinal vein occlusion (CRVO) is among the most common primary veno-occlusive disorders of the retina.[2] The frequency of CRVO ranges from 0.2% to 0.8% in population-based studies.[2] At the onset of CRVO some eyes may have associated cilioretinal artery occlusion (CLRAO).

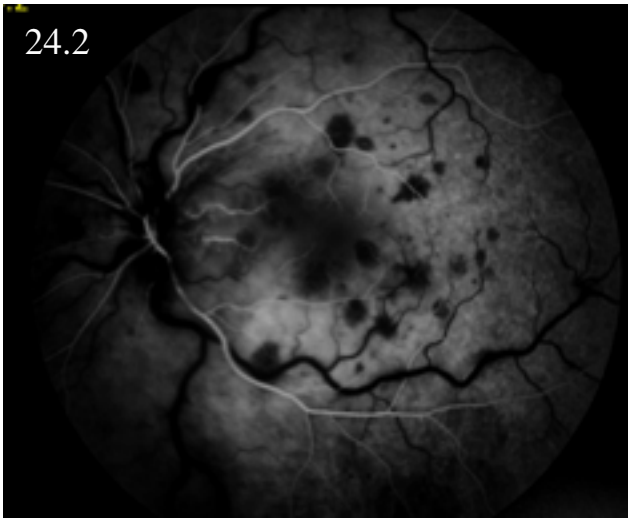
The combination of CRVO and CLRAO was first described in 1968.[3] The pathogenesis of CLRAO in patients with CRVO is not precisely known. Numerous therapies (e.g., surgical embolectomy, Nd:YAG embolysis) have been used to treat retinal arterial occlusive disorders. Supplemental oxygen is administered to maintain retinal function and restore vision via diffusion from the choroidal circulation to the inner layers of the retina.[4] Hyperbaric oxygen treatment (HBOT) administered as early as possible within 24 hours after the diagnosis of occlusive vascular disease of the retina is being used in some centres with some success in selected patients.[5–7] We present a patient with CRVO and CLRAO who was successfully treated with HBOT, and summarise the pathogenesis of this dual entity.

Case report

A 43-year-old male presented with sudden onset of painless, blurred vision in his left eye. He reported having visual obscurations during the week prior to this. The patient's ophthalmic and systemic history was negative prior to this visual complaint. At presentation, visual acuity was 20/20 in the right eye (OD) and 20/200 in the left (OS). Intraocular pressures were 16 mmHg OD and 18 mmHg OS. Slit-lamp examination was unremarkable. Dilated fundoscopic examination of the left eye showed left optic disc swelling, multiple small intra-retinal haemorrhages in the papillomacular bundle, deep blot haemorrhages in the entire posterior pole, as well as increased vessel tortuosity and venous dilatation. Retinal whitening was observed along the course of the CLRA. Examination of the right eye was normal. Visual field testing was unavailable at the time due to technical problems with the equipment.

Fundus fluorescein angiography (FFA) of the left eye showed delayed filling of the central retinal vein and prolonged arteriovenous filling time. The CLRA began to fill as dye appeared in the retinal arteries 24.2 s after injection of the dye. At 33.7 s the retinal veins had just begun to fill proximally with dye, which indicated prolonged retinal arteriovenous transit time (Figures 1 and 2). Based on these findings, the patient was diagnosed as having combined CRVO and CLRAO. Systemic examination showed previously undetected hypertension. A full blood

Figure 1
Fundus fluorescein angiography of the left eye showing slow filling of the CLRA with dye (image taken at 24.2 s)



count, coagulation screen, C-reactive protein, fasting blood glucose, homocysteine level, and liver function were all normal, as were electrocardiography, chest X-ray, carotid ultrasonography and transthoracic echocardiography. The only abnormalities noted were high LDL-cholesterol (157 $mg \cdot dl^{-1}$) and triglyceride (244 $mg \cdot dl^{-1}$) levels. The patient was begun on anti-hyperlipidaemia treatment. His blood pressure was not lowered during the event but later on he was started on antihypertensive medications with beta-blockers on a regular basis.

After the diagnosis was established, he was transferred to a hyperbaric facility elsewhere for daily 2-h HBOT at 253 kPa, which was continued for 14 consecutive days without incident. After the final HBOT, his visual acuity had increased to 20/20 OS. Dilated fundoscopic examination of the left eye showed that the intra-retinal haemorrhages in the entire retina and the retinal whitening along the course of the CLRA had completely resolved. There were small refractile yellow-white iridescent crystals noted at the end of the CLRA. Fundus fluorescein angiography showed a normal dye arteriovenous transit time of 16.6 s and a lack of abnormal florescence (Figure 3).

Discussion

Cilioretinal artery occlusion has been reported in association with embolism, CRVO and a variety of medical conditions as well as with pregnancy.[1] Combined CRVO and CLRAO was first described in 1968, and subsequently reported to account for 40% of all CLRA obstructions.[3,7] There are three forms of CLRAO: isolated non-arteritic; associated with giant cell arteritis, and associated with CRVO.[8] CLRAO associated with CRVO is a clinical entity thought to be due to transient haemodynamic blockage of the CLRA caused by a sudden sharp increase in intraluminal pressure in the retinal capillary bed to a level higher than that in the CLRA.

Figure 2
Fundus fluorescein angiography of the left eye showing delayed filling of the central retinal vein and prolonged arteriovenous filling time in the left eye; dilatation and tortuosity of the retinal vessels was also noted in all four quadrants (image taken at 33.7 s)

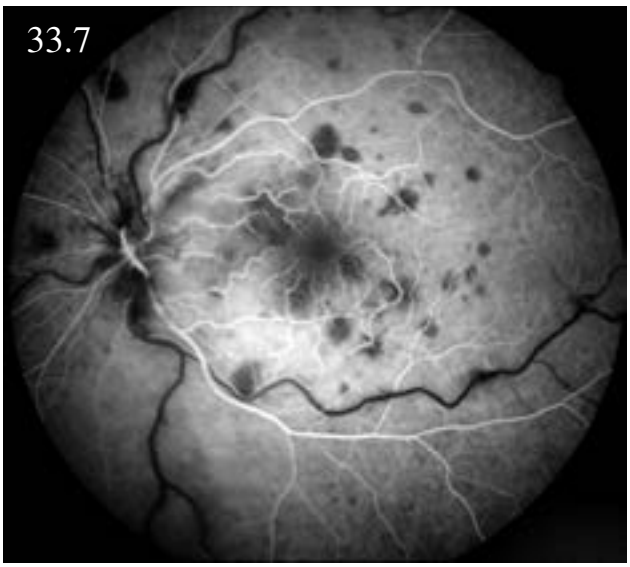
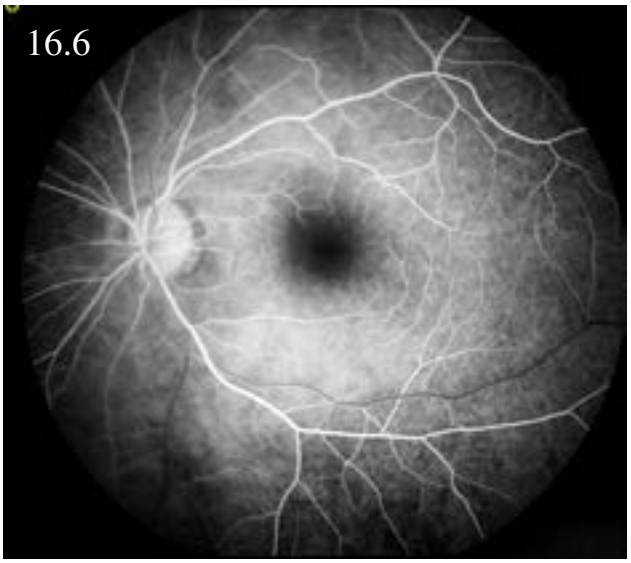


Figure 3
Fundus fluorescein angiography of the left eye following 14 HBO treatment showing a normal dye transit time and lack of abnormal florescence (image taken at 16.6 s)



The pathogenic mechanism of CLRAO combined with CRVO remains unknown. One hypothesis is that CLRAO develops secondary to elevated capillary pressure caused by CRVO.[9] Another is that a primary reduction in the perfusion pressure in the cilioretinal and retinal arteries causes a

decrease in retinal circulation, and subsequent venous stasis and thrombosis.[10] In eyes with a cilioretinal supply, the probability that cilioretinal infarction will complicate retinal vein occlusion is thought to increase as the severity of venous obstruction increases and as the origin of CLRA increases distally from the posterior ciliary artery tree.[11] Indicators of the degree of venous obstruction that may be necessary to instigate cilioretinal infarction include: a very prolonged (defined as more than 30 seconds) dye transit time in the central circulation, increases in venous cyanosis and tortuosity, perivenous cotton wool sentinels and macular perivenular whitening.[11]

Another hypothesis is that a primary reduction in central retinal arterial and CLRA perfusion, or arterial vasospasm, produces secondary venous hypoperfusion and stasis, promoting thrombosis.[10,12] A further hypothesis is based on the fact that arterial perfusion pressure must overcome venous pressure to maintain circulation, and that a marked increase in intraluminal retinal capillary bed pressure due to venous blockage exceeds intraluminal CLRA perfusion pressure, resulting in occlusion.[13] Experimental studies have also shown that arterial constriction following venous obstruction is attributable to a decrease in local levels of nitric oxide, which might contribute to reduced CLRA perfusion.[14] The central retinal artery has sufficient auto-regulatory capacity to maintain perfusion, in contrast to the CLRA arising from the choroidal vascular bed.[13] Furthermore, perfusion pressure in the choroidal vascular bed is lower than that in the central retinal artery.[15]

Fluorescein fundus angiography provides useful information in eyes with CLRAO. Normally, the CLRA begins to fill immediately before the central retinal artery at the optic disc, although in some eyes the cilioretinal and the central retinal arteries begin to fill at the same time.[13] However, in eyes with CRVO and CLRAO, the CLRA filling time depends upon the time between the onset of visual symptoms and fluorescein angiography. Observation of eyes within a couple of hours of the onset of visual symptoms reveals a classical oscillating blood column in the CLRA (i.e., the artery fills for a variable distance from the optic disc during diastole), whereas in eyes observed two to three days after the onset of symptoms, the CLRA begins to fill earlier. The shorter the time interval between the onset of visual symptoms and signs (i.e., the greater the retinal venous stasis), the longer it takes for the artery to fill.[13] The time it takes for the CLRA to fill depends on: the severity of retinal venous stasis; the speed with which the venous collaterals develop in the optic nerve, and the time between the onset of visual symptoms and angiography.[1,9]

Patients with CRVO and CLRAO generally present with a history of an episode(s) of transient visual blurring before the onset of persistent blurred vision, which is first experienced upon waking from sleep or in the morning when the need for fine central vision first arises. In the eyes of patients with non-ischaemic CRVO without foveal involvement from CLRAO, marked improvement in visual acuity may occur; however, when the retinal infarct involves the foveal zone, central scotoma is irreversible. A detailed discussion of the primary differences between ischaemic and non-ischaemic CRVO is to be found elsewhere.[13] In the presented case, because visual obscurations were reported prior to sudden visual loss, it was thought that there was partial occlusion in the central retinal vein and that the CLRAO was secondary to this.

There is no treatment proven to be effective for CLRAO associated with CRVO.[1] The challenge is to administer supplemental oxygen soon enough after the onset of visual loss to prevent irreversible retinal damage. Supplemental oxygen as a treatment option in retinal arterial occlusions showed promising visual results. In experimental models of complete central retinal arterial occlusion the ischaemic time window before permanent retinal damage occurs is 91 mins; in clinical settings in which occlusion may be incomplete vision may be restored even after 8–24 h.[5,6] In patients with retinal arterial occlusion that present within 24 h of visual loss, supplemental oxygen should be started immediately. Recent studies have suggested that HBOT is a safe, easily administered, low-cost and effective treatment in patients with non-arteritic CLRAO.[17] If the patient responds to HBOT, follow-up treatment with supplemental oxygen should be customized to maintain retinal viability until the obstructed retinal artery is re-canalized, which typically occurs within 72 h.[5] HBOT was reported as a safe and effective treatment for a case of cystoid macular edema secondary to retinal vein occlusion.[19] There are no clear recommendations with regard to the number or frequency of HBOT in this clinical situation, though guidelines are available for acute central retinal artery obstruction (CRAO).[5]

The major parameters for visual prognosis are the time from onset of symptoms to the beginning of HBOT, and the time until retinal reperfusion begins.[4] HBOT not only increases oxygenation and perfusion pressure, but also probably reduces intraocular and episcleral venous pressure, which moves a thrombus to a more distal site.[1,17,18]

In conclusion, the combination of CLRAO and CRVO comprises a discrete clinical entity. Even though there are many hypotheses concerning this condition, it is most likely the result of elevated intraluminal pressure in the retinal capillaries due to CRVO that exceeds the pressure in the CLRA. Prospective controlled trials are needed to investigate more fully the role of HBOT as a treatment of choice for CRVO-associated CLRAO and for CRAO.

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Retractions

Young DA, Blake DF, Brown LH: Transcutaneous oximetry measurement: normal values for the upper limb. *Diving Hyperb Med.* 2016 March;46(1):54. Retraction of: Young DA, Blake DF, Brown LH. *Diving Hyperb Med.* 2012 December;42(4):208-213.

Consistent with the Committee on Publication Ethics guidelines, we the above authors are initiating the retraction of our paper: Young DA, Blake DF, Brown LH: Transcutaneous oximetry measurement: normal values for the upper limb. *Diving Hyperb Med.* 2012;42(4):208-213.

We wish to make the following statement:

"The authors voluntarily retract this article after discovering a critical error associated with the instrumentation used in the study, namely the fitting of incorrect sensor membranes on the electrodes of the transcutaneous oximetry device used in the study. This resulted in transcutaneous oxygen tension ($P_{tc}O_2$) measurements that were consistently lower than those that would have been recorded with the correct electrode membranes in place. We recently confirmed this by comparing the two membrane types once we discovered the error. We are in the process of replicating our work using the correct $P_{tc}O_2$-specific membranes."

Submitted: 16 December, 2015

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Blake DF, Young DA, Brown LH: Transcutaneous oximetry: normal values for the lower limb. *Diving Hyperb Med*. 2016 March;46(1):54. Retraction of: Blake DF, Young DA, Brown LH: *Diving Hyperb Med*. 2014 September;44(3):146-153.

Consistent with the Committee on Publication Ethics guidelines, we the above authors are initiating the retraction of our paper: Blake DF, Young DA, Brown LH: Transcutaneous oximetry: normal values for the lower limb. *Diving Hyperb Med.* 2014 September;44(3):146-153.

We wish to make the following statement:

"The authors voluntarily retract this article after discovering a critical error associated with the instrumentation used in the study, namely the fitting of incorrect sensor membranes on the electrodes of the transcutaneous oximetry device used in the study. This resulted in transcutaneous oxygen tension ($P_{tc}O_2$) measurements that were consistently lower than those that would be recorded with the correct electrode membranes in place, which we recently confirmed by comparing the two membrane types once we discovered the error. We are in the process of replicating our work using the correct $P_{tc}O_2$-specific membranes."

Submitted: 24 November 2015

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Partial retraction

Blake DF, Naidoo P, Brown LH, Young DA, Lippmann J: A comparison of the tissue oxygenation achieved using different oxygen delivery devices and flow rates. *Diving Hyperb Med*. 2016 March;46(1):55. Partial retraction of: Blake DF, Naidoo P, Brown LH, Young DA, Lippmann J: *Diving Hyperb Med*. 2015;45:79-83.

Consistent with the Committee on Publication Ethics guidelines, we the above authors are initiating a partial retraction of our paper: Blake DF, Naidoo P, Brown LH, Young DA, Lippmann J: A comparison of the tissue oxygenation achieved using different oxygen delivery devices and flow rates. *Diving Hyperb Med*. 2015;45:79-83.

We wish to make the following statement:

"The authors voluntarily retract aspects of this article after discovering a critical error associated with the instrumentation used in the study, namely the fitting of incorrect sensor membranes on the electrodes of the transcutaneous oximetry device used in the study. This resulted in transcutaneous oxygen tension ($P_{tc}O_2$) measurements that were consistently lower than those that would be recorded with the correct electrode membranes in place. This measurement error was consistent across all arms of the study. This non-differential information error would have created a bias toward the null hypothesis. Therefore, whilst the absolute values for the data were incorrect, the direction and implications of the significant associations reported in this study are unchanged."

Submitted: 16 December 2015

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Letters to the Editor

Hyperbaric oxygen therapy for osteoradionecrosis

Dr Sames and colleagues are to be commended on their thought-provoking article about regional variation in hyperbaric oxygen treatment (HBOT) provision for oro-facial osteoradionecrosis (ORN) across Australia and New Zealand.[1] The four-fold difference between jurisdictions requires further elucidation. As co-directors of the only comprehensive hyperbaric facility in Tasmania, the state with the highest ORN treatment rate, we believe a number of issues pertaining to the Australian situation warrant further consideration.

1. Disease prevalence

Comparisons between regions require consideration of socio-economic conditions. Tasmania has Australia's highest proportion of people living below the poverty line.[2] The increased prevalence of multiple conditions linked to lower socio-economic status (smoking, alcohol, obesity, cardiovascular disease) is reflected in our higher than average age-standardised mortality rates for cancer, diabetes, ischaemic heart disease and stroke.[2,3] Although lack of a specific ICD-10 code for oro-facial ORN prevents estimation of hospital-based incidence or treatment rates, as the authors rightly point out, it is reasonable to assume that Tasmania's figures will reflect known trends and exceed the national average.

2. Chamber logistics

Physical and staffing constraints affect availability of hyperbaric 'places' for patients. Most States and Territories (except Australian Capital Territory (ACT)) have one major public hyperbaric chamber. The minimum physical size of a comprehensive hyperbaric facility is determined by the Medicare requirement for it to manage ventilated and invasively-monitored intensive care (ICU) patients.[4] Depending upon configuration, the Royal Hobart Hospital (RHH) multi-place chamber can accommodate either one ventilated ICU patient or five seated patients. Routine hyperbaric treatments take about two hours, and staffing levels generally limit facilities to providing two to three elective chamber runs per day safely. Although physical chamber size varies between units, New South Wales (NSW) + ACT for example (combined population eight million) cannot provide sixteen times more public hyperbaric 'places' than Tasmania (population 516,000).[5] Relative under supply of public hyperbaric services may, therefore, artificially lower ORN treatment-rates in more populous states.

3. Administrative systems

Tasmania's four acute-care public hospitals are administered by a single Health Service. Most complex specialties (including major head-and-neck surgery and hyperbaric medicine) are centralized at the state's sole tertiary-level facility (RHH). Strong political emphasis is placed on equity of access to these centralized services, wherever the patient lives in Tasmania. Patient travel assistance programmes, outreach clinics at regional hospitals, and lack of bureaucratic territoriality ensure free flow of patients throughout the region.

This contrasts with the situation encountered in more populous eastern states where multiple tertiary-level hospitals in separate area health services (sometimes several in a single city) vie for supremacy. Acute diving-related injuries may be referred across administrative boundaries, but chronic medical conditions seldom are. Points 2 and 3 are neatly illustrated in Figure 1 of Sames et al's paper.[1] A clear dichotomy is evident between the more populous multi-hospital, multi-health-service eastern states (Victoria/Queensland/NSW+ACT), which treat < 10 cases per million population; and less populous states (Western Australia (WA)/South Australia/Tasmania/Northern Territory) with fewer tertiary-level hospitals, servicing a higher proportion of their population (12–19 cases per million).

4. Regional geography

Residual variation between comparable states may be due to local geography and population distribution. Amongst the less populous states identified above, Tasmania is the smallest (land area 68,400 km^2). Driving times to RHH from anywhere in Tasmania seldom exceed four hours. A very different situation exists in, say, WA (land area 2.52 **million** km^2) where distance may preclude routine land-based travel from outlying regions.

Local data indicate that *per capita* hyperbaric activity levels (across a range of Medicare-approved diagnoses) are consistently higher in Tasmania than elsewhere. We believe this reflects the unique environment in which we work. Tasmania is a small, geographically isolated island-state administered as a single Health Service. Specialized services at the single tertiary facility are easily accessible by the entire population. Socio-economic factors affect the prevalence of several conditions approved for HBOT, and a pro-active approach to service provision is encouraged. Hyperbaric staff routinely participate in multidisciplinary head-and-neck, diabetic-high-risk-foot and wound clinics within RHH, and provide outreach clinics at regional facilities. These factors combine to optimise patient access in Tasmania. We would encourage our colleagues in the hyperbaric medicine and health administration communities to view the results of this paper as potentially indicative of unmet need in lower treatment-rate regions.

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Key words
Hyperbaric facilities; health; economics; osteoradionecrosis: evidence; letter (to the Editor)

Retraction of three papers investigating transcutaneous oxygen tensions in healthy volunteers

In this issue, we have retracted two papers and partially retracted a third that we published in *Diving and Hyperbaric Medicine* (DHM).[1–3] These papers described upper and lower limb transcutaneous oxygen measurements ($P_{tc}O_2$) in healthy volunteers or $P_{tc}O_2$ values using different oxygen delivery devices. We recorded lower $P_{tc}O_2$ levels than had been described previously, and in the papers on normal values raised "*the possibility of a diffusion barrier*" as a potential explanation.

We have now determined that those findings were the result of measurement error associated with the use of incorrect membranes that cover the oxygen sensors; specifically, the testing incorporated membranes designed for combined $P_{tc}O_2$ and transcutaneous carbon dioxide tension ($P_{tc}CO_2$) measurement and not solely for $P_{tc}O_2$ measurement. As a result, the values for both upper and lower limb $P_{tc}O_2$ that we reported in healthy volunteers are systematically low.

In a comparison of the two membrane systems in a group of 12 healthy volunteers breathing room air, lower limb readings obtained using the correct ($P_{tc}O_2$) membranes were a median of 12 mmHg (interquartile range 5–20 mmHg; $P < 0.001$) higher; upper limb readings obtained using the correct ($P_{tc}O_2$) membranes were a median of 10 mmHg (interquartile range 3–19 mmHg; $P < 0.001$) higher.

In the third study, in which we used the same device to compare the $P_{tc}O_2$ achieved with various oxygen delivery devices, this measurement error would have been consistent across all arms of the study. This non-differential information error would have created a bias toward the null hypothesis. Therefore, whilst the absolute values for the data were incorrect, the direction and implications of the significant associations reported in that study are sound.[3]

We are in the process of replicating our work using $P_{tc}O_2$-specific membranes. In the meantime, we sincerely apologize for this mistake.

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3 Blake DF, Naidoo P, Brown LH, Young DA, Lippmann J. A comparison of the tissue oxygenation achieved using different oxygen delivery devices and flow rates. *Diving Hyperb Med*. 2015;45:79-83.

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Key words
Transcutaneous oximetry; retraction; letters (to the Editor)

Tissue oxygenation using different oxygen delivery devices and flow rates

We read with interest the recent comparison by Blake et al. of the tissue oxygenation achieved using different oxygen (O_2) delivery devices.[1] This study explored the tissue partial pressure of O_2 ($P_{tc}O_2$) in healthy volunteer scuba divers administering O_2 with a non-rebreather mask (NRB) or with a demand valve with oronasal mask. The authors found that tissue oxygenation was greatest when O_2 was delivered via the NRB at 15 L·min^{-1}. We believe that these conclusions are unwarranted because of a critical methodological flaw of the current study.

As the authors noted, the nasal cannula for measuring end-tidal carbon dioxide may have contributed to a compromised mask seal. Additionally the valve of the demand valve device required an inspiratory pressure for opening. Significant differences between four demand systems have been demonstrated previously.[2] In some systems the inspiratory valve needs a higher pressure difference, whereas a relatively low pressure difference opens the expiration valve and thus leads to the inflow of ambient air. In the present study, the findings for the demand valve were unexpected. We believe that the low tissue oxygenation is a hint to this phenomenon. Meanwhile Blake et al. reported a measurement error associated with the use of incorrect membranes that cover the oxygen sensors.[3] This resulted in $P_{tc}O_2$ measurements that were consistently lower. In our opinion the direction and implications of the significant associations reported in this study were still the same.

We also studied an oxygen delivery device at 15 L·min^{-1} with an open mask (OxyMask™ Adult, Southmedic, Ontario) in an anesthesiology setting prior to cardiac surgery. All patients provided informed consent for an arterial line and blood sampling as part of their routine care. In accordance with the findings of Blake et al., we found similar arterial oxygen partial pressures (P_aO_2) while breathing O_2 spontaneously. We used continuous mandatory ventilation (CMV) in intubated patients as a reference (Table 1).

On-site 100% oxygen first-aid treatment remains unchanged in guideline recommendations.[4] This is difficult to achieve in practice. However, based on the reported $P_{tc}O_2$ or P_aO_2 values of the continuous-flow-rate delivery devices, a demand system would be the best alternative.

Table 1
Demographics and arterial oxygen measurements in five patients

Characteristic	Mean	SD
Age (years)	69.3	5.2
Heart rate (beats·min^{-1})	73	8.8
Respiratory rate (breaths·min^{-1})	16	1.7
P_aO_2 on room air (mmHg)	64	11.6
P_aO_2 on 15 L·min^{-1} for 3 min (mmHg)	249	56.6
P_aO_2 on CMV F_iO_2 1,0 for 10 min (mmHg)	339	60.4

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Key words
First aid; equipment; performance; transcutaneous oximetry; letter (to the Editor)

Reply:

We appreciate the concerns raised by Jüttner et al.[1] regarding our recent paper on first-aid oxygen delivery devices and flow rates.[2] Our unexpected results with the use of the demand valve have been an area of much discussion both within our research group and at the SPUMS 2015 Annual Scientific Meeting. We agree this issue is complex and the lower than expected values we observed with demand valve ventilation may be attributable to several variables, however any leak caused by the nasal cannula should be minimal, and would not fully explain our findings.

Although the data presented by Jüttner et al. are interesting, it is important to note that experiments in the anaesthesia environment might not adequately capture the realities of out-of-hospital care. In our study, we tried to replicate the types of equipment, personnel and process of use as experienced in the pre-hospital environment. That said, the data presented by Jüttner et al. in many ways corroborate our premise that $P_{tc}O_2$ can be used as a surrogate marker for P_aO_2, and that our use of a head hood as our reference standard

(which produced $P_{tc}O_2$ values in the upper limb similar to the P_aO_2 values obtained by Jüttner et al.) was appropriate.

Of course we all agree that the gold standard for oxygen administration in first aid for decompression sickness is an inspired fraction of 100% in order to obtain optimal tissue oxygenation. This should be achievable using the DAN oxygen kit demand valve, but clearly further work is required to identify the device modifications and methods of deployment required to ensure that it does achieve this. In the meantime, our data should reassure first responders without access to a demand valve, or who are unable to achieve adequate oxygenation using the device, that a non-rebreather mask with 15 $L \cdot min^{-1}$ oxygen flow rate can achieve reasonably high values of $P_{tc}O_2$.

References

1 Jütter B, Großheim M, Theiss K. Tissue oxygenation using different oxygen delivery devices and flow rates (Letter). *Diving Hyperb Med*. 2016;46:58.

2 Blake DF, Naidoo P, Brown LH, Young D, Lippmann J. A comparison of the tissue oxygenation achieved using different oxygen delivery devices and flow rates. *Diving Hyperb Med*. 2015;45:79-83.

Denise F Blake[1,2], Lawrence H Brown[3,4]

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[2] Emergency Department, The Townsville Hospital, Townsville, Queensland, Australia
[3] Mount Isa Centre for Rural and Remote Health, James Cook University, Townsville, Australia
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Key words
First aid; equipment; performance; transcutaneous oximetry; letter (to the Editor)

Vale Carl Edmonds

I would like to take this opportunity to thank all my diving medical colleagues, and my fellow divers, for their generous help and comradeship over the last 50 years. I have now retired from active medical practice in this my octogenarian year and with diminishing vision and slower synapsing of the little grey cells. Snorkelling is now my thing. I have donated my library (i.e., my research resource) to the Hyperbaric Unit in Hobart, and also no longer have secretarial access. All I have to offer now are anecdotes and experience – a euphemism for remembered mistakes! – and then only over a glass or two of wine.

My previous overviews of diving medicine, international, Australasian and personal, were described in the *SPUMS Journal*.[1,2] Most of my research, reviews and lectures were also reported there and my admiration abounds for this publication (now *Diving and Hyperbaric Medicine*) and its editors.

2015 was my swan song. I updated our free internet text, *Diving Medicine for Scuba Divers*, on the <www.divingmedicine.info> site. There is no copyright, so please use it as you wish. Informative chapters can be downloaded for specific patients. With the assistance of Mike Bennett, John Lippmann and Simon Mitchell, we published the fifth edition of *Diving and Subaquatic Medicine* – a best seller for 40 years!

My greatest satisfaction of 2015 came as we finally comprehended the conundrum of scuba divers, pulmonary oedema (SDPE), after more than a decade of analysing detailed case histories, investigations and experiments.[3] I agree with Charles Dent and Oliver Sacks – our patients teach us more than our surveys and statistics.

Thank you all.

References

1 Edmonds C. Australian diving medicine, a retrospective 1965-95. *SPUMS Journal* 1995;25:

2 Edmonds C. Diving medicine through a corrected lens face mask. *SPUMS journal*. 2003;33:41-5.

3 Edmonds C. The evolution of scuba divers pulmonary edema. *Undersea Hyperb Med*. 2016;43:83-91.

Carl Edmonds
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Editors note: Carl is a Founder Member of SPUMS, a former Editor of the *SPUMS Journal* and an indispensible resource of diving medical knowledge for as long as this Editor can remember. You may think that you have retired Carl, but I'll still find you for advice wherever you are!

Book reviews

Diving and Subaquatic Medicine

Carl Edmonds, Michael Bennett, John Lippmann, and Simon Mitchell

5th edition; hard cover, paperback and eBook (almost 40 MB) 865 pages, 35 colour and 166 black and white illustrations
ISBN 978-1-482260-12-0
CRC Press; 2015
Available from: https://www.crcpress.com/Diving-and-Subaquatic-Medicine-Fifth-Edition/Edmonds-Bennett-Lippmann-Mitchell/9781482260120.
RRP: £120.00 (currently £102.00 Book + eBook); £84.00 (eBook only)
or: http://www.amazon.com/Diving-Subaquatic-Medicine-Fifth-Edition/dp/1482260123. Various prices
For librarians: Available on CRCnetBASE

When I received this heavy brick for review (with electronic version downloaded from the Publisher's website for offline use on either PC/Mac, iPhone/iPad, Android device or Kindle Fire) I was familiar with the fourth edition published in 2002, so my first question was whether it had changed much from the previous edition? Then I realized that there were some younger colleagues who would consider buying this book for the very first time and they would be more interested in an opinion on how this textbook compared with other books on diving medicine available on the market. So I decided to review it keeping in mind those two aims: *de novo* evaluation of the content and its comparison to previous edition(s).

I must agree with the general description of the book on the Publisher's website that:

- it is "*clinically based*", which means that it has been specifically written to assist medical practitioners in diagnosis, on-site first aid and further treatment of injured diver;
- it is "*highly structured*", which means that the list of contents is built logically, every chapter has highlighted key points, boxed case reports and discussions and many illustrations, including in colour;
- it is "*authoritative*", which means that every sentence was written and later reviewed by some of the world's most experienced diving physicians known from other scientific publications and excellent lectures to everyone involved in diving medicine.

The book covers all aspects of diving medicine, with the chapters logically structured into general subjects concerning:

1. Diving introduction, presenting a brief history of diving, physics and physiology, diving equipment and the undersea environment;
2. dysbaric diseases – barotrauma;
3. decompression sickness, including pathophysiology, manifestations, prevention and treatment;
4. effects of abnormal gas pressures;
5. drowning as the main aquatic disorder;
6. other aquatic disorders, including seasickness, thermal problems, infections, trauma, poisoning and underwater explosions;
7. specific diving diseases, describing virtually every health problem that can be met in diving;
8. diving accidents, including risk factors, first aid and emergency treatment, as well as how to conduct a *post-hoc* investigation;
9. medical standards for both recreational and professional divers;
10. specialized diving topics, e.g., female divers, breath-hold diving, technical diving, divers with disabilities, occupational groups, diving in contaminated water, deep/saturation diving, and long-term effects on health, and
11. hyperbaric medicine, including a description of hyperbaric oxygen treatment (HBOT) and hyperbaric chamber equipment.

There are also appendices with the US Navy Standard Decompression Tables, the US Navy recompression therapy tables, recompression therapy options including in-water recompression schedules and lists of suggested books, training organisations and medical organisations.

The very first edition, published in 1976 in Australia, and written by Carl Edmonds, Christopher Lowry and John Pennefather was primarily orientated towards diving doctors, instructors, professional divers and the serious sport divers <http://classicdivebooks.customer.netspace.net.au/oeclassics-hyperbaric.html>. [accessed 2016 January 23]. It was relatively cheap and was rapidly recognised as a valuable text. By the 1990s it was published overseas for a somewhat more 'academic' price of AUD275, which is still the price for the new edition, now for both paper and electronic versions. Whilst very readable and understandable for the well-educated layman or paramedic, the intended audience is clearly that of medical practitioners.

Since three of the four authors from the fourth edition have departed the scene (Christopher Lowry, John Pennefather and Robyn Walker), the current edition has been reviewed by the main author Carl Edmonds with three new collaborators. More experienced practitioners would be hard to find as all of them are internationally-known experts whose opinions are always good to hear. The text is fluent, written in an informative and accessible style with a perfect balance between basic knowledge and scientific background. The

many flow charts, diagrams and illustrations included are very useful educational tools. There are many real case descriptions presenting excellent practical examples to support the imparted knowledge. These case descriptions, in particular, make this a unique publication that reflects the authors' extensive experience.

Regrettably, as usually happens with subsequent editions of a previous text, there are some imbalances. Some chapters have been well updated, e.g., these on fatal diving accidents, ear barotrauma and hearing loss, modern decompression planning as a part of DCS prevention, diving with asthma or diabetes mellitus and management of the unconscious diver underwater. Others have been extensively rewritten like the one on scuba divers' pulmonary oedema or on HBOT, whilst some are completely new. The updating of some chapters has led to the deletion of interesting and educational information included in previous editions, such as on the different decompression algorithms (Hempleman single-tissue model or Hills thermodynamic approach for instance). Missing topics which this reader believes should have been included in a such book include omitted decompression without DCS, preconditioning of divers with oxygen pre-breathing, exercise and thermal stress physiology, diving with neoplastic diseases and their complications, like post-surgical stomas and implants (excluding mammary implants which are covered in the text), dysbaric bone necrosis in recreational divers and inclusion of in-chamber staff of HBOT facilities in the group of professional workers exposed to occupational risks from hyperbaric exposures, similarly to commercial divers and compressed-gas workers.

Nevertheless, in summary, *Diving and Subaquatic Medicine* is a very comprehensive book which is a must for the library of every diving medicine specialist as well as other medical practitioners interested in this field. I am sure that everyone involved in this subject will find it useful, especially in its electronic format, where everything can be found instantly, with the proverbial 'single-click' access. In my personal opinion, it is the perfect entry point for novice physicians starting their adventure with diving medicine. For me, it will also serve as a reliable source of information for educational purposes.

Jacek Kot

Professor and Director, National Centre for Hyperbaric Medicine Institute of Maritime and Tropical Medicine Medical University of Gdansk, Poland

E-mail: *<jkot@gumed.edu.pl>*

Undersea and Hyperbaric Medical Society

Guidelines for Hyperbaric Facility Operations, 2nd edition

Workman WT, editor

Soft cover or eBook format
31 pages
ISBN: 978-193-0536-82-1
North Palm Beach, FL: Best Publishing Company; 2015
Available from: http://www.bestpub.com
Price: Softcover USD$35.00; eBook USD$30.00; package of both USD$50.00

This is the UHMS's third publication offering guidance related to training, staffing, safety, responsibility and quality assurance for hyperbaric medicine facilities. This edition incorporates previous UHMS position statements on clinician attendance (2009) and credentialing and privileging (2014). It also benefits from extensive input by the UHMS Associates who have provided expert advice regarding nursing and technical personnel.

At the outset it must be stated that these are a set of guidelines and recommendations which do not in any way override local state or federal standards or legislation. Also, these guidelines have been formulated around the way hyperbaric medicine is practised in the USA and there are some significant differences between these guidelines and the (hopefully) soon to be released AS/NZS 4774.2 2015, particularly with regard to chamber technical staff. I am not sufficiently familiar with details from Europe to comment on how it might relate to practice there.

With these provisos, this publication is well laid out and concise. It offers six sections dealing with: Recommended training; job descriptions and responsibilities; staffing numbers; safety programme; physician credentialing, and quality assurance.

Each section offers excellent dot-point guidance for the various personnel required to staff both Class A and Class B clinical hyperbaric facilities. For physicians and nurses, these guidelines have a useful position in the Antipodes; however, it was disconcerting to find training for chamber operations staff, Safety Director and Technical Director listed under nursing personnel.

Technical training and staffing for hyperbaric facilities has evolved differently 'down under' to the extent that the job descriptions (not the training requirements) for both Safety Director and Technical Director match the job descriptions of most technical staff in Australian public hospital hyperbaric units.

Differences in practice notwithstanding, this is a handy reference to have on the shelf with an excellent list of recommended reading for physicians and a very useful bibliography, references to other supporting documents are also available in the quality assurance section.

Steve Goble

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Key words
Hyperbaric facilities; safety; standards; training; book reviews

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Deep into deco: the diver's decompression Textbook

Asser Salama

Softcover or eBook format 120 pages
ISBN 978-1-930536-79-1
Best Publishing Company
North Palm Beach, FL, USA
E-mail: <info@bestpub.com>
Available from: http://www.bestpub.com
Price: US$29.99 softcover US$19.99 eBook US$39.99 package softcover + eBook

The book review of *Deep Into Deco* published in *Diving Hyperb Med*. 2015;45:263 twice commented on the apparent lack of an index. However, the softcover edition does indeed include an index. The review was based on the eBook edition, which has had the index removed (most eBook readers provide a keyword search function).

The reviewers apologise for this oversight.

Greg van der Hulst

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Key words
Decompression; decompression tables; computers - diving; models; book reviews

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Conjoint Professor Michael Bennett

On 12 November 2015, Michael Bennett was appointed to the position of Conjoint Professor in the Prince of Wales Clinical School, Faculty of Medicine, University of New South Wales, Sydney, Australia.

The relevant academic and research areas he will be working in are anaesthesia, diving and hyperbaric medicine. Mike says that it is his prerogative as to how these fields of interest are defined for the future.

SPUMS and EUBS congratulate him on this highly deserved appointment and wish him the very best in his new role within the UNSW Faculty of Medicine.

Back articles from *Diving and Hyperbaric Medicine*

After a one-year embargo, articles from *Diving and Hyperbaric Medicine* (DHM) are placed on the Rubicon Foundation website: <www. http://rubicon-foundation.org/>.

Rubicon is an open-access database, available free of charge and containing many thousands of other publications not available in the public domain anywhere else. Examples are *Undersea Biomedical Research*, back issues of *Undersea and Hyperbaric Medicine*, UHMS reports, research reports from the US and Royal Australian navies, DCIEM in Canada and the University of Pennsylvania and many other items.

All *SPUMS Journal* and DHM to early 2012 are searchable. At present, this is not fully up-to-date for DHM beyond 2012 but more articles are being uploaded regularly. All DHM articles to the end 2014 should be on-line within the next few months.

More recent articles or other enquiries about articles should be sent to: <editorialassist@dhmjournal.com>. Embargoed articles will be charged for – fee on application.

Complete back issues of DHM are available and may be purchased from the SPUMS Administrator at: <admin@spums.org.au>.
Price: AUD30.00 (incl P&P)

The
Diving and Hyperbaric Medicine Journal
website is at

<www.dhmjournal.com>

Notices and news

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

42nd EUBS Annual Scientific Meeting 2016

Dates: 13–16 September
Venue: Geneva, Switzerland

Save the date for the next appointment with our friends from all around Europe to talk about diving and hyperbaric medicine. It will be the occasion to improve and update our knowledge with the latest studies and research in the field. Speakers and guests will be welcomed in the international conference centre in Geneva (CICG), the perfect venue for our annual scientific and social meeting.

Conference website: <http://www.eubs2016.com>
Abstract submission and registration is open.

Important dates:
Deadline for Abstract Submission – 16 May 2016
Early bird registration – 31 May 2016

Hotel selection is possible when going through the registration process; the hotels that are proposed have been carefully selected for their quality/price ratio and location. However, please note that you might find cheaper prices on the web. Usually these cheaper offers come with stricter cancellation policies.

It is of course still possible to support the EUBS Conference by providing a sponsorship. This way, your company or institution will clearly show its involvement and dedication to advancing the field of hyperbaric/diving medicine and physiology; furthermore, you will have a perfect targeted company exposure to potential clients and customers; details to be downloaded from the website <www.eubs2016.com> .

The Science of Diving

Support EUBS by buying the PHYPODE book "*The science of diving*".

PHYPODE research fellows, <www.phypode.org>, have written a book for anyone with a keen interest in the latest research trends and results in diving physiology and pathology. Edited by Tino Balestra and Peter Germonpré, the royalties from this book are being donated to the EUBS. Need more reason to buy? TB and PG don't think so!

Available from: Morebooks <https://www.morebooks.de/store/gb/book/the-science-of-diving/isbn/978-3-659-66233-1>

ECHM Consensus Conference

Lille, 14–15 April 2016

It is not too late to register for this important meeting - see advertisment on page 66 of this issue for details.

Associate Professor Jacek Kot

In February 2016, Jacek Kot, President of the EUBS, was appointed to the position of Associate Professor at the Medical University of Gdansk.

EUBS and SPUMS would like to warmly congratulate him on this academic appointment.

Jacek is also Head of the Department of Hyperbaric Medicine and Sea Rescue, National Centre of Hyperbaric Medicine, Poland

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/>

Notices and news

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

SPUMS Annual Scientific Meeting 2016

Diver resuscitation: in and out of the water

Dates: 15–21 May
Venue: Intercontinental Fiji Golf Resort and Spa, Natadola Coast

Keynote speaker: Chris Lawrence, Forensic Pathologist, Hobart, Tasmania
Other speakers: Simon Mitchell, John Lippmann, Mike Bennett
Workshop: A diving-focused Advanced Life Support Course (recognised for CME points; waiting list only now)

Convenor: Douglas Falconer <asm2016@spums.org.au>
Full information is on the SPUMS website: www.spums.org.au
Follow along @
Facebook: www.facebook.com/spums2016
Twitter: www.twitter.com/spums2016
The conference is already heavily booked, so register now!

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

The ANZCA Certificate in Diving and Hyperbaric Medicine (DHM) is currently under review. ANZCA has not been accepting new trainee registrations since 01 August 2013 and this situation will continue until the Working Party recommendations have been finalised. The Diploma of DHM that is organised by the South Pacific Underwater Medicine Society (SPUMS) is not included in the review.

In accordance with a recommendation from a previous ANZCA Working Party, trainees who were registered for the ANZCA Certificate DHM prior to 01 August 2013 are able to complete and sit the examination. ANZCA has confirmed examination dates for 2016.

To be eligible to sit the above mentioned examination(s), candidates must have:

- Been registered with ANZCA for the DHM certificate prior to 01 August 2013 and paid all relevant fees;
- Successfully completed a Fellowship with a specialist medical college recognised by ANZCA Council (e.g,. FANZCA, FACEM, FCICM);
- Achieved the SPUMS Diploma of Diving and Hyperbaric Medicine or The University of Auckland Postgraduate Diploma in Medical Science – Diving and Hyperbaric Medicine or equivalent;
- Completed their workbook and/or formal project (for the Auckland diploma this is having completed either MED718 or MED719 as part of the course).

Please note that documentation of the above must be received by ANZCA on or before the closing dates of the nominated examination to allow verification by a DPA Assessor.

Periodic updates on the review of the DHM Certificate will be made available on the ANZCA website. All interested parties are advised to regularly visit the webpage <http://www.anzca.edu.au/training/diving-and-hyperbaric-medicine> to ensure you are kept up to date.

For further information contact: <dhm@anzca.edu.au>

2016 examination dates for the ANZCA Certificate in Diving and Hyperbaric Medicine examination

Closing date for exam registration	Friday 22 April	Friday 09 September
SAQ examination	Friday 10 June	Friday 04 November
Oral viva examination	Friday 15 July	Friday 02 December

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 the 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 (EO) for assessment as a diploma paper. If the paper has been accepted for publication or published in another journal, then evidence of this should be provided.

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

Additional information – prospective approval of projects is required

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

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

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

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

Projects will be deemed to have lapsed if:

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

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

The Academic Board reserves the right to modify any of these requirements from time to time.

As of January 2016, the SPUMS Academic Board consists of:
Dr David Wilkinson, Education Officer, Adelaide;
Associate Professor Simon Mitchell, Auckand;
Dr Denise Blake, Townsville.

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

Capita Selecta Diving Medicine Academic Medical Centre, University of Amsterdam, The Netherlands

Course calendar 2016

CSD offers advanced courses (content conforms to ECHM-EDTC Level 1, 2D).

24 September–01 October: Mini-congress *Diving Medicine* (5 plenary lectures by Adel Taher, 10 invited lectures, free contributions, 18 cp); Paradise Bay, Malta
November: *Exercise under water and working under pressure* (6 cp); AMC, Amsterdam

For further information: <www.diveresearch.org>

European Committee for Hyperbaric Medicine 10th Consensus Conference

Dates: 15–16April 2016
Venue: Lille, France

The European Committee for Hyperbaric Medicine (ECHM) has in its objectives the continuous improvement in the quality of care and safety in hyperbaric medicine. One of the tools used to achieve this is the organization of consensus conferences to develop guidelines. Nine such conferences have been organized and their recommendations widely promulgated. Two of these, in 1994 and 2004, were especially focused on the organization, indications and quality of care in hyperbaric medicine. Ten years on, it is time to review and update these guidelines based on advances in medical knowledge and the experience gained in clinical practice during that period.

In 1994, the guidelines were developed by a jury from expert reports and discussion with the conference audience. In 2004, these guidelines were improved by grading the recommendations based on the level of evidence for and the clinical importance of each recommendation. In 2016, ECHM wishes to take this a step further by reviewing each recommendation and enhancing the grading system. Recognized experts in each field will produce a report on a topic with an exhaustive literature survey, a synthesis of the evidence and a proposal for revised recommendations. These reports will be circulated amongst the expert group and each will be asked to weight their assessment of the proposed recommendations. During the conference, the reports and expert opinions will be presented to the audience which will have an opportunity to discuss and amend the reports before a final consensus on each recommendation is issued.

For information: <www.echm-lille-consensus-2016.org>

Scott Haldane Foundation

The Scott Haldane Foundation is dedicated to education in diving medicine, organizing 230 courses over the past 20+ years. In 2016 SHF is targeting more and more on an international audience with courses world wide.

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

SHF courses for 2016
1–2 April: Basic Course Diving Medicine (level 1 part 1); Zeist, NL
9, 15 and 16 April: Basic Course Diving Medicine (level 1 part 2); Amsterdam, NL
21–28 May: *NEW* In-depth course HBOt and decompression; São Vincente, Cape Verde
4–11 June: *NEW* Basic course Lungs and Diving; Bonaire, Netherlands Caribbean
21–22 September: Basic Course Diving Medicine (level 1 part 1); Al Sifah, Oman
24 Sept–01 October: Basic Course Diving Medicine (level 1) part 2; Al Sifah, Oman
October: *NEW* Refresher course Diving Accidents; NL
5–12 November: Basic Course Diving Medicine (level 1 part 1); tbd
12–19 November: *NEW* 24th In-depth Course Diving Medicine; tbd
19–26 November: *NEW* 24th In-depth Course Diving Medicine; tbd
Tbd: In-depth course "*A life-long diving*" (level 2); Loosdrecht, NL
Tbd: *NEW* Ultrasound hands-on workshop; Europe

For further information: <www.scotthaldane.nl/en/>

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>

Department of Biomedical Sciences University of Padua 2015/16

Level II Master's Course in Hyperbaric Medicine

12-month course – 60 course credits (European Credit Transfer System)
Pre-requisite: medical degree
Submit applications online: <www.unipd.it/medicina-iperbarica>

High Education Course in Technical and Health Management in the Hyperbaric Chamber Environment

6-month course – 15 course credits (European Credit Transfer System)
Pre-requisite: high school diploma (technical/science subjects) and/or bachelor's degree in health sciences/nursing
Submit applications online: <www.unipd.it/corsi/aggiornamento-formazione-professionale/corsi-alta-formazione>

Please visit: <https://www.facebook.com/Hyperbaric-School-Padua-1589083271327695/?fref=ts>

Undersea and Hyperbaric Medical Society 2016 Annual Scientific Meeting

Venue: Tropicana Las Vegas Casino Hotel Resort, Las Vegas, Nevada
Dates: 08–11 June 2016

For more information/registration: <https://www.uhms.org/annual-scientific-meeting/registration.html>

British Hyperbaric Association ASM 2016

Dates: 28 November – 02 December or 05–09 December
Venue: Cayman Brac, Cayman Islands, hosted by Cayman Hyperbaric Services

Further information in next issue or contact:
<http://www.hyperbaric.org.uk/>

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>

Royal Adelaide Hospital Hyperbaric Medicine Unit Courses 2015

Medical Officers' Courses
04–08 April: Basic
11–15 April: Advanced

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>

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:
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Instructions to authors

A downloadable pdf of the 'Instructions to Authors' (revised August 2015) can be found on the *Diving and Hyperbaric Medicine* (DHM) website: <www.dhmjournal.com>. Authors must read and follow these instructions carefully.

All submissions to *DHM* should be made using the portal at <http://www.manuscriptmanager.com/dhm>. Before submitting, authors are advised to view video 5 on how to prepare a submission on the main Manuscript Manager web site <http://www.manscriptmanager.com>.

In case of difficulty, please contact the Editorial Assistant by e-mail at <editorialassist@dhmjournal.com>.

DIVER EMERGENCY SERVICES PHONE NUMBERS

AUSTRALIA
1800-088200 (in Australia, toll-free)
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NEW ZEALAND
0800-4DES-111 (in New Zealand, toll-free)
+64-9-445-8454 (International)

ASIA
+81-3-3812-4999 (Japan)

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

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

UNITED KINGDOM
+44-7740-251-635

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 nonšfatal 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>

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