Diving and Hyperbaric Medicine

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SPUMS

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EUBS

Liver injury in decompression illness

Field study of deep stops in technical diving: no advantages?

Otitis externa is common but mild in navy diver trainees

An unusual presentation of cerebral DCI

ECG changes in Turkish professional divers

ECHM recommendations for hyperbaric oxygen treatment

The Grattan Report: poor methods and erroneous conclusions

Infusion devices for hyperbaric use

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PURPOSES OF THE SOCIETIES

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

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DIVING AND HYPERBARIC MEDICINE

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The Editor's offering

The importance of the interaction between the vascular endothelium and blood constituents in the evolution of decompression illness (DCI) was first recognised many years ago. For instance in the 1990s, stripping of the surfactant lining of the vascular endothelium in the brain was proposed as an important mechanism for vascular and other organ injury.[1] Also stopping the adhesion of neutrophils to the damaged vascular wall after gas embolism prevented subsequent local cerebral circulatory impairment.[2] Since then, many papers have established the important role of the local and circulatory nitric oxide and pro-inflammatory systems and the potential role of circulating microparticles in the development of the injury from circulating gas bubbles.

Most readers probably think of DCI largely in terms of central nervous system symptoms and joint pain. However, DCI is a multi-organ injury, and the study in this issue on liver injury in rats using a pressure profile known to produce severe DCI demonstrates this.[3] There are also clinical reports of gastrointestinal tract involvement[4] and renal failure,[5] and the acute lung injury, colloquially known as the "*chokes*", has been recognised for many decades. Likewise, the diversity of CNS symptoms with which DCI may present is epitomised by the unusual case report of visual anosognosia.[6]

The validation of decompression tables is a complicated, time consuming and expensive undertaking requiring large numbers of dives with different depth/time profiles. In practice, particularly in technical diving using multiple gas mixtures, decompression protocols are largely based on modelling and/or a fair amount of trial and error. Since the vascular pathophysiology and inflammatory response following diving can be measured, the concept of using biological 'markers' to estimate 'decompression stress' is explored in the paper on two different types of decompression protocols for a standard deep trimix dive.[7]

Hyperbaric oxygen treatment (HBOT) is under threat in a number of countries around the world, and poorly performed clinical research, such as that to which readers' attention was drawn in a September 2016 editorial,[8] does not help. In this issue, a highly critical analysis is presented of a report, focusing predominantly on HBOT, from the Grattan Institute in Australia.[9] The Grattan Institute is an organisation "*dedicated to developing high quality public policy for Australia's future*". They claim to be "*independent*", "*rigorous in obtaining the best available evidence*" and "*practical in articulating what governments should do to improve the lives of all Australians*". However, the Institute's report entitled "*Questionable care: stopping ineffective treatments*"[10] is a classic example of the presentation and interpretation of "*alternative facts*" (Conway K, "*Meet the press*", 22 January 2017) conducted by an entirely non-clinical research group.

The hyperbaric community is partly to blame for these attacks on the 'stuff of life' in failing over decades to produce the necessary solid clinical evidence base for many of the proposed applications for HBOT[11] and by its over-use by 'charlatans'. As a result HBOT is still regarded by many clinicians as a 'fringe medicine' therapy. The hyperbaric medical community has much work still to do to establish firmly the place of HBOT in modern medicine.

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Key words
Decompression illness; Hyperbaric medicine; Evidence; General interest; Editorials

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Front page photo by Dr Andrew Fock at Truk Lagoon (with kind permission). Decompressing from a deep technical dive is not always boring! SPUMS Associate Member Rob Cook enjoying the company of his dive buddy.

The Presidents' pages

David Smart, President SPUMS

I trust that all SPUMS members had a safe and happy Christmas and New Year. By now, all SPUMS members will have received membership renewal notices and possibly reminders if your first notice was not acted upon. Thank you for your continuing support of SPUMS.

Last year was a busy year for the SPUMS Executive Committee with the website development, changing our banking to ANZ and setting a new strategic direction for the journal *Diving and Hyperbaric Medicine* to move to an electronic format in 2018. After initially planning for the Philippines for the ASM in 2017, we made a strategic but fairly late decision to change to Bali. We are very grateful to Katie Commons, Clinton Gibbs (conveners) and Denise Blake (scientific convener) for their efforts in bringing together what should be a terrific scientific meeting in such a short period of time. Conference registrations are looking very healthy at this stage. The Asian Diving and Hyperbaric Medicine Association meeting will also overlap with our conference, providing some positive networking opportunities for both societies.

It also gives me great pleasure to announce that the new SPUMS website is now operational, with a level of functionality that already exceeds the previous website. Thanks to Nicky Telles and Joel Hissink for your great work. Members will notice the website further evolve as it is populated with material, including SPUMS' organisational history, with the intent that it truly becomes a platform from which to operate our society in the future. It has been worth the effort.

In parallel with the website, SPUMS has been reviewing and updating its corporate governance. We now have terms and conditions of membership, which all members are asked to read and agree to before joining or renewing their membership, <https://www.spums.org.au/content/terms-and-conditions>. This policy includes a description of the membership year which runs from 01 January to 31 December. Members are reminded that they need to pay their subscription between 01 January and 31 March to remain current. We are progressively automating processes so that renewals and reminders are sent to members automatically. The process will also assist SPUMS to better meet its financial obligations as they occur, and also better gain an idea of our membership census.

We also have produced a privacy policy, <https://www.spums.org.au/content/privacy-policy>. A key component of the new website is the Diving Doctors List. This now has a Google Maps functionality, permitting an individual to search for doctors near where they live, who are trained in diving medicine. To join the Diving Doctors List requires a Member to 'opt in' to join the list and provide their practice details. The accuracy of these details is the responsibility of the doctor, and Members can update their details at any time to ensure they are current, including changing their practice address. Only SPUMS members registered in Australia and New Zealand may appear in the list. Doctors also need to confirm that they are current with their continuing medical education (CME). Although SPUMS, as a voluntary society, has no authority to mandate CME, there is an expectation that doctors on the list update their knowledge by undertaking courses in diving and hyperbaric medicine, or attend scientific meetings such as the SPUMS ASM. Of course, a major contributor to members' CME is this journal!

SPUMS Membership numbers have been static at around 500 now for a number of years. To grow and develop, we need more members. On behalf of the Executive, I encourage all members to approach colleagues who have an interest in diving or hyperbaric medicine, to join our organisation. Growing our membership will be a key component of our strategic direction for 2017 and beyond. As we further develop our website, there will be a greater number of resources and services available in the 'Members only' section of the website, to increase the value we provide to members.

Key words
Medical society; General interest

The

SPUMS

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

The new website has now been launched. Members are encouraged to log in and update their personal details.

Jacek Kot, President EUBS

We have updated our by-laws and the Constitution of the EUBS as described in my last President's letter published in the December 2016 issue of *Diving and Hyperbaric Medicine*. Most of our members supported this proposal – thank you so much. The new, updated version of this fundamental document for our Society, effective from 2017, is available on our website <www.eubs.org>.

Another important change for the Society is the change of our Treasurer/Secretary, which two positions have been held for more than thirteen years by Mrs Tricia Wooding from London, UK. In fact, she was running our home office in such an imperceptible and smooth way that the full value of her service to the Society was only clearly apparent when we started to look for her successor after she decided to step down. I had hoped to change her decision, but finally we had to face the facts. Fortunately, Tricia stayed with us longer than originally expected, allowing a smooth transition to a new incumbent. On behalf of all EUBS members, I would like to say to Tricia, thank you so much for being Tricia and supporting us so wonderfully for all those years! Since the beginning of 2017, Ms Kathleen Pye from Orkney, Scotland, took over the Treasurer/Secretary roles and has become part of our Executive Committee – welcome on board, Kathy. As Kathleen, like Tricia, is from the UK, regardless of brooding "*Brexit*", the Society's business will remain within that country. Keep your British pounds in your wallet at least for next year's EUBS membership fees!

This year we have two important international conferences on diving and hyperbaric medicine in Europe and the best solution for our members would be to attend them both. Of course, the first 'must-be' is the EUBS Annual Scientific Meeting to be held in Ravenna, Italy, 13–16 September. We all know from past experience Pasquale Longobardi and his team's ability to organise an unforgettable event. Please prepare a report of your recent work, submit the paper and make a reservation for your flights and accommodation. More information can be found at <www.eubs2017.org>.

Another important meeting in Europe this year is the International Congress on Hyperbaric Medicine (ICHM). Originally started in 1963 by Professor Ite Boerema in Amsterdam, The Netherlands, the ICHM is a three-yearly meeting organised each time on a different continent. The last one, in 2014, was in South America, in Buenos Aires, Argentina. This year's meeting will be held in Belgrade, Serbia, 11–14 May. It would be unwise not to take advantage of this Congress being in Europe and not to join it at least this once in your life-time. Check all options for yourself at <www.ichm2017.com>.

As already announced in Geneva during last year's EUBS meeting, we have found that our original plans to have the next Tri-Continental meeting (in 2018) of EUBS, SPUMS and SAUHMA in Oman must be changed for political reasons (see the Minutes from the last General Assembly). To cut a long story short, we communicated this with our partners, namely SPUMS and SAUHMA and cancelled the location. Now, representatives of all three societies are looking for an alternative site and the best date available. So we keep our options open to have the Tri-Con meeting in 2018, but where and when exactly is yet to be determined. In any case, stay tuned to the EUBS website at <www.eubs.org> for further updates.

Key words
Medical society; General interest

The

website is at
<www.eubs.org>

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

The new, revamped EUBS website <www.eubs.org> is online. Its layout has been drastically modified for easy viewing on smartphones, tablets and computers, while offering the same functionality as before. The new website structure allows for easier and faster announcement of events and news items. Also, we will gradually expand the content with Position Statements and Committee activity reports.

Check it out!

Original articles

Otitis externa in military divers: more frequent and less harmful than reported

Thijs T Wingelaar, Pieter-Jan AM van Ooij and Rob A van Hulst

Abstract

(Wingelaar TT, van Ooij PJAM, van Hulst RA. Otitis externa in military divers: more frequent and less harmful than reported. *Diving and Hyperbaric Medicine*. 2017 March;47(1):4-8.)

Introduction: Although otitis externa (OE) is a common disease, data related to (military) divers are limited. This study aimed to determine the incidence of OE in military divers during their initial training. We also wished to consider seasonal influences on incidence and whether early detection increases completion of the diving course.

Methods: From January 2011 to October 2016 the Royal Netherlands Navy Diving School trained 189 divers. Up to December 2015 we used the training records for the analyses. From January 2016 onward all divers were prospectively screened. Pearson's χ^2 and Fisher's exact tests were used to analyse the data.

Results: In the 162 included divers, 30 cases of OE were identified. The incidence in 2016 was significantly higher than in 2011–2015 (17/35 (49%) versus 13/127 (10%), $P < 0.001$). Almost all cases developed after three weeks of diving. No influence of season was found ($P = 0.354$). Early diagnosis and treatment of OE does not seem to affect completion of diving courses ($P = 0.280$). Only in three cases did a diver have to discontinue the course due to OE.

Discussion: This study suggests that OE is more frequent among military divers than earlier reported, most likely caused by prolonged water exposure. Diving activities can often be continued with standard topical treatment.

Key words

Scuba diving; Ear infection; Treatment

Introduction

Infection of the outer ear canal, otitis externa (OE), is a common disease in general practice. Lifetime prevalence is estimated at 10%, while the yearly incidence ranges from 1–1.4%.[1–4] There is a profound seasonal effect in the general population, with the highest incidence in the summer.[5,6] This has been attributed to increased aquatic activities and rising ambient temperatures, generating the ideal circumstances for developing OE.[7–9] Although contaminated fresh water lakes, pools and hot tubs are known to cause epidemics, sufficiently filtered and chlorinated water can also cause OE.[5,6,10] Prolonged exposure to (any type of) water macerates the ear canal and washes away the acidic cerumen, making the ear vulnerable to infection.[5,11,12] Bacterial overgrowth is responsible for more than 90% of the cases of OE, with *Pseudomonas aeruginosa* and *Staphylococcus aureus* being the most common pathogens.[1,2,13,14] The remaining 10% is caused by mycosis (*Candida* and *Aspergillus*), which is more common in tropical climates.[7,12]

Data on the incidence in aquatic athletes and scuba-divers is surprisingly limited. OE was reported to be 2.5 times more frequent in swimmers and water polo players than in football players.[5] A survey among experienced sport divers showed a 'diving career prevalence' of 43.6%.[15] Diving activities are highly likely to be discontinued when OE occurs in divers.

There is much debate on preventive or therapeutic interventions in OE, with some stating there should be no difference in the treatment of divers compared with non-aquatic athletes.[16] The use of prophylactic acidic drops has not proven effective.[1,2,9,17] Unless there are signs of systemic inflammation, there is no place for systemic antibiotic treatment.[1,2,8,12,18] Evidence is unclear which topical agent is preferred to treat OE.[1,18,19] While OE is treated effectively with a course of eardrops, the cornerstone of treatment is to keep the outer ear canals dry and clean.[8,18,19] This is particularly difficult in the case of military diving, since diving activities are continued as long as possible for operational reasons.

While sport diving is a leisure activity, military diving must be considered as hard work in harsh environments. It seems plausible that OE in military diving is far more frequent than earlier reported. The aim of this study was to determine the incidence of OE among military divers during their initial diving training. We were also interested in seasonal effects on the incidence of OE and whether early detection and treatment reduces interference with the diving course.

Methods

STUDY CONTEXT

The Royal Netherlands Navy Diving School (NDS) is responsible for training of all military divers in the Netherlands. While follow-up training depends on their

trade (e.g., clearance diver, construction, special forces, etc.), the initial training is a six-week course with three weeks in pool water followed by three weeks of training in open water. Although the locations of various elements of the course have changed over the years, the basic outline has remained the same. The NDS operates throughout the year. All trainees are healthy candidates who passed thorough dive medical screening in accordance with the European Diving Technology Committee (EDTC) guidelines prior to entering the course.[20] The Medical Ethics Committee affiliated with the Amsterdam Medical Centre approved our methods for handling personal details and privacy and concluded that they were concordant with the guidelines of the Association of Universities in the Netherlands and the Declaration of Helsinki (document reference: W16-281).

In 2013, the deep pool exercises switched from a naval sonar maintenance pool to an indoor pool solely used for diving. As of 2014, the free ascents from 15 metres' depth could be practiced in the naval harbour, which previously had to be practiced in an indoor pool in Belgium. During the entire study period, all diving locations (pools and outside) were tested monthly regarding water quality and all met the quality and safety conditions according to both Dutch and international standards.[21,22]

DATA COLLECTION

The NDS keeps detailed records of course results of all diving trainees, including medical problems. The training records of all diving trainees from January 2011 to October 2016 were reviewed. Up to December 2015, each diver could request a consultation with a dive medical nurse or physician. The diver can also be ordered by the instructors to visit medical staff if they suspect a medical problem. As of January 2016, one dive medical physician and two nurses actively engaged the trainees and performed regular checkups on all divers. All data up to the end of December 2015 were gathered retrospectively, while data from January 2016 onwards were acquired prospectively. During the entire training period, OE was defined as a combination of: 1) otalgia, itching or otorrhoea, and 2) oedema or erythema of the external ear canal or pain when manipulating the tragus.[3] Training records with incomplete data were excluded from the analysis. All information was documented in a database that registered: 1) occurrence of OE, 2) whether the diver missed any diving days and 3) whether the diver was able to successfully complete the course. The two latter parameters were categorized into those that were caused by OE, or were due to other reasons.

TREATMENT PROTOCOL

Our treatment protocol was based on best practice and is in accordance with Dutch guidelines, primarily using acidic drops and switching to topical steroids with a cotton wick if the ear canal was severely swollen.[1,8,18] If topical steroids proved to be insufficient, a combination of dexamethasone, framycetin and gramicidin (Sofradex®) was used. In the Netherlands, the use of ciprofloxacin is reserved for post-surgery and chronic external otitis. In line with the literature, we refrained from giving systemic antibiotic treatment.[1,2,8,12,18] Bacterial culture is not part of our standard practice. A diving physician could order a patient to discontinue diving activities when complaints seemed to be incompatible with diving.

Table 1

Distribution of diver trainees by quarter of the year (Q) for the period 2011–2015 and for 2016; for each quarter the upper line is the number of divers with adequate medical records (total $n = 162$), the bottom line the number of patients with otitis externa

	2011–2015	2016	Total
Q 01	29	11	40
	3	8	11
Q 02	61	24	85
	7	9	16
Q 03	7	0	7
	0	0	0
Q 04	30	0	30
	3	0	3
Total	127	35	162
	13	17	30

ANALYSIS

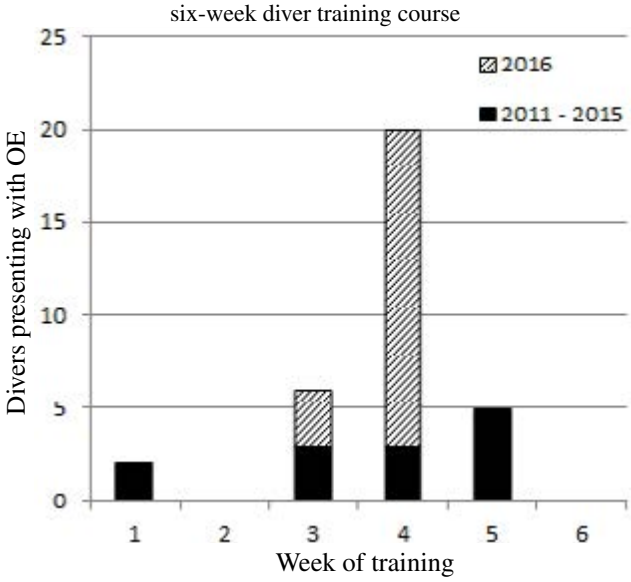
All data were binary (either OE or no OE). Statistical analyses were performed with SPSS Statistics for Windows (IBM Corp; Armonk, NY: 2015, version 23.0), using Pearson's χ^2-test for hypothesis testing. To determine any seasonal influence, we categorized the results per quarter (i.e., Q1 from January–March, Q2 from April–June, etc.) and performed a Fisher's exact test. To measure the effect of early detection and treatment, we compared the incidence in the period 2011–2015 with that in 2016. Statistical significance was assumed when $\alpha < 0.05$.

Results

In the period January 2011 to October 2016, a total of 189 divers were trained by the NDS. All training records were reviewed and 15 records (8%) were excluded because they contained no data. In 12 records (6%), information on medical status was missing, leaving a total of 162 divers for the present study. Although females are allowed in military diving, of the 162 included divers, 155 of the included subjects (96%) were male. Table 1 shows the distribution of divers over the quarters for the retrospective and prospective groups. Thirty cases of OE were identified, none in the seven female divers.

Compared with that in the previous years (10%), the increased incidence in 2016 (17/35, 49%) was significant

Figure 1
Onset of otitis externa (OE); number of cases in each week of the six-week diver training course



($P < 0.001$ for χ^2). The onset of OE is presented in Figure 1: 2016 is presented separately from the previous years to show the effect of active screening. The highest incidence of OE is in week four, after three weeks of diving in pool water. However, in 2016 all but three divers in week four presented themselves before starting open water training. In 2016, we found no cases of OE in week five and, throughout the study period, onset of OE did not occur after the fifth week.

The quarterly incidence of OE did not differ significantly (Fisher's exact test $P = 0.354$). We also tested the incidence of 2011–2015 separately to correct for the increased incidence of 2016, this difference was also not significant ($P = 0.959$). According to measurements by the Dutch Ministry of Infrastructure and the Environment, the water temperature during the study ranged from 2°C in the winter to 22°C in the summer, with ambient temperatures ranging from -10°C to 35°C.

Up to December 2015, a total of 13 divers were identified with OE, of whom 12 (10%) had to discontinue diving for at least one day due to OE. In 2016, OE caused at least one missed day of diving in five of the 35 divers (14%); this slight increase was not significant ($P = 0.280$). Thirty-two of the 162 divers (20%) failed the course either for insufficient results (12 divers) or for medical reasons (20 divers). Of these 20 divers, only three were due to OE, all of which occurred in the period of 2011–2015. In these cases, OE was so severe that continuation of diving would be too painful.

Our treatment protocol did not change during the study period. In four divers (13%), including two who had to stop the diving course, topical antibiotic treatment was given due to treatment failure of topical steroids. All other cases of OE were treated with acidic drops, with or without steroids.

Discussion

This study provides a six-year overview of the incidence of OE in naval diving trainees and its impact on their diving activities. The incidence found is much higher than reported in the literature. This might be explained by frequent and continuing water exposure during the six-week diving course. There was no seasonal influence. The study shows that early detection and treatment has no effect on participation in diving activities.

ACTIVE SCREENING

Up to December 2015, divers contacted medical staff when they experienced complaints. In 12 of the 13 divers the OE was severe enough to miss at least one diving day, and in three divers the infection was so severe that the diving course could not be completed. This is why we decided to actively screen the divers for OE and found a much higher incidence. In our opinion, this increase can be attributed to previous underreporting. In 2016, all divers had some complaints (either pain or itching), but the majority did not consider their complaints severe enough to consult a physician.

One could argue that the behaviour of the divers might have changed due to the regular screening we performed. However, we feel that this effect is negligible, since instructions to rinse and dry the ears after diving and to refrain from using objects to clean the outer ear canal were already standard practice in the diving course.[21] Also, we consider the possibility of traumatic injury and subsequent development of OE due to the screening itself to be very low, since all medical staff were trained in handling the otoscope and performed all examinations carefully.

PROLONGED EXPOSURE TO WATER

Almost all our cases of OE developed in the third and fourth weeks. Although we cannot exclude the contribution of chlorination because our study lacks a control group in unchlorinated water, studies support our observation that long exposure to water makes the outer ear canal susceptible to OE.[5,11,12] Also, although diving locations have changed over the years, the locations were similar (i.e., inside or outside training) and the water quality at all dive sites remained well within international regulations.[22] We feel this is an additional argument to conclude that OE in these divers can be attributed to the frequent and prolonged exposure to water, rather than possible contaminated or type of water.

SEASONAL INFLUENCE

As the diving school operates throughout the year, we were able to test whether seasonal conditions had any influence on the development of outer ear infection. We hypothesized that the incidence would be highest when ambient temperature was higher (i.e., in Q2 and Q3). Although our Q3 group is

small compared to the groups in the other quarters (partly due to 15 blank records in 2011 which had to be excluded), we found no significant effect. Also, the behaviour of the divers is likely to change with changing weather conditions, e.g., wearing a woolen hood when working at the surface in the winter, or just a simple cap in the summer. In contrast to the literature, we feel that our study indicates there is no significant seasonal effect on the development of OE in military divers.

EARLY DETECTION AND TREATMENT

One might suggest that early detection and treatment would lead to higher participation in the course. However, we found no significant change in missed diving days. If any, there might be a slightly lower participation. In view of the high incidence and low number of divers that had to stop the diving course, we might conclude that prolonged water exposure or continuing diving operations with OE is less harmful than earlier thought. Even severe cases of OE could be treated topically, while none of the cases required systemic antibiotic treatment.

STRENGTHS AND LIMITATIONS

To our knowledge, there are no publications on the incidence of OE in military divers. The present study combines retrospective and prospective data, providing an overview of the impact on operational diving. The study design allowed us to evaluate the effect of active screening and determine the incidence of OE in military divers. Unfortunately some divers had to be excluded due to insufficient data; a prospective design might serve to limit this influence. Although all divers were screened according to EDTC guidelines, we did not register any risk factors (such as a narrow auditory canal or history of eczema) which could predispose for OE. This information could help us determine which divers are more at risk. To our knowledge, there is no validated grading system to stratify the severity of OE. This might have provided more insight into the effects of early diagnosis and treatment. Whereas this study does provide some insight into effects of topical treatment on participation in diving courses, it does not determine which treatment is optimal to continue diving operations.

Conclusions

Otitis externa is much more frequent in military divers than earlier assumed, but continuing to dive with OE would appear to be less harmful than previously thought. We were unable to demonstrate a seasonal influence on the development of OE, as reported in the literature. Screening and early treatment do not seem to prolong diving activities and, with standard treatment using topical agents, our divers were able to continue their diving course without worsening of OE. We plan a prospective study aiming to determine the optimal treatment regimen for military divers.

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Assistance from interested physicians in preparing critical appraisals (CATs) is welcomed, indeed needed, as there is a considerable backlog. Guidance on completing a CAT is provided. Contact Professor Michael Bennett: <m.bennett@unsw.edu.au>

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A comparative evaluation of two decompression procedures for technical diving using inflammatory responses: compartmental versus ratio deco

Enzo Spisni, Claudio Marabotti, Luigia De Fazio, Maria Chiara Valerii, Elena Cavazza, Stefano Brambilla, Klarida Hoxha, Antonio L'Abbate and Pasquale Longobardi

Abstract

(Spisni E, Marabotti C, De Fazio L, Valerii MC, Cavazza E, Brambilla S, Hoxha K, L'Abbate A, Longobardi P. A comparative evaluation of two decompression procedures for technical using inflammatory responses: compartmental versus ratio deco. *Diving and Hyperbaric Medicine*. 2017 March;47(1):9-16.)

Introduction: The aim of this study was to compare two decompression procedures commonly adopted by technical divers: the ZH-L16 algorithm modified by 30/85 gradient factors (compartmental decompression model, CDM) versus the 'ratio decompression strategy' (RDS). The comparison was based on an analysis of changes in diver circulating inflammatory profiles caused by decompression from a single dive.

Methods: Fifty-one technical divers performed a single trimix dive to 50 metres' sea water (msw) for 25 minutes followed by enriched air (EAN50) and oxygen decompression. Twenty-three divers decompressed according to a CDM schedule and 28 divers decompressed according to a RDS schedule. Peripheral blood for detection of inflammatory markers was collected before and 90 min after diving. Venous gas emboli were measured 30 min after diving using 2D echocardiography. Matched groups of 23 recreational divers (dive to 30 msw; 25 min) and 25 swimmers were also enrolled as control groups to assess the effects of decompression from a standard air dive or of exercise alone on the inflammatory profile.

Results: Echocardiography at the single 30 min observation post dive showed no significant differences between the two decompression procedures. Divers adopting the RDS showed a worsening of post-dive inflammatory profile compared to the CDM group, with significant increases in circulating chemokines CCL2 ($P = 0.001$) and CCL5 ($P = 0.006$) levels. There was no increase in chemokines following the CDM decompression. The air scuba group also showed a statistically significant increase in CCL2 ($P < 0.001$) and CCL5 ($P = 0.003$) levels post dive. No cases of decompression sickness occurred.

Conclusion: The ratio deco strategy did not confer any benefit in terms of bubbles but showed the disadvantage of increased decompression-associated secretion of inflammatory chemokines involved in the development of vascular damage.

Key words

Scuba diving; Decompression tables; Inflammation; Chemokines; Bubbles; Echocardiography

Introduction

Decompression sickness (DCS) after scuba diving is probably more common than previously thought.[1] DCS is associated with different pathophysiological conditions. The first is an increase in intravascular inert gas bubbles directly related to the degree of inert gas supersaturation of tissues. These bubbles in turn activate inflammatory responses. Intravascular inert gas bubbles have been linked to the elevation of circulating microparticles (MPs) observed both in humans and in experimental animal models of diving and associated with inflammation and neutrophil activation.[2] MPs have a physiological role in inflammation.[3] Elevated circulating MPs in divers have been clearly linked to neutrophil and endothelial activation, triggering a response cascade able to increase circulating inflammatory molecules.[4,5] Several studies have recently focused on the effects of decompression on the vascular endothelium, even in divers without DCS.[6] Altered endothelial function may exert a negative effect on the maintenance of vascular homeostasis after diving. A post-dive decrease of endothelial function has been demonstrated following a single air dive that produced few post-dive bubbles and no clinical symptoms of DCS.[7] The alterations of endothelium include an increased expression of endothelial adhesion molecules.[2] These responses were recorded soon after diving and constitute early physiological responses to decompression.[8] Moreover, these studies demonstrated that endothelial physiology is modified even after safe dives. These modifications in vascular physiology may be useful, early, sensitive biomarkers able to monitor the adverse effects of decompression linked to inflammation and endothelial activation.

For more than a century, compartmental decompression models (CDM) have been proposed to describe mathematically tissue desaturation mechanisms and thereby limit DCS. These models have been statistically evaluated by DCS cases, and over time have gradually included bubble formation biophysics.[9,10] Technical divers perform deep mixed-gas 'square' dives, with a relatively long duration at the target depth and very long decompressions, which are often outside the validation of the algorithms used by these divers.[11] For these reasons, an increasing number of technical divers use decompression schedules generated without using dive tables, decompression software or a dive

computer in the hopes of producing safer decompression. The basis for calculating these decompression schedule using a 'ratio decompression strategy' (RDS) are relatively simple and generally driven by anecdote. Commonly adopted compartmental decompression algorithms express exponential profiles favouring gradually longer decompression stops approaching the surface. The RDS expresses a 'S'-shaped ascent curve, extending the duration of decompression stops at which the switch to the first oxygen-rich 'deco' gas takes place. This S-shaped ascent curve would also take advantage of a greater number of deep stops aimed to better control microbubble formation.[12] There is widespread belief that bubble algorithms and the RDS, which redistribute decompression in favour of deeper decompression stops, are more efficient than compartmental shallow-stop algorithms. This is despite recent hyperbaric chamber studies not supporting this view.[13,14]

With regard to the pathophysiological approach to decompression, what we know currently is not enough to predict which decompression procedures are better than others in terms of DCS prevention. At present, the only way to compare different decompression strategies is to test them in underwater practice, but this means monitoring a huge number of dives, which is expensive and difficult to achieve in a reasonable amount of time, especially for technical dives.

This study is based on the assumption that inflammation and modification of vascular physiology, monitored by post-dive circulating inflammatory molecules, can produce biomarkers able to evaluate the quality of decompression, even in the absence of DCS events. We studied two decompression procedures commonly adopted by technical divers, comparing their post-dive inflammatory profiles elicited by the same dive. We focused on the circulating pro-inflammatory cytokines and chemokines involved in endothelial activation. Thus, we propose an innovative approach to compare decompression procedures in underwater practice.

Methods

STUDY POPULATION

The research was conducted on 74 healthy volunteer divers and 25 healthy volunteer swimmers. All subjects provided written informed consent, and the study was conducted in conformity with the principles of the Declaration of Helsinki. The local ethics committee approved the study protocol (Ethics Committee of the Azienda Ospedaliera-Universitaria Pisana; approval number 2805).

Subjects were selected after exclusion of disease and the use of anti-inflammatory drugs (steroidal or non-steroidal) within seven days before diving. Body mass index (BMI) >30 kg·m^{-2} was also considered an exclusion criterion. Divers were divided into three groups based on their dive and decompression procedures:
23 recreational divers (Rec) were 40.0 ± 8.1 (mean ± SD) years old and had a BMI of 24.7 ± 4.2 kg·m^{-2};
23 technical divers adopting a compartmental decompression model (Tech CDM; ZH-L16 algorithm modified with 30/85 gradient factors) had a mean age of 40.5 ± 6.7 years and mean BMI 25.3 ± 2.7 kg·m^{-2};
28 technical divers adopting the ratio deco decompression strategy (Tech RDS) had a mean age of 41.0 ± 4.7 years and mean BMI 22.8 ± 2.3 kg·m^{-2}.
A group of 25 swimmers (mean age 41.1 ± 9.1 years and mean BMI 24.9 ± 3.4 kg·m^{-2}) was enrolled as a control group to assess the effects of exercise alone on the inflammatory profile. Swimmers performed moderate surface exercise (slow breaststroke-style swimming), comparable to that performed by the divers, for a similar duration of 60 min.

DIVES AND DECOMPRESSION PROFILES

All dives were performed with open-circuit scuba equipment and with dry suits to avoid the effects of cold on circulatory and vascular physiology. Bottom temperatures ranged from 17–19°C while surface temperature ranged from 22–26°C. Technical dives (Tech CDM and Tech RDS) were based on the presence of trimix bottom gas (18% oxygen, 45% helium, 37% nitrogen) and two stage bottles, enriched air nitrox 50 (EAN50) and 100% oxygen, with the switch gases fixed at 21 metres' sea water (msw) and 6 msw respectively (switch PO_2 = 1.6 bar). All the dives were performed in the vicinity of the Giannutri Island Marine National Park, Tuscany, Italy. The technical dives were carried out on the ferry wreck, *Nasim II*, at 50 msw for 25 min. A descent shot line and a path line along the wreck were placed up to the point where the ascent began in order to keep the amount of swimming during the dive similar for each diver. Ascent was performed in open water towards the coast. The two technical diving decompression schedules were selected by the Tech divers as typical for the dive; all divers followed closely the prescribed schedules, as verified by analyzing their diving computer records.

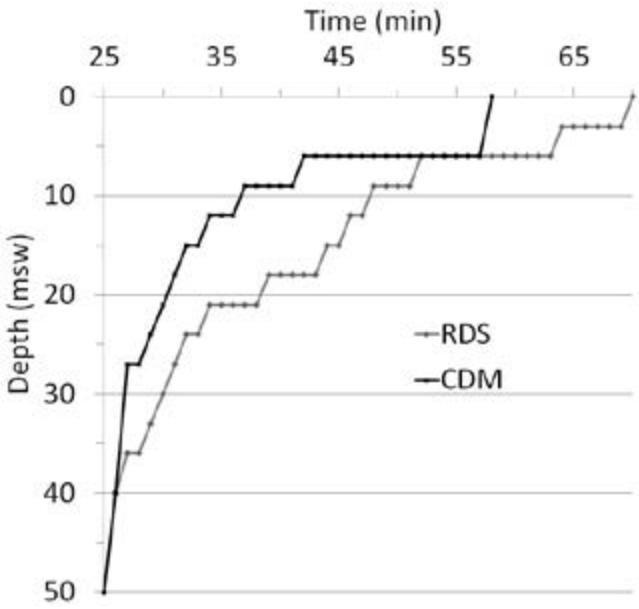
The recreational decompression dive was a 30 msw air dive within the no-stop limits prescribed by the US Navy Air Decompression Table. The maximum depth was reached after 2 min, and divers remained at 30 msw up to 25 min of dive time. The ascent was at 10 m·min^{-1} up to a safety stop at 3 msw for 3 min and then they surfaced at an ascent rate of 3 m·min^{-1}.

The CDM was generated by Deco Planner software based on the Bühlmann algorithm (ZH-L16 algorithm modified with gradient factors 30/85), one of the most commonly used by technical divers (Table 1). This profile (Figure 1) calculates the decompression timing according to the exponential kinetics of the inert gases in tissues. The software considers the behavior of tissues and assigns gradually longer decompression stops as divers near the surface. The ascent

Table 1
Two different decompression schedules – ratio decompression strategy (RDS) and compartmental decompression (CDM) – for a technical dive with a total descent and bottom time of 25 min; depth at which the diver is located (msw) against run time (min)

Run time (min)	RDS (msw)	CDM (msw)
25	50	50
26	40	40
27–28	36	27
29	33	24
30	30	21
31	27	18
32–33	24	15
34–36	21	12
37–38	21	9
39–41	18	9
42–43	18	6
44–45	15	6
46–47	12	6
48–51	9	6
52–57	6	6
58	6	0
59–63	6	
64–69	3	
70	0	

Figure 1
Two technical diving decompression profiles – ratio decompression strategy (RDS, light grey) and compartmental decompression (CDM, dark grey); the descent and bottom-time profile (0–25 min, not shown) was identical for both RDS and CDM dives



to the first decompression stop (27 msw) was 10 m·min^{-1} and 3 m·min^{-1} thereafter.

The RDS adopts a coded concept of set points that fixes a ratio of bottom time and decompression time for various depths to calculate the decompression times (40 msw ratio 1:1; 60 msw ratio 1:2; 75 msw ratio 1:3). Additional rules are used to interpolate between set point depths. The total decompression time obtained from the RDS is distributed among decompression stops according to a set of rules (Table 1). The total decompression time for RDS divers was longer than that generated by the CDM profile, but what changed most was the shape of the ascent profile (Figure 1), with lengthening of the time at the gas switch. The decompression develops in several steps with a first deep stop at 75% of the maximum depth (1 min) and a second deep stop at 50% of maximum depth (1 min). These two stops at a conservative depth during the ascent phase are proposed to help to control the critical volume of inert gas which is correlated to the radius of the microbubbles. The ascent to the first decompression stop (37 msw) was 10 m·min^{-1} and thereafter 3 m·min^{-1} up to the gas switch and subsequent stops.

BLOOD SAMPLE COLLECTION AND DETECTION OF CYTOKINES

For the diver groups, 5 ml of venous blood was collected from the antecubital fossa of the left arm into a Vacutainer® (BD Science) containing ethylene diamine tetraacetic acid (EDTA). In swimmers, 300 µl of blood was collected by digital puncture and transferred to Eppendorf tubes containing EDTA. Blood was collected 60 min before and 90 min after diving or swimming. Blood samples were kept at 4°C for 24 h, then centrifuged at 1000 g for 15 min. Plasma was collected and stored at -80°C until analysis. Cytokines present in plasma were quantified in triplicate (plasma dilution 1:4) by using a customized detection panel (BioRad, USA): interleukin 6 (IL-6), interleukin 8 (IL-8); C-X-C motif chemokine 10 (CXCL10), C-C Motif Chemokine Ligand 2 (CCL2), Macrophage Inflammatory Protein-1 beta (MIP-1β) and C-C Motif Chemokine Ligand 5 (CCL5). The assays were performed in 96-well filter plates by multiplexed Luminex®-based immunoassay as previously described,[15] following the manufacturer's instructions, at the Proteomic Unit CRR, University of Bologna.

Samples were analysed as a single batch, after performing validation and calibration of the instrument (Bioplex Validation & Bioplex Calibration Kits, Biorad, USA). Microsphere magnetic beads coated with monoclonal antibodies against the different target analysates were added to the wells. After 30 min incubation, the wells were washed and biotinylated secondary antibodies were added. After further incubation for 30 min, beads were washed and then incubated for 10 min with streptavidin-PE conjugated to the fluorescent protein, phycoerythrin (streptavidin/phycoerythrin). After washing, the beads (a minimum of 100 per analysate) were analyzed in the BioPlex 200 instrument (BioRad, USA). Sample concentrations were estimated from the standard curve using a fifth-order polynomial equation and expressed as pg·ml^{-1} after adjusting for the dilution factor (Bio-Plex Manager software 5.0). Samples

below the detection limit of the assay were recorded as zero, while samples above the upper limit of quantification of the standard curves were assigned the highest value of the curve. The intra-assay coefficients of variability (CV) averaged 12%.

BUBBLE ANALYSIS AND GRADING

After surfacing, divers returned to the diving centre by fast boat (20 min trip, seated) then rested seated for 10 min. Finally, they lay supine for 2D echocardiography performed 30 min after surfacing. A 30-sec clip of each of the following echocardiographic views was acquired: apical four-chamber (to evaluate right ventricle and right atrium), heart base short-axis (to evaluate right atrium, right ventricular outflow tract and main pulmonary artery), inferior vena cava and right atrium subcostal scan. A visual search for circulating bubbles was made offline on recorded loops. The use of a single evaluation of circulating bubbles is sub-optimal for proper assessment, but we had to limit ultrasonic evaluations due to protocol constraints.

Echocardiography evaluation was at the time (30 min post dive) that previous reports indicate as the time of peak venous gas emboli (VGE),[16] and each ultrasonic evaluation was protracted for 90 sec (30 sec for each of the three analyzed views) to reduce the likelihood of underestimating bubble grades owing to spontaneous variability of the number of VGE. Bubbles were graded as the maximum in any view by an operator unaware of the decompression procedures followed by the diver, according to the Eftedal-Brubakk grading.[17] Bubble grades were divided into high (grades 3–5) and low bubble grade groups (grades 0–2).

URINE COLLECTION AND ANALYSES

Urine specific gravity has been used to assess hydration status in sportsmen.[18] Urine samples (15 ml) were collected in polypropylene bottles from all divers 60 min before and 90 min after the dive. Combur-Test® strips (Roche, Germany) were immediately used for the detection of leukocytes, proteins, glucose and blood. Analyses were repeated at least twice for each sample. No diver showed values outside the normal range. Urine specific gravity was evaluated in triplicate by using a refractometer (Atago, Japan).

Oxidative damage was analyzed by measuring 8-hydroxy-2-deoxy guanosine (8-OH-dG) and creatinine in urine, which has been used to evaluate the effect of exposure to systemic reacting oxygen insults.[19] Urinary 8-OH-dG (Abcam Inc., USA) was measured in triplicate using a commercially available ELISA kit following the manufacturer's instructions. 8-OH-dG, a frequently used biomarker of oxidative DNA damage, is removed from DNA by the base excision repair pathway, and subsequently transported into saliva, urine and plasma. Creatinine was determined by means of a modified Jaffe reaction (alkaline picrate method) using the Wako Creatinine-Test (Wako Pure Chemical Ind, Ltd. Japan).

STATISTICAL ANALYSIS

Continuous variables are expressed as mean ± SD of at least three independent determinations. Normality of distribution was verified with the D'Agostino-Pearson and Shapiro-Wilk tests and the homogeneity of variances (homoscedasticity) with the F-test. Statistical differences between groups were determined by Student's *t*-test. GraphPad Prism 6 (GraphPad Software Inc., San Diego, CA, USA) was used for all analyses. Categorical variables are expressed in total counts and percentage of counts, and were compared using χ^2 tests. Differences were considered significant at $P < 0.05$.

Results

BUBBLE ANALYSIS

Echocardiographic bubble analysis made at one time point (30 min) post dive showed no significant differences between the two groups of technical divers (Figure 2), although high bubble grades (grades 3–4) were more frequent in the RDS group (2/23 in Tech CDM divers *vs.* 4/28 in Tech RDS divers). There were no statistical differences in bubble grading between the two decompression procedures, either comparing low with high grade frequencies or grade zero against all other grades.

PRO-INFLAMMATORY MARKERS

The 60 min of moderate exercise did not modify the inflammatory profile of swimmers (Figure 3A), whereas the Rec diver group showed a significant increase in circulating CCL2 (1.4 fold; $P < 0.001$) and CCL5 (1.2 fold, $P = 0.003$) after diving; IL-6, IL-8, CXCL10 and MIP-1β were unaffected Figure 3B). A similar increase in CCL2

Figure 2

Bubble grades 30 min after surfacing using two different decompression schedules – ratio decompression strategy (RDS) and compartmental decompression model (CDM) for a 50 msw, 25 min bottom time technical dive; no grade 5 bubbling was detected

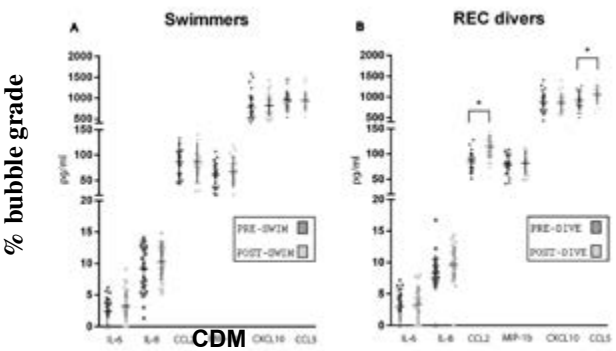
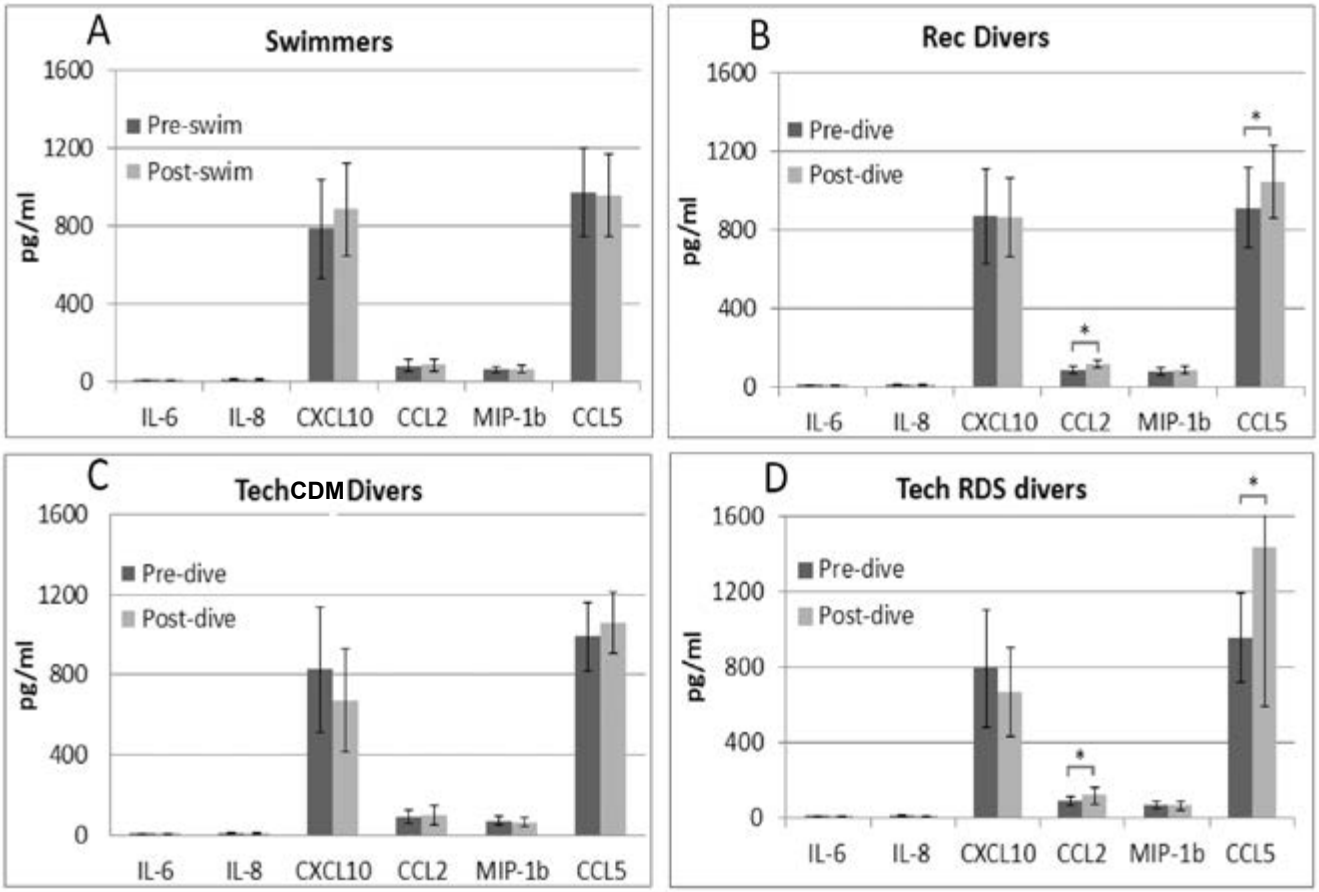


Figure 3

Circulating cytokines and chemokines detected in swimmers before and 90 min after surface swimming, and in three groups of divers (mean +/- SD shown) before and 90 min after surfacing from their different dives: the concentrations of interleukin 6 (IL-6); interleukin 8 (IL-8); C-X-C motif chemokine 10 (CXCL10); C-C motif chemokine ligand 2 (CCL2), macrophage inflammatory protein-1 beta (MIP-1ß) and C-C motif chemokine ligand 5 (CCL5) were simultaneously measured in the plasma of swimmers and divers by multiplexed Luminex®-based immunoassay; * indicates statistically significant differences (see text for details)



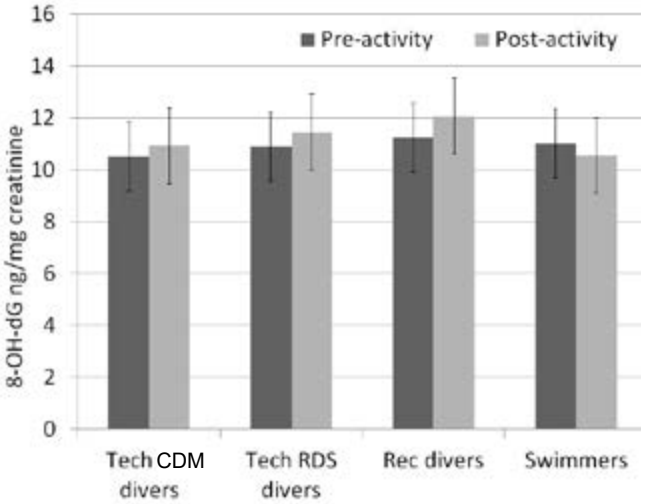
(1.4 fold, $P = 0.001$) and CCL5 (1.5 fold, $P = 0.006$) was observed in Tech RDS divers (Figure 3C). By contrast, Tech CM divers showed only a slight, non-significant decrease in the mean value of CXCL10 (from 827 to 674 pg·ml^{-1}) and MIP1-ß (from 73 to 65 pg·ml^{-1}) (Figure 3D). Comparing the pro-inflammatory markers in all three groups of divers, it was evident that only Rec and Tech RDS divers showed a worsening of their inflammatory profile, particularly in circulating CCL2 and CCL5 levels, while inflammation was unchanged after diving in Tech CM divers. There was no correlation between bubble grades and circulating CC2 or CCL5 levels after diving.

URINE ANALYSIS

Most of the divers had an urinary specific gravity above 1.020 before diving (average 1.022) but there were no differences in urinary specific gravity observed pre or post dive among the three diver groups. Increased oxygen exposure during the dives did not modify urinary 8-OH-dG levels in any of the three dive groups (Figure 4).

Figure 4

Urinary 8-hydroxy-2'-deoxyguanosine (8-OH-dG) taken 90 min after surface swimming and in three groups of divers before and 90 min after surfacing from their different dives (mean +/- SD)



Discussion

The RDS is widely used by technical divers for their decompression procedures. Nevertheless, decompression protocols with experimental deep stops added, when tested in simulated dives in hyperbaric chambers, have never shown any real advantages over more traditional compartmental models.[13,14] However, the conditions under which these laboratory studies were conducted differ from conditions in typical technical diving. Field studies can allow decompression procedures to be evaluated under typical conditions encountered by technical divers.

Studies comparing different decompression models in terms of decompression effectiveness require a vast number of analyzed dives since they are based on statistical analyses of DCS cases and statistical analyses of Doppler and echocardiographic bubble counts. On the other hand, we do not know enough about the pathophysiology of DCS to predict the goodness of fit of decompression models. An in-depth analysis of real decompression accidents clearly shows that the majority of DCS cases reported by DAN occur after dives conducted following appropriately prescribed decompression.[20] This suggests that as yet unknown pathophysiological factors are involved in the onset of DCS.

It is known that physical activity may alter circulating IL-6, IL-8, MIP-1β and other pro-inflammatory molecules.[21] The modification of the inflammatory profile after scuba diving, but not after the comparable swimming exercise in our study, suggests that it is decompression that causes an increase in some circulating chemokines, namely CCL2 and CCL5, and not with the physical exercise performed during the dive. While CCL2 and CCL5 increased after diving in both the Rec group and in the RDS group, they remained unaffected 90 min after diving in the CDM dive. This suggests that the recreational air dive to 30 msw was more proinflammatory than the CDM dives to 50 msw. This apparent paradox may be explained partially by the documented protective effects of helium on the endothelium.[22] Given the increased levels of these two pro-inflammatory chemokines after RDS-controlled dives, we conclude that the RDS ascent profile caused a worsening in diver inflammation compared with the CDM ascent profile. This fits with the chamber evidence of no advantage to deeper stops.[13,14]

The chemokine CCL5 or RANTES (regulated on activation, normal T cell expressed and secreted) is a member of the CC chemokine family stored in and released from platelets and activated T lymphocytes. Circulating chemokine CCL5 is known to contribute to endothelal activation and the interaction between endothelial cells and monocytes.[23] It was reported recently that CCL5 secretion facilitates endothelial progenitor cell recruitment and increases nitric oxide production in endothelial cells.[24] Thus, CCL5 may be considered a good circulating marker of vascular damage. As platelet degranulation enhances the release of circulating CCL5, it has been proposed also as a potential index for evaluating decompression stress.[25] Our results suggest that CCL5 could be a circulating marker of the endothelial activation involved in decompression stress, linking platelet activation and endothelial dysfunction, two events clearly involved in decompression physiology.[26] CCL2, also called monocyte chemoattractant protein 1 (MCP-1), is a pro-inflammatory chemokine involved in tissue inflammation and produced by tissue injury.[27] Interestingly, circulating CCL2 and CCL5 concentrations increase in hypertension[28] and have been considered as 'early endothelial chemokines' given their role in vascular inflammation.[29]

It remains possible that the increase in cytokine levels after the RDS dives compared to the CDM group could be attributed to the longer exposure to the environment and high oxygen partial pressures in the breathing gases. Nevertheless, the similar increase in cytokines in the Tech RDS and Rec groups argues against this possibility since Rec divers were exposed to the environment for a shorter period and did not breathe oxygen-enriched decompression gases. As we found no detectable changes in 8-OH-dG levels during these dives, we conclude that the hyperoxia associated with the dive profiles did not give rise to systemic oxidative stress of any importance.

Increased circulating chemokines and higher bubble grades may be two phenomena that are physiologically disconnected. That is, bubble development and the increased inflammation likely induced by vascular modifications might be independent phenomena, both able to enhance divers' susceptibility to develop DCS. However, endothelial physiology, which also depends on individual genetics, is certainly linked to the inflammatory response trigger elicited by circulating bubbles. Further studies will be necessary to correlate circulating chemokines with differences in accepted measures of decompression stress such as the incidence of DCS, VGE evolution or different dive profiles with unequivocal differences in decompression stress.

Urine specific gravity measurements demonstrated that moderate dehydration before diving was common even in highly experienced technical divers. This finding suggests divers are not able to adopt proper hydration strategies in the hours preceding their dives. Dehydration certainly worsens during diving, due to physical exercise, immersion diuresis and loss of water vapour with breathing. The consequent increase in plasma osmolality may concentrate bubbles and also circulating pro-inflammatory molecules. Ninety min after the end of the dive, urine specific gravity tended to decrease in all divers, since they were able to urinate and drink after surfacing from their dives.

We are aware that our study has important limitations, namely the quite low number of divers enrolled, the fact that only a single dive profile – 50 msw, 25 min bottom

time – was tested and the use of a single evaluation of circulating bubbles, which is likely to be sub-optimal. On the other hand, its strength is that it analyzed non-professional divers in the conditions commonly encountered during their recreational dives.

Conclusions

This study does not establish any association between the decompression model chosen and the likelihood of DCS. A single echocardiographic observation of bubble grades is insufficient to draw any useful comparison between CDM and RDS-controlled decompression for this 50 msw dive. However, the RDS has the disadvantage of decompression-associated increased secretion of chemokines involved in the development of vascular damage. This increased secretion of pro-inflammatory chemokines seems related to the decompression system rather than to the longer exposure to high partial pressures of oxygen that RDS divers undergo. Tech RDS and Rec Divers showed very similar inflammatory profiles after the dives. Overall, our findings contradict the idea that adding longer and/or deeper stops is useful to achieve a more effective decompression. A major limitation is that only a single dive profile – 50 msw, 25 min bottom time – was studied and the findings cannot be extrapolated to other dive profiles.

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Preventive effect of rosiglitazone on liver injury in a mouse model of decompression sickness

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Abstract

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Background and aims: Severe decompression sickness (DCS) is a multi-organ injury. This study investigated the preventive effects of rosiglitazone on liver injury following rapid decompression in mice and examined the underlying mechanisms.

Methods: Mice were randomly divided into four groups: a control group, vehicle group, and rosiglitazone (5 and 10 mg·kg^{-1}) groups, the latter three being exposed to a pressure of 911 kPa. Haematoxylin and eosin staining, plasma levels of alanine transaminase (ALT), aspartate transaminase (AST) and lactate dehydrogenase and blood cell counts were used to evaluate liver injury at 30 min after rapid decompression. The expression of endothelial and inducible nitric oxide synthase (iNOS) and its phosphorylation were measured to uncover the underlying molecular mechanisms.

Results: A significant increase in plasma ALT, red blood cells and platelets, and a decrease in neutrophils were observed in the vehicle group. Furthermore, the expression of iNOS, E-selectin and the total level of NO in hepatic tissue, and soluble E-selectin in the plasma were significantly elevated in the vehicle group. Rosiglitazone pre-treatment prevented the increases in ALT (and AST), soluble E-selectin concentration, red blood cells and platelet counts. Moreover, rosiglitazone reduced over-expression of iNOS and the NO level, prevented the fall in neutrophil count and promoted the phosphorylation of iNOS in the liver.

Conclusions: Pre-treatment with rosiglitazone ameliorated liver injury from severe DCS. This preventive effect may be partly mediated by stimulating endothelial NO production, improving endothelial function and limiting inflammatory processes.

Key words

Animal model; Diving research; Injuries; Nitric oxide; Pharmacology

Introduction

Decompression sickness (DCS) is caused by bubbles formed in the blood and tissues during or after a rapid reduction in environmental pressure and is a multi-organ injury.[1] Although use of an effective decompression plan can prevent DCS, it is difficult to completely avoid it happening especially in emergencies. Thus, other preventive methods targeting the pathophysiological processes have become an important strategy to reduce the severity of DCS. Research has mainly focused on the central nervous system injury,[1,2] but other injuries such as to liver and endothelial tissue cannot be ignored;[3–6] thus we investigated how injury to the liver could be reduced.

Previous research found that promoting nitric oxide (NO) generation and release by various methods, such as agent-mediation and appropriately timed exercise pre-diving, could reduce bubble generation and prevent DCS injury especially in the CNS.[7–11] Whereas administration of the nitric oxide synthase (iNOS) inhibitor N(G)-nitro-L-arginine methyl ester (L-NAME) increased bubble formation and mortality in rats,[12] the effects of L-NAME treatment on the susceptibility to DCS in male and female rats were different.[13] These reports suggest that stimulated production of endothelium-derived NO via the activation of endothelial nitric oxide synthase (eNOS) and preservation of endothelial integrity might decrease liver injury induced by rapid decompression.

Rosiglitazone is an hypoglycaemic agent cleared for use in the USA but prohibited in Europe because of its potential adverse side effects. However, studies on rosiglitazone are still on-going, and several have shown its action in promoting the phosphorylation of eNOS Ser-1177 and stimulating NOS in cultured endothelial cells via an AMP-activated protein kinase-dependent (AMPK) mechanism.[14,15] In addition, rosiglitazone may play a protective role in ischaemic brain or hepatic ischaemia/reperfusion injury, which may be partially mediated by alterations in the NO pathway, specifically eNOS and inducible nitric oxide synthase (iNOS).[16–18] Based on the role of eNOS/NO in the pathophysiological processes of DCS and the effect of rosiglitazone on eNOS/NO, the present study investigated its preventive effect on liver injury following rapid decompression and the possible underlying mechanisms with the use of specific markers.

Materials and methods

ANIMALS

Male ICR mice (6–9 weeks of age) were provided by the Experimental Animal Centre of Nantong University. All procedures were performed according to the rules of Jiangsu Province Animal Care Ethics Committee and approved by the Animal Care and Use Committee of Nantong University (Approval ID: SYXK (SU) 2007–0021). Mice were housed in a common cage and maintained on a regular day (06:00–18:00)/night (12 h) cycle with free access to food

Table 1
Number of mice used for each component of the study;
Ros5 – Rosiglitazone 5 mg·kg^{-1}; Ros10 – 10 mg·kg^{-1}; n = 160

Test	Control	Vehicle	Ros5	Ros10
Total (deaths)	40 (0)	50 (10)	20 (4)	50 (7)
Liver function	10	8	8	9
Histology	4	4	–	4
Blood counts	10	8	8	9
Total NO	10	8	–	9
sE-selectin	–	6	–	6
Western-blot	6	6	–	6

and water. The temperature was maintained at 22 ± 1^{O}C. The changes of mice in behaviour, posture and appearance were monitored daily.

Mice were exposed to compressed mixed gas to induce DCS after rapid decompression. The mice were randomly divided into four groups: a control group (n = 40), vehicle group (n = 50) and two rosiglitazone (5 mg·kg^{-1}, Ros5 and 10 mg·kg^{-1}, Ros10) groups (n = 20 and 50, respectively).[16,18] Mice in the vehicle and rosiglitazone groups were subjected to hyperbaric exposure.

Rosiglitazone was administered intraperitoneally at 45 min before hyperbaric exposure, while the animals in both the vehicle group and the control group were administered with an equal volume of saline (0.1 ml/20 g body weight). The numbers of animals used for each assay are listed in Table 1.

HYPERBARIC EXPOSURE

Ten mice at a time were placed in a 100-litre tank (Wuhu Diving Equipment Factory, Anhui, China) and were free to move in the cage during each hyperbaric exposure. One hundred and twenty mice in total were exposed to hyperbaric mixed gas. In our pre-experiments, male ICR mice exposed to 911 kPa (absolute) nitrox did not show significant signs of anaesthesia according to electroencephalographic and motor function tests. Compressed air was not used to avoid the potential toxic effect of a high partial pressure of oxygen (21 kPa × 9 = 189 kPa) on the mice, and hyperbaric nitrox was likely to make any DCS symptoms more apparent, thus we chose nitrox for the study.

The chamber pressure was increased at a rate of 16.7 kPa·sec^{-1} up to 203 kPa (atmosphere absolute) using compressed air and then to 911 kPa with pure N_2 (Nantong Tianyuan Gas Co., Ltd., Jiangsu, China) at the same rate to give a nitrox mix of approximately 95/5 N_2/O_2. The chamber pressure was maintained at 911 kPa for 45 min. The concentration of O_2 and CO_2 were monitored continuously. Oxygen was supplemented manually while exhaled CO_2 was absorbed using soda lime. Rapid decompression was performed at a rate of 100 kPa·s^{-1} to the surface to induce DCS injury.

LIVER FUNCTION

At 30 min after decompression under isoflurane anesthesia, about 1 ml blood plasma was collected via the retro-orbital venous plexus from 35 rats (n = 10 in control group, n = 8 both in vehicle and Ros5 group, n = 9 in Ros10 group, Table 1). 500 µl were put into a disposable vacuum tube without addition of anticoagulant and centrifuged at 1,000 g for 10 min. The plasma levels of alanine transaminase (ALT), aspartate transaminase (AST) and lactate dehydrogenase (LDH) were detected with a biochemical analyzer (AU2700, Olympus, Japan).

BLOOD CELL COUNTS

500 µl of blood was put into a vacutainer containing K_2EDTA (BD Franklin Lakes, NJ, USA). Blood cell counts were performed using an automatic analyzer (XT-1800i, SYSMEX, Japan). White blood cells including lymphocytes and neutrophils, red blood cells, haemoglobin and platelets were measured. The measurements were not self-controlled (before/after pressurisation) as the volume of blood necessary to do so would have been too great to ensure the normal physiological state of mice and thus might have influenced the subsequent results.

HAEMATOXYLIN AND EOSIN STAINING

At 30 min after decompression, 12 mice (n = 4 of the control, vehicle and Ros10 groups, Table 1) were anaesthetized intraperitoneally with ketamine (70 mg·kg^{-1}) and xylazine (10 mg·kg^{-1}) and then perfused with 50 mL of normal saline through the left ventricle followed by a 50 mL 4% paraformaldehyde solution. The hepatic tissue was removed quickly and post-fixed for 24 h in 4% paraformaldehyde solution. After paraffin embedding, coronal sections were cut with a thickness of 5 µm on a paraffin microtome (RM2245, Leica, Bensheim, Germany). Sections were then deparaffinized, rehydrated, stained with haematoxylin and eosin, mounted with neutral balata and covered with coverslips. Finally, the sections were examined under a microscope (DM 4000B, Leica, Germany).

TISSUE PROTEIN EXTRACTION

At 30 min after the end of decompression, livers (n = 16 in the control group, n = 14 in the vehicle group and n = 15 in the Ros10 group, Table 1) were quickly removed from mice killed by decapitation under anaesthesia then homogenized in Radio Immunoprecipitation Assay Lysis Buffer (Beyotime, Jiangsu, China), centrifuged at 14,000 g at 4°C for 30 min; the supernatant was then collected and the total protein concentration was determined using a BCA Protein Assay Kit (Thermo Scientific, Rockford, USA).

TOTAL NO CONCENTRATION MEASUREMENT

Total NO concentration in the hepatic tissues of the mouse

was measured using a NO assay kit (nitrate reductase method, Jiancheng Bioengineering Institute, Nanjing, China). The livers of mice (n = 10 in control group, n = 8 in vehicle and Ros5 groups and n = 9 in the Ros10 group, Table 1) were harvested at 30 min after decompression as described above and homogenized 1:9 (w:v) in 0.9% saline. The homogenates were then centrifuged at 2,500 rpm for 10 min at 4°C, and the supernatants were taken for NO assay according to the manufacturer's instructions and total protein determination.

SOLUBLE E-SELECTIN DETECTION

About 200 µl blood was obtained from the tip of the tail before compression and at 30 min after decompression (n = 6 vehicle and Ros10 groups, Table 1). The samples were coagulated at 4°C, and the soluble E-selectin (sE-selectin) concentration in the supernatant was subsequently detected using an ELISA kit (Cloud-Clone Corp., Houston, USA). The concentration of soluble E-selectin in serum collected before compression was defined as the baseline level.

WESTERN BLOT ANALYSIS

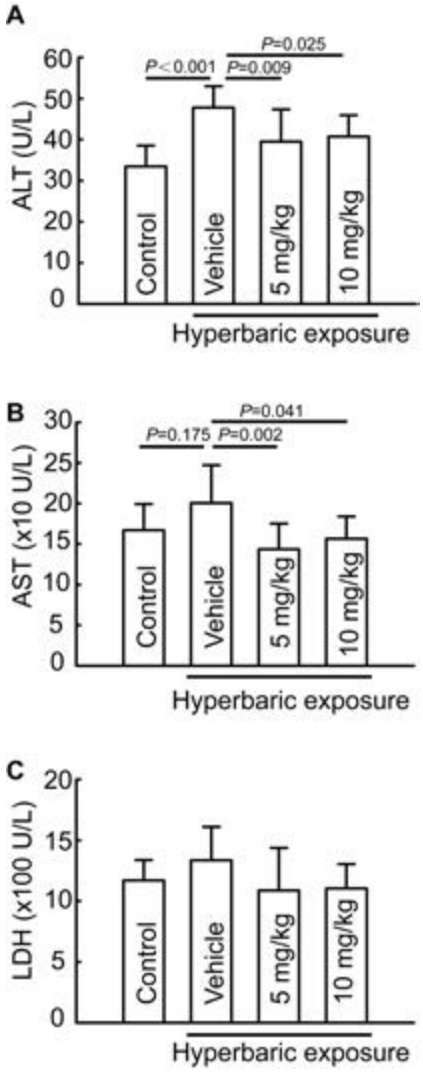
Eighteen protein samples (n = 6 in control, vehicle and Ros10 groups, Table 1) mixed with loading buffer were electrophoresed using 10% sodium lauryl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and electrically transferred onto a polyvinylidene fluoride (PVDF) membrane. The membrane was incubated at 4°C overnight in tris buffered saline (TBS) containing 5% defatted milk and detected with the following primary antibodies: eNOS (C–20) (1:200, sc–654, Santa Cruz, Dallas, USA), phosphorylated eNOS (p-eNOS) at Ser1177 (1:500, sc-12972, Santa Cruz), β-actin (1:10,000, Sigma-Aldrich, St. Louis, USA), iNOS (1:1000, #13120, CST, Denver, USA), and E-selectin (H-300) (1:500, SC-14011, Santa Cruz). After several washes in TBS, the samples were incubated for 2 h at room temperature with secondary IRDye 800 CW goat anti-mouse or rabbit (1:10000, Li-COR, Nebraska, USA). Immunoreactivities were captured using a fluorescence scanner (Odyssey Lix, LI-COR) and quantified using the software Image-pro Plus 5.1. Data were obtained from at least three independent preparations.

STATISTICAL ANALYSIS

Normal distribution was tested for with a Shapiro-Wilk Test using SPSS 17.0 software. Data were presented as the mean ± SD, one-way analysis of variance (ANOVA) was used for multiple comparisons (LSD) with variables that were normally distributed. AST levels and the lymphocyte counts were not distributed normally, so these were transformed into ranks and analyzed with univariate analysis of variance. The significance level was established at $P < 0.05$.

Figure 1

Effect of rosiglitazone 5 mg·kg^{-1} (Ros5) and 10 mg·kg^{-1} (Ros10) pre-treatment on liver injury in DCS mice; plasma ALT, AST and LDH (mean +/- SD) at 30 min after rapid decompression from 911 kPa (n = 10 in control group, n = 8 in vehicle and Ros5 groups, n = 9 in Ros10 group)



Results

Twenty-one of the 120 rats (18%) subjected to pressurisation died, leaving 139 for the various analyses (Table 1). There were no significant differences in mortality between the vehicle and rosiglitazone groups.

LIVER INJURY (FIGURE 1)

The levels of ALT, AST and LDH in the vehicle group were increased to different extents compared to the control group. ($P < 0.001$ for ALT, Figure 1A–C). Both doses of rosiglitazone significantly inhibited these elevations (Ros5, P = 0.009; Ros10, P = 0.025).

Figure 2
Haematoxylin and eosin staining of liver sections at 30 min after decompression from 911 kPa; the arrowheads refer to a disordered lobular structure; scale bar 100 µm

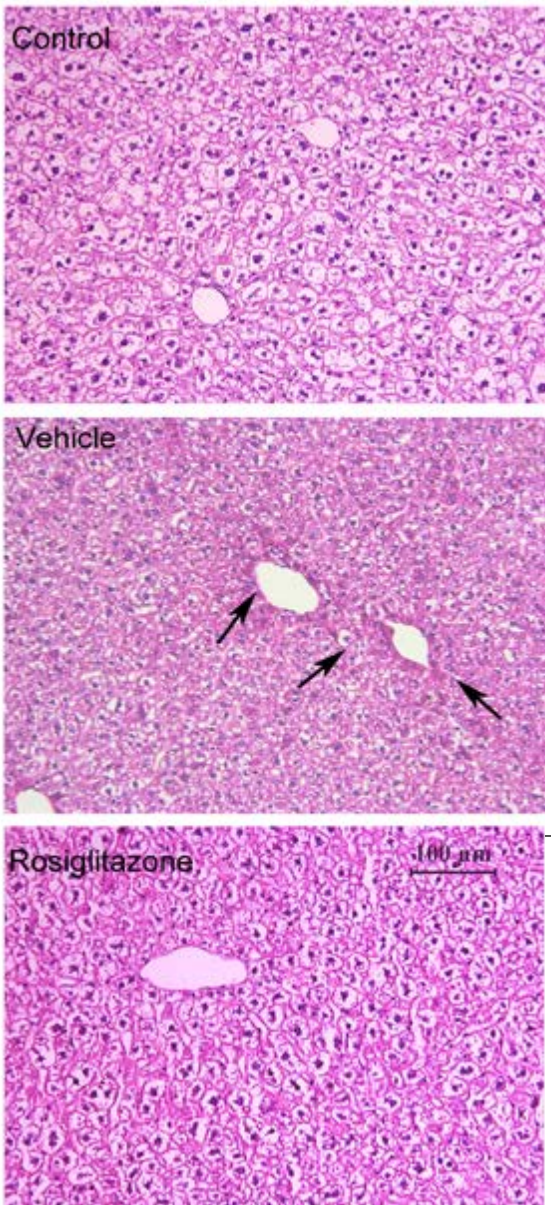
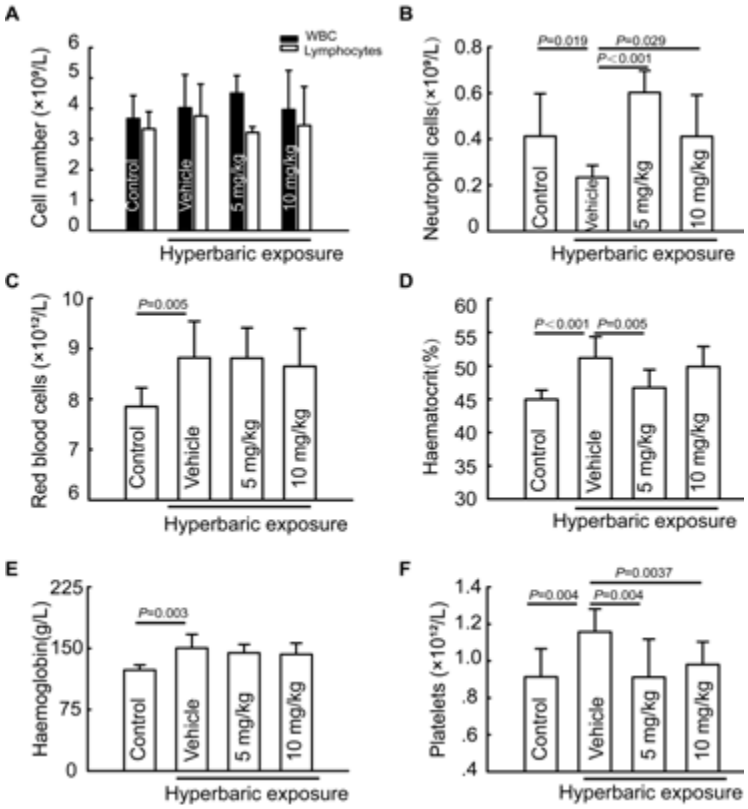


Figure 3
Effect of rosiglitazone pre-treatment on blood cell counts 30 min after decompression from 911 kPa (mean +/- SD); A–F: white blood cells, lymphocyte, neutrophil and red blood cell and platelet counts, haematocrit and haemoglobin concentration (n = 10 in control group, n = 8 in vehicle and Ros5 groups, n = 9 in Ros10 group)



A clear lobular structure and organized hepatic cell cords were observed in control mice, whereas disorganized hepatocytes and a disordered lobular structure were observed in the vehicle group (Figure 2). However, normal hepatic architecture was preserved in the Ros10 group.

BLOOD CELL COUNTS (FIGURE 3)

Red blood cell counts and haematocrit (Figure 3C and D), haemoglobin (Figure 3E) and platelets (Figure 3F) were significantly increased after decompression in the vehicle group. The increase in haematocrit was prevented in the Ros5 group compared to the vehicle group (P = 0.005), and in both rosiglitazone groups the levels of platelets were significantly reduced (Ros5 P = 0.004 and Ros10 P = 0.037, Figure 3). Additionally, the neutrophil counts were significantly decreased after rapid decompression (P = 0.019, Figure 3B), and this reduction was prevented by both rosiglitazone groups (Ros5 P < 0.001 and Ros10; P = 0.0029, Figure 3B).

HEPATIC TOTAL NO PRODUCTION AND iNOS EXPRESSION (FIGURE 4)

Total NO production and iNOS expression in hepatic tissue were significantly elevated in the vehicle group after decompression (P < 0.001 and P = 0.016, respectively *vs*. the control group), however, these elevations were inhibited by rosiglitazone pre-treatment (Ros5 P < 0.001 and Ros10 P = 0.048, respectively *vs*. the vehicle group, Figure 4).

SERUM SE-SELECTION CONCENTRATION AND HEPATIC E-SELECTIN EXPRESSION (FIGURE 5)

Following rapid decompression, the concentration of sE-selectin in the serum and E-selectin expression in hepatic tissue in the vehicle group were remarkably elevated (P = 0.017 and P = 0.011, respectively). Pre-treatment

Figure 4

Effect of rosiglitazone pre-treatment on total NO production and iNOS expression in the liver (mean +/- SD) at 30 min after decompression from 911 kPa; A: total NO concentration; (n = 10 in control group, n = 8 in vehicle group, n = 9 in Ros10 group); B: examples of iNOS expression; C: iNOS levels (n = 6 in each group)

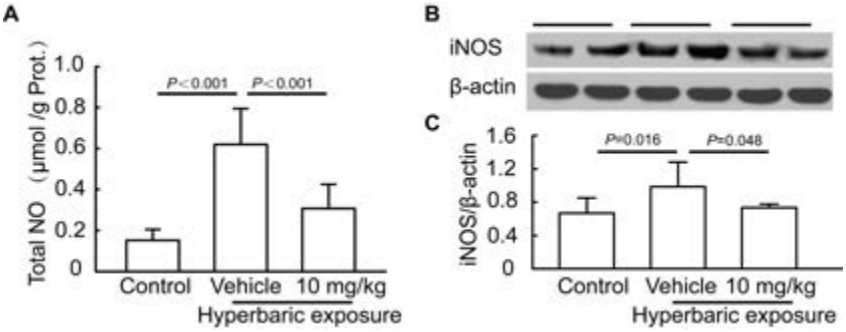


Figure 5

Effect of rosiglitazone pre-treatment on the levels of serum sE-selectin concentration and E-selectin expression in hepatic tissue (mean +/- SD) at 30 min after rapid decompression from 911 kPa; A – change in sE-selectin (n = 12 in the control group, and n = 6 in the vehicle and rosiglitazone groups); B – examples of E-selectin expression (Western blot); C – mean values of E-selectin in the liver

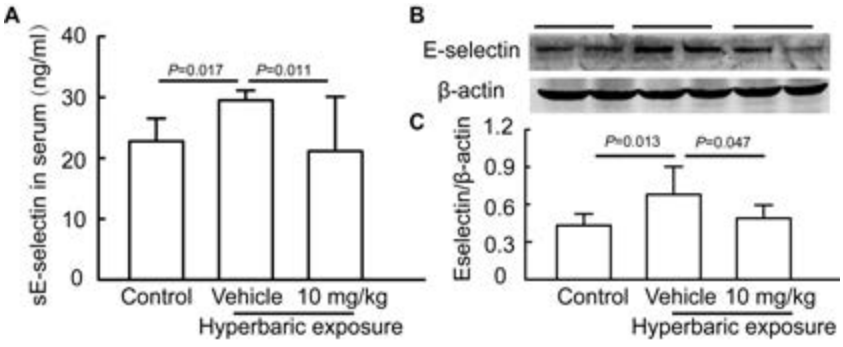
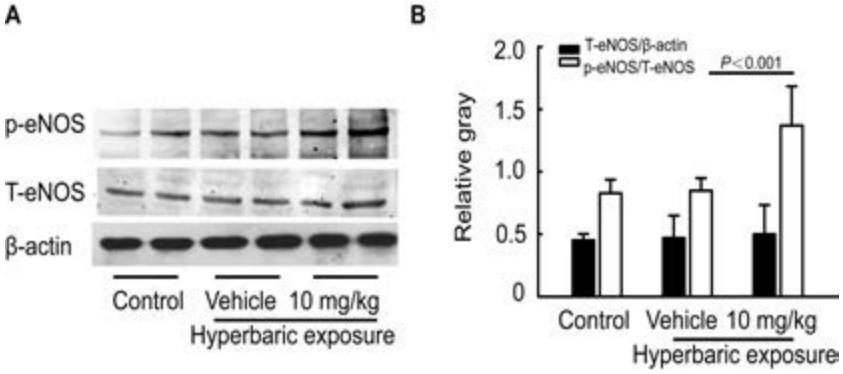


Figure 6

Effect of rosiglitazone pre-treatment on the phosphorylation of eNOS in the liver (Western blot analysis) at 30 min after rapid decompression from 911 kPa; A: examples of T-eNOS, p-eNOS and -actin expression; B: T-eNOS and p-eNOS level relative to β – β-actin (mean +/- SD, n = 6 in each group)



with rosiglitazone prevented these elevations (Ros5 P = 0.013 and Ros10 P = 0.047, Figure 5).

PHOSPHORYLATION OF eNOS (FIGURE 6)

The expression of T-eNOS remained unchanged after decompression and in the presence of rosiglitazone. Moreover, rapid decompression did not change the level of p-eNOS; however, pre-treatment with rosiglitazone (Ros10) elevated the expression level of p-eNOS and the ratio of p-eNOS / T-eNOS in the hepatic tissue (P < 0.001, Figure 6).

Discussion

The main finding in this study was that pre-treatment with rosiglitazone reduced liver injury in mice following rapid decompression, as assessed by morphological hepatic lobule alterations, the ALT and AST levels and blood cell counts. In addition, we found that rosiglitazone pre-treatment significantly decreased sE-selectin level in the serum and promoted the phosphorylation of eNOS in the liver of mice after rapid decompression. These results suggest that the reduction in liver injury by rosiglitazone pre-treatment may be mediated via stimulation of eNOS and the resultant elevation of endothelial function. Moreover, the decreases in iNOS expression, total NO production in the liver and of neutrophil counts in blood suggest that rosiglitazone also may have an anti-inflammatory action.

Nitrogen bubbles that appear in the blood, extracellular space, and intracellular space during decompression can promote neutrophil activation, stimulate the release of inflammatory mediators IL-6, as well as cell adhesion molecules E-selectin, L-selectin and intercellular adhesion molecule-1, thereby triggering inflammatory cascades in tissues.[6,19] In this study, sE-selectin, a marker of endothelial activation and systemic inflammatory response syndrome,[20] was elevated in serum after decompression. In addition, damage to the vascular endothelium by gas bubbles in DCS may provoke diapedesis, which may be the reason for the decrease in neutrophil counts in the present study. Furthermore, stimulation of NO production through up-regulation of iNOS expression, may promote inflammatory responses contributing to tissue injury that is accompanied by increased leukocyte activation and endothelial adherence.

Rosiglitazone pre-treatment significantly prevented the increase in ALT and the decrease in neutrophils as well as inhibiting iNOS expression and total NO production. This suggests a potential inhibitory effect of rosiglitazone on inflammatory responses and consequently, exerting a protective effect during DCS. We believe that this protective effect of rosiglitazone may be partially mediated by inhibiting iNOS activity.[21] Previous studies have also shown that rosiglitazone can attenuate inflammatory responses and exert a protective effect in experimental models of ischaemia and intracerebral haemorrhage.[22] Thus, the present results of rosiglitazone treatment on liver injury induced by rapid decompression are consistent with the literature.

Bubble precursors (gas nuclei) adhering to the endothelium are able to grow into bubbles during decompression.[12] To some extent, the amount and size of bubble formation during decompression is dependent on the basal synthesis of NO, specifically for NO derived from eNOS in the endothelium.[8,12] Thus, altering the properties of the vascular endothelium via exogenous NO administration or mediators of endogenous NO up-regulation might reduce DCS risk and severity, which may be mediated by altering the endothelial surface tension and ultimately interfering with bubble formation.[7,23] In this study, we found an increase in the endothelial activation marker sE-selectin in the serum and E-selectin expression in hepatic tissue following decompression, indicating an activation of the endothelium. These increases were inhibited by rosiglitazone, suggesting that its protective effect may involve actions on endothelial function.

Rosiglitazone has been reported to be able to acutely stimulate NOS in cultured endothelial cells via an AMPK-dependent mechanism. eNOS-mediated NO generation can serve a protective function, thereby preserving endothelial integrity, improving tissue perfusion, and abrogating injury.[7,14] Rosiglitazone promoted the phosphorylation of eNOS in the liver in the present study. In general, damage to endothelium during rapid decompression will increase the microvascular permeability and extravasation of plasma, which will result in haemoconcentration.[24] The haematolical data suggest that some level of haemoconcentration had occurred and that rosiglitazone pre-treatment prevented this. Thus, a potential effect of rosiglitazone may be to alleviate endothelial injury during rapid decompression.[25,26]

As there were no significant differences in the results between the two rosiglitazone groups, we did not measure the effects of 5 $mg \cdot kg^{-1}$ rosiglitazone on indices including E-selectin, total NO level and the level p-eNOS. The present findings suggest a mechanism underlying rosiglitazone-induced protection that involves the phosphorylation of eNOS, that increases endothelial NO production, preserves vascular integrity and function and, as a result, the liver function of mice after rapid decompression.

Conclusions

The present study demonstrated that pre-treatment with rosiglitazone could protect mice against the liver injury induced by rapid decompression. This preventive action may be mediated, at least in part, by limiting inflammatory processes and preserving endothelial integrity and function. Therefore, targeting eNOS/NO pathways may serve as a strategy to reduce liver injury in DCS.

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Consensus Conference

Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment

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Abstract

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The tenth European Consensus Conference on Hyperbaric Medicine took place in April 2016, attended by a large delegation of experts from Europe and elsewhere. The focus of the meeting was the revision of the European Committee on Hyperbaric Medicine (ECHM) list of accepted indications for hyperbaric oxygen treatment (HBOT), based on a thorough review of the best available research and evidence-based medicine (EBM). For this scope, the modified GRADE system for evidence analysis, together with the DELPHI system for consensus evaluation, were adopted. The indications for HBOT, including those promulgated by the ECHM previously, were analysed by selected experts, based on an extensive review of the literature and of the available EBM studies. The indications were divided as follows: Type 1, where HBOT is strongly indicated as a primary treatment method, as it is supported by sufficiently strong evidence; Type 2, where HBOT is suggested as it is supported by acceptable levels of evidence; Type 3, where HBOT can be considered as a possible/optional measure, but it is not yet supported by sufficiently strong evidence. For each type, three levels of evidence were considered: A, when the number of randomised controlled trials (RCTs) is considered sufficient; B, when there are some RCTs in favour of the indication and there is ample expert consensus; C, when the conditions do not allow for proper RCTs but there is ample and international expert consensus. For the first time, the conference also issued 'negative' recommendations for those conditions where there is Type 1 evidence that HBOT is not indicated. The conference also gave consensus-agreed recommendations for the standard of practice of HBOT.

Key words

Medical conditions and problems; Evidence; Systematic review; Symposium; European Committee for Hyperbaric Medicine

Introduction

The European Committee for Hyperbaric Medicine (ECHM) has in its objectives the continuous improvement in the quality of care and the safety of hyperbaric medicine.[1] One of the tools used to reach this target is the organization of consensus conferences to issue guidelines which could be recognized and accepted as widely as possible. Two such consensus conferences have been organized previously in 1994 and 2004. In 1994, the guidelines were elaborated by a jury from expert reports and discussion with the conference audience.[2] In 2004, the guidelines report was improved in grading the recommendations both by the level of evidence supporting the recommendation and their importance for clinical practice.[3] Twelve years on, it was time to review and update these guidelines based on the advances in medical knowledge and the experience gained in clinical practice during that period. For the 2016 guidelines, ECHM wished to go a step further in reporting not only recommendations with their clinical importance and evidence level, but also how confident the conference audience was in those recommendations. A preliminary report with the short list of indications for hyperbaric oxygen treatment (HBOT) was published recently.[4] Here, we present the full report, including methodology and detailed recommendations given at the conference. Additional files with literature queries and analysis of published evidence using the GRADE system can be found on the ECHM website (www.ECHM.org).

Methodology

Evidence based medicine (EBM) methodology has gained a widespread acceptance and is presently an integral part of modern medical practice. The approach and tools used in EBM involve using scientific evidence to provide answers to specific questions. However in the real world, there are different levels of evidence depending on the source of information and the design of the study (e.g., from case reports to randomised controlled trials RCTs). This results in the concept of a pyramid of evidence with a decreasing chance of bias as the methodological rigour improves moving up the pyramid. For interested readers, we provide a useful reference on EBM.[5]

The process of issuing new recommendations for clinical practice is typically based on three components: 1) the

level of evidence (i.e., the quality of available data;) 2) the interpretation of the evidence (i.e., what the data suggest and how concordant these data are regarding a particular problem) and 3) the type or strength of the recommended practice (i.e., the extent to which a physician is able to recommend a particular intervention on the basis of the first two considerations). This method may be used either by an individual physician or by a group of experts who could be expected to arrive at the same conclusion.

For clinical research, the various levels of evidence are the following:

Level A: At least two concordant, large, double-blind RCTs with no or little methodological bias;
Level B: Double-blind RCTs but with methodological flaws, studies with only small samples or one study only;
Level C: Consensus opinion of experts;
Level D: Only uncontrolled studies with no consensus opinion of experts;
Level E: No evidence of beneficial action, or methodological or interpretation bias precluding any conclusion;
Level F: Procedure not indicated by existing evidence.

Even though the hyperbaric medicine community has made considerable effort to achieve high quality clinical studies, we must recognize that many questions remain with insufficient evidence to give a definite answer. Therefore, it is hardly surprising that, from the current list of clinical indications for HBOT, only a small number of clinical entities in which HBOT is conventionally used is supported by the highest level of evidence. Physicians should remember that clinical decisions are usually based on some level of evidence that is less than absolute proof and that no evidence of a benefit is not the same as evidence of no benefit. In the view of the ECHM, there are some clinical situations in which it is extremely difficult or even virtually impossible to undertake high quality, controlled trials, for example:

- Using HBOT in a particular condition, unsupported by a high level of evidence, is so logical that it has become universally accepted to such an extent that it would be grossly inappropriate to consider omitting it to establish proof of efficacy or even that it would be considered a violation of accepted standards of care to deny a patient the benefit of the therapy for the purpose of a study (e.g., HBOT for decompression illness (DCI) or arterial gas embolism (AGE));
- where the disease or condition of interest is so complex or where there are so many variables that it would be impossible to design a study sufficiently powerful to assess any single procedure (e.g., HBOT and gas gangrene);
- where no current higher level of evidence exists, but experts are able to report, not only from their own experiences but also by producing comprehensive literature reviews from which consensus can provisionally be reached, pending the outcome of future studies (e.g., HBOT and neuroblastoma).

In such situations, an alternative approach should be sought. In the opinion of the ECHM, the search for a consensus by experts is a way to convert the best evidence available into clinical guidelines.

ECHM consensus conferences aim to create an objective and complete review of the current literature and knowledge on a particular topic or field. This method has the advantage of involving a diverse group of participants from a broad range of relevant backgrounds to provide consideration of all aspects of the chosen topic and maximum objectivity. The opportunity to meet with other experts in the same field and share comments and information is also a valuable aspect of these meetings. At a consensus conference, experts present their reviews of the literature relating to a specific topic before a jury and an audience. Thereafter, the jury gathers in a secluded place to discuss the presentations, and presents its finding in a consensus statement that includes recommendations for clinical practice based on the evidence that was presented. These recommendations are published in one or more medical journals.

The application of EBM methodology to the consensus process helps the jury members to reach a consensus and strengthens the recommendations. Thus, each jury member assesses the literature and the evidence presented by the experts and grades these according to their quality. In the ECHM conferences, each jury member used the same grading scale (from 1 to 4) for the level of evidence as follows:[2,3]

For both basic studies (tissue, cellular or subcellular level) and for animal studies with a control group:

- Level 1: Strong evidence of beneficial action;
- Level 2: Evidence of beneficial action;
- Level 3: Weak evidence of beneficial action;
- Level 4: No evidence of beneficial action or methodological or interpretation bias preclude any conclusion.

For human studies:

- Level 1: Strong evidence of beneficial action based on at least two concordant, large, double-blind, RCTs with no or only weak methodological bias;
- Level 2: Evidence of beneficial action based on double-blind RCTs but with some methodological bias, or concerning only small samples, or only a single study;
- Level 3: Weak evidence of beneficial action based only on uncontrolled studies (historical control group, cohort study);
- Level 4: No evidence of beneficial action (case reports only) or methodological or interpretation bias preclude any conclusion.

Jury conclusions have been made according to the level of supporting evidence (Table 1):

Table 1
Consensus-based and GRADE scaling for recommendations; GRADE – Grading of Recommendations Assessment, Development and Evaluation System

Strength of recommendation (consensus-based)	Level of evidence (based on GRADE system)
Level 1 = Strong recommendation = "*We recommend…*" The course of action is considered appropriate by the large majority of experts with no major dissension. The panel is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.	Grade A = High level of evidence The true effect lies close to our estimate of the effect.
Level 2 = Weak recommendation = "*We suggest…*" The course of action is considered appropriate by the majority of experts but some degree of dissension exists amongst the panel. The desirable effects of adherence to the recommendation probably outweigh the undesirable effects.	Grade B = Moderate level of evidence The true effect is likely to be close to our estimate of the effect, but there is a possibility that it is substantially different.
Level 3 = Neutral recommendation = "*It would be reasonable…*" The course of action could be considered appropriate in the right context.	Grade C = Low level of evidence The true effect may be substantially different from our estimate of the effect.
No recommendation No agreement was reached by the group of experts.	Grade D = Very low level of evidence Our estimate of the effect is just a guess, and it is very likely that the true effect is substantially different from our estimate of the effect.

- Type 1 recommendation, which means "*strongly recommended*", recommendations or standards are supported by Level 1 evidence;
- Type 2 recommendation, which means just "*recommended*", recommendations or guidelines are supported by Level 2 evidence;
- Type 3 recommendation, which means "*optional*", statements are supported only by Level 3 evidence.

During the 2004 ECHM consensus conference, after having listened to the experts and with the assistance of literature reviewers, the jury graded the existing evidence using the scale we have described above (levels from A to F).[3] Conditions where the use of HBOT was supported by level A, B or C evidence were considered as accepted indications. However, in order to make the jury discussion and decision on conditions not considered accepted indications for HBOT more transparent, the levels D, E, and F were also reported with the jury's evaluation of the existing evidence.

For the 2016 European Consensus Conference, the ECHM decided to adopt the modified GRADE system for evidence analysis,[7,8] together with the DELPHI system for consensus evaluation.[9,10] As for the previous conferences, ECHM asked a panel of experts in each field to prepare reports based on a literature survey, a synthesis of the evidence for each and a proposal for recommendations (Table 1).[6–8]

In order to take into account the changes proposed to improve the quality of guidelines elaboration, we introduce two additional steps:

- All the reports were circulated within the expert group and each expert was asked to weight the clinical importance and the level of evidence each proposed recommendation (Delphi method).
- During the conference, reports and expert opinions were presented and discussed. The audience then voted on each recommendation and the agreement between audience participants was measured and reported. Final consensual recommendations with weighted evidence and audience confidence were then issued.
- We expect that, using such a methodology, every individual reading the conference conclusions will be immediately able to assess the strength of each statement and how it could be applied in their own practice.

Results

Recommendations on the clinical indications for HBOT have been presented separately for accepted indications (Table 2), non-accepted indications (Table 3) and those conditions in which HBOT is not recommended (Table 4).

ACCEPTED INDICATIONS

Carbon monoxide (CO) poisoning

- We recommend HBOT in the treatment of CO poisoning (Type 1 recommendation, Level B evidence).
- We recommend 100% oxygen be applied immediately to any CO poisoned person as a first aid treatment (Type 1 recommendation, Level C evidence).
- We recommend HBOT for every CO poisoned person who presents with altered consciousness alteration, clinical neurological, cardiac, respiratory or psychological signs whatsoever the carboxyhaemoglobin level at the time of hospital admission (Type 1 recommendation, Level B evidence).
- We recommend HBOT in CO-poisoned pregnant women whatever their clinical presentation and

Table 2
Recommendations on the indications accepted for HBOT (there was no Level A evidence)

Condition	Level of evidence		Agreement level
	B	C	
Type 1			
CO poisoning	X		Strong agreement
Open fractures with crush injury	X		Strong agreement
Prevention of osteoradionecrosis after dental extraction	X		Strong agreement
Osteoradionecrosis (mandible)	X		Strong agreement
Soft tissue radionecrosis (cystitis, proctitis)	X		Strong agreement
Decompression illness		X	Strong agreement
Gas embolism		X	Strong agreement
Anaerobic or mixed bacterial infections		X	Strong agreement
Sudden deafness	X		Strong agreement
Type 2			
Diabetic foot lesions	X		Strong agreement
Femoral head necrosis	X		Strong agreement
Compromised skin grafts and musculo-cutaneous flaps		X	Strong agreement
Central retinal artery occlusion (CRAO)		X	Strong agreement
Crush Injury without fracture		X	Agreement
Osteoradionecrosis (bones other than mandible)		X	Agreement
Radio-induced lesions of soft tissues (other than cystitis and proctitis)		X	Agreement
Surgery and implant in irradiated tissue (preventive treatment)		X	Agreement
Ischaemic ulcers		X	Agreement
Refractory chronic osteomyelitis		X	Agreement
Burns, 2nd degree more than 20% BSA		X	Agreement
Pneumatosis cystoides intestinalis		X	Agreement
Neuroblastoma, stage IV		X	Agreement
Type 3			
Brain injury (acute and chronic TBI, chronic stroke, post anoxic encephalopathy) in highly selected patients		X	Agreement
Radio-induced lesions of larynx		X	Agreement
Radio-induced lesions of the CNS		X	Agreement
Post-vascular procedure reperfusion syndrome		X	Agreement
Limb replantation		X	Agreement
Selected non-healing wounds secondary to systemic processes		X	Agreement
Sickle cell disease		X	Agreement
Interstitial cystitis		X	Agreement

carboxyhaemoglobin level at hospital admission (Type 1 recommendation, Level B evidence).

- It would be reasonable to treat patients with minor CO poisoning either by 12 hours normobaric oxygen or HBOT (Type 3 recommendation, Level B evidence).
- We do not recommend treating with HBOT asymptomatic patients seen more than 24 hours after the end of CO exposure (Type 1 recommendation, Level C evidence).

Open fractures with crush injury

- We recommend HBOT in the treatment of open fractures and/or with crush injury (Type 1 recommendation, Level B evidence).
- We recommend early application of HBOT following severe open fractures because it can reduce complications such as tissue necrosis and infection. Gustilo 3B and 3C injuries are considered indications for HBOT and less severe injuries should be considered for treatment when host- or injury-related risk factors are present (Type 1 recommendation, Level B evidence).
- We suggest that HBOT may offer benefit in crush injuries with open wounds but without fracture, where tissue viability is at risk or where there is significant risk of infection (Type 2 recommendation, Level C evidence).

- It would be reasonable to provide HBOT for closed crush injuries where tissue viability is clinically judged to be at risk (Type 3 recommendation, Level C evidence).
- It would be reasonable to provide HBOT for closed crush injuries where there is a potential for compartment syndrome, but where compartment syndrome requiring fasciotomy is not established and where it is possible to monitor progress and response to treatment either clinically or via compartment pressure or oxygenation monitoring (Type 3 recommendation, Level C evidence).
- We recommend that HBOT centres treating crush injury should have equipment for transcutaneous oximetry measurement (TCOM) under pressure as this has predictive value in some situations (Type 1 recommendation, Level B evidence).

Radionecrosis or radition-induced lesions

- We recommend HBOT in the treatment of mandibular osteoradionecrosis (Type 1 recommendation, Level B evidence).
- We recommend HBOT for the prevention of mandibular osteoradionecrosis after dental extraction (Type 1 recommendation, Level B evidence).
- We recommend HBOT in the treatment of haemorrhagic radiation cystitis (Type 1 recommendation, Level B evidence).
- We recommend HBOT in the treatment of radiation proctitis (Type 1 recommendation, Level A evidence).
- We suggest HBOT in the treatment of osteoradionecrosis of other bone than the mandible (Type 2 recommendation, Level C evidence).
- We suggest HBOT for preventing loss of osseointegrated implants in irradiated bone (Type 2 recommendation, Level C evidence).
- We suggest HBOT in the treatment of soft-tissue radionecrosis (other than cystitis and proctitis), in particular in the head and neck area (Type 2 recommendation, Level C evidence).
- It would be reasonable to use HBOT for treating or preventing radio-induced lesions of the larynx (Type 3 recommendation, Level C evidence).
- It would be reasonable to use HBOT in the treatment of radio-induced lesions of the central nervous system (Type 3 recommendation, Level C evidence).

Decompression illness (DCI)

- We recommend HBOT in the treatment of DCI (Type 1 recommendation, Level C evidence).
- We recommend 100% normobaric oxygen first aid (Type 1 recommendation, Level C evidence).
- We recommend intravenous fluid resuscitation with non-glucose containing crystalloid solutions (Type 1 recommendation, Level C evidence).
- We recommend HBOT/recompression therapy tables (US Navy Treatment Table 6 or helium/oxygen (Heliox) Comex Cx30 or equivalent) for the initial treatment of DCI (Type 1 recommendation, Level C evidence). US Navy Treatment Table 5 can be used as the first recompression schedule for selected mild cases.
- We recommend appropriate HBOT treatment tables for residual manifestations of DCI (Type 1 recommendation, Level C evidence).
- We recommend the use of low-molecular weight heparin for the prophylaxis of deep venous thrombosis for immobile or paralyzed cases of DCI (Type 1 recommendation, Level C evidence).
- We suggest the use of lignocaine (lidocaine) and Heliox recompression tables for serious neurological DCI (Type 2 recommendation, Level C evidence).
- We suggest oral tenoxicam (or similar NSAID) for appropriately selected DCI cases (Type 2 recommendation, Level B evidence).

Gas embolism

- We recommend HBOT in the treatment of gas embolism (Type 1 recommendation, Level C evidence).
- We recommend the use of HBOT in cases of arterial and venous gas embolism with neurological and/or cardiac manifestations. Even if a short interval (< 6 h) between embolism and hyperbaric treatment is associated with a better outcome, response to hyperbaric treatment with substantial clinical improvement has been observed in many case reports with a longer interval and even in small series of patients after 24 hours or more (Type 1 recommendation, Level B evidence).
- We recommend the immediate administration of 100% oxygen in case of noticed embolism. However, even if the signs/symptoms resolve, because secondary deterioration can occur later, HBOT is still recommended (Type 1 recommendation, Level B evidence).
- We do not recommend high pressure treatment tables (>405 kPa) because of lack of good evidence. Consideration of the use of heliox or nitrox at higher pressure must be undertaken by each unit based on experience and logistic arguments (Type 2 recommendation, Level B evidence).
- We suggest the use of adjunctive therapy for isolated AGE, such as lidocaine (Type 2 recommendation, Level B evidence) aspirin and/or NSAID (Type 3 recommendation, Level C evidence).
- It would be reasonable to use anticoagulants as adjunctive therapy for isolated AGE (Type 3 recommendation, Level C evidence).

Anaerobic and mixed bacterial infections

- We recommend HBOT in the treatment of anaerobic and mixed bacterial infections (Type 1 recommendation, Level C evidence).

- We recommend HBOT for the treatment of necrotizing soft tissue infections in all locations, particularly perineal gangrene. (Type 1 recommendation, Level C evidence).
- We recommend HBOT be integrated in a treatment protocol combined with immediate and adequate surgery and antibiotics targeting the most probable anaerobic and aerobic involved bacteria (Type 1 recommendation, Level C evidence).
- We recommend HBOT be integrated in the treatment protocol of intra-cranial abscess when one of the following criteria is met: multiple abscesses; abscess in a deep or dominant location; compromised host; contra-indication to surgery, lack of response or further deterioration in spite of standard treatment (Type 1 recommendation, Level C evidence).
- We suggest HBOT be integrated as a second-line measure in the treatment of other anaerobic or mixed anaerobic-aerobic tissue infections such as pleuropulmonary or peritoneal infection (Type 2 recommendation, Level C evidence).

Sudden deafness (idiopathic sudden sensorineural hearing loss, ISSNHL)

- We recommend HBOT in the treatment of ISSNHL (Type 1 recommendation, Level B evidence).
- We recommend HBOT combined with medical therapy in patients with acute ISSNHL who present within two weeks of disease onset (Type 1 recommendation, Level B evidence).
- We do not recommend the use of HBOT alone or combined with medical therapy in patients with ISSNHL who present after six months of disease onset (Type 1 recommendation, Level C evidence).
- It would be reasonable to use HBOT as an adjunct to corticosteroids in patients presenting after the first two weeks but not later than one month, particularly, in patients with severe and profound hearing loss (Type 3 recommendation, Level C evidence).

Delayed wound healing

- We suggest using HBOT in the treatment of diabetic foot lesions (Type 2 recommendation, Level B evidence).
- We suggest using HBOT in the treatment of ischaemic ulcers (Type 2 recommendation, Level C evidence).
- It would be reasonable to use HBOT in the treatment of selected non-healing wounds secondary to systemic processes (Type 3 recommendation, Level C evidence).
- We recommend HBOT in ischaemic lesions (ulcers or gangrene) without surgically treatable arterial lesions or after vascular surgery:
  a. In the diabetic patient, the use of HBOT is recommended in the presence of a chronic critical ischaemia as defined by the European Consensus Conference on Critical Ischemia (see note below), if TCOM readings under hyperbaric conditions (253 kPa, 100% oxygen) are higher than 100 mmHg (Type 1 recommendation, level A evidence).
  b. In the arteriosclerotic patient, HBOT is recommended in case of a chronic critical ischaemia (see note below), if TCOM readings under hyperbaric conditions (253 kPa, 100% oxygen) are higher than 50 mmHg (Type 2 recommendation, Level B evidence).
  c. Note: Chronic critical ischaemia can be recognised when there is: periodic pain, persistent at rest, needing regular analgesic treatment for more than two weeks, or ulceration or gangrene of foot or toes with ankle systolic pressure <50 mmHg in the non-diabetic or toes systolic pressure < 30 mmHg in the diabetic.[11]
  d. However, despite the strong agreement on the validity of the criteria listed above to properly select patients for HBOT, the jury acknowledges the fact not all hyperbaric centres are able to perform TCOM under hyperbaric conditions (253 kPa, 100% oxygen). Therefore, owing to this limitation, we suggest HBOT in diabetic foot ulcers (grade 3 and above of Wagner classification, stage B, grade 3 and above of University of Texas classification) that have failed to respond to adequate basic wound care after four weeks (Type 2 recommendation, Level B evidence).
- For the same reason as above, it would be reasonable to use HBOT in delayed-healing (chronic), non-diabetic wounds and in recurrent, multiple non-healing wounds due to vasculitis (especially those who have not responded to immunosuppressive therapy) (Type 3 recommendation, Level C evidence).
- We recommend, as standard of care, that HBOT should always be used as part of a holistic, multidisciplinary, treatment plan with ongoing wound care on a regular basis and not as a stand-alone therapy (Type 1 recommendation, Level B evidence).
- We recommend that, prior to HBOT, standard wound care has been provided during at least four weeks (including appropriate debridement, vascular screening for significant peripheral arterial disease and/or local wound hypoxia, adequate offloading and infection management) (Type 1 recommendation, Level C evidence).
- We recommend that, prior to HBOT, vascular screening, including imaging procedures, is undertaken in order to evaluate if any revascularization procedure is indicated (Type 1 recommendation, Level C evidence).
- We recommend the use of TCOM as the best technique to monitor the local tissue pressure of oxygen and to select patients for HBOT (Type 1 recommendation, Level C evidence).
- We suggest that the therapeutic dose of HBOT (pressure, time and length of treatment course) should be adapted to patient, type of chronic wound and evolution (Type 2 recommendation, Level C evidence).

- It would be reasonable to consider HBOT as part of a multi-interventional approach in the treatment of chronic calciphylaxis (Type 3 recommendation, Level C evidence).

Compromised skin graft and flap

- We suggest using HBOT in the treatment of compromised skin graft and flap (Type 2 recommendation, Level C evidence).
- We recommend HBOT in all cases of compromised skin grafts and flaps as soon as possible after the diagnosis of compromised grafts/tissues (Type 1 recommendation, Level B evidence).
- We suggest tissue viability be evaluated by clinical judgement and more objective methods including measurement of TCOM or assessment of capillaries by laser Doppler (Type 1 recommendation, Level B evidence).
- We suggest HBOT at a pressure between 203 and 253 kPa for at least 60 minutes per session (preferably 90–120 min), repeated two or three times in first day, then twice per day or once daily until tissues declared alive or necrotic (Type 2 recommendation, Level C evidence).
- We recommend HBOT be used both pre- and post-operatively in cases where there is an increased risk for compromised skin grafts and flaps, e.g., irradiated or infected wound bed, immuno-compromised patient (Type 1 recommendation, Level C evidence).

Limb replantation

It would be reasonable to consider HBOT for limb replantation (Type 3 recommendation, Level C evidence).

Post-vascular procedure reperfusion syndrome

It would be reasonable to consider HBOT for post-vascular procedure reperfusion syndrome (Type 3 recommendation, Level C evidence).

Refractory chronic osteomyelitis

- We suggest HBOT be used in the treatment in chronic refractory osteomyelitis (Type 2 recommendation, Level C evidence).
- We suggest compromised hosts be identified as, in particular, they may benefit from HBOT (Type 2 recommendation, Level C evidence).
- We suggest HBOT protocol be individualized based on the condition and compliance of the patient (Type 2 recommendation, Level C evidence).
- We recommend the effects of HBOT be evaluated repeatedly during and after treatment using the same diagnostic methods as used pre HBOT. HBOT treatment should last at least 11–12 weeks, approx. 60 sessions, before any significant clinical effect should be expected. (Type 1 recommendation, Level C evidence).

Femoral head necrosis (FHN)

- We suggest HBOT be used in the treatment of the initial stage of FHN (Type 2 recommendation, Level B evidence).
- We suggest daily treatment of ≥ 60 min, 100% oxygen, 5–6 days a week, and 4–5 weeks per cycle, at 243–253 kPa, at the initial stage of FHN (Type 2 recommendation, Level B evidence).
- We suggest scheduling MRI and orthopaedic clinical evaluation at 3–4 weeks from the end of the HBOT cycle (Type 2 recommendation, Level C evidence).
- We do not recommend HBOT be used as an isolated treatment but be integrated in a multidisciplinary protocol including minimizing weight-bearing, weight reduction, physiotherapy where applicable and smoking cessation through the HBOT course (Type 1 recommendation, Level C evidence).

Burns

- We suggest HBOT be used in the treatment of second degree burns >20% body surface area (BSA) (Type 2 recommendation, Level C evidence).
- We recommend that only highly specialised HBOT centres, in the immediate vicinity of a burns centre, treat burns as an adjunct to classical burns care, taking care of optimal monitoring and fluid management. (Type 1 recommendation, Level C evidence).
- We suggest that the most benefit is obtained in severe scald burns patients (>20% BSA), with a large proportion of partial-thickness burns (Type 2 recommendation, Level C evidence).
- We suggest that burns to the face (ear, nose), neck, hands and fingers and perineum may benefit even if the total surface burned is <20% (Type 2 recommendation, Level C evidence).
- We suggest that HBOT be initiated within six (at the most eight) hours after the burn injury, and that two sessions per day (at 253 kPa, 100% oxygen) be given for a minimum of three days (Type 2 recommendation, Level C evidence).

Central retinal artery occlusion (CRAO)

- We suggest considering HBOT for patients suffering from CRAO, to be applied as soon as possible (Type 2 recommendation, Level C evidence).

Pneumatosis cystoides intestinalis

- We suggest HBOT in the treatment of pneumatosis cystoides intestinalis (Type 2 recommendation, Level C evidence).

Table 3
Recommendations on the non-accepted indications for HBOT; all have only Level D evidence

Condition	Level of evidence D	Agreement
Post sternotomy mediastinitis	X	Agreement
Malignant otitis externa	X	Agreement
Acute myocardial infarction	X	Agreement
Retinitis pigmentosa	X	Agreement
Facial (Bell's) palsy	X	Agreement

Table 4
Recommendations on those indications for which HBOT should not be used; no Level A evidence

Condition	Level of evidence A	B	C	Agreement
Autism spectrum disorders		X		Agreement
Placental insufficiency			X	Agreement
Multiple sclerosis		X		Agreement
Cerebral palsy		X		Agreement
Tinnitus		X		Agreement
Acute phase of stroke			X	Agreement

Sickle cell disease

- It would be reasonable to consider HBOT as a second-line treatment in sickle cell disease crisis in addition to opioids (Type 3 recommendation, Level C evidence).
- It would be reasonable to consider HBOT as an adjunct to standard wound care in patient with non-healing skin ulcer due to sickle cell disease (Type 3 recommendation, Level C evidence).

Interstitial cystitis

- It would be reasonable to consider HBOT for interstitial cystitis (Type 3 recommendation, Level C evidence).

Brain injury in highly selected patients

- It would be reasonable to consider HBOT in acute moderate-severe traumatic brain injury (TBI) patients and in a highly selected group of patients with chronic TBI who have clear evidence of metabolically dysfunctional brain region(s) (Type 3 recommendation, Level B evidence).
- We recommend HBOT use in TBI to be used only in the context of an investigational study protocol approved by an ethics committee and performed according to clinical research good practice (Type 1 recommendation).
- We do not recommend HBOT use in the acute phase of stroke (Type 1 recommendation, Level C evidence).
- It would be reasonable to consider HBOT in the frame of an investigational clinical study in a highly selected group of patients with chronic stroke who have clear evidence of metabolically dysfunctional brain regions that are mismatching with the necrotic brain regions (Type 3 recommendation, Level C evidence).
- It would be reasonable to use HBOT as an adjunctive measure in the treatment of post anoxic encephalopathy after near hanging (Type 3 recommendation, Level C evidence).

Neuroblastoma

- We suggest HBOT in the treatment of neuroblastoma stage IV (Type 2 recommendation, Level C evidence).

NON-ACCEPTED INDICATIONS (TABLE 3)

Owing to very low levels of evidence (Grade D), no specific recommendations on HBOT are given for the following clinical conditions:

- Post sternotomy mediastinitis
- Malignant otitis externa
- Acute myocardial infarction
- Retinitis pigmentosa
- Facial (Bell's) palsy

CONDITIONS FOR WHICH HBOT IS NOT INDICATED (TYPE 1 INDICATION, TABLE 4)

Evidence of lack of clinical effect of HBOT allows Type 1 recommendations to be given for not using HBOT in:

- Autism spectrum disorders (Type 1 recommendation, Level B evidence)
- Placental insufficiency (Type 1 recommendation, Level C evidence)
- Multiple sclerosis (Type 1 recommendation, Level B evidence)
- Cerebral palsy (Type 1 recommendation, Level B evidence)
- Tinnitus (Type 1 recommendation, Level B evidence)
- Acute phase of stroke (Type 1 recommendation, Level C evidence).

PRACTICE OF HYPERBARIC OXYGEN TREATMENT

- We recommend that all European hyperbaric facilities comply as a minimum with the European Code of Good Practice and this ECHM list of clinical indications for HBOT as the basis for accreditation processes and national reimbursement policies.
- We recommend conditions in which HBOT is considered not to be indicated are discussed in a benefit/risk balance for each specific patient before using HBOT.
- We recommend medical education and training of hyperbaric centre medical staff comply with the standards developed and mutually agreed by ECHM and

the European Diving Technology Committee (EDTC).

- We recommend education and training of hyperbaric centre non-medical staff comply with the standards developed by the European Baromedical Association for nurses, operators and technicians (EBAss) and agreed by ECHM.
- We recommend physicians involved in hyperbaric centres are trained and participate in clinical as well as basic research.
- We recommend the hyperbaric community at large increases its participation in the research effort in order to improve the level of evidence supporting the ECHM recommendations.

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Technical reports

An assessment of the performance of the Baxter elastomeric (LV10) Infusor™ pump under hyperbaric conditions

Stephen Perks, Denise F Blake, Derelle A Young, John Hardman, Lawrence H Brown, Iestyn Lewis and Tilley Pain

Abstract

(Perks S, Blake DF, Young DA, Hardman J, Brown LH, Lewis I, Pain T. An assessment of the performance of the Baxter Elastomeric (LV10) Infusor ™ pump under hyperbaric conditions. *Diving and Hyperbaric Medicine*. 2017 March;47(1):33-37.)

Introduction: There are limited data on the use of elastomeric infusion pumps during hyperbaric oxygen treatment.

Aim: This study evaluated the flow rate of the Baxter elastomeric LV10 Infusor™ pump under normobaric (101.3 kPa and three hyperbaric conditions of 203 kPa, 243 kPa and 284 kPa.

Methods: Elastomeric pumps were secured to participants in the same manner as for a typical patient, except that a container collected the delivered antibiotic solution. Pumps and tubing were weighed before and after the test period to determine volume delivered and to calculate flow rates at sea level and the three commonly used hyperbaric treatment pressures at two different time periods, 0–2 hours (h) and 19–21 h into the infusion.

Results: The mean flow rates in $ml \cdot hr^{-1}$ (SD) were: 9.5 (0.4), 10.3 (0.6), 10.4 (0.6), 10.4 (0.5) at 0–2 h and 10.5 (1.0), 12.2 (0.6), 9.4 (0.5), 10.3 (0.9) at 19–21 h for the normobaric, 203 kPa, 243 kPa and 284 kPa conditions respectively. There was no significant association between flow rate and time period ($P = 0.166$) but the 203 kPa flow rates were significantly faster than the other flow rates ($P = 0.008$). In retrospect, the 203 kPa experiments had all been conducted with the same antibiotic solution (ceftazidime 6 g). Repeating that experimental arm using flucloxacillin 8 g produced flow rates of 10.4 (0.8) $ml \cdot h^{-1}$, with no significant associations between flow rate and time period ($P = 0.652$) or pressure ($P = 0.705$).

Conclusion: In this study, the flow rate of the Baxter LV10 Infusor™ device was not significantly affected by increases in ambient pressure across the pressure range of 101.3 kPa to 284 kPa, and flow rates were generally within a clinically acceptable range of 9–12 $ml \cdot h^{-1}$. However, there was evidence that the specific antibiotic solution might affect flow rates and this requires further study.

Key words

Hyperbaric oxygen therapy; Infectious diseases; Drugs; Equipment; Treatment; Flow rate

Introduction

Electronic medication infusion pumps are often used to deliver long-term intravenous (IV) antibiotic therapy to patients with infections such as necrotizing fasciitis, myonecrosis, refractory osteomyelitis and infected diabetic and venous foot ulcers; conditions which might also benefit from hyperbaric oxygen treatment (HBOT).[1,2] While some electronic medication infusion pumps have been modified to function in the hyperbaric environment,[3,4] others cannot be used during HBOT for a variety of reasons, most particularly the presence of lithium batteries which are a fire hazard under hyperoxic conditions. Therefore, non-electronic pumps, such as balloon-driven elastomeric infusion pumps, may be considered a safer alternative for the hyperbaric setting. These pumps typically have a medication-filled balloon reservoir that deflates at a consistent rate, pushing the antibiotic solution through a flow restrictor into the IV tubing and delivering it to the patient via a peripherally inserted central catheter (PICC) line.[5] Historically, elastomeric infusion devices have been disconnected from patients prior to entering a hyperbaric chamber due to concerns about the potential effects of the hyperbaric environment on the deflation rate of the balloon. This practice could result in two hours (h) or more of infusion time being lost each day, and requires additional manipulations of the PICC access increasing the risk of iatrogenic infections.

The purpose of this study was to assess the flow rates delivered by one type of elastomeric infusion pump, the Baxter elastomeric LV10 Infusor™, under various hyperbaric conditions. The two null hypotheses tested were:

- that the volume of solution delivered by the device during routine hyperbaric compression was the same as the volume of solution delivered under normobaric conditions; and
- that the volume delivered was within the appropriate clinical range.

Methods

Ethical approval for the study was obtained from the Townsville Hospital and Health Service Human Research Ethics Committee (HREC/15/QTHS/7).

Unused LV10 pumps filled with antibiotic solution were

Table 1
Antibiotic and dose for each time frame and pressure exposure; * primary analysis (Table 2); † secondary analysis (Table 3)

Time frame (h)	Pressure	Antibiotic	Dose (g)	no. of pumps
0–2	101.3 kPa	cefepime	3	3
		flucloxacillin	8	2
	203 kPa	cefepime	3	2
		flucloxacillin	8	3
	243 kPa	cefepime	3	5
	284 kPa	cefepime	3	3
		flucloxacillin	8	1
		cefoxitin	12	1
19–21	101.3 kPa	cefoxitin	6	2
		ceftazidime	6	1
		cephazolin	6	1
		piperacillin/ tazobactam	13/0.5	1
	203 kPa	ceftazidime*	6	5
		flucloxacillin†	8	5
	243 kPa	piperacillin/ tazobactam	13/0.5	1
		benzylpenicillin	10.8	4
	284 kPa	benzylpenicillin	10.8	3
		cefoxitin	6	2

sourced from the hospital pharmacy. Pumps were used within 14 days of the antibiotic expiration date and within the expiration date of the infusor device itself. Normal saline (NS) was the diluent for all antibiotics. The specific antibiotics and doses used in this study are listed in Table 1.

Pump flow rates were evaluated using mock infusions under both normobaric and hyperbaric conditions. Healthy volunteers were recruited for the normobaric tests, whilst hyperbaric staff, marine biology students and routine hyperbaric patients were recruited to participate in the compression tests which were conducted during clinical HBOT sessions. All participants were afebrile as measured on the forehead using an infrared thermometer (Thermofocus, Tecnimed Srl, Varese, Italy). Written informed consent was obtained from all participants. The study did not involve any deviation from the Hyperbaric Unit's normal clinical practice.

Pumps were warmed to room temperature for one hour and then attached to the research subject in a manner similar to that used for actual infusions. The luer-lock connecter of the infusion line was secured to the upper arm with an overlying single adhesive island dressing and a piece of Tubifast®. The flow restrictor is located just proximal to the luer-lock connection and is required to be secured to the patient at approximately 31°C to achieve the nominal flow rate.[5] Pilot data from five participants demonstrated the temperature (Vital Signs Monitor 300 Series, Welch Allyn, New York, USA) under the single island dressing was always near 31°C (SD 0.07), so no further effort was made to measure or control the temperature of the antibiotic solution at the flow restrictor. The pump was placed in a carry bag on the participant's chest so that the luer-lock connector and pump were secured at the same level. Finally, a short length of connecter tubing was attached to the luer-lock connector, with the other end draining into a small container strapped to the upper arm instead of infusing into the subject (Figure 1).

Figure 1
A short length of connecter tubing was attached to a luer-lock connector with the other end draining into a small container strapped to the upper arm instead of infusing into the patient

Pumps were tested at 101.3 kPa (sea level) and at 203, 243 and 284 kPa in a multiplace chamber to replicate commonly used hyperbaric treatment pressures. For each normobaric/ hyperbaric pressure, pumps were tested over two time intervals: at the beginning (0–2 hours, h) and near the end (19–21 h) of the 24-h infusion timeframe. The rate of the infusion fluctuates during the 24 h with the pump running slightly faster at the end of the infusion. Therefore, we used the 19–21 h time frame so that this increased flow rate would not impact on our results.[6] Separate pumps were used for each test to limit the compounding of any intrinsic error from a single pump; the pumps that were tested at 19–21 h were run for the first 19 hours in an incubator at 31.1°C.

The infusion pumps were weighed pre- and post-compression (Pelican® Digital Bench Scale: d = 0.01g, Class 3) to calculate the amount of solution delivered. Change in pump weight was used as a surrogate marker for volume delivered on a 1:1 ratio since the difference of weight and volume of NS, the primary diluent, is less than half of one percent (i.e., 1 mg of solution = 1 ml of solution). The duration of the compression was logged to enable calculation of the rate of the infusion as $ml \cdot h^{-1}$. The pre- and post- compression weight of collection containers was also determined to verify flow

Table 2

Flow rates from 0–2 hours and 19–21 h at differing treatment pressures (primary analysis) at an infusion rate of 10 ml·h^{-1}; the number of infusions that were outside the clinically acceptable range (9–12 ml·h^{-1}) were recorded

Time frame (h)	Pressure (kPa)	Flow rate (ml·h^{-1}) Mean	(SD)	Min	Max	95% CI	*n* <9 ml·h^{-1}	*n* >12 ml·h^{-1}
0–2	101.3	9.5	(0.4)	9.1	10.1	9.1–10	–	–
	203	10.4	(0.5)	9.7	10.9	9.7–11.2	–	–
	243	10.7	(0.4)	10.1	11.1	9.8–11.2	–	–
	284	10.5	(0.5)	9.7	11.1	9.9–11.2	–	–
19–21	101.3	10.5	(1.2)	8.4	11.3	9.4–11.8	1	–
	203	12.2	(0.6)	11.2	13.0	11.5–12.9	–	4
	243	9.4	(0.5)	8.6	9.8	8.9–10.1	1	–
	284	10.4	(1.0)	9.1	11.5	9.3–11.5	–	–

rate as determined by change in pump weight.

STATISTICAL ANALYSIS

According to Baxter, the elastomeric pump flow rate is expected to be 10 ml·h^{-1} ± 10% (nominal accuracy variation) using 5% dextrose as a diluent solution and may be 10% faster than the labelled rate (i.e., 11 ml·hr^{-1}) when NS is used as the diluent.[5] Therefore, we assumed a clinically acceptable range for infusion flow rates of 9 ml·h^{-1} (10 ml·h^{-1} - 10%) to 12 ml·h^{-1} (11 ml·h^{-1} + 10%).

A flow rate within 10% of expected is clinically acceptable, but a flow rate 20% less than recommended may mean that the patient would not receive the whole medication dose within the nominal delivery time, and a flow rate 20% higher than expected would result in the 24-hr pump running out prior to the intended completion time. Therefore, we powered the comparative component of this study to detect a 20% (2.2 ml·h^{-1}) difference in flow rate. We determined a sample size of five pumps in each group would provide a greater than 90% power (with $\alpha = 0.05$) to detect a 2.2 ml·h^{-1} difference in flow rates.

To compare flow rates across time periods and pressures, we first confirmed normal distribution of the data using the Shapiro-Wilk test and Q-Q plots.[7,8] We then compared mean flow rates for the two time periods and four pressure conditions using two-factor analysis of variance (ANOVA), with $P < 0.05$ used to establish statistical significance. All statistical analyses were performed using Stata release 11.2 (StataCorp, College Station, TX, USA).

Results

Forty mock infusions were completed. The room temperature for the study did not change as the hospital is an air-conditioned environment and remained at 22.5°C for all normobaric tests. The average chamber temperature during the administration was 24.6°C (SD 1.3), ranging from 15.0°C to 29.7°C. We did not prospectively measure or adjust for outside atmospheric pressure, but retrospective weather data available for ten of the 17 study days revealed generally stable barometric pressures ranging from 1011 to 1026 hPa (mean: 1019 (SD 4.4) hPa).[9]

The average volume delivered during the mock administrations was 19.7 (SD 2.0) ml, ranging from 15.8 to 23.8 ml. Compression times varied for the study due to treatment tables being different lengths of time; the mean duration of administration was 113 (SD 7.2) minutes, ranging from 100 to 121 minutes. The average calculated flow rate for all time periods and pressure groups was 10.5 (SD 1.0) ml·h^{-1}.

Table 2 shows the primary results for each time period and pressure. In the 0–2 h period, flow rates ranged between 9.1 and 11.1 ml·h^{-1}; in the 19–21 h time period, flow rates ranged between 8.6 ml·h^{-1} and 13.0 ml·h^{-1}. All of the 0–2 h observations were within the clinically acceptable window of 9 to 12 ml·h^{-1}, but six of the 19–21 h observations were outside that range: two observed flow rates (one at 101.3 kPa and one at 243 kPa) were less than 9 ml·h^{-1}, and four observed flow rates (all at 203 kPa) were greater than 12 ml·h^{-1}. Two-factor ANOVA revealed a statistically significant difference in flow rate among the four pressures ($F = 4.61$, $P = 0.008$), but not between the two time periods ($F = 2.00$, $P = 0.166$).

As can be seen in Table 2, the flow rates for the 9–21 h trials at 203 kPa were higher than for the remaining trials. Notably, all five of the 203 kPa 19–21 h trials were conducted with the same antibiotic and dose - ceftazidime 6 g - and four of the five observed flow rates were above 12 ml·h^{-1}. These results were not consistent with the rest of the data and could not be logically attributed to the increase in pressure.

To clarify this, the 19–21 h 203 kPa experiments were repeated using pumps filled with flucloxacillin 8 g, a drug and dosage commonly used in combination with HBOT. The mean (SD) flow rate for those trials was 10.4 (0.8) ml·h^{-1}, ranging from 9.6 to 11.5 ml·h^{-1} (Table 3). Repeat ANOVA (secondary analysis) performed

Table 3
Flow rates at 203 kPa at 19–21 h comparing ceftazidime and flucloxacillin

Antibiotic	Dose	Mean (SD)	Min	Max
Ceftazidime	6 g	12.2 (0.6)	11.2	13.0
Flucloxacillin	8 g	10.4 (0.8)	9.6	11.5

on the flucloxacillin data at 203 kPa at 19–21 h instead of ceftazidime found no significant differences between the flow rates among the pressures or time periods tested (pressure, F = 0.47, P = 0.705; time period, F = 0.21, P = 0.652).

A post-hoc comparison using Student t-test confirmed that the observed 19–21 h 203 kPa flow rates for the original five ceftazidime pumps (mean 12.2 ml·h^{-1}, SD 0.6) were greater than those for the replacement 203 kPa flucloxacillin pumps (mean 10.4 ml·h^{-1}, SD 0.7) (Table 3).

Discussion

Antibiotic infusions are often required for both inpatients and outpatients undergoing HBOT. Although technology continues to advance, early studies found substantial incompatibilities between electronic infusion pumps and HBOT, with both significant variations in pump flow rates and outright pump failures in hyperbaric settings.[10,11] Many newer generation electronic pumps perform well in hyperbaric conditions[3] but some electronic pumps used for monoplace chambers are no longer being manufactured.[4] Also, even modern pumps that use lithium batteries cannot be used during HBOT due to the risk of fire.[4]

Elastomeric infusion devices can deliver antibiotic infusions without any electronic elements, but there are limited data on their reliability in HBOT settings. Flow from elastomeric pumps filled with water was unaffected so long as the flow restrictor and the balloon reservoir were exposed to the same pressure conditions.[12] No difference in solution flow rates from LV10 pumps in normobaric and hyperbaric conditions were reported in another study but they observed flow rates that were 35% lower than expected in both conditions.[13] These findings might be explained by the use of long out-of-date solutions and not warming the flow restrictor to the recommended 31°C.[13]

In our experiments, we used in-date infusion devices with antibiotic solutions within 14 days of their expiry date, and attached the flow restrictor to the mock patient's arm to achieve the necessary warming, as would be done during clinical care. The results of our study suggest that antibiotic delivery using LV10 pumps achieve flow rates within acceptable parameters during HBOT at 203, 243 and 284 kPa.

We did initially observe faster than expected flow rates in one arm of the study (203 kPa at 19–21 h), but there was no dose-response relationship in the data. That is, the flow rates returned to normal at even higher pressures. In retrospect, all of the initial experiments in that study arm were conducted with the same antibiotic solution: ceftazidime 6 g. At the time of this study, there was no literature suggesting that the type and/or dose of antibiotic solution could affect the flow rate through an elastomeric device; therefore, we simply used any available elastomeric pumps for our experiments. However, when we recreated that study arm using pumps containing flucloxacillin 8 g we found clinically acceptable flow rates that were not statistically different from those of the other study arms. Because of these divergent data we cannot dogmatically conclude that elastomeric infusion pumps are always safe in HBOT settings, and we encourage future research on the role of specific antibiotic (and other medication) solutions on elastomeric pump performance.

LIMITATIONS

For proper operation, the flow restrictor on the LV10 pump should be at 31.1^{O}C.[5] We did not mechanically control the temperature of the flow restrictor, but rather connected it to a participant using an island dressing in a manner similar to what would happen in clinical practice. Although pilot data indicated a temperature of approximately 31°C under the dressing, we did not definitively measure the flow restrictor temperature in our study.

This study was performed using various available antibiotics at varying dosages, again as might occur in the clinical setting. Our data suggest there might be variations in the flow rates achieved with different antibiotic solutions, and further research exploring that issue would be valuable.

We only studied one specific elastomeric device, and did not compare the flow rates achieved with the Baxter LV10 Infusor™ to those achieved with other elastomeric devices, electronic pumps or other delivery technologies such as syringe pumps.

Finally, although this study closely replicated the clinical environment, it was not a clinical study per se. The pumps delivered solution into a collection container rather than intravenously, which might affect the observed flow rates. The methodology was consistent across all arms of the study, however, which should provide confidence in the comparative results. Future studies evaluating clinical use of elastomeric pumps during HBOT are warranted.

Conclusion

In this study, the flow rate of the Baxter elastomeric LV10 Infusor™ device was not significantly affected by increases in ambient pressure across the pressure range of 101.3 kPa to 284 kPa, and flow rates were generally within a clinically acceptable range of 9–12 ml·h^{-1}. However, there was some

evidence that the specific antibiotic solution might affect flow rates and this requires further study.

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Performance of the BBraun Perfusor Space syringe driver under hyperbaric conditions

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Abstract

(Frawley L, Devaney B, Tsouras T, Frawley G. Performance of the BBraun Perfusor Space syringe driver under hyperbaric conditions. *Diving and Hyperbaric Medicine*. 2017 March;47(1):38-43.)

Background: The BBraun Perfusor Space™ syringe driver is already in use by ambulance services and retrieval teams but has not previously been assessed for hyperbaric chamber use.

Methods: Pump flow accuracy was tested at rates between 1 and 40 ml·hr^{-1} using three different brands of 50 ml syringe. Function of the occlusion alarms was assessed using the same syringes. The hyperbaric profile involved pressurisation to 284 kPa at 30 kPa·min^{-1}, 30 min at 284 kPa and decompression at 30 kPa·min^{-1}. Output was recorded from differences in weight of collection containers. A single device was tested.

Results: Performance was highly dependent on the syringe type used, with two of the three 50 ml syringes used demonstrating 'stiction' at both low and high occlusion pressure alarm settings, most marked during pressurisation. On decompression from 284 kPa all syringes alarmed at significantly lower pressures. Because of the stiction problems only the flow measurements for the BBrown Omnifix 50 ml syringes are reported. At a pressure of 284 kPa, the difference between programmed and delivered rates was within the manufacturer's specification of 10%: at 40 ml·h^{-1} (median variation 1.25%, IQR 0.5–1.7%), 10 ml·h^{-1} (8.6%, IQR 8–9.2%), 5 ml·h^{-1}(-8.8%, IQR -1.6–8.8%) and 1 ml·h^{-1} (-4%, IQR 4–12%). Pressurisation was associated with significantly lower flow rates whilst decompression was associated with significantly increased rates. Limited testing at 405 kPa was also within the manufacturer's specifications.

Conclusion: A BBraun Infusor Space syringe driver performed within acceptable performance criteria but is highly dependent on syringe type and flow rates. The potential for the device to under deliver on pressurisation and over deliver on depressurisation, however, suggests vigilance and appropriate rate adjustments may be necessary during these phases.

Key words

Equipment; Hyperbaric medicine; Intensive care medicine; Pharmacology

Introduction

Hyperbaric oxygen treatment (HBOT) is indicated in selected patients with critical illnesses, including necrotising soft tissue infections and cerebral arterial gas embolism.[1–5] Many of these patients are intubated, ventilated and receiving intensive care (ICU) management, including inotropic support. For ICU patients on inotropic support, consistent delivery is dependent on the infusion devices maintaining function under hyperbaric conditions. If the devices are not hyperbaric-approved, the need to change devices imposes the risk of unexpected boluses of inotropes during device changeover and potentially significant morbidity. Haemodynamic instability during HBOT is a recognised entity particularly during compression and decompression. Possible causes of this instability include the physiological response to pressurisation and malfunction of infusion devices.[1]

Whilst ICU patients can be managed in a monoplace chamber with infusion devices external to the treatment chamber,[6] the vast majority of ICU patients are managed in multiplace units. As such, all medical devices should be tested for compatibility within an hyperbaric environment.[7,8] Previous studies, case reports and letters have demonstrated that some devices fail completely at normal treatment pressures whereas others deliver inconsistent flow rates.[9,10] Some of the syringe drivers previously evaluated for hyperbaric use are no longer manufactured but may be still in use.[11–15]

The primary aim of this project was to evaluate the performance of a current generation syringe driver in wide use and its suitability for hyperbaric chamber use. The BBraun Perfusor Space™ syringe driver (BBPS; BBraun, Melsungen, Germany) is currently used by ambulance services and retrieval teams, including the Royal Flying Doctor Service, but has not previously been assessed for use under increased pressure. The null hypothesis to be tested was that delivery rates of the syringe driver are not influenced by hyperbaric conditions. A secondary hypothesis was that the occlusion alarm function does not alter under hyperbaric conditions so that the alarm settings do not need to be modified for some syringe/pump combinations to be practicable.

In addition, intermittency and obstruction caused by the high static friction relative to dynamic friction between the plunger seal and the syringe wall (combined static friction and sticking or 'stiction') can increase under pressure so that safe drug administration in the hyperbaric environment may require either changes in usual protocols or the exclusion of some driver/syringe combinations.

Methods

All measurements were performed in the inner lock of a rectangular, triple-lock hyperbaric chamber (Fink Engineering, Australia). The researchers were fit for hyperbaric chamber attendance (Australian Standard 4774.2-2002, *Work in compressed air and hyperbaric oxygen facilities*). Testing was conducted solely by the researchers. There were no other human subjects involved in the testing of this device. The Alfred Hospital Research and Ethics Committee were contacted prior to commencing the study and they deemed that no approval was needed as this was an *in vitro* study, no patients were involved in the study and there was no impact on patient care or confidentiality.

APPARATUS

A single BBPS device was evaluated at ambient atmospheric pressure and under increased pressure, with particular regard to the accuracy of volume delivery. The BBPS is an electromechanical peristaltic syringe driver powered by a stepper motor. The device's external AC power supply was removed and all testing was performed on its internal NiMH battery pack. The syringe driver loaded with a 50 ml syringe of 0.9% saline was tested in the inner lock of the multiplace hyperbaric chamber of the Alfred Hospital Hyperbaric Unit. The syringes evaluated were the BBraun Omnifix 50 ml syringe (BBraun, Melsungen, Germany), the Terumo 50 ml syringe (Terumo, Laguna, Philippines) and the Becton Dickinson 50 ml syringe (BD Luer-Lok, Sydney, Australia). The syringes were connected to a 250 cm Infusomat Space PVC line (BBraun, Melsungen, Germany) which emptied directly into the measuring containers. All air bubbles were thoroughly removed before measurements commenced. The delivered volume was measured using an electronic precision weighing balance (Classic Light PL-L, Mettler Toledo); this is subject to independent, annual quality assurance calibration and accreditation and is considered to be accurate to four decimal places.

Prior to testing, a biomedical engineer (author TS) examined the BBraun syringe driver using the Alfred Hyperbaric Unit testing matrix. This matrix has been used for many new items of equipment and comprises verification of basic suitability and function with test pressurisations to 304 kPa and a pressurisation rate of 10 kPa·min^{-1}.[16] This standardised testing pathway covers our requirements for routine HBOT and is primarily used as a screening tool to identify equipment that may be adversely affected by pressure or pressure changes or represents an ignition risk. In order to complete an oxygen risk assessment, the unit was partially disassembled and an internal inspection conducted to identify any items requiring further evaluation with respect to oxygen enriched environments, including electronic components, the internal battery and any lubricating grease.

FORCE GENERATION TESTING

Performance verification tests were conducted prior to 284 kPa treatment profiles. A calibrated force gauge was used to determine force generated with the pump running at 100 ml·h^{-1} and the occlusion alarms set at the lowest value (10 kPa or P1) and the highest value (120 kPa or P9). All results were cross referenced with the manufacturer's specifications for allowable tolerances.

OCCLUSION ALARM PARAMETERS

The output line from each pump was connected via a pressure transducer to a tap, the syringe, line and transducer filled with water, all air bubbles flushed and the pressure monitor zeroed against ambient pressure. The pump was started at 100 ml·h^{-1} and when the flow rate was stabilised the tap was closed. At the moment the pump halted with an occlusion alarm, the pressure reading (measured accuracy 1 kPa) and time duration were recorded.

FLOW RATE ACCURACY

The accuracy of the BBPS syringe driver's flow rates were tested at flow rate settings of 1, 5, 10 and 40 ml·h^{-1}. The volume delivered was collected at 5-min intervals directly into laboratory-supplied sample containers with lids, which were labelled and weighed prior to test dives. Timing was performed by a hyperbaric technician with a stopwatch outside the chamber. Infusion flow rates were determined from differences in weight of the containers and time. After completion of each pressure profile, the test tubes were weighed by the researchers using the precision measuring scales.

HYPERBARIC PROFILE

The hyperbaric profile involved pressurisation to 284 kPA at 30 kPa·min^{-1}, 30 min at 284 kPa and decompression at 30 kPa·min^{-1}. This profile was chosen because it represents standard hyperbaric treatments for emergency and intensive care throughout Australia. The chamber atmosphere was controlled by the outside technicians and internal chamber temperature, humidity and gas composition were monitored and kept within defined limits. Temperature ranged from 24–25°C and humidity from 40–60%. For control purposes, a 30-min sampling phase (six samples) occurred at ambient pressure in the chamber prior to each 'dive' commencing. The syringe driver with a 50 ml BBraun syringe also underwent unmanned tests at 405 kPa whilst programmed to deliver 10 ml·h^{-1}over a 60-min infusion period.

Departmental safety protocols mandated constraints on depth, duration and the number of dive profiles able to be completed per week in order to minimise risk of decompression illness in the researcher. The testing durations were calculated to be less than the maximum allowable no

Table 1

Occlusion pressures during pressurisation in a multiplace chamber at 30 kPa.min^{-1} to maximum pressure 284 kPa and decompression at 30 kPa.min^{-1}; all tests at a flow rate of 100 ml.h^{-1}; P1 (10 kPa) the lowest occlusion alarm setting and P9 (120 kPa) the highest; time-to-occlusion specifications: BBraun 50 ml syringe – 96 s on P1 setting and 13.46 s on P9; Becton Dickinson (BD) 50 ml syringe – 173 s on P1 and 934 s on P9; (mean times and pressures rounded to nearest whole number)

Test stage	Expected occlusion pressure (kPa)	Syringe	Acceptable range (+/-10%) (kPa)	Time to occlusion (sec) mean (SD)		Measured occlusion pressure (kPa) mean (SD)		Error in occlusion pressure (%)	Comment
Baseline	P1 10	Terumo 50 ml	9–11	29	(17.3)	5	(1.6)	-51	Syringe sticking
		BD 50 ml	9–11	42	(8.4)	8	(0.3)	-22	
		BBraun 50 ml	9–11	59	(18)	11	(3.7)	+13	
	P9 120	Terumo 50 ml	108–132	332	(31.9)	103	(1.4)	-14	Syringe sticking
		BD 50 ml	108–132	340	(8.6)	123	(4.4)	+3	
		BBraun 50 ml	108–132	319	(6.9)	113	(2.9)	-6	
Pressurisation#	P1 10	Terumo 50 ml	9–11						Fail repeatedly
		BD 50 ml	9–11	20	(6.5)	8	(2.4)	-20	Fail
		BBraun 50 ml	9–11	10	(1.2)	9	(1.1)	-12	
	P9 120	BBraun 50 ml	108–132	399	(53.7)	109	(1.4)	-9	
At Pressure*	P1 10	BD 50 ml	9–11	9	(7.5)	7	(0.4)	-32	
		BBraun 50 ml	9–11	10	(1.2)	9	(1.0)	-12	
	P9 120	BBraun 50 ml	108–132	98	(1.6)	110	(0.6)	-8	
Decompression#	P1 10	BBraun 50 ml	9–11	7	(3.3)	8	(1.4)	-25	
		BD 50 ml	9–11	5	(1.0)	5	(0.9)	-45	
	P9 120	BBraun 50 ml	108–132	4	(6.8)	116	(0.6)	+4	

Table 2

Flow rates (ml.h^{-1}) delivered at different stages of hyperbaric exposure using a new BBraun 50 ml syringe for each test (see text for details of pressure profile); baseline – normobaric pressure; data normally distributed except for that at pressure; * $P < 0.001$

	Baseline				Pressurisation				At pressure				Decompression			
Set flow (ml·h^{-1})	Actual flow (ml·h^{-1})		% diff		Actual flow (ml·h^{-1})		% diff		Actual flow (ml·h^{-1})		% diff median (IQR)		Actual flow (ml·h^{-1})		% diff	
40	40.3	(0.1)	1	(0.9)	32.4	(2.7)*	-14	(0.1)	41.1	(0.7)	1	(-0.7–11.3)	43.4	(2.5)	+5	(0.2)
10	10.6	(0.1)	6	(5.2)	10.5	(0.2)*	-14	(0.2)	10.9	(0.3)	9	(8 to 9.2)	14.1	(0.9)	+41	(4.5)
5	4.8	(0.2)	-5	(5.1)	3.6	(0.6)*	-28	(0.3)	4.4	(0.2)	-9	(-8 to -9.2)	7.6	(1.1)	+52	(5.0)
1	1.0	(0.1)	0	(0.2)	0.7	(0.3)	-16	(0.5)	1.1	(0.1)	-4	(-4 to -12)	1.4	(0.9)	+20	(4.1)

decompression limit (NDL) duration for the dive depths under study in accordance with Canadian Defence and Civil Institute of Environmental Medicine (DCIEM) tables currently utilised by Hyperbaric Units in Australia.

STATISTICAL ANALYSIS

Descriptive statistics were calculated for all variables. Normality of data was assessed by the skewness/kurtosis test for normality and the Shapiro-Wilk test. Paired Student's *t*-tests were performed to test for differences in programmed and delivered volumes for each of the administration sets. Non-normally distributed data were reported as median and interquartile range and compared between groups by the Kolmogorov-Smirnov and Kruskal-Wallis tests. A general linear model (ANOVA) and a Scheffe post hoc test to isolate differences were fitted to the standardised values to determine the effect of day of testing on the accuracy of volume delivery.

Results

OCCLUSION ALARM TESTS

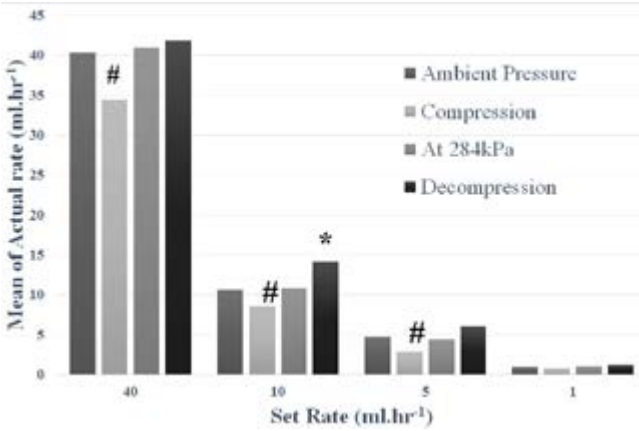
The force generated by the syringe driver at 100 ml·min^{-1} was 12.85 (SD 0.2) Newton on the lowest occlusion alarm setting and 71.9 (SD 0.2) Newton on the highest occlusion alarm setting. Both values were within the manufacturer's specifications. Performance was highly dependent on the syringe type used (Table 1). The Terumo and Becton Dickinson 50 ml syringes demonstrated significant stiction on pressurisation to 284 kPa. The performance of these syringes was unacceptable and all further testing was performed with the BBraun 50 ml syringe. The BBraun syringe had a markedly stiffer barrel and the plunger O-rings were further apart causing less lateral plunger movement than the Terumo or BD syringes. In addition, the plunger end has ridges which may reduce slippage of driver on plunger. The BBraun syringes performed within the manufacturer's specifications (+/- 5%) and were clinically acceptable during pressurisation, at 284 kPa and on decompression. On the lowest occlusion pressure setting, BBraun syringes alarmed at a significantly lower pressure (-12%, $P = 0.01$) and earlier time ($P = 0.01$) at 284 kPa. On the high occlusion pressure setting during decompression, BBraun syringes alarmed at a significantly lower pressure (-25%, $P = 0.01$) and earlier time ($P = 0.01$).

ACCURACY OF VOLUME DELIVERY

Following the unacceptable occlusion testing, all flow rate calculations reported are exclusively for the BBraun 50 ml syringe. Measured flow rates were dependent on the flow rate set and the stages of pressurisation (Figure 1). During pressurisation mean flow rates decreased by 13.9%, 13.6%, 28% and 16% on the 40 ml·h^{-1}, 10 ml·h^{-1}, 5 ml·h^{-1} and 1 ml·h^{-1} settings, respectively. At 284 kPa the rate increased by a median of 1.2%, 8.6% and 4% at 40 ml·hr^{-1}, 10 ml·hr^{-1} and 1ml·hr^{-1} respectively and decreased by 8.8% at 5 ml·hr^{-1}. All rates at 284 kPa were within the manufacturer's allowable flow rate tolerance for the BBPS of 10%. On decompression, increases of 4.7%, 41%, 52% and 20% occurred (Table 2). There was no day-to-day variation in performance (F = 0.866, $P = 0.55$).

Figure 1

Calculated delivered rates during hyperbaric testing of a BBraun Space syringe driver with 50 ml BBraun syringe of 0.9% saline; normobaria; pressurisation at 30 kPa·min^{-1}; 284 kPa; decompression at 30 kPa·min^{-1}; rates calculated from volume delivered over 5-min increments; statistically significant variation from set rates are marked as under-delivery (#) and over-delivery (*)



At 405 kPa the syringe driver with a 50 ml BBraun syringe set to deliver 10 ml·hr^{-1} had a calculated actual flow rate of 10.06 ml·hr^{-1} (+ 0.6% of target).

Discussion

This study has shown that the performance of the BBraun Perfusor™ Space device is dependent on the set flow rates and on the make of syringe used. We have reported here only the volumes delivered with the 50 ml BBraun syringe. In general, the device delivered small increases in volume infused at 284 kPa compared with rates at ambient pressure. These were statistically significant and may be clinically significant. The major changes in delivery occurred on compression (under-delivery) and decompression (over-delivery). Whilst modest errors in the average rate of infusion may not be critical, transient interruptions and unintended boluses could be clinically relevant. When inotropes are being infused, this could seriously impact a critically ill patient. Noradrenaline has a half-life of 1–2 min and a standard dilution for adults is 60 µg·ml^{-1} delivering 1 mcg·min^{-1} at 1 ml·h^{-1}. Variations in delivery of 10–40% would mean the actual rate is 0.6–0.9 µg·min^{-1} on compression and 1.1–1.4 µg·min^{-1} on decompression. For paediatric inotrope infusions, the standard dilution is 30 µg·ml^{-1} delivering 5 mcg·kg^{-1}·min^{-1} at 1 ml·h^{-1} and the variation may be more relevant.

There have been only three syringe drivers tested for use in multiplace hyperbaric chambers (Terumo, Graseby and Atom 235).[9,13,16] The Atom syringe pump is now discontinued and the Terumo and Graseby drivers have been superseded. The Fresenius Pilote Hyperbaric (Vial Infusion Technology) syringe pump is CE-marked but not FDA-cleared for use in multiplace hyperbaric chambers. The battery powered Argus 600 syringe pump (Codan Triplus) has been used successfully at the Karolinska Hyperbaric unit but has not undergone rigorous peer review.[17]

A number of syringe characteristics affect the volume infused under pressure. It is likely that deformation of the syringe during pressurisation and decompression significantly impacted on delivery.[18–20] The thinner barrel, lack of O-rings on the plunger and a non-serrated plunger end of the Terumo syringe permitted torsion of the plunger and an asymmetrical alignment resulted in significant stiction and delivery failure. A contributing factor is the gas space between the two sealing rings of many types of syringes, which is air filled and hence subject to Boyle's Law forces. On pressurisation, distortion of the plunger seal occurs causing it to bind more tightly against the syringe barrel and trigger the occlusion alarm to stop the infusion. In general, the larger the syringe and the lower the flow rate the more pronounced the stiction effect. In our series, the changes in flow rate were most marked at low set flow rates and stiction may have played a significant role in exceeding occlusion alarms and under-delivery of saline.

Using the same type of infusion device in the ICU, during transport and in the hyperbaric chamber not only reduces delays before treatment starts but also removes the need for interruption of dose-critical infusions and reduces the risk of change-over errors.[21,22] On balance, the risk associated with over- or under-delivery during compression and decompression is likely to be markedly less than the risk of inadvertent boluses on transfer from one infusion system to another prior to treatment. The under-delivery on compression, however, may well compound the haemodynamic changes occurring as a result of exposure to hyperbaric oxygen. Cardiovascular responses to hyperbaric hyperoxia include a rate-dependent reduction in cardiac output and systemic vasoconstriction with an increase in peripheral vascular resistance and a decrease in pulmonary vascular resistance.[23,24] This results in a decrease in heart rate, cardiac output, and cardiac work, possibly related to baroreceptor stimulation.[25] All left ventricular performance indices decrease, without a change in preload or afterload. Pulmonary vascular resistance decreases whilst pulmonary arterial pressure does not change.[26] Although these effects are well tolerated in normal individuals, patients undergoing HBOT can have compromised cardiac function as evidenced by reports of acute pulmonary oedema (with one death) during monoplace HBOT in three patients with markedly reduced left ventricular ejection fractions.[27]

LIMITATIONS

A limitation of this study is the use of only one syringe driver during testing. Some variability in performance between devices could be expected but it is likely this would be small. Our standard compression rate (30 kPa·min^{-1}) to a treatment pressure permitted only five minutes to document syringe performance on compression and decompression. As such there were fewer observations during this phase of the study and less precision in the estimate of effect size. The potential for sampling bias thus exists. We also did not test the dynamic performance of the driver following transfer through the medical lock at pressure. This is a possible clinical scenario, and it is possible that the rapid rate of pressurisation could affect subsequent performance at pressure by causing mechanical distortion.

Conclusions

The BBraun Infusor™ Space syringe driver performs within acceptable performance limits but is highly dependent on syringe type and set flow rates. From a clinical perspective, the errors in overall volume delivery were relatively small and should be interpreted as clinically acceptable error and of clinically insignificant risk to patients. However, the potential for the device to under-deliver on pressurisation and over-deliver on depressurisation suggests vigilance and appropriate rate adjustments may be necessary during these phases. This is important in order to avoid adverse shifts in haemodynamics, compounded by physiological responses related to exposure to hyperbaric oxygen.

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Scientific integrity review

Identifying and acting on inappropriate metadata: a critique of the Grattan Institute Report on questionable care in Australian hospitals

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Abstract

(Cooper PD, Smart DR. Identifying and acting on inappropriate metadata: a critique of the Grattan Institute Report on questionable care in Australian hospitals. *Diving and Hyperbaric Medicine*. 2017 March;47(1):44-54.)

Introduction: In an era of ever-increasing medical costs, the identification and prohibition of ineffective medical therapies is of considerable economic interest to healthcare funding bodies. Likewise, the avoidance of interventions with an unduly elevated clinical risk/benefit ratio would be similarly advantageous for patients. Regrettably, the identification of such therapies has proven problematic. A recent paper from the Grattan Institute in Australia (identifying five hospital procedures as having the potential for disinvestment on these grounds) serves as a timely illustration of the difficulties inherent in non-clinicians attempting to accurately recognize such interventions using non-clinical, indirect or poorly validated datasets.

Aim: To evaluate the Grattan Institute report and associated publications, and determine the validity of their assertions regarding hyperbaric oxygen treatment (HBOT) utilisation in Australia.

Methods: Critical analysis of the HBOT metadata included in the Grattan Institute study was undertaken and compared against other publicly available Australian Government and independent data sources. The consistency, accuracy and reproducibility of data definitions and terminology across the various publications were appraised and the authors' methodology was reviewed. Reference sources were examined for relevance and temporal eligibility.

Results: Review of the Grattan publications demonstrated multiple problems, including (but not limited to): confusing patient-treatments with total patient numbers; incorrect identification of 'appropriate' *vs*. 'inappropriate' indications for HBOT; reliance upon a compromised primary dataset; lack of appropriate clinical input, muddled methodology and use of inapplicable references. These errors resulted in a more than seventy-fold over-estimation of the number of patients potentially treated inappropriately with HBOT in Australia that year.

Conclusion: Numerous methodological flaws and factual errors have been identified in this Grattan Institute study. Its conclusions are not valid and a formal retraction is required.

Key words

Critical appraisal; Data; Economics; Evidence; Health; Hyperbaric oxygen therapy; Policy

Introduction

The identification and prohibition of ineffective medical therapies is of considerable economic interest to funding bodies. Regrettably, the identification of such therapies has proven problematic and a recent paper in the *Medical Journal of Australia* (*MJA*) illustrates the difficulties inherent in accurately recognizing such interventions from non-clinical, indirect or poorly validated datasets.[1]

Published in August 2015, this peer-reviewed article from the Grattan Institute attempted to develop a model to measure potentially inappropriate care in Australian hospitals and was based on a report previously prepared by that organization, but omitted from their published references.[1,2] The authors utilized de-identified patient-level data from the Australian Institute of Health and Welfare (AIHW) to identify the hospital-specific incidence of selected diagnosis-procedure pairs that were allegedly deemed 'inappropriate' in previous literature. All Australian public and private hospital separations (discharges, deaths, transfers) in financial year 2010–11 were included. Five hospital procedures, including hyperbaric oxygen treatment (HBOT) were identified as having potential for disinvestment on these grounds, and punitive measures were recommended against healthcare providers with "*illegitimate variation*" in service provision.[2]

Of the five 'do-not-do' procedures scrutinized in the *MJA* article and its source document, HBOT *"for a range of conditions"* was surprisingly prominent, contributing 79% of the procedures identified as potentially inappropriate.[1] The authors stated that "*(m)ore than 4500 people a year get hyperbaric oxygen therapy when they do not need it*".[2] However, this figure far exceeded the known total number of individuals treated across all Australian facilities (public and private, civilian and military, 1,276 patients) in 2010–11.[3] Likewise, claims that *"(o)ne in four hyperbaric oxygen treatments should not happen*"[2] appeared questionable when their list of 'inappropriate' indications included diagnoses that had been funded for HBOT under the Australian *Medicare Benefits Schedule* (*MBS*)[4,5] following rigorous review of the available evidence by the Government's own Medical Services Advisory Committee (MSAC).[6]

Aim

To critically evaluate the Grattan Institute Report and associated publications, and determine the veracity of their conclusions regarding HBOT in Australia.

Methods

The following processes were used to critically review the publications:

- Utilising existing published source data, the accuracy of the numbers presented in the Grattan papers was assessed against published data for 2010–11 from the Hyperbaric Technicians and Nurses Association (HTNA), AIHW and Medicare Australia.
- Basic data definitions and terminology relating to HBOT were reviewed to determine consistency and reproducibility across all documents. It was expected that definitions and terminology would be accurate and consistent.
- References were examined for consistency, relevance, source data, vertical integration and temporal applicability to ensure post-dated publications were not applied retrospectively.
- If other fundamental problems with the methodology, analysis or conclusions were identified during the review, these were documented.

Our analysis was confined to HBOT data only and excluded the four surgical procedures scrutinized in this report, which seldom occur more than annually in any patient.

Results

1. PATIENT *versus* TREATMENT NUMBERS

HBOT, as a non-surgical treatment (like antibiotics, plasmapheresis, radiotherapy), is commonly prescribed as a course of 20 to 30 sessions ('doses') for any individual. HBOT is formally classified in the *Australian Classification of Health Interventions* (*ACHI*) as being amongst the "*(n)on-invasive, cognitive and other interventions*", and appears as such in AIHW data.[7,8] Of 5,888 procedures identified as 'inappropriate' by the Grattan Institute 4,659 were HBOT (79%).[1,2] The authors interpreted this as indicating that "*(m)ore than 4500 people a year get hyperbaric oxygen therapy when they do not need it*".[2] These figures were vastly more than documented patient numbers from other databases. Over the last 20 years, all comprehensive (Medicare-eligible) hyperbaric facilities in Australia have routinely provided their unit activity data to the HTNA for annual publication.[3] This independent dataset shows 1,276 patients ***in total*** were treated Australia-wide in 2010–11, receiving 26,873 'doses' all told (average: 21 per patient).

The Grattan Report explains that de-identified AIHW data "*were released as one record per admission, so it was not possible to link records to derive data on a per-person basis*".[1] Therefore, each admission was assumed to represent a separate patient. This is incorrect. The Report notes that the inability to correct for readmissions may deflate their hospital 'do-not-do' rates, making their analysis conservative – citing as an example "*a person who had multiple treatments, one of which was a do-not-do treatment, would thus be counted once in the numerator and multiple times in the denominator*" in their data.[1] Comparison against the HTNA's independent dataset demonstrates that this supposition is also incorrect. Failure to recognize HBOT as a multi-dose medical therapy inflates the numerator rather than the denominator, exaggerating the effect the authors seek to measure. This methodological flaw skews their results and misrepresents HBOT when compared against the four surgical procedures. It would have been more appropriate to examine the number of patients treated rather than the number of HBOT doses provided. Unfortunately the study methodology does not permit this. This single failure of clinical understanding leads to a 21-fold overestimation of the stated problem.

Table 1
Diagnostic indications for hyperbaric oxygen treatment deemed 'potentially inappropriate' by the Grattan Institute [1]

Osteomyelitis
Cancer
Non-diabetic wounds/ulcers
Skin graft survival
Crohn's disease
Tinnitus
Bell's palsy
Soft tissue radionecrosis
Cerebrovascular disease
Peripheral obstructive arterial disease
Sudden deafness and acoustic trauma
Carbon monoxide poisoning

The Grattan Report's raw data have not been published, preventing independent re-analysis of the HBOT results by diagnosis. However, applying the average number of treatments-per-patient derived from the HTNA dataset permits a reasonable first approximation. When divided by 21 the 4,659 'inappropriate' episodes of HBOT equate to approximately 222 discrete HBOT courses. This filter reduces the total number of individuals subjected to the five 'do-not-do' procedures from 5,888 to 1,451 and the fractional contribution of HBOT from 79% (4,659/5,888) to 15% (222/1,451).

2. SELECTION OF 'INAPPROPRIATE' INDICATIONS

The next substantial contribution to the over-representation of HBOT arose from the selection of indications for which HBOT was deemed 'inappropriate' (Table 1). The authors state that they "*took a selection of treatments that evidence*

Table 2
Medicare-approved (MSAC) indications for HBOT in 2010–11[4,5]

	MBS item	Year approved
	13020	2000[9]
Decompression illness		
Air or gas embolism		
Gas gangrene		
Necrotising fasciitis and Fournier's gangrene		
Diabetic wounds inc. diabetic gangrene and foot ulcers		
Prevention of osteoradionecrosis		
Treatment of osteoradionecrosis		
	13015	2003[6]
Soft tissue radionecrosis		
Refractory non-diabetic hypoxic wounds*		

**de-listed in 2012 (MSAC)*[10]

clearly shows should not be done routinely, or at all", and "*(o)nly guidance published before our data period (2010–11) was used*".[1]

The evidence base underlying HBOT has undergone three external reviews in Australia over the last 17 years. Following rigorous evaluation by MSAC, HBOT was approved for Medicare-funding for seven conditions in 2000 (Table 2).[9] The list of conditions for which HBOT was deemed 'inappropriate' by the Grattan authors derived from those excluded from funding in this initial MSAC report.[9] None of the references cited in the *MJA* article, other than these MSAC reviews, refer to HBOT.[1,2] Following appeal by the profession, two further conditions (soft tissue radiation injury (STRI) and refractory non-diabetic hypoxic wounds (NDHW)) were subsequently funded under a 3C Ministerial Determination, and formally appeared in the *MBS* following MSAC's 2003 review.[6] This approval spanned from April 2003 to October 2012.[10–12] From November 2012 public funding for STRI was confirmed but NDHW was de-listed.[13,14] Even as NDHW was being de-funded, MSAC acknowledged that their analysis did "*not take into account improvements in quality of life following successful treatment or any reduction in quality of life following surgery or due to unsuccessful treatment. Evidence suggests that the impact on patient's quality of life may be substantial. Consequently the actual benefit to the patient of providing HBOT is likely to be underestimated.*"[10,15] Both STRI and NDHW were legitimate indications for HBOT in 2010–11 (the period studied in the Report), as evidenced by reference to the *MBS*.[4,5] Provision of HBOT for these two indications cannot be retrospectively regarded as inappropriate.

Review of the HTNA dataset demonstrates that STRI and NDHW accounted for over 37% of all patients treated with HBOT in 2010–11 (483/1,276), and 73% (483/659) of those individuals who would be regarded as receiving 'potentially inappropriate' HBOT using Grattan methodology.[3]

Again, the failure to publish original data precludes independent re-calculation of the results by diagnostic group but a reasonable first approximation of this error's impact may be achieved. The approximately 222 patients (from point 1) potentially subject to 'inappropriate' HBOT may be reduced by a further 73% – resulting in a reduction in patient numbers to approximately 60 individuals. This further reduces the total number of patients subjected to all five 'do-not-do' procedures from 1,451 to 1,289 and the fractional contribution of HBOT from the original 79% (4,659/5,888) to < 5% (60/1,289).

Of the 1,276 patients treated with HBOT Australia-wide according to HTNA data, 176 (13.8%) were for non-Medicare-funded indications.[3] These figures are very different from the 4,500+ patients and 25% of HBOT that "*should not happen*" according to these authors.[2] Further breakdown of this group reveals that the majority (131/176, 74.4%) were treated for indications which, whilst not currently Medicare-funded, are recognized as potentially amenable to HBOT by international professional scientific societies active in this field (South Pacific Underwater Medicine Society, Undersea and Hyperbaric Medical Society (USA) and European Committee for Hyperbaric Medicine),[16–18] with the remaining 45 patients classified as miscellaneous/other. This last group would include patients participating in formal clinical research trials.

Amalgamating legitimate indications with non-Medicare-funded ones in the 'do-not-do' category is an error of sufficient consequence to single-handedly nullify the conclusions of this study.[1,2] When combined with the confusion surrounding patient- *vs.* treatment-numbers (point 1) the incidence of 'inappropriate' HBOT falls to 1.3% (60/4,659) of that reported. A seventy-fold overestimation of effect size is of sufficient magnitude as to invalidate any paper and mandate retraction. Several further concerns about this paper are identifiable, but their effects are harder to quantify.

3. INTERNAL VALIDITY OF PRIMARY DATA SOURCE

The AIHW is the Government agency responsible for providing *"reliable, regular and relevant information and statistics on Australia's health and welfare"*.[19] Diagnosis and procedure data submitted to the AIHW's hospital database are extracted retrospectively from individual patients' medical records by clinical coders at each institution. The internal validity of this dataset however is questionable. Although self-proclaimed as a source of "*Authoritative information and statistics to promote better health and wellbeing*",[17] interrogation of the 2010–2011 Procedures Data Cube reveals unexplained discrepancies.[8] A total of 17,326 instances of '*Therapeutic Intervention 1888 Hyperbaric oxygen therapy*' were documented that year, but drilling down to the next level of data elicits only 15,485 episodes [15,278 episodes of code 13020-00 (HBOT duration > 90min, ≤ 3hr) and 207 episodes of code 13025–00

(HBOT duration > 3 hr)], leaving 1,841 HBOT episodes unaccounted for (10.6%).

Since the *ACHI* only provides three possible codes for HBOT it is tempting to assume that all missing episodes fall under the third code which, for reasons unknown, was omitted from that year's data-cube.[7,8] Unfortunately this assumption raises more questions than it answers. The third code, 96191-00 (HBOT duration ≤ 90min), only applies to HBOT sessions that are not routinely used in clinical practice. The estimated incidence of such abbreviated treatments (e.g., due to patient logistics, aborted HBOT because of ear-clearing problems, oxygen toxicity, etc.) is only ~2% (personal communications, all Australian hyperbaric facilities, 2015/2016). A significant fraction of the missing HBOT episodes in the AIHW dataset therefore remain unaccounted for.

4. EXTERNAL VALIDITY OF PRIMARY DATA SOURCE

The data for this study derived from information provided annually by State and Territory health authorities to the AIHW. Comparison with the annual activity data published by the HTNA demonstrates no correlation.[3,8] Since HTNA data derive directly from individual hyperbaric facility databases (collected contemporaneously by front-line clinical personnel) it appears reasonable to assume that it should be at least as accurate as the 'official' data collected retrospectively by clerical staff in the hospital coding departments.

According to HTNA data, 26,873 hyperbaric treatments were provided by comprehensive hyperbaric facilities Australia-wide in 2010–11.[3] Only 17,326 (64%) of these episodes were recorded in the AIHW dataset.[8] Failure to capture over a third of the relevant information in this patient population appears to arise from two sources. First, the data only include admitted inpatients and exclude outpatients. Administrative systems vary between jurisdictions and facilities, with some hospitals providing HBOT as an outpatient service and others as a day-admission. Therefore, those providing HBOT on an outpatient basis are not included in this dataset. The second issue arises from uncertainty amongst coders about whether to record multiple HBOT sessions during a single admission as (a) multiple discrete episodes or (b) a cumulative intervention to be recorded only once. The rules governing this aspect of inpatient hyperbaric coding nationally were only clarified in March 2016.[20] Our companion paper illustrates this problem.[21] Of 22 inpatient admissions where > 1 episode of HBOT was provided (132 HBOT sessions in total), none recorded more than a single episode.[21] The AIHW dataset therefore fails to reliably capture HBOT patients treated either as outpatients or as overnight inpatients – providing a semblance of reality for day-admissions only.

Even for the day-admissions, questions remain. AIHW data record 207 instances of HBOT of duration > 3 hr (code 13025-00) out of 17,326 total instances (1.2%).[8] This duration of HBOT is only approved for use in Australia for decompression illness (DCI) or air/gas embolism (AGE).[4,5] However, HTNA data only record 148 patients being treated with HBOT for DCI/AGE in 2010–11.[3] No hyperbaric facility in the country routinely provides more than a single treatment of this duration to DCI/AGE patients, nor do they use such treatments for any other HBOT indication (personal communications, all Australian hyperbaric facilities 2015/2016). Hence, no more than 148 instances of code 13025–00 should be available for recording in the AIHW dataset. Comparing AIHW and HTNA datasets leads to the fractional incidence of this service falling from 1.2% (207/17,326) to < 0.6% (148/26,873). This halving of the incidence of this specific service is direct evidence of inaccurate data capture by coders.

Further doubt is cast upon the credibility of the AIHW dataset in our accompanying paper.[21] Seventy percent of the HBOT patients treated at our institution in 2010–11 had one or more errors in their diagnosis and/or procedure codes as recorded by the hospital's coders. Multiple discrete error types were identified, including (but not limited to): missing patients; missing treatments; 'additional' treatments; 'additional' patients, incorrect procedure codes and incorrect diagnosis codes. Incidental observations of surgical, anaesthetic and intensive care coding errors within this cohort confirmed that problems were not restricted to hyperbaric medicine.[21] Although regional variations may exist, publications from other centres indicate that these problems are not unique to this institution or State.[22]

5. LACK OF CLINICAL EXPERTISE

Whilst not medically trained themselves, the Grattan authors claim that the clinical relevance of their 'do-not-do' list was evaluated by "*a panel of general clinical experts and then a selection of specialists relevant to each treatment*".[23] These experts are not listed in the *MJA* article, but some are acknowledged in the original Report.[1,2] No-one with recognizable clinical expertise or qualifications in hyperbaric medicine are identifiable amongst those listed.[2] This lack of relevant clinical input helps to explain the elementary flaws outlined above.

Many smaller details reinforce the impression that appropriate clinical input was not provided, including:

- *Inclusion of irrelevant diagnoses in their 'inappropriate' code list* – e.g., T59.7 "*toxic effects of carbon dioxide*".[23] Any medical practitioner would be aware of the very different physiological roles and toxicological effects of carbon monoxide and carbon dioxide, and no specialist in the field would consider carbon dioxide toxicity as an indication for HBOT.[7] (*refer to footnote p.48)
- *Inclusion of irrelevant diagnoses in their 'potentially legitimate' code list* (Table 3).[23] Multiple codes including the words 'necrosis/necrotising/gangrene' have been

Table 3
Grattan Institute 'potentially legitimate' HBOT codes with descriptions[7,23]

Code	
A480	Gas gangrene, clostridial
A690	Other spirochaetal infections, necrotising ulcerative stomatitis
E10-E14	Diabetes mellitus codes
G374	Other demyelinating diseases of central nervous system, subacute necrotising myelitis
I775	Necrosis of artery
K041	Necrosis of pulp, pulpal gangrene (tooth)
K102	Inflammatory conditions of jaws
K520	Gastroenteritis and colitis due to radiation
K627	Radiation proctitis
L598	Other specified disorders of skin and subcutaneous tissue related to radiation
L599	Disorder of skin and subcutaneous tissue related to radiation, unspecified
M31	Other necrotising vasculopathies
M318	Other specified necrotising vasculopathies, hypocomplementaemic vasculitis
M319	Necrotising vasculopathy, unspecified
M726	Necrotising fasciitis
M8731	Other secondary osteonecrosis, shoulder region
M8738	Other secondary osteonecrosis, other site
M8785	Other osteonecrosis, pelvic region and thigh
M8788	Other osteonecrosis, other site
M8795	Osteonecrosis, unspecified, pelvic region and thigh
M8798	Osteonecrosis, unspecified, other site
M962	Post-radiation kyphosis
N304	Irradiation cystitis
N498	Inflammatory disorders of other specified male genital organs
N768	Other specified inflammation of vagina and vulva
O24	Diabetes mellitus in pregnancy
O240	Pre-existing diabetes mellitus, Type 1, in pregnancy
O241	Pre-existing diabetes mellitus, Type 2, in pregnancy
O242	Pre-existing diabetes mellitus, other specified type, in pregnancy
O243	Pre-existing diabetes mellitus, unspecified, in pregnancy
O244	Diabetes mellitus arising during pregnancy
O249	Diabetes mellitus in pregnancy, unspecified onset
P77	Necrotising enterocolitis of foetus and newborn
T66	Unspecified effects of radiation, **radiation sickness**
T703	Other effects of decompression and barotrauma
T790	Air embolism (traumatic)
T800	Air embolism following infusion, transfusion and therapeutic injection
T875	Necrosis of amputation stump
Z298	Other specified prophylactic measures, related to communicable disease, **fluoride**
Z923	Personal history of irradiation, therapeutic radiation

regarded as 'potentially legitimate', irrespective of their relevance to hyperbaric medicine.[7] This confusion with approved diagnoses such as necrotising fasciitis, gas gangrene or diabetic gangrene demonstrates lack of appropriate clinical guidance. Similarly, T66 "*radiation sickness*" was included erroneously; confusing the life-threatening effects of acute radiation sickness with the chronic post-radiotherapy injury for which HBOT is approved. Perhaps hardest to explain however is the inclusion of Z29.8 "*Other specified prophylactic*

*** Footnote**
A large table listing the Grattan Institute 'do-not-do' HBOT codes with descriptions[7,23] is available on request from the authors or from the DHM office <editorialassist@dhmjournal.com>. Because of its size it was not possible to include it here.

measure (related to communicable diseases)", which covers the prophylactic administration of fluoride for dental health purposes (Table 3).

- *Omission of relevant diagnoses from their 'potentially legitimate' list*. Several pertinent codes for air or gas embolism are missing from their 'potentially legitimate' list, including those arising from obstetric or cardiothoracic causes (e.g., O88.0 "*Obstetric air embolism*", O08.2 "*Embolism following abortion and ectopic and molar pregnancy; air embolism*", P25.8 "*Other conditions related to pulmonary air leak syndrome originating in the perinatal period; air embolism*", T81.7 "*Vascular complications following a procedure, not elsewhere classified; air embolism*").[7] Likewise, the most appropriate code for patients undergoing HBOT to prevent osteoradionecrosis developing as a result of upcoming dental surgery, Z51.4 "*Preparatory care for subsequent treatment, not elsewhere classified*", was omitted (Table 3).
- *Confusion of unrelated clinical conditions*. Several months prior to official publication of the *MJA* article and its underlying Grattan report, a near-identical 'draft' version of the Grattan report was circulated at high levels within relevant Australian Federal Government agencies.[24] This draft lists *"diabetic wounds and ulcers"* amongst the 'do-not-do' indications for HBOT. Although subsequently changed to *"non-diabetic wounds and ulcers"* in the final version, the fact that misrepresentation of this condition as its exact opposite went undetected prior to dissemination of the report beyond the Grattan Institute further strengthens the impression of a lack of appropriate clinical involvement.[2,24]

6. MUDDLED METHODOLOGY

Soft-tissue radionecrosis (STRI) is clearly listed as a 'potentially inappropriate' indication for HBOT in the published *MJA* article.[1] Curiously, it is not mentioned by name at all in the main Grattan report (which only alludes to *"a range of conditions including osteomyelitis, cancer, and non-diabetic wounds and ulcers"* in their 'do-not-do' list without specifying which, if any, other conditions were included).[2] Scrutiny of that report's separate methodological supplement however reveals that multiple STRI codes were included in their 'potentially legitimate' list (e.g., K52.0, "*gastroenteritis and colitis due to radiation*"; K62.7, "*radiation proctitis*"; N30.4, "*irradiation cystitis*" (Table 3).[23] Without original source data, it is impossible to determine whether STRI was analysed as an 'inappropriate' or 'legitimate' diagnosis. In point 2, we have assumed that the *MJA* article (being the last-published and only peer-reviewed document arising from this study) provides the definitive answer, and STRI was analysed alongside NDHW as an 'inappropriate' indication. If, however, the *MJA* article is incorrect and STRI was analysed as a 'potentially legitimate' indication (as per the methodological supplement) then the approximation in point 2 will be incorrect. The HTNA dataset included 659 patients who would be viewed as receiving 'inappropriate' HBOT by *MJA*-article criteria (219 STRI, 264 NDHW, 176 other). If STRI is removed, the proportion of their 'do-not-do' patients incorrectly identified as receiving 'inappropriate' HBOT fall from 73% (483/659) to 60% (264/440). Under these circumstances the number of patients potentially subject to 'inappropriate' HBOT increases by ~ 50%, from 60 (27% x 222) to 89 (40% x 222), but remains far short of the 4,500+ individuals claimed in the Grattan report.[2]

7. TRANSPARENCY OF METHODOLOGY

From 2011 onwards, the *MJA* stopped publishing full research articles and their associated references in print. The casual reader is, therefore, presented with a single-page, reference-free 'executive summary', and obliged to trust that the peer-review and editorial processes have appropriately assessed the veracity of an author's assertions. The more interested reader needs to access the online edition to peruse the full article and supporting references. Even here, however, article word limits (2,500 words and 25 references for original research) work against full disclosure of all pertinent information.[25] This issue is not unique to the *MJA* and many journals now provide the opportunity to include supplementary material in an on-line appendix. No such appendix was provided with this *MJA* article, nor was any reference made to supplementary material being available elsewhere.[1] Therefore, even the interested reader was left with inadequate methodological information and data to independently verify the results. Similarly, an impression was created that the 23 listed references provided all the supporting information upon which the authors framed their original hypothesis and developed their methodology.[1]

It is only by dint of a general internet search that the concerned reader might, eventually, identify the unreferenced, differently-titled and non-peer-reviewed Grattan Institute report upon which the *MJA* article was based.[2] This 43-page document, written more as a political discussion document than an academic research paper, includes 106 references (only 13 common to the *MJA* article) but contains little additional methodological information. To locate this the most assiduous reader is finally referred to a separate 17-page methodological supplement containing a further six references (four new).[23] The methodology however remains opaque as the 'potentially legitimate' and 'do-not-do' diagnoses and procedures are not defined in full. The (now exhausted) reader is confronted with a list of over 560 three- to seven-digit alphanumeric codes that are meaningless without access to the relevant coding manuals – currently available as a five-volume set for AUD490.00 (excluding GST) or in electronic format under licence through a registered institution.[7,26] It is only upon 'cracking' these codes that many of the fundamental methodological issues described previously become apparent (*refer to footnote p.48).

8. USE OF REFERENCES

Further muddying the waters was the whimsical manner in which supporting documents were referenced. References are essential to the readership's ability to assess the validity of an author's claims. Several areas of inconsistency or concern were identifiable in this article:

In the Medical Journal of Australia:
Despite using only 23 of their available 25 reference slots, there is no reference to the source documents (Grattan Institute report and methodological supplement) in the peer-reviewed publication.[1] There is no evidence that reviewers or editorial staff were aware of the existence of this supplementary material. In the absence of this knowledge the references listed in the *MJA* would appear to be the extent of the background evidence upon which the authors based their arguments.

The authors state that "*(p)otentially ineffective treatments were drawn from published lists of, or recommendations about, inappropriate care*", but "*(o)nly guidance published before our data period (2010–11) was used*".[1] However, of their 23 references, 9 were published after these dates, including 3 of the 14 references apparently drawn upon to provide clinical guidance about the appropriateness, or otherwise, of various procedures.[10,27,28] It was inappropriate to expect medical practitioners in 2010–11 to have applied the conclusions of these reports to their practice.

Of the 14 clinical references, only the three MSAC reviews described above (point 2) make any reference to HBOT, but only two of these were published prior to the study period.[6,9,10] Their 'do-not-do' indications for HBOT were drawn from just the first, and the approval of HBOT for two further indications (STRI and NDHW) in the second was ignored – leading to their incorrect inclusion in this paper's 'do-not-do' list.[6,9] The third MSAC report, withdrawing funding of NDHW, was published after the 2010–11 period studied and was, therefore, irrelevant.[10] This post-dated reference was also cited inaccurately, omitting the words "*non-neurological soft tissue radiation injuries*" from the title.[1] Apparently intended to provide credibility to the *MJA* article, this document actually contradicts their assertions regarding STRI.[10] It is curious that, if the authors deemed this document sufficiently important to include despite publication outside their selected timeframe, the dissenting report of the clinical experts on that third MSAC review (available on-line at the same Government website) was not also included amongst their references.[29]

In the Grattan Institute Report:
This document reiterates that "*advice about more than 1200 treatments was publicly available during the period covered by our data*" and "*(f)indings published during or after our data period (2010-2011) were not used*".[2] Of the 106 references listed, however, 38 were published during or after these dates, including 5 of the 31 references apparently drawn on to provide guidance about the clinical appropriateness of a given intervention.[27,28,30–32]

Of the 31 clinical references, only two contain any reference to HBOT. Closer scrutiny reveals that the second of these references is actually a duplicate, simply cited differently.[2] Both citations refer to the original MSAC 1018–1020 (2000) report.[9] No reference is made to the second (2003) or third (2011) hyperbaric-relevant MSAC reports and it would appear that these documents were subsequently added to the *MJA* article's reference list as an afterthought.[1] This omission could explain how STRI and NDHW ended up on the 'do-not-do' list. Likewise, duplication of the single HBOT-relevant reference and omission of the relevant 2003 report from the Grattan document, together with the inclusion of the two later MSAC reports in the *MJA* article (even if they were not used), make it appear that the supporting evidence base was more comprehensive than was actually the case.

In the Methodological Supplement:
Of the six references listed in the Grattan Institute's methodological supplement, four are new.[23] Only one of these was published prior to 2010–11. This is the 2004 Cochrane review of HBOT for chronic wounds.[33] This systematic review reported no compelling evidence of benefit in wounds of non-diabetic aetiologies and concluded that "*the routine management of such wounds with HBOT is not justified by the evidence*". This is a critical issue as, in Australia, HBOT has never been a routine therapy for NDHW, but rather a 'salvage' intervention when standard care has failed. This appears to have been the only hyperbaric-relevant reference, other than the initial 2000 MSAC report, utilised by the Grattan authors.

Extensive use of secondary sources (review articles) was made to guide decisions in the Grattan Report. This might be appropriate for non-clinicians, since they would lack the requisite skill-set to meaningfully appraise the primary studies themselves. However, failure to consult primary sources is an increasing problem even in clinical circles, as thousands of new articles are published each month. This increasing dependence on secondary sources comes at significant cost. With so much primary research being published, secondary articles rapidly become progressively less relevant. The Cochrane review referenced in the Grattan's methodological supplement illustrates this point. Five clinical trials were reviewed in 2004, but by the time the next version came out (2012) there were nine trials to include.[33,34] All four of the new trials were published before or during 2010–11 and could reasonably be expected to have influenced clinical practice during the study period.

Although many of the primary studies upon which the secondary-source authors based their recommendations were published prior to 2010–11, backtracking to the primary studies upon which the Grattan articles' references were based reveals many that were still subject to robust scientific

Table 4
IHPA costings for hyperbaric oxygen therapy 2009–10 to 2013–14[40–43]

Financial year	2009–10	**2010–11**	2011–12	2012–13	2013–14
Average cost	$479	**$1,445**	$570	$ 479	$478

debate amongst clinicians and should not have been used as the basis for definitive statements on the legitimacy of a given therapeutic intervention. Furthermore, secondary sources provide filtered information that cannot always be assumed to be free of bias. By selecting reviews that support their own agenda, whilst omitting those that do not, authors of tertiary studies such as this *MJA* article can (intentionally or otherwise) obscure the original science, with all its limitations, behind layers of superposed opinion to provide 'definitive' advice which will ultimately prove to be incorrect.

Recommendations that "*the Australian Commission on Safety and Quality in Health Care publishes up-to-date do-not-do lists*" and that "*the Commission should review them at least every two or three years*",[2] whilst superficially appealing, are likely to prove unworkable in practice. Such lists become obsolete long before their next planned update (denying patients timely access to the latest developments in medical care) and the costs of the bureaucracy required to comprehensively review every indication for every procedure in the *MBS* every two to three years would likely dwarf any potential cost-savings accruing from whatever restrictions they might recommend. Furthermore, since those who are best placed to appropriately interpret new research are those with the greatest training and experience in the relevant field, such guidelines would require the diversion of limited clinician resources away from direct patient care, further compromising health outcomes.

9. TEMPORAL MISREPRESENTATION

The timeline confusion described in point 8 is not restricted to use of reference material but carries over into the discussion. Assertions that "*the procedures used here as examples have either been shown in academic studies to be inappropriate or are recommended against in guidelines, or both. What we have shown is that, despite this advice, and even defunding in the Medicare Benefits Schedule, the procedures are still being performed*"[1] appear disingenuous when it is realized that this 2015 paper was based on 2010–11 data and that the defunding of NDHW in the *MBS* did not occur until November 2012.[10–14] Current practices cannot be inferred from five-year-old data when the regulations governing those practices have changed in the interim.

10. REGIONAL VARIATION

Tasmania was illustrated as the most remarkable outlier by State, with a rate of 'do-not-do' HBOT ten times higher than any other jurisdiction.[2] This figure was not consistent with our knowledge of local hyperbaric medicine practices and required explanation. Tasmania has only a single comprehensive clinical hyperbaric facility and we, its medical co-directors, have an obligation to our patients, colleagues, funding bodies and the broader community to detail the multiple issues that negate this study's conclusions.

In Tasmania, the Royal Hobart Hospital hyperbaric database reveals that 1,734 individual hyperbaric treatments were provided to a total of 100 patients in 2010–11. Of those, 1,613 (93%) were for Medicare-approved indications in a total of 87 patients, and 121 treatments (7%) in 13 patients were for non-Medicare-funded indications.[21] These figures compare favourably with HTNA data, which demonstrate a national average of 13.8% of patients being treated for non-Medicare-funded indications.[3] Of these 13 Tasmanian patients, nine were provided with HBOT as an emergency life-, limb- or sense-saving intervention for indications recognized as potentially amenable to HBOT by the international scientific societies mentioned previously, and for which no alternative treatments with higher levels of supporting evidence were available. Clearly identification of Tasmania as an outlier is erroneous.

Multiple reasons for regional variation in the provision of HBOT have been identified previously.[35] Disease prevalence, chamber logistics, Health-service administrative systems, local geography and population distribution relative to the regional hyperbaric facility all contribute to such variation. It has been suggested that rather than demonstrating inappropriate over-utilization in high treatment-rate locations this variation is potentially indicative of unmet need in lower treatment-rate regions.[35] However, the importance of administrative systems in that article was limited to the potential for bureaucratic territoriality to hinder patient flow across health-service boundaries.[35] This issue is not encountered in Tasmania, with its single health service. However, administrative systems can also create factitious variation between regions. As discussed in point 4, hospitals providing HBOT on an outpatient rather than a day-admission basis were not included in the AIHW dataset. Furthermore, our forthcoming companion article illustrates that regional variation in coding error-rates may also exist, varying from 25 to 70% in different locations.[21,22]

Researchers have an ethical obligation to apply due diligence and ensure their data validity prior to publication. Identification of outliers (if genuine) can be an important source of progress in scientific research, informing new directions of enquiry. The authors of the *MJA* paper do not describe what, if any, steps they took to confirm data

validity. It may be that they accepted AIHW at face value as a source of "*(a)uthoritative information and statistics*".[19] However the presence of such dramatic outliers as Tasmania should have triggered a cross-check of data validity against other available data sources. Even basic cross-referencing against other (albeit incomplete) Government datasets would have alerted the authors to re-examine their source data. Medicare data, for example, demonstrate major regional inconsistencies in HBOT use when compared against AIHW figures. Of 15,579 hyperbaric treatments billed nationally to Medicare in 2010–11, only two were from Western Australia – several orders of magnitude fewer than in the AIHW dataset.[36]

11. FINANCIAL IMPACT

The methodological supplement uses data from the Independent Hospital Pricing Authority (IHPA) to estimate the average cost of their various 'do-not-do' procedures. The IHPA is the Government agency responsible for determining the "*National Efficient Price*" for public hospital services.[37–40] The Grattan authors' analysis of these data reported an average cost for HBOT in 2010–11 (adjusted to 2014–15 dollars using the IHPA's indexation rate of 4.7%) of $1,298.[23] This figure approximates the IHPA's own published cost of $1,445 for 2010–11.[37] However, that year was an outlier in the IHPA data, with an average cost more than three times greater than the previous (AUD479) and succeeding years (Table 4).[37–40] It is ironic that the Report utilized a financial outlier as source data whilst seeking to eliminate clinical outliers. Whether this profound variation reflects a typographical error or a deeper issue (e.g., alteration in data collection or statistical analysis) is unclear. It was appropriate that the authors used IHPA data for the relevant year, but use of this non-representative figure leads to a significant overestimation of the cost of 'inappropriate' HBOT.

A more realistic service price of $501.50 (the average of the other four years' publicly-available IHPA data) for HBOT is 6–8 times lower than their calculated costs for the 'do-not-do' surgical procedures (vertebroplasty, arthroscopy, uterine nerve ablation) they assessed (AUD3,252–4,412).[23] This failure to compare like-with-like calls into question the author's claims that "*(w)e identified in just five examples more than 5,000 unnecessary procedures happening every year. This means there are probably 5,000 people who need surgery who aren't getting it*".[41] Statements to the media of this nature seriously misrepresent the financial reality.

12. PUBLICATION STRATEGY

Of particular concern is the manner in which the authors chose to disseminate their questionable results. A draft version of the Grattan Institute report was circulated "*for discussion purposes*" in policy-influencing circles several months prior to general publication.[24] The final version of this report was then published on-line, together with an associated media release, the day prior to publication of the peer-reviewed *MJA* article.[1,2,42] These actions appear to contravene the *MJA*'s publication requirements, which state: "*Manuscripts and letters must be offered exclusively to the Journal. This means that all submissions should not be submitted simultaneously to other journals nor made available to others, including news reporters, while they are being considered for publication in the MJA. This embargo continues up to 12.01 am on the day of publication for all submissions that are accepted*".[25] A co-ordinated multi-media campaign then started before sunrise on the day of official *MJA* publication.[41,43–47] This strategy pre-empted broader clinical scrutiny of their paper and undermined legitimate scientific debate. The time and resources necessary to disprove incautious generalizations (based upon misinterpretation of unrepresentative data by individuals disconnected from the provision of clinical care) would be better invested elsewhere.

Conclusions

This review identifies major concerns about this Grattan Institute report. Confusion of basic terminology, inappropriate selection of 'do-not-do' indications, lack of appropriate clinical input, muddled methodology, compromised data sources, retrospective application of post-dated references, use of non-representative financial information and a publication strategy that undermines the established scientific peer-review process all combine to invalidate its conclusions. We have not analysed their other 'do-not-do' treatments, but the errors identified from HBOT alone are of sufficient magnitude to necessitate withdrawal of this paper.

Impetuously embracing the results of a dramatic new study, no matter how worthy its intentions, is unwise before it is subject to appropriate scrutiny and debate. Calls to enforce a particular agenda with punitive measures are premature if the data upon which that agenda was predicated are flawed. The Australian public have a right to expect that the health economic data used to support disinvestment in healthcare are as robust as the clinical evidence necessary to support applications for new investment. A level playing-field must exist in debates of this importance to the nation's health.

The underlying assumptions of the Gratan Institute Report are incorrect, its data source compromised, its methodology problematic and its conclusions erroneous. If the Grattan Institute wishes to regain academic credibility, the *MJA* paper and its underlying report must be formally retracted.

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Declaration of interests:

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Short communication

The prevalence of electrocardiogram abnormalities in professional divers

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Abstract

(Gunes AE, Cimsit M. The prevalence of electrocardiogram abnormalities in professional divers. *Diving and Hyperbaric Medicine*. 2017 March;47(1):55-58.)

Background: The underwater environment presents physiological challenges for the cardiovascular, renal and pulmonary systems. Increases in external hydrostatic pressure reduce the capacity of the venous compartment and cause blood to move toward the lung. The aim of this study was to evaluate retrospectively electrocardiographic (ECG) changes in a cohort of professional divers.

Methods: Between January 2009 and January 2012, 225 randomly selected professional divers, 204 male (91%) and 21 female (9%) attended our clinic for their biannual diving medical assessment. Their ECG records were evaluated retrospectively.

Results: The most common ECG abnormality observed was incomplete right bundle branch block (IRBBB) in 30 divers (13.3%). Eleven divers (4.9%) showed right QRS axis deviation (seven with IRBBB). Six divers had a sinus tachycardia; in four divers there was early repolarization; three divers had ventricular extrasystoles; one diver had ST elevation in lead V3; there was one with sinus arrhythmia and another with T-wave inversion in leads V2, V3 and aVF. These ECG changes were evaluated retrospectively by a cardiologist who made various recommendations for further review including bubble-contrast echocardiography for IRBBB.

Conclusions: No serious ECG abnormalities were identified, but IRBBB should be further investigated because of its association with persistent (patent) foramen ovale. Rapid cardiological review of ECGs could be achieved using modern communications technology, such as telecardiography, and further clinical investigations directed by specialist recommendation arranged promptly if indicated.

Key words

Diving at work; Electrocardiography; Health status; Fitness to dive; Diving research

Introduction

The underwater environment presents physiological challenges, particularly for the cardiovascular, renal and pulmonary systems.[1] Immersion reduces the capacity of the venous compartment and causes blood to move toward the lung.[2] Immersion also results in an increased cardiac output, a rise in stroke volume and increased arterial pulse pressure, leading to fluid loading on the left heart.[1] The increased pulmonary blood volume results in increased residual volume and reduced vital capacity.[3] Increasing environmental pressure reduces systolic left and right ventricular function and decompression may cause endothelial dysfunction.[4] Because of their sustained exercise, professional divers create adaptations to the underwater environment, include the myocardium, which may be associated with electrocardiographic (ECG) changes.[5] Pathological ECG findings may offer important clues about structural abnormalities of the heart, e.g., left ventricular hypertrophy, persistent (patent) foramen ovale (PFO) and the possible causes of sudden death in divers.[6]

In Turkey, occupational divers are required to undergo bi-annual examination conducted by physicians who specialize in underwater medicine. This includes laboratory tests and ECG recordings. The aim of this study was to evaluate retrospectively the ECG findings of a cohort of professional divers assessed in our clinic.

Method

The study was conducted in the Istanbul University Faculty of Medicine Underwater and Hyperbaric Medicine Clinic between 01 January 2009 and 31 January 2012. Permission was obtained from the Directors of the Department of Underwater Clinical Medicine to conduct the research. The aim of the study was explained to the divers who gave written consent for their information to be used for medical research purposes in this and other potential studies.

The case records were selected by stratified randomisation from a larger number over that time frame. The records of 225 professional divers, 204 male (91%) and 21 female (9%), aged between 18 and 46 years, presenting to the clinic for routine biannual examination were evaluated retrospectively. Demographic parameters were stored in a Microsoft Excel 2010 database and simple descriptive statistical evaluation was performed using the SPSS 17.0 programme (SPSS Inc., Chicago, IL, USA). A standard 12-lead digital ECG (EDAN SE-1200 Express 12-channel ECG) was recorded after the diver had rested supine for at least three minutes. Standard diagnostic criteria were used for the identification

Table 1
Anthropometric characteristics of 225 professional divers

Characteristic	Mean	(SD)
Males	204	
Females	21	
Age (y)	26.5	(5.7)
Height (cm)	177	(7.2)
Weight (kg)	78	(10.6)
Body mass index (kg·m^{-2})	23.4	(2.8)
Diving experience (y)	11	(2.7)

of ECG abnormalities.[8–10] Abnormal ECGs were assessed retrospectively by a cardiologist.

Results

Table 1 summarises the demographics of the 225 divers. The most common ECG abnormality was incomplete right bundle branch block (IRBBB) in 30 divers (13.3%), 22 males and eight females. Eleven divers (4.9%, eight males) showed right axis QRS deviation; seven of these 11 were in the IRBBB group. Nine divers (4%) had sinus bradycardia. A number of other abnormal ECG findings were noted. These included six divers (2.7%) with sinus tachycardia, four divers with early repolarization, three with ventricular extrasystoles, a diver who had ST elevation in V3, a diver with sinus arrhythmia, and a diver who had a negative T-wave in V2, V3 and aVF. Table 2 summarises the types and frequency of the abnormal ECG findings.

RETROSPECTIVE CARDIOLOGICAL ASSESSMENT

Retrospective cardiological review of the abnormal ECGs resulted in a number of recommendations for further assessment. Firstly, it was suggested that IRBBB and right axis deviation should be referred for transthoracic bubble-contrast echocardiography. If indicated, trans-oesophageal bubble-contrast echocardiography and cardiac magnetic resonance imaging may be recommended as the next step. Pre-syncope and hypotensive episodes need to be evaluated in sinus bradycardia and, if insertion of a cardiac pacemaker is recommended, no diving permit is given. Systemic disease should be investigated for in sinus tachycardia. Where ventricular extrasystoles and ST and T-wave changes are present, investigation for ischaemic heart and valvular disease should be considered. Electrophysiological studies may be required for ventricular extrasystole. Table 2 also summarises the cardiologist's opinion of what further investigations were indicated.

Discussion

This was a retrospective study of a cohort of professional divers undergoing biannual medical clearance. According to the regulations for professional divers in Turkey, if abnormal findings are detected, they are not allowed to dive until further specialist assessment has been completed. For treatable abnormalities or those not considered having a diving safety impact, the diving permit can be obtained; otherwise, those divers with irreversible abnormalities cannot dive again.

Serious ECG abnormalities are important factors for sudden death.[7] The rate of IRBBB at 13.3% in this study is quite high. IRBBB in an ECG recording is usually a benign finding in asymptomatic healthy people.[8] The prevalence of IRBBB and RBBB is higher in men than it is in women, and increases with age in men.[9] There were too few women (mostly underwater technology college students and civil defense staff) in our study to allow us to assess any sex differences. In healthy, young college athletes, IRBBB was not predictive of any structural abnormalities of the myocardium.[10] In addition, a study on 134 asymptomatic middle-aged men with IRBBB found no increased risk for cardiovascular disease in a 20-year follow-up.[11] However, another study reported an increased risk of sudden death in patients with RBBB.[12]

Atrial septal defect (ASD) is the most frequent congenital

Table 2
Abnormal ECG finding in 225 professional divers and retrospective comments by a cardiologist regarding recommended follow-up; EPS – electrophysiological studies; IRBBB – incomplete right bundle branch block; MPS – myocardial perfusion scintigraphy; MRI – magnetic resonance imaging; NS – no suggestion; TEE – trans-oesophageal echocardiography; TTE – trans-thoracic echocardiography

Abnormal ECG finding			Cardiological assessment recommendations	
	n	(%)	1st stage	2nd stage
IRBBB	30	13.3	TTE (bubble-contrast)	TEE or Cardiac MRI
Right QRS axis deviation	11	4.8	TTE (bubble-contrast)	TEE or Cardiac MRI
Sinus bradycardia (<60)	9	4	Cardiac pacemaker if symptomatic	NS
Sinus tachycardia (>100)	6	2.6	Investigate for systemic disease	NS
Early repolarization	4	1.7	Risk for sudden cardiac death	NS
Ventricular extrasystoles	3	1.3	24-h Holter monitor; MPS or exercise testing	Coronary angiography; EPS
Negative T-waves	2	0.8	Exercise test; MPS	Coronary angiography
Sinus arrhythmia	1	0.4	NS	NS
ST elevation	1	0.4	Coronary angiography	NS

cardiac abnormality in adults.[13] Ostium secundum ASD is frequently associated with IRBBB and right QRS axis deviation.[14] Our study found right QRS axis deviation to be the second most common ECG finding (4.8%). In addition, PFO has a prevalence of 25% in the general population. The presence of a right-to-left shunt is often seen in divers with decompression sickness (DCS).[15] If defects in the atrial septum are not identified, the diver may be at increased risk of presenting acutely with DCS.[21]

Ventricular extrasystoles, observed in three patients, are seen in sleep apnoea, hypertension, and structural heart disease.[16] Further investigations are needed in these cases, such as 24-h Holter monitoring, and treatment as indicated. The uncommon finding of sinus tachycardia, the incidence of which was 2.6%, was attributed mainly to anxiety over the impact that the medical review might have on their diving career.

The changes observed in the ECGs of athletes are largely viewed as physiological adaptations.[17] The European Society of Cardiology divides ECG changes in athletic people into two categories: physiological changes that are associated with training and pathological changes that are not linked to training. Sinus bradycardia, which is the most commonly found ECG change seen in athletes, occurs as a result of increased parasympathetic activity.[18] Sinus arrhythmia is also found frequently in athletes.[17] As a result of abnormal repolarization, IRBBB is believed to be a right ventricular adaptation to strenuous exercise,[19] whereas complete RBBB is considered to be a pathological finding; evidence of right ventricular cardiomyopathy or Brugada syndrome.[19] T-wave inversion may indicate left ventricular hypertrophy, which could be either exercise-induced or pathological.[17] However, early repolarization is classified as a benign ECG change in elite athletes,[20] but can lead to a fatal incident in later life.[21]

Professional divers may work in deep waters where cardiopulmonary difficulties caused by the high ambient pressure and increased gas densities can lead to ventricular decompensation. Therefore, diagnosis of RBBB and other clinically important ECG changes in professional divers is important. In routine practice, expert ECG interpretation may be lacking in a diving medicine clinic and consideration should be given to routine ECG evaluation by a cardiologist. With modern technology, such as telecardiography via a smart phone or similar device, the ECG could be read within a few minutes.[22] The diving medical examination could then continue or be suspended pending further specialist assessment.

As a result of forwarding these cardiological opinions to the directors of the Department of Underwater Clinical Medicine, new protocols are being considered in the divers' clinic. Before medical clearance for diving is given, the ECG could be sent via smartphone for a cardiological opinion.

Conclusions

The ECG is necessary for early diagnosis of cardiovascular pathology. Changes that are not related to exercise should be carefully assessed cardiologically, possibly including transthoracic bubble-contrast echocardiography, exercise ECG testing and cardiac magnetic resonance screening. Bubble-contrast echocardiography may be particularly suitable in divers; it is a readily available, cheap, non-invasive technique. With modern technology, the ECG could be read by a cardiologist within a few minutes.

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Insulin-requiring diabetes and recreational diving: Australian Diabetes Society position statement, December 2016

In 2015, the Australian Diabetes Society (ADS) commissioned a working group to review and revise its position statement on scuba diving in people with diabetes. A thorough literature review was performed and all available evidence was summarised and a new position statement was drafted and submitted to the ADS Council for approval and is now released.[1] The scope of this document is restricted to recreational (not professional) diving and targeted at insulin-requiring (both type 1 and type 2) diabetes, as traditionally this group has been excluded from recreational diving.

The academic literature in this area consists of a simulation study in a hyperbaric chamber, questionnaires for divers with diabetes, and seven prospective studies in open water. A 2005 workshop jointly sponsored by the Undersea and Hyperbaric Medical Society and Divers Alert Network brought together over 50 experts to review the existing literature and compared different protocols and reach consensus guidelines.[2] The consensus guidelines reached have formed the basis for development of several subsequent guidelines from different authorities and different countries. In light of the above evidence and in consultation with Australian experts and divers with diabetes, the updated ADS guidelines contain three sections:

1) suitability for diving,
2) scope of diving and
3) blood glucose management on the day of diving.

These recommendations bring the ADS in line with the South Pacific Underwater Medical Society and authorities from other countries.

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Key words
Policy; Fitness to dive; Evidence; Medical society

Case report

Anton's syndrome as a presentation of decompression illness

Charles P Azzopardi, Lyubisa Matity and Stephen Muscat

Abstract

(Azzopardi CP, Matity L, Muscat S. Anton's syndrome as a presentation of decompression illness. *Diving and Hyperbaric Medicine*. 2017 March;47(1):59-61.)
We present a case of a patient with Anton's syndrome due to decompression illness (DCI) after recreational scuba diving. Visual anosognosia, or denial of loss of vision, which is associated with lack of awareness regarding visual loss in the setting of cortical blindness, is known as Anton's syndrome (also termed Anton-Babinski syndrome). Our patient presented with progressive neurological DCI treated with repeated recompression. The anosogosia resolved after 48 h. Subsequent echocardiography revealed a persistent (patent) foramen ovale.

Key words
Decompression sickness; Central nervous system; Anosognosia; Case reports

Introduction

Decompression illness (DCI) is caused by bubble formation in blood or tissues after a reduction in ambient pressure following compressed gas diving. Clinically, DCI involving the central nervous system may present with a spectrum of neurological symptomatology, including rare and atypical syndrome presentations, making diagnosis difficult. We present one of these rare cases, with anosognosia presenting as Anton's syndrome post recreational diving.

Case report

A 57-year-old male PADI-certified recreational Master Diver with 260 logged dives, with a background of essential hypertension, as well as a longstanding history of recurrent migraine with aura, was brought to the emergency department. He complained of a sudden onset of severe back pain, followed by lethargy, tingling sensation and inability to move both legs 45 minutes after surfacing from his second dive of the day. This was to a maximum depth of 29 metres' sea water (msw) for a total dive duration of 44 minutes on air. He had performed another dive on the same day to a maximum depth of 30.7 msw for a total dive duration of 47 minutes on air, with a 105-minute surface interval between the dives, wherein he ate a beef burger and drank a bottle of carbonated beverage. This was the last of seven separate dives over four days, and he admitted drinking five units of alcohol on the evening before the day of the incident.

On admission, the patient was obtunded and disorientated, and exhibited bilateral lower limb weakness of 2/5 on the MRC Muscle Strength Scale, with up-going left plantar reflex, together with brisk knee and ankle jerks bilaterally; neurological examination of his upper limbs was unremarkable. The patient was unable to perform Romberg's or Unterberger's tests in view of his inability to stand. On cranial nerve testing the most striking clinical feature on examination was severe impairment of visual acuity, with only light perception in both eyes. Despite an objective diminution of his vision, our patient exhibited anosognosia, with regards to his visual defect; when asked to grasp a simple object, he was quick to reach out to grasp it, but he was unable to visually locate it. He started confabulating answers at finger counting wherein no fingers were being displayed by the examining doctor. Pupillary reflexes were intact (suggesting an intact anterior visual pathway), with fundoscopy being unremarkable. His body-mass index was calculated at 39 $kg{\cdot}m^{-2}$, and he was eupnoeic, afebrile, and hypertensive with a blood pressure of 190/100 mmHg, a blood glucose of 9.9 $mmol{\cdot}L^{-1}$ and oxygen saturation of 96% on air. He was able to pass urine normally. He was administered one litre 0.9% sodium chloride intravenously prior to being transferred urgently to the hyperbaric unit for recompression therapy of spinal and cerebral DCI.

He was treated with a COMEX 30 table with 50/50 heliox, with the first 60 minutes at 30 msw (405 kPa), and a total therapeutic table time of 450 minutes excluding compression. The treatment was complicated by profuse vomiting of dark material after reaching 18 msw (284 kPa) during the decompression profile. He exhibited significant resolution of lower limb weakness within the first 60 minutes at 30 msw (405 kPa) and continued to pass urine normally whilst in the recompression chamber. He was admitted to the neurology inpatient service and managed with 4 mg dexamethasone intravenously, urinary catheterization, physiotherapy, intravenous rehydration with 0.9% saline, thromboembolic deterrent (TED) stockings and subcutaneous low molecular weight heparin. The cortical visual defect with associated anosognosia persisted for the first 48 hours, but resolved on follow-up treatment with five daily US Navy Treatment Table 5.

Figure 1
Occipital lobe involvement, showing right occipital enhancement on MRI (FLAIR)

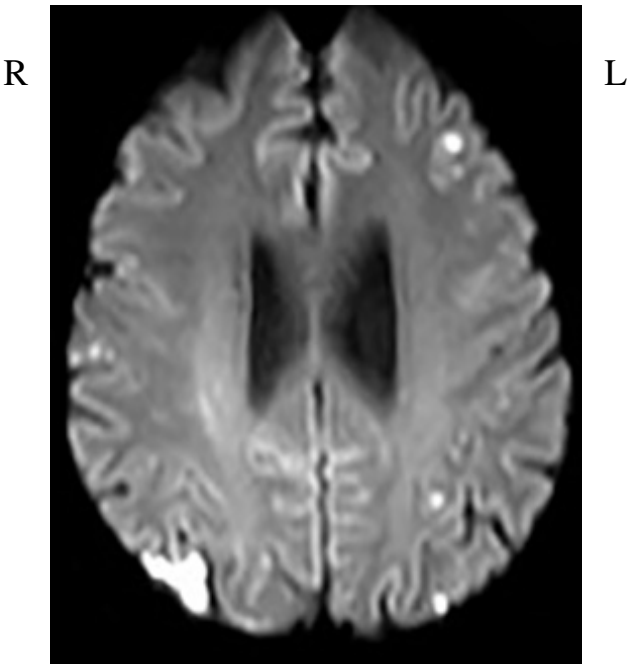
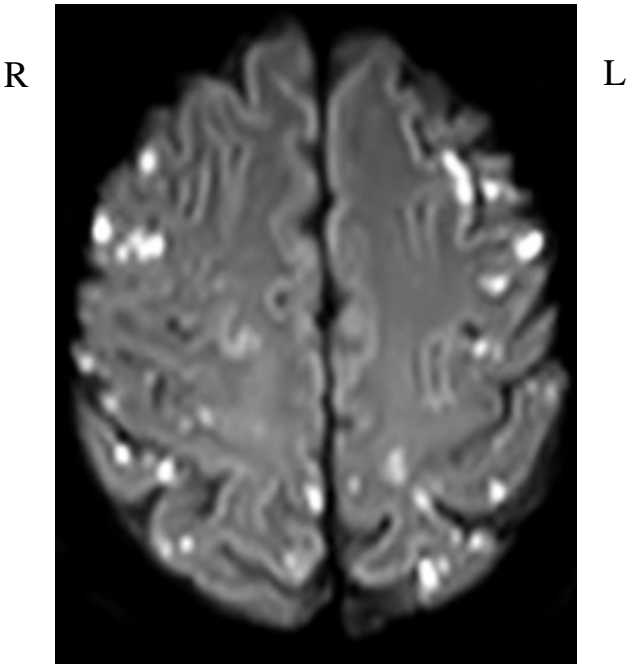


Figure 2
Parietal lobe involvement, showing enhancement subsequent to multiple emboli on MRI (FLAIR)



Magnetic resonance imaging (MRI) of the brain demonstrated evidence of widespread, bilateral multiple foci of gyral oedema throughout the cerebral hemispheres and also involving the cerebellum, with corresponding restricted diffusion noted in these regions, consistent with multiple acute emboli bilaterally. Magnetic resonance (MRI) of the spine showed no discernible pathology, despite the patient showing overt neurological signs of spinal DCI. Subsequent trans-thoracic echocardiography showed a persistent (patent) foramen ovale (PFO), with manifest right-to-left shunting through the PFO. All his symptomatology and signs resolved, except for residual bilateral lower limb weakness at 4/5 on the MRC Muscle Strength Scale.

Discussion

The first documented description of a patient who appeared unaware of his own blindness was by the French writer Montaigne (1533–1592), as he described it in his second book of *Les Essais*.[1] Three centuries later, the neuropsychiatrist Gabriel Anton (1858–1933) described a cohort of patients with blindness and deafness who showed a distinctive lack of awareness of their deficits associated with brain pathology.[2] Joseph François Babinski (1857–1932) later coined the term "*anosognosia*" to describe this unusual symptomatology.[3]

Anton's syndrome is the blatant denial of loss of vision (visual anosognosia) associated with confabulation in the setting of overt visual loss and cortical blindness. Frequently, patients with damage to the occipital lobes bilaterally also have damage to their visual association cortex, which may potentially explain their lack of awareness of the visual deficit.[4] Additionally, as suggested by Anton, damaged visual areas are effectively detached from functioning areas, such as speech-language areas; these often confabulate a response to the missing sensory visual information.[5] Cerebrovascular disease is by far the most commonly recognized cause of Anton's syndrome,[6] although the syndrome has also been reported in hypertensive encephalopathy with pre-eclampsia,[7] obstetric haemorrhage with hypo-perfusion[8] and trauma.[9]

Our patient with embolic occipital infarcts causing cortical blindness and visual anosognosia appears to fulfil the classical description for Anton's syndrome. He maintained a striking belief in his visual aptitude despite an obvious deficit. The mechanism for cerebral injury in this case is shunting of nitrogen bubbles through a demonstrated PFO. The time of onset of symptoms, 45 minutes in our case, supports this aetiology, wherein in cases of cerebral arterial gas embolism secondary to pulmonary barotrauma, the onset of symptoms is usually close to or immediately post-surfacing from the dive in question.[10] We believe this is the first published case of Anton's syndrome in a recreational scuba diver as part of the clinical presentation of DCI.

We decided to proceed with a COMEX 30 table as opposed to a fully extended US Navy Treatment Table 6 (USN TT6) based on international guidelines, such as DMAC 23 rev. 1,[11] and on the 30 years of experience at our hyperbaric centre. In cases of life-threatening DCI, USN TT6 may

be insufficient, even if extended; the Comex 30 is a more radical tool for shrinking any remaining bubbles and flushing out nitrogen from tissues. Dexamethasone was prescribed by the admitting neurologist, despite being advised by the hyperbaric consultant that there is no evidence base for its use in DCI.[12] We postulate that the patient's episode of vomiting during the decompression phase was due to central nervous system oxygen toxicity whilst breathing 100% oxygen at a partial pressure of 284 kPa.[13] The ingestion of carbonated beverages and a heavy meal immediately prior to diving, with a gastric carbonated gas bubble prone to expansion in keeping with Boyle's law on ascent, could also have contributed to his episode of vomiting during recompression.

Our patient's diving history and profiles are considered to be provocative for DCI in terms of multi-day repetitive diving, obesity, dehydration and alcohol ingestion. His history of recurrent migraine with aura led us to suspect the possible presence of a right-to-left shunt at either pulmonary or cardiac level, and the presence of a PFO was confirmed. PFO is associated with an increased risk for the development of neurological DCI.[14]

MRI of the brain of divers suffering from DCI frequently shows evidence of cortical involvement, especially on FLAIR sequences, although imaging of the spinal cord sometimes fails to evidence any overtly discernible pathology.[15] Our patient had clinical evidence of spinal DCI despite the absence of discernible pathology on MRI.

Good recovery of visual function has been noted in hypertensive encephalopathy and cortical hypo-perfusion causing Anton's syndrome.[7,8] Correction of the causative factor often leads to resolution of symptoms, and, in our case, prompt recompression therapy led to resolution of the visual deficit and anosognosia within 48 hours from presentation.

Conclusion

This case illustrates the need to maintain a high index of suspicion in assessing the possibility of DCI, in view of the deceptive presentation of DCI when the diver himself is unaware of his deficit and thus not in a position to forward any symptomatology. A thorough neurological examination is an essential part of the assessment of any diver presenting to medical attention post diving.

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Conflicts of interest: nil

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World as it is

British Sub-Aqua Club (BSAC) diving incidents report 2015

Compiled by Brian Cumming and Claire Peddie, Diving Safety and Incidents Advisors
<www.bsac.com/core/core_picker/download.asp?id=26912>

In 1980, BSAC started collecting and reporting on diving incidents and have done so annually since then. These reports remain available.[1,2] Over the years, they have striven to improve the amount and the quality of information collected with the audit of these incidents. Although these data are mainly from reports made by club members, other sources are also used.[3,4] Analysis has allowed the identification of common errors and mistakes leading to changes in training to reduce these errors. The reports have been summarised in this journal since 2006 with the earlier reports detailing the data collecting methods, which remain unchanged.[3,4]

The 2015 report covers primarily the United Kingdom though also contains a few reported incidents by BSAC divers while overseas. There were 226 incidents reported, with fewer than in previous years in all categories including the fatalities and decompression illness (DCI) sections. The efforts channelled into reducing ascent incidents since their peak of 99 in 2006 has proven successful with only 35 in 2015. This may also be a contributing factor in the reduction in DCI reports.

The number of reported incidents by month follows a sinusoidal form with the lowest in the northern hemisphere winter months; however, the previous springtime (April to July) rise was absent, suggesting better care by divers at the beginning of the season. There was less involvement by the Coastguard, the Royal National Lifeboat Institute and Search and Rescue helicopters than in previous years.

Fatalities

It is heartening to see that in 2015 there were only nine reported diving fatalities, the lowest number for 20 years. BSAC members only accounted for three of these, well below the previous 10 year's average of 6.2. Unlike previous reports of diving fatalities in other publications,[5] the BSAC report sometimes does not provide the same quality and depth of information, making it difficult to determine a root cause, though in most cases an appropriate educated assessment can be made. Also, more than one cause may be at play when things start going wrong. Broadly the causes of these fatalities were similar to previous years:

- The nine fatalities were aged between 44 and 59 years, average 52 years;
- Five cases involved the casualty falling unconscious underwater, thus creating a more problematic rescue;
- Three confirmed cases suffered a 'non-diving' related medical incident (e.g., heart attack) whilst in the water;
- In two additional cases, a medical event while underwater was very likely;
- Five cases involved divers diving in a group of three;
- Two cases involved a rapid ascent whilst carrying out an alternative gas source ascent;
- Four cases involved a separation of some kind and in three of these they were diving in a group of three;
- One case was a solo rebreather diver; insufficient information was available to determine the cause(s).

A comparison to a recent publication of fatalities from Denmark shows that in their region the incidence is rising while their average age is lower at 38.9 years.[6] From the fatalities section of the BSAC 2015 report:

Case 1

"On the second day of a deep diving course an instructor was conducting the first shore dive of the day with two students and a support diver. The group had descended to a maximum depth of 35 m without incident and were ascending up a slope. At 20 m the instructor stopped to demonstrate filling a small bottle with gas when his regulator free flowed. The instructor was provided with an alternate source and the ascent continued to around 5 m when he suddenly made a rapid ascent to the surface. The rest of the group ascended immediately, with a dive time of 24 min, and found the instructor lying face down and unresponsive. He was removed from the water, CPR and oxygen were administered and an ambulance called but he did not recover."

Case 2

"A group of divers carried out a wreck dive to 32 m from a [rigid hull inflatable] *RHIB. As a diver and his buddy, diving on a twin-set, prepared to dive it was noticed that one of the buddy's regulators was leaking. On checking the buddy's equipment it was found that the contents gauge hose was loose. This was tightened as well as all other hoses checked. The divers descended the RHIB's anchor line to the wreck with the divers exchanging 'OK' signals several times. As the visibility was low and as discussed during their dive brief, the diver attached a reel to the anchor line so they could return to it for their ascent. The divers arrived back at the anchor line, unclipped the reel and ascended. The diver had checked his computer which showed a 2 min stop at 3 m and noticed that his buddy had switched her regulators. They made a steady ascent but at 17 m the buddy suddenly grabbed the diver's BCD chest strap but looked 'OK'. To reassure the buddy, the diver held her by the shoulder and he ascended backwards up the line so he could see her all the time and they exchanged 'OK' signals.*

At around 4 m the diver moved the buddy's hand from his chest strap and onto the anchor line while he checked his computer; his decompression stop requirement had cleared. The buddy gave what the diver understood to be an 'out of air' signal so the diver gave her second regulator to her. The diver checked his buddy's contents gauges which showed 150 bar in one and 50 bar in the other and he had handed her the regulator for the 150 bar cylinder. The buddy was still signalling so the diver gave her his own spare regulator which she took. The pair had now ascended to 3 m and the diver, holding onto the buddy, took her to the surface where he made them both buoyant. Their dive time was around 25 min to a maximum depth of 32 m. The buddy still had the regulator in her mouth but was now unresponsive and not breathing. The diver was assisted to recover the buddy aboard the RHIB and CPR was immediately started. The Coastguard was alerted and a rescue helicopter was sent to the scene together with a lifeboat. The diver was airlifted to hospital but pronounced dead on arrival."

Case 3

"Six students and two instructors entered the water during the first day of a rescue training course which was in open water. They swam on the surface to a training platform. The visibility in the water was around 1 to 1.5 m. The students had been briefed to descend to an approximate depth of 5 m in their buddy pairs. One instructor and four students went to a buoy at one end of the platform whilst the second instructor with two other students went to the opposite buoy on the same platform. The second instructor did not descend straight away because one student had difficulties with a leaking drysuit and this student swam on the surface to the shore and exited the water. The second instructor and the last student then descended down onto the platform. During a rescue scenario, in which the last student was rescuing the first instructor, the last student became separated and the first instructor came to the surface without the last student. Both instructors looked for bubbles from the surface and one instructor then descended back down onto the platform and searched the platform area. He then extended his search moving off the platform and found the casualty unresponsive on his back, face up with his fins slightly raised. He did not have his regulator in his mouth. The instructor brought the casualty to the surface and indicated to the surface support that this was a real emergency. As they were close to the exit he towed the victim to shore and the other divers assisted moving him up onto the slipway. CPR attempts were made but he did not recover. A post mortem indicated that a cardiac episode had occurred."

Decompression illness (DCI)

There were 39 decompression incidents reported, the lowest for many years and markedly reduced compared to the last six years. Analysis of the causal factors are similar to previous reports:

- Eight involved repetitive diving;
- Seven involved rapid ascents;
- Seven involved diving to depths greater than 30 metres' sea water;
- Four involved missed decompression stops;
- Three involved repetitive diving with a reverse profile.

Some cases involved more that one factor. It is noteworthy that eleven of the DCI cases arose from dives reported to be within decompression limits; divers should be warned to be alert to DCI symptoms arising from any dive. The content and order of this list is virtually identical to previous years. It is again felt that a number of the *"diver injury/illness"* reports (40) are probably also DCI cases, though the rate of reporting is less than that of previous years. From the DCI section:

Case 4

"A group of four divers carried out a shore dive together in two buddy pairs. They had planned a no stop dive to 35 m including a 3 min safety stop. The divers descended a shotline to 34 m and then headed towards a wall ascending to a 27 m plateau. They slowly ascended to 10 m and started the final part of their ascent parallel to the wall. At 5 m the divers carried out their 3 min safety stop, which was a bit crowded with all the divers on the stop. Halfway through this stop one of the divers, diving nitrox 23 [sic, ?32] *as air, felt dizzy. He and his buddy signalled to each other that their computers were clear and they ascended to about 2 m when the dizzy diver appeared to hesitate. His buddy was about to give an 'OK' signal when he signalled 'Up'. Back on the surface, with a dive time of 33 min, the buddy asked the diver if he was 'OK'. He appeared to be a bit disorientated but responded by saying he felt dizzy. The buddy grabbed hold of his cylinder handle and started to tow him toward some steps to exit the water. Near the steps the diver began to vomit. As the buddy turned him around to try and get him out of the water, the diver was struggling to breathe and became unconscious; the buddy shouted for help. The other buddy pair had just exited the water and they, together with a group of doctors and paramedics who had been working nearby with a film crew, recovered the diver ashore. The diver was unconscious but breathing and his treatment, including oxygen administration, was taken over by the paramedics. The diver was transferred to an ambulance and an air ambulance arrived. The diver regained consciousness and it was decided by the doctor on the helicopter that the diver should be taken to hospital by the land ambulance. The diver was then transferred to a hyperbaric chamber where a doctor diagnosed arterial gas embolism and brain and spinal cord DCI. It was also the doctor's view that it was possible the diver had a PFO. The diver remained at the chamber for three weeks and underwent eleven sessions of recompression treatment and then spent another week in hospital. The diver made slow, gradual improvements during the course of his treatment. He also underwent intensive physiotherapy and was due for further spinal rehabilitation as the most essential part of his recovery."*

Case 5

"A trimix diver had completed a shore dive to 54 m for 52 min. After he de-kitted the diver complained of back pain which he tried to relieve by stretching. Five minutes later the diver complained of dizziness and nausea, was laid down and oxygen administered. Neurological checks were carried out by another diver who was also a paramedic. The diver was checked 15 min later and after another 15 min the diver was moved to a car for transfer to hospital. The diver was now extremely dizzy, required help to get into the vehicle and was sick. The emergency services had not yet been informed as the dive site had no mobile phone signal but a few minutes later a call was made to the Coastguard to inform them of the incident and confirm that the diver was on his way to hospital. The Coastguard rang back to confirm that a team had been paged to meet the diver at the hospital and a helicopter had been scrambled. The diver was now complaining of altered sensation in both legs, a 'tingling' sensation over his stomach, back pain and he appeared to be drowsy. 1 hour and 15 min after surfacing the diver arrived at the hospital where he was examined by a doctor and transferred by the helicopter to a hyperbaric chamber where he received recompression treatment."

Case 6

A group of divers were on a hardboat diving holiday and their fifth dive of the trip was on a wreck. A diver in the group wanted to go to 40 m to view a particular section of the wreck but his usual buddy did not want to go that deep so another experienced diver agreed to be his buddy. During their buddy check the diver mentioned that his drysuit dump valve had been leaking so he would tighten it underwater and release it for the ascent. The divers descended the shotline and headed down the deck of the wreck. At 40 m the diver passed below his buddy and then turned back to try and find the wreck feature. There was no indication of any problems at this point. The buddy became aware that the diver was no longer with him so he turned back and found him inverted and holding onto the wreck at 34 m with his torch apparently entangled in deck plating. The diver had disconnected his drysuit inflator hose as he had felt his drysuit's legs filling with air, he had double checked his shoulder dump was fully open and was now trying to get his legs down. The buddy attempted to lower the diver's legs without success. The diver pointed to his left chest and it was not clear to the buddy whether he was in pain or suffering from narcosis. The buddy decided to take the diver to the surface as slowly as possible so freed the diver's torch from the deck plates, dumped all the air from his own drysuit and BCD and held onto the buddy. The ascent became buoyant and took around 1 min from 32 m to the surface. The diver's regulator was maintained in place throughout but the buddy missed safety stops as the diver had lost consciousness during the ascent. The pair surfaced with a dive time of 16 min to a maximum depth of 41 m with the diver still unconscious but breathing. The buddy signalled the dive boat but, with all the other divers underwater, the skipper was the only person aboard. He and the buddy recovered the diver using the boat's dive lift. A neighbouring dive boat came across and the skipper came aboard with one of his diving group to assist. The diver was placed on oxygen and the Coastguard contacted. The diver recovered consciousness after about 5 min and the buddy, who was a diving doctor, spoke to a hyperbaric facility who agreed the diver should be evacuated to their chamber. Around forty minutes later a helicopter arrived and evacuated the diver to the chamber where he was diagnosed with a cerebral gas embolism and given recompression treatment. He made a full recovery and was released from hospital three days later."

The overall incidence of DCI and the numbers of fatalities continues to fall. This and previous reports demonstrate common failures and, as in the past, help to direct education and learning. Thanks go again to the efforts of Brian Cumming and his team at BSAC for collating this report. We again gratefully acknowledge the honesty of those who report on their failures and misdemeanours, allowing us to learn from them.

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Key words
Recreational diving; Diving deaths; Decompression illness; Abstracts; Case reports

Letters to the Editor

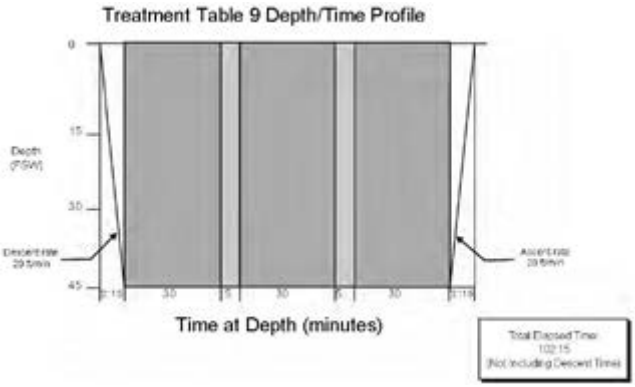
USN Treatment Table 9

The United States Navy (USN) introduced Treatment Table 9 (USN TT9) in 1999.[1] Its purpose is to provide a dosing protocol for cases of incomplete resolution of decompression sickness (DCS) and arterial gas embolism following initial provision of USN Treatment Table 6 (USN TT6). It also can be used for several non-diving-related acute toxicities. Prior to USN TT9, it was and remains common to use USN Treatment Table 5 (USN TT5) for 'follow-up' therapy. An exception might be cases of severe residual neurologic injury, where some prefer to repeat USN TT6. The primary role of USN TT5, however, is for treatment of 'pain only' (Type 1) DCS that has fully resolved within 10 minutes of the first oxygen breathing period at 60 feet of seawater (fsw) (284 kPa).[2]

It is thought helpful here to point out that USN TT9 offers certain safety and operational advantages over USN TT5. As USN TT9 employs a maximum pressure of 243 kPa, a marked risk reduction exists for the injured diver in terms of CNS oxygen toxicity. Seizures are reported during treatment of divers using US Navy protocols,[3] some as early as the second and in one case during the first oxygen breathing period at 284 kPa (Mitchell SJ, personal communication, 2016). The inside attendant likewise enjoys an iatrogenic DCS risk reduction. While air breathing exposure time at 60 fsw on USN TT5 appears modest at first blush, the table can be extended at 30 fsw (203 kPa) for two additional oxygen/air cycles.[2] Such extensions result in a not inconsiderable total exposure time of three hours. DCS risk is also increased if the treatment represents a repetitive dive for the attendant, a not uncommon event. Given the ongoing occurrence of inside attendant DCS, in some cases career ending and twice with fatal outcome, its mitigation should be aggressively pursued (author's personal files).

From an operational perspective, both treatment pressure and sequencing of oxygen/air breathing cycles during delivery of USN TT9 are essentially identical to that commonly employed during multiplace chamber delivery of hyperbaric oxygen treatment. Accordingly, it is straightforward enough to incorporate follow-up decompression illness cases into daily clinical practice. Not having this dosing 'match', i.e., using USN TT5, might otherwise disrupt regularly scheduled cases.

In my capacity as a medical claims adjudicator and clinical resource, I am involved, to varying degrees, in more than 300 cases of decompression illness each year. In those involving more than a single treatment, it is very much the exception, even after 17 years since its introduction, that USN TT9 is employed. The primary purpose of this correspondence, then, is to make mention of the advantages of USN TT9 and remind providers that it is indeed a standard of care



in cases of incomplete relief for those who choose to base decompression injury management decisions on USN treatment procedures.

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Key words
Decompression illness; Decompression sickness; Recompression; Letters (to the Editor)

Cerebral arterial gas embolism, ingestion of hydrogen peroxide and flight

We read with interest the recent report by Smedley et al. on an interesting case of cerebral arterial gas embolism (CAGE) after pre-flight ingestion of hydrogen peroxide (H_2O_2).[1] The authors discuss the safety of aero-medical transfer following H_2O_2 ingestion. We agree with the possible problems but the concern on the other side of the coin needs to be mentioned; can transfer be delayed is the big question? Indeed, as reported by others, ingestion of even a small amount of concentrated H_2O_2 can result in CAGE.[2] Hence, whether aero-medical transfer proceeds or not, severe, life-threatening embolism can occur. Since it was reported that "*complete neurologic recovery occurred quickly with hyperbaric therapy*", this supports the contention that the fastest transfer of the patient for hyperbaric treatment should be the primary focus.[3]

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Key words
Toxicology; Bubbles; Aviation; Letters (to the Editor)

Book review

Cherry Red

Neil B Hampson

Ebook, 156 pages
ISBN: 978-1-9305-3693-7 / 978-1-9305-3694-4 (ebook)
Library of Congress Control Number: 2016938682
North Palm Beach, FL: Best Publishing Company, 2016
Available from: <http://www.bestpub.com>
Price: USD14.99

It can be said that we all have a book in us, but few of us have the commitment to follow through and bring it (or them) into the world. After a distinguished career in clinical medicine and medical science publishing, Neil Hampson began exploring new directions in writing with the 2014 publication of a true crime story with a family connection.[1] He has now moved into murder mystery fiction with *Cherry Red*. This book brings together his intimate knowledge of hyperbaric medicine, carbon monoxide poisoning and the Pacific Northwest into a who- and how-done-it romp. Those who know the American hyperbaric medicine community will recognize slightly obscured or partial names of many players in the field. The protagonist of the story, Dr Bradley Franklin, is a hyperbaric physician practicing in Seattle who finds intrigue in a rash of unusual cases of carbon monoxide poisoning. The good doctor bears more than a passing resemblance to the author (Neil Bradley Hampson), with several of the benefits that one can bestow on an avatar, including an adjustment of birthdate and character commentary describing him as looking 10 years younger than his old college roommate!

The book provides a peek behind the curtain into the practices within clinical hyperbaric units and hospitals, and a novel (yes, pun intended) tutorial on the hazards, presentation, management, and avoidance of carbon monoxide poisoning. Insights into the Pacific Northwest experience and regional history add extra dimensions to entice the reader. There are also a few shining moments of humour, the best one being between Brad and his wife, that are quite engaging.

While well crafted, the book is not without flaws. The most significant is the somewhat stilted dialogue, most noticeable when it is used to communicate more backstory than would be normal for a conversation between colleagues, or as unnaturally formal conversation between friends. These, though, are forgivable errors in a sophomore book. The minor editing issues are less so: the inappropriate use of "*insure*" in place of "*ensure*", "*complimentary*" in place of "*complementary*" and the occasional missing or incorrect words. There is also a small amount of gratuitous character development. The most extreme example of this is found in the character of Candy, who adds little to the story with her breathless presence or her clothing choices.

I enjoyed *Cherry Red*. It is not high art, but it is a light vacation read that also serves to educate. It will be a good choice for those exposed to or associated with hyperbaric or diving medicine, those interested in medically-based mysteries, those who like education wrapped in a fiction package, and those wanting to check out fiction set in the Pacific Northwest. Even the flaws have grace, since they are certain to disappear in future creations by this writer.

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Key words
General interest; Carbon monoxide; Book reviews

Obituary

Norman (Nick) KI McIver OBE, MB ChB, LRCP, MRCS, FFOM

20 August 1940 – 15 September 2016

Dr Nick McIver was based at the North Sea Medical Centre at the Gorleston Medical Practice, Great Yarmouth, UK and was the key UK diving physician during the early years of the North Sea oil industry. He pioneered clinical treatments, medical support for the offshore gas industry and medical standards.

The rush to extract gas from the Southern Sector of the North Sea off East Anglia introduced a new offshore industry which constructed gas platforms and pipelines. The divers were required to spend as long as physiologically possible at 50 metres' sea water, which is the limit for air diving, in order to do heavy manual construction work underwater. Surface decompression, which was applied commercially in the southern gas fields, produced a high rate of spinal decompression sickness. The diver's danger money, primitive scuba diving equipment and the commercial pressures of the off-shore industry were a long way from the gaze of any health and safety inspector and produced many fatalities and permanent spinal injuries.

Nick came into this environment having done a spell in the Army. His impeccable clinical standards, manners and leadership skills challenged the 'cowboys' and began to improve diving and offshore safety. He flew offshore and went into diving chambers to resuscitate divers and prescribe recompression tables. Later he trained diver medics in neurological examination and practical procedures to speed up diagnosis and treatment. The North Sea environment required clinical innovation from first principles, an era in medicine when you had to 'just do it' without a multi-disciplinary team or easy communication and in a remote, hostile environment. The offshore diving industry was fortunate to have Nick's integrity, clinical skill and enthusiasm when it needed them most. He was a good networker and developed links with the Royal Navy, academics and occupational medicine specialists.

After establishing his diving medicine in the southern gas fields, the North Sea oil fields required another step change in the deeper waters off Aberdeen. The Forties Field was constructed in 1972 in 110 metres of hostile sea 180 km offshore. Saturation diving with diving bells and helium for the sea bed connections and construction had to be quickly implemented commercially from Naval experiments. Nick networked his new clinical experience, knowledge and training with the newly establishing Aberdeen diving doctors. He was secretary of the crucial Diving Medical Advisory Committee which was set up by the leading diving company to raise standards and agree safety policies across the new North Sea offshore diving industry.

He published widely, was in demand for international diving medicine conferences and ran many diving medicine courses. He was involved in developing the standards for statutory diving medicals over decades, which are the cornerstone for prevention of diving accidents offshore. He contributed to all the key published international workshops on decompression illness and managing illness in saturation.

In 1981 he was awarded the Craig Hoffman Award by the Undersea and Hyperbaric Medical Society USA for his contributions to diving safety. He was a founder member in 1993 of the British Hyperbaric Association which set standards for National Health Service (NHS) hyperbaric chambers throughout the UK. In 1996, using a redundant commercial chamber, a hyperbaric unit was established at James Paget Hospital, Yarmouth by a North Sea Medical Centre group lead by Nick and he became medical director, extending hyperbaric oxygen treatments to NHS patients for wound healing and carbon monoxide poisoning as well as divers with dysbaric illness.

He remained a humble and self-effacing man despite his professional status with his peers in the international industry. He bore his final neurological illness with great dignity and fortitude. He is survived by his wife Rita, three children and three grandchildren.

Dr James Douglas
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Editor's note: This is a shortened version of the obituary written by Dr Douglas.

Key words
Obituary; Occupational diving; Occupational health; Decompression illness; Diving industry

Notices and news

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

43rd EUBS Annual Scientific Meeting 2017

Dates: 12–16 September
Venue: Ravenna, Italy

Organising Committee: Paolo Pelaia (Ancona), Monica Rocco (Roma) and Pasquale Longobardi (Ravenna)

The EUBS Executive Committee and the local organising committee welcome you to Ravenna for the 43rd Annual Scientific Meeting of EUBS.

The dedicated conference website <www.eubs2017.org> is now active and provides practical information and registration for the conference. **Early registration ends on 31 March 2017**.

Do not forget to apply for the EUBS Student Travel Grant, the EUBS Research Grant, the Zetterstrom Award or the Musimu Award (all details can be found on the EUBS2017 website)

EUBS Member at Large Election

A new Member-at-Large to serve a three year term on the EUBS Executive Committee (ExCom) needs to be elected, either proposed by the current ExCom or by a sponsorship of 15 EUBS members. EUBS members are invited to propose candidates for this position by e-mail to <secretary@eubs.org>. Election will be conducted by internet ballot and will open on 01 July, 2017. This is your chance to participate actively in our Society – we know you can make a difference.

EUBS Affiliate Society agreements

For the year 2017, affiliate agreements have been made with the following societies and organisations:
Belgian Society for Diving and Hyperbaric Medicine: <www.sbmhs.bvoog.be>
German Society for Diving and Underwater Medicine: <www.gtuem.org>
Italian Society for Diving and Hyperbaric Medicine: <www.simsi.org>
Undersea and Hyperbaric Medicine Society: <www.uhms.org>
Scott Haldane Foundation, The Netherlands: <www.scotthaldane.org>
Members of these societies can benefit from a 10% discount on EUBS membership. These agreements are renewed annually upon written request by the Affiliate Societies, and are granted as long as a predetermined minimum number of their members have been EUBS members during the previous calendar year.

EUBS Membership Secretary/Treasurer

After 13 years of loyal service, Patricia (Tricia) Wooding, our Membership Secretary/Treasurer, has handed her tasks over to Kathleen (Kath) Pye.

The EUBS ExCom, on behalf of the membership, expresses our deep gratitude for the excellent work Tricia has done for the Society, helping to modernise the membership and financial management over past years. We have no doubt that Kath will be a great asset in the same way as Tricia has been. Kath can be reached through the same e-mail address: <secretary@eubs.org>

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>

Notices and news

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

SPUMS Annual Scientific Meeting 2017

Joint Conference with the

Asian Hyperbaric & Diving Medicine Association

Main Theme: Medical Support of Commercial Diving

Dates: 21–26 May 2017
Venue: Exclusive use of Rama Candidasa Resort and Spa, Bali, Indonesia

Keynote speakers: Dr Debbie Pestell, Canadian Undersea and Hyperbaric Medical Association
Dr Jurg Wendling, Dan Europe Suisse
Additional speakers: Neal Pollock, Ian Gawthrope, David Smart, Sarah Lockley, Martin Sayer
ADHMA: Dick Clarke, National Baromedical Services and National Board of Diving & Hyperbaric Medical Technology

Workshop: Hands-on diver-focused echocardiography with Neal Pollock, Ian Gawthrope and Jurg Wendling

Conveners: Katherine Commons and Clinton Gibbs <asm2017@spums.org.au>
Scientific Convener: Denise Blake <scientific.convener@spums.org.au>

Abstract submissions are now open via the registration site.

Registration: via the CVENT link at <http://spums.org.au/content/2017-spums-asm>

Facebook: facebook.com/spums2017

Australian College of Emergency Medicine CPD accreditation for SPUMS 2017 ASM

The following activity has been accredited for ACEM CPD: Activity ID: 36307 South Pacific Underwater Medicine Society (SPUMS) Annual Scientific Meeting 2017 – group learning, meetings, conferences, etc; non-ACEM 20 h.

The accreditation outcome and use of the supplied accreditation logo is valid until 30 June 2017, unless the activity is significantly changed. If necessary, participants can and should update the stated number of hours to reflect their individual activity.

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Key words
Meetings; MOPS (maintenance of professional standards)

ANZ College of Anaesthetists CPD accreditation for SPUMS 2017 ASM

The following information is regarding ANZCA CPD points for the SPUMS 2017 ASM.
Hands on workshops: Participants in the ANZCA CPD programme may claim this workshop under the Knowledge and skills activity; short format learning at 2 credits per hour.
Lectures: Participants in the ANZCA CPD programme may claim this workshop under the knowledge and skills activity; learning sessions at 1 credit per hour.

Professor Simon Mitchell PhD, FUHM, FANZCA

Simon Mitchell has been promoted to Professor at the University of Auckland, effective 01 February 2017. He is Head of the Department of Anaesthesiology, Faculty of Medical and Health Sciences. Simon is a member of the DHM Editorial Board and serves on the Research Committee of the ANZ College of Anaesthetists and the SPUMS Executive.
SPUMS and EUBS extend their warmest congratulations on this richly deserved appointment.

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;
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 2017

6–13 May: *Mini-congress Diving Medicine*
Venue: Marsa Shagra Eco-diving village, Marsa Alam, Egypt

Principal speaker: Adel Taher
Invited speakers: Jean Claude Le Péchon; Ulrike Preiml; Guy Vandenhoven; Mattijn Buwalda; Rienk Rienks; Nico Schellart; Marga Schweigmann; Peter Westerweel

15 cp; content conforms to ECHM-EDTC Level 1, 2D

For further information: <www.diveresearch.org> or
E-mail: <n.a.schellart@amc.uva.nl>

International Congress on Hyperbaric Medicine (ICHM) 2017

Date: 11–14 May
Venue: The Sava Centre, Belgrade, Serbia

The ICHM President, Miodrag Zaric, and the organising committee invite you to participate in the 19th ICHM, hosted by the Centre for Hyperbaric Medicine and the University of Belgrade School of Medicine. The ICHM is the only world-wide association in this field, with meetings held every third year across the globe. Key topics include research pathways in hyperbaric medicine, controversial and new/promising indications, pathogenesis of DCI, cost effectiveness and basic research. A practical, problem-orientated pre-congress workshop, as well as post-congress courses are also planned.

Website: <www.ichm2017.com>
E-mail: <office@ichm2017.com> or <chm@chm.rs>
Phone: (+381)-(0)11-3670-158

3rd International Conference on hyperbaric oxygen therapy and the brain 2017

Dates: 18–20 May
Venue: Yam Suf Hotel, Eilat, Israel
Host: Israeli Society for Hyperbaric and Diving Medicine

Preliminary programme (official language: English) includes traumatic, decompression and anoxic brain injuries: blast injuries; post-concussion syndrome; post traumatic stress disorder; chronic pain syndromes; 'reverse aging' concepts

Scientific enquiries:: <ramig@bgu.ac.il>
For further information, registration and submissions: <http://www.ishdm2017.com/>

Scott Haldane Foundation

As an institute dedicated to education in diving medicine, the Scott Haldane Foundation has organized more than 230 courses over the past 20 years. SHF is targeting more and more on an international audience with courses worldwide.

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

SHF Course Calendar 2017
1, 7 & 8 April: Basic course part 2, AMC, Amsterdam
18–19 May: Basic course part 1, Oman
20–27 May: Basic course part 2, Oman
23–24 June: In-depth course Diving in Extreme conditions, Loosdrecht, NL
04–11 November: Basic course part 1, Flores/Komodo, Indonesia
11–18 November: 25th in-depth course diving medicine, Flores/Komodo, Indonesia
18–25 November: 25th in-depth course diving medicine, Flores/Komodo, Indonesia

On request: Internship different types of diving (DMP certification), NL
On request: Internship hyperbaric medicine (DMP certification), NL/Belgium
For further information: <www.scotthaldane.org>

Undersea and Hyperbaric Medical Society 50th Annual Scientific Meeting 2017

Dates: 29 June–01 July
Venue: Naples Grande Beach Resort
Naples, Florida

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The Editor's offering

The importance of the interaction between the vascular endothelium and blood constituents in the evolution of decompression illness (DCI) was first recognized many years ago. Bubbles in the circulation may lead to the mechanical lifting of the vascular endothelium in the brain, recognized as an important mechanism for vascular and other organ damage. Bubbles may also cause platelet activation, lead to damaged vascular wall after gas embolism, per-vented subsequent local cerebral circulatory impairment.[1] Bruzzi et al. [2] have recently reviewed the interaction between the blood and atherosclerotic arterial wall, and per-ceived an interesting system and the potential role of circulating microparticles in the development of the injury from circulating gas bubbles.

Most readers probably think of DCI largely in terms of central nervous system symptoms and joint pain. However, DCI is a multi-organ injury, and the study in this issue on the effect of decompression illness on the kidneys is a reminder across DCI characteristics like: "Pain is not also clinical signs of gastrointestinal tract involvement" and cutaneous" and "Cutaneous manifestations are well known and have been recognized for many decades. Likewise, the diversity of CNS symptoms with which DCI may present is epitomized by the unusual case reported" could unexpected.

The hyperbaric community is partly to blame for these misdescriptive "and of lie" including over-decades to produce the necessary solid clinical evidence base for many of the treatments we use, and to "Hyperbaric Medicine" and "Hyperbaric" As a result HMOT is still regarded by many clinicians as a "fringe medicine" therapy. The hyperbaric community needs to do more than just "Hyperbaric" to establish firmly the place of HMOT in modern medicine.

References

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Pre-courses:
1. Hyperbaric oxygen safety: clinical and technical issues
2. Pre-hospital management of decompression illness: towards development of definitive modern guidelines.

For further information:
<https://www.uhms.org/index.php?option=com_civicrm&task=civicrm/event/info&reset=1&id=135>

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/>

Royal Adelaide Hospital Medical Officers' Course in Diving and Hyperbaric Medicine 2017

Dates: 28 August–08 September
Venue: The Royal Adelaide Hospital, Adelaide
Cost: AUD$2,500.00 (inclusive of GST)

Course Conveners: David Wilkinson and Suzy Szekely

Invited faculty includes: Professors Michael Bennett and Simon Mitchell

The course content includes:

- Physics and physiology of diving
- Recreational fitness-to-dive
- Occupational fitness-to-dive
- Decompression illness and non-dysbaric injuries
- Medical management and return to diving
- Technical and professional diving
- Marine envenomation
- Introduction to hyperbaric medicine

Contact for information:
Ms Lorna Mirabelli, Course Administrator
Phone: +61-(0)8-8222-5116
Fax: +61-(0)8-8232-4207
E-mail: <Lorna.Mirabelli@sa.gov.au>

British Hyperbaric Association Annual Scientific Meeting 2017

Dates: 20–21 October
Venue: In or near to Birmingham (to be confirmed)

The meeting will be held jointly with the UK Diving Medical Committee and will be aligned to refresher training for HSE Approved Medical Examiners of Divers. The dates will be arranged around the Dive Show being held in Birmingham 21–22 October.

More information soon: < 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>

Instructions to authors

A downloadable pdf of the 'Instructions to authors' (most recently revised February 2017) can be found on the *Diving and Hyperbaric Medicine* (DHM) website: <www.dhmjournal.com>.
Authors must read and follow these instructions carefully.

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For further information contact:
E-mail: <folke.lind@karolinska.se>

German Society for Diving and Hyperbaric Medicine (GTÜeM)

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

DIVER EMERGENCY SERVICES PHONE NUMBERS

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

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)
+27-828-106010 (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 incidents. All information is treated confidentially with regard to identifying details when utilised in reports on fatal and non-fatal cases. Such reports may be used by interested parties to increase diving safety through better awareness of critical factors. Information may be sent (in confidence unless otherwise agreed) to:

DAN Research
Divers Alert Network Asia Pacific
PO Box 384, Ashburton VIC 3147, Australia
Enquiries to email: <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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