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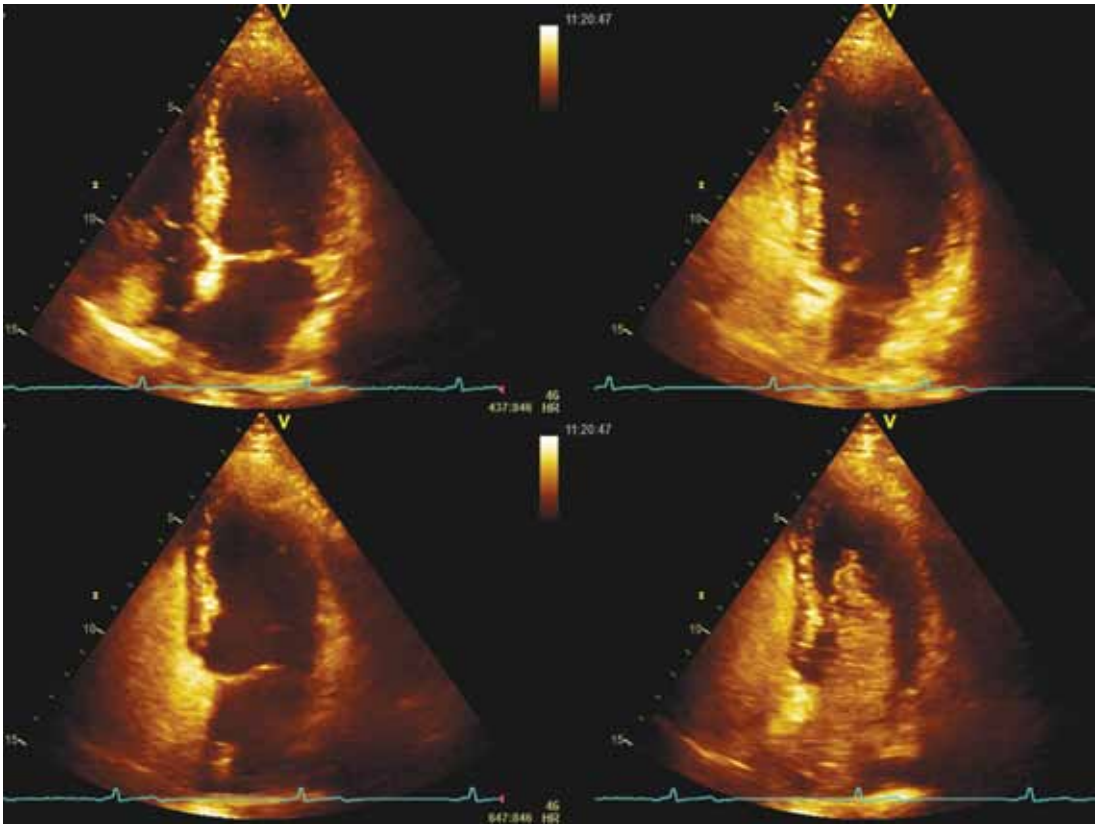

Special issue

Persistent foramen ovale and decompression illness

First-aid O_2 devices for injured divers: which and how much O_2?

Are skin bends due to brain injury in decompression illness?

Does alcohol protect rats from decompression sickness?

Survival from 'poppers' and alcohol: a role for HBOT?

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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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Editorial

Persistent (patent) foramen ovale (PFO): implications for safe diving

Diving medicine is a peculiar specialty. There are physicians and scientists from a wide variety of disciplines with an interest in diving and who all practice 'diving medicine': the study of the complex whole-body physiological changes and interactions upon immersion and emersion. To understand these, the science of physics and molecular gas and fluid movements comes into play. The ultimate goal of practicing diving medicine is to preserve the diver's health, both during and after the dive. Good medicine starts with prevention. For most divers, underwater excursions are not a professional necessity but a hobby; avoidance of risk is generally a much better option than risk mitigation or cure. However, prevention of diving illnesses seems to be even more difficult than treating those illnesses.

The papers contained in this issue of DHM are a nice mix of various aspects of PFO that divers are interested in, all of them written by specialist doctors who are avid divers themselves. However, diving medicine should also take advantage of research from the "non-diving" medicine community, and PFO is a prime example. Cardiology and neurology have studied PFO for as long, or even longer than divers have been the subjects of PFO research, and with much greater numbers and resources. Unexplained stroke has been associated with PFO, as has severe migraine with aura. As the association seems to be strong, investigating the effect of PFO closure was a logical step. Devices have been developed and perfected, allowing now for a relatively low-risk procedure to 'solve the PFO problem'. However, as with many things in science, the results have not been spectacular as hoped for: patients still get recurrences of stroke, still have migraine attacks. The risk-benefit ratio of PFO closure for these non-diving diseases is still debated.[1,2]

For diving, we now face a similar problem. Let there be no doubt that PFO is a pathway through which venous gas emboli (VGE) can arterialize, given sufficiently favourable circumstances (such as: a large quantity of VGE, size of the PFO, straining or provocation manoeuvres inducing increased right atrial pressure, delayed tissue desaturation so that seeding arterial gas emboli (AGE) grow instead of shrink, and there may be other, as yet unknown factors). [3–6] There is no doubt that closing a PFO, either surgically or using a catheter-delivered device, can reduce the number of VGE becoming AGE.[7] There is also no doubt that the procedure itself carries some health risks which are, at 1% or higher risk of serious complications, an order of magnitude greater than the risk for decompression illness (DCI) in recreational diving.[8,9]

Scientists seek the 'truth', but the truth about how much of a risk PFO represents for divers is not likely to be discovered nor universally accepted. First of all, the exact prevalence of PFO in divers is not known. As it has been pointed out in the recent literature, a contrast echocardiography (be it transthoracic or trans-oesophageal) or Doppler examination is only reliable if performed according to a strict protocol, taking into account the very many pitfalls yielding false negative results.[10] The optimal procedure for injection of contrast medium was described several years ago, but has not received enough attention.[11,12] Indeed, it is our and others' experience that many divers presenting with PFO-related DCI symptoms initially are declared "PFO-negative" by eminent, experienced cardiologists!

Failing a prospective study, the risks of diving with a right-to-left vascular shunt can only be expressed as an 'odds ratio', which is a less accurate measure than is 'relative risk'. The DAN Europe Carotid Doppler Study,[13] started in 2001, is nearing completion and will provide more insight into the actual risks of DCI for recreational divers.

The degree of DCI risk reduction from closing a PFO is thus not only dependent on successful closure but also (mostly?) on how the diver manages his/her dive and decompression in order to reduce the incidence of VGE. It has been convincingly shown that conservative dive profiles reduce DCI incidence even in divers with large PFOs,[14,15] just as PFO closure does not protect completely from DCI if the dive profiles are aggressive.[7,16] Prospective studies should not only focus on the reduction of DCI incidence after closure, but should take into account the costs and side effects of the procedure, as has been done in the cardiology and neurology studies.

Imagine lung transplants becoming a routine operation, costly but with a high success rate; imagine also a long-term smoker suffering from a mild form of obstructive lung disease and exercise-limiting dyspnoea. Which of two options would you recommend: having a lung transplant and continue smoking as before, or quit smoking and observe a progressive improvement of pulmonary and cardiac pathology? As opposed to patients with thrombotic disease and migraine, divers can choose to reduce DCI risk. In fact, all it takes is acceptance that some types of diving carry too high a health risk – whether it is because of a PFO or another 'natural' factor.[17] It would be unethical to promote PFO closure in divers solely on the basis of its efficacy of shunt reduction. Unfortunately, at least one device manufacturer has already done so in the past, citing various publications to specifically target recreational divers. Some technical diving organizations even have recommended preventive PFO closure in order to undertaking high-risk dive training.

As scientists, we must not allow ourselves to be drawn into intuitive diver fears and beliefs. Nor should we let ourselves be blinded by the ease and seemingly low risk of the

procedure. With proper and objective information provided by their diving medicine specialist, divers could make an informed decision, rather than focus on the simplistic idea that they need 'to get it fixed' in order to continue diving. A significant relationship between PFO and cerebral damage, in the absence of high-risk diving or DCI, has yet to be confirmed.[18-20] Studying PFO-related DCI provides us with unique opportunities to learn more about the effect of gas bubbles in various tissues, including the central vascular bed and neurological tissue. It may also serve to educate divers that safe diving is something that needs to be learned, not something that can be implanted.

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Key words
Persistent foramen ovale; decompression illness; editorials

Front page: sequential images (duration 2.5 sec) of a contrast-transthoracic echocardiography demonstrating patency of the foramen ovale; courtesy Germonpré P, Obeid G, Centre for Hyperbaric Oxygen Therapy and Cardiology Department, Military Hospital, Brussels.

Original articles

A rat model of chronic moderate alcohol consumption and risk of decompression sickness

Peter Buzzacott, Aleksandra Mazur, Qiong Wang, Kate Lambrechts, Michael Theron and François Guerrero

Abstract

(Buzzacott P, Mazur A, Wang Q, Lambrechts K, Theron M, Guerrero F. A rat model of chronic moderate alcohol consumption and risk of decompression sickness. *Diving and Hyperbaric Medicine*. 2015 June;45(2):75-78.)

Introduction: This study aimed to establish if chronic, moderate, pre-dive alcohol consumption had any affect upon susceptibility to decompression sickness (DCS) in rats.

Methods: A treatment group of 15 rats were given water containing 12 mL·L^{-1} of ethanol for four weeks. Controls (n = 15) were given water. Both groups were compressed with air to 1,000 kPa, followed by staged decompression. An additional 30 control rats from a similar previous experiment were added, raising the control-treatment ratio to 3:1.

Results: Rats in the treatment group consumed the equivalent of an 80 kg man drinking 2 L of 5% alcohol by volume beer per day, which is three times the recommended daily limit for men. Overall, comparing the treatment group with the combined control groups neither weight (P = 0.23) nor alcohol consumption (P = 0.69) were associated with DCS.

Discussion: We observed that chronic, moderate alcohol consumption prior to compression was neither prophylactic nor deleterious for DCS in young, male rats.

Key words

Animal model; decompression illness; risk factors; hyperbaric research; regression analysis

Introduction

Decompression sickness (DCS), occurs after ascending from depth, when previously dissolved gas is liberated in the form of bubbles rather than harmlessly diffusing out of a diver's tissues and blood.[1] Prior alcohol consumption is often cited as a risk factor for DCS, though evidence for this is lacking. The history of this caution dates back to 1874 when Dr Alphonse Jaminet, physician for the construction of the Eads Bridge over the Mississippi River at St Louis, rejected 25 of 133 (19%) job applicants for intemperance.[2] More recently in an editorial in this journal, it was stated that "*almost certainly excessive alcohol intake contributed to one case of neurological decompression sickness at a SPUMS Annual Scientific Meeting some years ago*",[3] though it remains equally possible that the case could have been worse were it not for the previous night's consumption.

In the UK, the recommended daily benchmark for alcohol consumption is 30–40 mL of pure alcohol per man.[4] Surveys of British recreational divers have consistently found that around 25% exceed the recommended weekly threshold and around 16% report regular binge drinking, commonly defined as twice the Government's recommended daily benchmark.[4–6] Both chronic and acute alcohol consumption may, therefore, be as common among divers as in non-divers. Whether acute or chronic, how habitual alcohol consumption affects risk of DCS remains unclear. Case-series reviews of decompression illness have not shown higher consumption among injured divers compared with either uninjured divers or non-divers.[6–10] Acute administration of alcohol following decompression has been shown to be beneficial in preventing or treating DCS in rabbits and humans. The aim of this study was to establish if chronic, moderate, pre-dive alcohol consumption has any affect in rats upon their susceptibility to DCS.

Methods

Male Sprague-Dawley rats (n = 30) were obtained from Janvier SAS (Le Genest St Isle, France) at age 10 weeks. Before commencing the experiment, the rats were housed for one week in the Faculty of Sciences and Techniques Vivarium in standard conditions (mean temperature 21.2°C ± 0.2 SD, relative humidity 27% ± 16% SD, 12-hour light:dark cycle, 0700–1900 h), during which they had access to rat chow ad libitum. Rats in the treatment group (n = 15) were then given 50 mL of water per day containing 12 mL·L^{-1} of ethanol (12 mL of alcohol was mixed with 988 mL of tap water to form 1 L) for 28 or 29 days, depending on the day of compression. Fifty mL just exceeds the typical water consumption measured during previous experiments. Control rats (n = 15) were given water only ad libitum. The rats were weighed each week and on the day of diving before being compressed in a 170-litre hyperbaric chamber (Comex, Marseille, France). All dives commenced in the morning after 0800 h. Hydration was withdrawn from both groups 30 mins before compression.

The 15 alcohol-treated rats in this study are a convenience sample of vehicle-control animals from separate studies yet to be reported. The duration of alcohol treatment was

Table 1
Mean weight (SD) at compression and number (*n*) of rats with decompression sickness (DCS) by group; * $P < 0.05$; † Not significant compared to the combined control group

	Control groups		Alcohol group
	Previous	Current	
	(*n* = 30)	(*n* = 15)	(*n* = 15)
Mean weight (g)	455 (27)*	414 (14)*	434 (15)†
No DCS (*n*)	6	6	5†
Survived DCS (*n*)	4	2	2†
Dead DCS (*n*)	20	7	8†

based on the requirements of these other studies. Fifteen water-only control rats were contemporaneous with these alcohol-treated rats. An additional 30 control rats from a previous experiment were added to the 15 control rats in this study, thus reducing the number of animals used while still raising the control to treatment ratio to 3:1. These additional control rats were the same age, sex and strain, housed under the same housing/cage/light/food/water/humidity/temperature conditions and underwent the same compression/decompression protocol and observation period, at the same time of day. This study and the previous experiment were approved by the French Ministry of Agriculture and the Universite de Bretagne Occidentale Animal Research Ethics Committee (R-2011-FG-01).

Since acute post-decompression alcohol administration has been shown to increase survival from DCS in rabbits, we selected a compression/decompression profile that resulted in > 50% mortality among control rats, expecting this proportion to fall significantly in the treatment group.[11] Compression with air to 1,000 kPa occurred at the rate of 100 kPa·min^{-1}. Maximum pressure was maintained for 45 minutes followed by decompression at 100 kPa·min^{-1} to 200 kPa. Decompression was thereafter staged with 5 min at 200 kPa, five min at 160 kPa and 10 min at 130 kPa.

This protocol has been shown to produce DCS signs in a predictable proportion of male Sprague-Dawley rats aged 10 to 11 weeks.[12,13] Following decompression, the rats were immediately removed from the chamber and observed for signs of DCS for one hour. The classification used was 0 – No observable DCS (*n*DCS); 1 – respiratory distress or paralysis (*s*DCS); 2 – death within one hour (*d*DCS). Two observers agreed the diagnosis in each case. Time of death was recorded as occurring at 0 minutes if observed when the chamber was opened or at time since surfacing in all other cases. The observation period ended at 60 minutes and mortality or survival noted.

ANALYSIS

Data were analysed using SAS ver 9.3 (SAS, Cary, North Carolina). Distribution of DCS between the two water-only groups was assessed for significant difference using cumulative logistic regression. The modelled probability (p) of a DCS outcome of state $\leq j$ (*n*DCS or *s*DCS), is shown in Equation 1:

$$Ln\left(\frac{p_j}{1-p_j}\right) = \underline{\alpha} + \beta_1 Group \quad (1)$$

where $\underline{\alpha} = [\alpha_1, \alpha_2]$ intercepts, α_1 for the logit of the probability of *n*DCS and α_2 for the logit for either *n*DCS or *s*DCS. The probability of *d*DCS is 1 – (probability of *n*DCS + probability of *s*DCS); *Group* was either of the two water-only groups. Differences in weight between groups were tested for significance by the Kruskal-Wallis test of Wilcoxon (rank sum) scores. Significance of alcohol consumption and weight upon DCS were assessed using a second cumulative logistic regression model (Equation 2) with p, j and $\underline{\alpha}$ as described above. Weight on the day of compression was included since weight is known to have a significant effect upon likelihood of DCS:[13]

$$Ln\left(\frac{p_j}{1-p_j}\right) = \underline{\alpha} + \beta_1 Alcohol + \beta_2 Weight \quad (2)$$

Alcohol was the control (0) or treatment (1) group and *Weight* was in grams. Significance in either regression model, determined by Maximum Likelihood Wald chi-square test for coefficient difference to a value of zero, was accepted at $P < 0.05$.

Table 2
Odds ratios for the two regression models combined; CI – confidence interval

Parameter	Point estimate	95% Wald CI	*P*-value
New water-only group vs. old (*n* = 45)	0.43	0.12, 1.40	0.15
Weight (per g; *n* = 45)	1.01	0.99, 1.03	0.23
Alcohol (*n* = 60; 0 vs. 1)	1.26	0.40, 3.94	0.69

Results

Twelve of the 15 rats consumed a mean 1.3 mL·kg^{-1} (1.0 g·kg^{-1}) of alcohol per rat per day (consumption was not measured for three of the rats), the mean weights (SD) and DCS outcomes are shown for each group in Table 1.

Distribution of DCS across *n*DCS, *s*DCS or *d*DCS did not significantly differ between control groups (Equation 1, χ^2 test $P = 0.15$). Weight at compression was significantly different between control groups ($P < 0.0001$), but was not significantly different between the combined control groups and the alcohol group ($P = 0.50$). Overall, comparing the treatment group with the combined control groups (Equation 2) neither weight (χ^2 $P = 0.23$) nor alcohol consumption (χ^2 $P = 0.69$) were associated with DCS. Odds ratios with confidence intervals are shown in Table 2.

Discussion

Rats in our treatment group consumed a mean of 1.3 mL kg^{-1} (1.0 g·kg^{-1}) of alcohol per day in a 1.2% alcohol tap-

water solution. In terms of raw alcohol consumption, this is the equivalent of an 80 kg man drinking 2 L of Fosters beer per day, which is three times the recommended daily limit for men,[4] although it must be noted that the metabolic rate of ethanol likely differs between the two species. Rats are naturally nocturnal and consumption mostly took place at night. The lights came on at 0700 h and the rats would usually settle down to sleep. Compression commenced later in the morning after alcohol and/or water were withdrawn at least 30 mins before. Therefore, it is unlikely that any rats were under the influence of alcohol at the time of compression, though this was not measured. This mimics the human population of interest, namely divers who drink chronically and then sleep before diving.

This is a relatively moderate dose of alcohol that has been shown to induce various behavioural and physiological responses in adult rats such as anxiolytic effects,[14] and raised acylated and total ghrelin levels in peripheral blood.[15] Far higher doses (5–10 $g \cdot kg^{-1} \cdot day^{-1}$) are commonly used experimentally; however, our rats were conveniently selected for this analysis from two separate, unrelated experiments, wherein they were the vehicle-control groups (unpublished data).[17] Higher doses or longer chronic ethanol consumption may well alter the risk of DCS but that remains to be investigated.

Investigating the effect of acute alcohol treatment, 32 New Zealand rabbits were compressed to 608 kPa for 30 minutes and then returned to one atmosphere.[11] Sixteen rabbits were given alcohol-saline injections (25% ethanol by volume, 3 $mL \cdot kg^{-1}$) immediately following decompression and 16 were injected with saline only.[11] All the rabbits given alcohol survived decompression whereas half the control rabbits died within 10–35 minutes.

In a pilot study, four marine fishery divers and two salvage divers who presented with acute DCS after rapid decompression were given 50–75 mL dry alcohol in a glucose drink soon after symptoms began. Sixty minutes later, four of the divers had fully recovered and all had fewer detectable circulating VGE.[16] The authors suggested "*it may be that inexpensive wine, which contains alcohol, could be an effective substitute for compression if administered shortly after the onset of acute DCS*".[16]

Four potential mechanisms have been proposed whereby ethanol may protect against DCS:[11]

- by enhancing the solubility of nitrogen in blood (the solubility of nitrogen is ten-fold greater in ethanol than in either blood or water);
- lowering the surface tension of bubbles by a factor of three and thereby acting as a de-frothing agent;
- reducing the adherence, aggregation and coagulation of platelets;
- increasing vasodilation and, thus, accelerating gas washout.

All four of these mechanisms require a blood alcohol concentration and, given the low dosage and delay between removing access to fluids and compression, it is unlikely the rats in this study had a blood alcohol level sufficiently high during decompression for the above mechanisms to play a role. This may approximate a similar circumstance to divers who drink regularly every night, sleep and then arrive at the dive site with a low or zero blood alcohol concentration. However, extrapolation from rats to the human condition can only be tentative.

Furthermore, if the addition of ethanol to the circulation does enhance nitrogen solubility then, in the case of chronic alcohol consumption, (as in this study), the degree of solubility enhancement would be symmetrical, whereas in the rabbit studies, with post-decompression ethanol solution injection, the addition of ethanol to the blood after decompression would create asymmetrical gas uptake and washout.

A limitation of our study is that we used a compression/decompression profile known to elicit a predictable proportion of three DCS outcomes[13] and to target slower tissues in the rat.[17] Therefore, a profile that generates DCS by targeting faster compartments, for example, by rapid ascent or ascent to altitude, may produce different results. Another potential limitation of this study is that the treatment and control groups arrived at the vivarium at age 10 weeks and, therefore, chronically consumed alcohol throughout sexual maturation. Since both alcohol and hormones are known to have cardiovascular effects we caution that a similar study using older animals, or females, may yield different results. The effects of chronic, higher doses of and/or longer exposure to ethanol remain to be investigated.

In conclusion, though acute alcohol consumption may prevent HPNS in rats,[18] ameliorate symptoms of experimental DCS in rabbits[11] and/or may prove an effective treatment in humans,[16] we report that chronic, moderate alcohol consumption prior to compression was neither prophylactic nor deleterious for DCS in young adult male rats.

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A comparison of the tissue oxygenation achieved using different oxygen delivery devices and flow rates

Denise F Blake, Philip Naidoo, Lawrence H Brown, Derelle Young and John Lippmann

Abstract

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

Introduction: High-concentration normobaric oxygen (O_2) administration is the first-aid priority in treating divers with suspected decompression illness. The best O_2 delivery device and flow rate are yet to be determined.

Aim: To determine whether administering O_2 with a non-rebreather mask (NRB) at a flow rate of 10 or 15 L·min^{-1} or with a demand valve with oronasal mask significantly affects the tissue partial pressure of O_2 ($P_{tc}O_2$) in healthy volunteer scuba divers.

Methods: Fifteen certified scuba divers had $P_{tc}O_2$ measured at six positions on the arm and leg. Measurements were taken with subjects lying supine whilst breathing O_2 from a NRB at 10 or 15 L·min^{-1}, a demand valve with an adult Tru-Fit oronasal mask and, as a reference standard, an oxygen 'head hood'. End-tidal carbon dioxide was also measured.

Results: While none of the emergency delivery devices performed as well as the head hood, limb tissue oxygenation was greatest when O_2 was delivered via the NRB at 15 L·min^{-1}. There were no clinically significant differences in end-tidal carbon dioxide regardless of the delivery device or flow rate.

Conclusion: Based on transcutaneous oximetry values, of the commonly available emergency O_2 delivery devices, the NRB at 15 L·min^{-1} is the device and flow rate that deliver the most O_2 to body tissues and, therefore, should be considered as a first-line pre-hospital treatment in divers with suspected decompression illness.

Key words

Scuba diving; decompression illness; first aid; oxygen; equipment; transcutaneous oximetry; medical kits; DAN (Divers Alert Network)

Introduction

Scuba diving is a pastime enjoyed by many people around the world. Decompression sickness (DCS) and arterial gas embolism (AGE) are risks for divers, collectively termed decompression illness (DCI). The depth and time of the dive as well as the mixture of the breathing gas used by the diver are major factors affecting the amount of inert gas, such as nitrogen, absorbed. DCS is caused when this inert gas is released from solution in the form of bubbles that accumulate in body tissues, lymphatic ducts and blood vessels.[1] AGE is typically the result of pulmonary barotrauma, but may also be released de novo in severe DCS. Inert gases are eliminated from the body through respiration, and breathing a high concentration of oxygen (O_2) increases the diffusion gradient for the inert gas between blood in the pulmonary capillaries and the alveoli, such that more gas moves into the alveoli to be exhaled. Oxygen should be given early to a diver with symptoms and signs of DCI, allowing them to better 'off gas' the excess inert gas and to supply more O_2 to hypoxic tissues.[2–5]

The current first-aid and pre-hospital care recommendation is that O_2 be delivered at the highest possible concentration to divers with symptoms and signs of DCI.[6] Divers Alert Network (DAN) America reports that the most commonly used O_2 delivery device for divers is the non-rebreather mask (NRB),[3] although this might not be the case in other parts of the world. The recommended initial O_2 flow rate with the NRB mask for divers with suspected DCI has historically been 15 L·min^{-1}.[6] Recently, DAN America reduced its recommended flow rate to 10–15 L·min^{-1}, largely based on extending the duration of often limited O_2 supplies in the field, while still providing increased oxygenation.[7] However, it is not known what effect, if any, this lower flow rate would have on tissue oxygenation.

This study used transcutaneous oximetry measurement (TCOM) to determine tissue oxygenation in subjects breathing O_2 via an NRB at both 15 and 10 L·min^{-1} flow rates, as well as via a demand valve with an oronasal mask. TCOM is a non-invasive technique that uses heated electrodes on the skin to measure the partial pressure of tissue oxygen ($P_{tc}O_2$).[8] The primary null hypothesis was that there would be no difference in the $P_{tc}O_2$ achieved after 10 minutes of breathing O_2 with any of the devices or flow rates.

Methods

Ethics approval was granted from The Townsville Health Service District Human Research Ethics Committee (HREC12/QTHS/203). The participants were healthy, volunteer, certified scuba divers recruited from the students and staff at The Townsville Hospital and James Cook University in Townsville. Participants were at least 18 years of age and had performed at least one dive within the previous twelve months. Each was given a study information sheet and provided written, informed consent. Participants were asked not to smoke and to refrain from consuming food or caffeine or performing heavy exercise for

Figure 1
Non-rebreather mask *(with permission)*

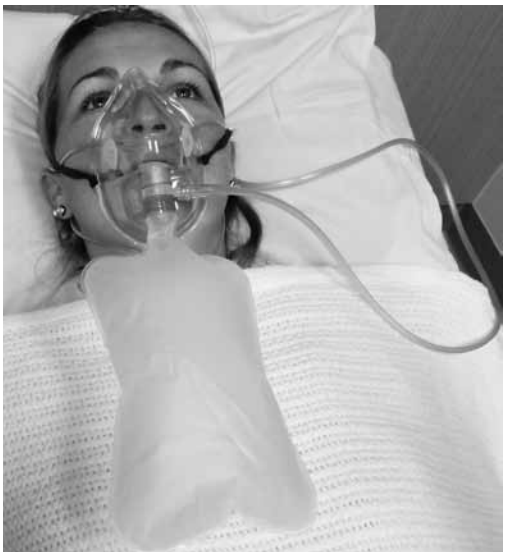
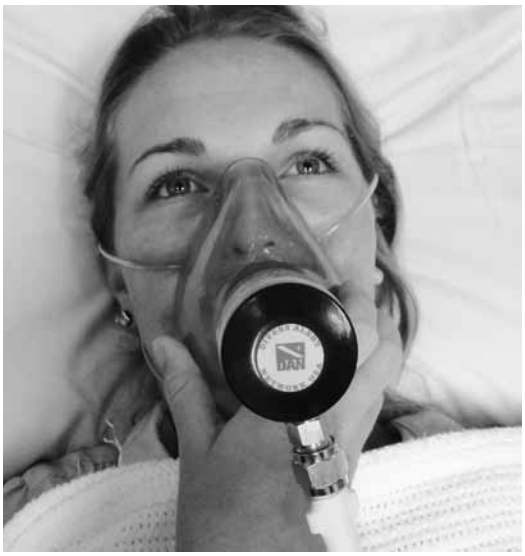


Figure 2
Demand valve *(with permission)*



two hours prior to participating in the study. Tidal volume (V_T) was measured using the EasyOne Spirometer (ndd Medical Technologies, Andover, MA, USA) according to the manufacturer's instructions. The participants were then placed in a supine position on a hospital stretcher with their head slightly raised on one pillow for the duration of the study. The room temperature was maintained at 22.0–22.5^{O}C; participants were offered a blanket for comfort and to limit any vasoconstrictive effects of being cold.

Baseline characteristics were documented, including age, gender, height, weight, O_2 saturation and blood pressure. A nasal cannula with an end-tidal carbon dioxide ($ETCO_2$) sensor (MAC-SAFE™ nasal cannula, Vital Signs Inc., West Sussex, UK) was positioned and attached to a bedside monitor (GE Carescape Monitor B650, GE Healthcare Finland OY, Helsinki, Finland) via a water trap (GE Mini D-fend™, GE Healthcare Finland OY, Helsinki, Finland).

Tissue oxygenation was measured using the TCM400 Transcutaneous Oxygen Monitoring System (Radiometer, Copenhagen, Denmark) with tc Sensor E5250. The $P_{tc}O_2$ electrodes were calibrated using room air prior to each monitoring period, as per the manufacturer's recommendations. To compensate for the environmental relative humidity and barometric pressure, a 'humidity correction factor' calculated from the room temperature, saturated water vapour pressure and relative humidity was entered into the TCM machine. All TCOM assessments were performed by the same technician. The TCM400 displays $P_{tc}O_2$ values in units of mmHg.

Six TCOM sensors were used, three on one leg and three on one arm.[9,10] The sensor sites were prepared by shaving hair if necessary, wiping clean, rubbing with an alcohol swab, and drying with gauze. One sensor was placed mid-way between the highest bony point on the shoulder and the olecranon process on the lateral aspect of the upper arm. One sensor was five centimetres distal to the brachial crease on the lateral aspect of the lower arm, and one over the thenar eminence. One leg sensor was placed 10 cm distal to the lateral femoral epicondyle, one 5 cm proximal to the lateral malleolus and one on the dorsum of the foot between the first and second metatarsal heads attempting to avoid large, superficial vessels. The leads were secured in place with tape to minimize pull on the sensor. The participants rested quietly while the sensors were placed. They were requested to minimise talking during the study, but not allowed to sleep. The investigator remained in the room for the duration of the data collection.

Initial normobaric, room air readings from all sensors were recorded after a minimum 20 minute equilibration period that allowed all sensors to stabilize. The participants were then asked to breathe O_2 for 10 minutes using each of four different O_2 delivery methods:

- NRB mask (Figure 1; Topster SM-H051, Sturdy Industrial Co Ltd) at 10 L·min^{-1};
- NRB mask at 15 L·min^{-1};
- demand valve (Figure 2; L324-020, Allied Healthcare Products, St. Louis, MO, USA) with tight-fitting adult Tru-Fit oronasal mask;
- clear plastic 'head hood' and rubber neck dam (not shown) at 15 L·min^{-1}.

DAN has designed a variety of portable O_2 delivery units to provide divers with O_2.[6,7] These units have two common components: (1) a constant flow capability for use with a NRB mask or other constant-flow delivery device; and (2) a pressure-cycled demand valve. We therefore evaluated both the constant-flow and demand valve delivery mechanisms. In Australia, a TCOM assessment normally involves a 100%

normobaric O_2 challenge using a clear head hood with a neck seal at an O_2 flow rate of 15 L·min^{-1}. Therefore, we used the hood as our reference standard.[9,10]

The order of the four O_2 delivery devices was randomised. Sensor readings were recorded at the end of the 10-minute O_2 breathing period, once stabilized. A pilot study confirmed that 10 minutes on O_2 and 10 min between devices was adequate. After each 10-min O_2 breathing period, participants breathed room air for 10 min, allowing all TCOM levels to return to baseline before the next device was trialled.[11] Medical grade O_2 was supplied from a wall outlet, or from a C-size cylinder for the demand valve. New NRB masks and $ETCO_2$ nasal cannulas were used for each participant.

The NRB masks were examined to ensure that the three one-way valves were in place, and then primed with O_2 to inflate the reservoir bag. The mask was positioned on the participant's face and adjusted to obtain the best possible seal. The participants were asked to breathe normally and the reservoir bag was monitored for collapse during the breathing periods. When breathing O_2 with the demand valve and oronasal mask, the participant was asked to breathe a little more deeply to trigger the valve.[12]

ANALYSIS

The primary outcome of this study was a determination of the differences between $P_{tc}O_2$ readings in healthy volunteer divers breathing O_2 via a hood, through an NRB at 15 and 10 L·min^{-1} and through a demand valve with oronasal mask. Based on previous research, we expected mean $P_{tc}O_2$ values between 300 mmHg (forearm) and 380 mmHg (upper arm), with a sample standard deviation of 68 mmHg, when subjects breathed 100% O_2.[9] Using the mid-point of that range (340 mmHg), assuming a decrease of 75 mmHg would be clinically significant, and allowing for substantial correlation (r = 0.90) between the repeated measures, a sample size of 13 subjects would provide a power of 80% (with α = 0.05) to detect clinically significant changes in tissue oxygenation.

Because of the small sample size, none of the data were normally distributed (that is, the histograms were skewed) despite having similar medians and means, and generally narrow standard deviations. Thus, differences between median $P_{tc}O_2$ readings using the various delivery devices and flow rates were analysed using the Friedman Test, as were the $ETCO_2$ readings. Wilcoxon Sign Rank test with Bonferroni correction was used for post-hoc paired analyses.

Results

Fifteen healthy volunteers, five male and 10 female, met all of the inclusion criteria and completed the study protocol. Their demographic and baseline data, including interquartile range (IQR), are shown in Table 1. Baseline measures of perfusion were clinically unremarkable in all participants.

Table 1
Demographics and baseline characteristics of the 15 participants

Characteristic	Median	(IQR)	Range
Age (years)	27	(23–36)	21–56
Heart rate (beats·min^{-1})	62	(57–71)	50–76
Systolic BP (mmHg)	120	(112–128)	109–133
Diastolic BP (mmHg)	65	(62–74)	58–77
Respiratory rate (breaths·min^{-1})	15	(12–18)	10–20
Demand valve rate (breaths·min^{-1})	9	(8–11)	6–19
Oxygen saturation (%)	99	(98–100)	97–100
Tidal volume (ml)	700	(620–790)	500–1150
Number of scuba dives	80	(20–396)	6–5000

Tables 2 and 3 display median IQR for the $P_{tc}O_2$ readings, the significance levels across all sensor sites, oxygen delivery devices and flow rates and a summary of the post hoc analysis across all the devices and sensor sites. As expected, $P_{tc}O_2$ values were highest when subjects breathed near 100% O_2 wearing the head hood, with median $P_{tc}O_2$ readings above 300 mmHg for all but the most distal sites. The NRB at 15 L·min^{-1} achieved statistically better oxygenation than the NRB at 10 L·min^{-1} and the demand valve at all sites, although the difference between the NRB at 15 L·min^{-1} and the NRB at 10 L·min^{-1} did not exceed our a priori clinically significant level (75 mmHg). The difference between the NRB at 15 L·min^{-1} and demand valve was also statistically significant (Table 2) and exceeded our threshold for clinical significance at all sensor sites. Oxygenation achieved with the NRB at 10 L·min^{-1} was statistically similar to the oxygenation achieved with the demand valve, although the NRB at 10 L·min^{-1} achieved clinically better oxygenation than the demand valve at all of the arm sensor sites.

$ETCO_2$ was statistically higher when patients breathed O_2 using the NRB at 10 L·min^{-1} compared to NRB at 15 L·min^{-1} (Table 2), but the difference (approximately 1 mmHg) would not be clinically relevant, and there were no statistically significant differences between $ETCO_2$ levels among any of the other device comparisons.

Discussion

O_2 is the first-aid treatment of choice for divers suspected of having DCI.[2,3,6,7,13,14] Oxygen has been shown to improve symptoms and decrease the number of hyperbaric treatments required.[3,14] An understanding of the factors influencing the delivered O_2 concentration from different devices is important in selecting first-aid O_2 equipment.[15] Near 100% O_2 via a head hood performed the best of all the devices tested in this study but it is not practical for use in the field. Of the commonly available first-aid or pre-hospital O_2 devices, the NRB at 15 L·min^{-1} is the device and flow rate that achieves the highest level of tissue oxygenation.

Table 2

Transcutaneous oxygen partial pressures (mmHg) while breathing oxygen from different delivery devices (median and inter-quartile range shown); NRB – non-rebreather mask; L – litres; min – minute; NRB 10 – NRB at 10 L·min^{-1}; NRB 15 – NRB at 15 L·min^{-1}; $ETCO_2$ – end-tidal carbon dioxide; (*P*-values based on the Friedman test)

	NRB 10 L·min^{-1}	NRB 15 L·min^{-1}	Demand valve	Head hood	*P*-value
Sensor 1 (upper arm)	261 (222, 301)	307 (269, 337)	158 (143, 244)	396 (358, 414)	0.005
Sensor 2 (lower arm)	230 (166, 260)	255 (199, 304)	141 (125, 164)	346 (314, 384)	0.002
Sensor 3 (palm hand)	236 (172, 264)	264 (212, 290)	169 (111, 219)	328 (279, 357)	< 0.001
Sensor 4 (lateral leg)	182 (145, 205)	215 (175, 259)	100 (77, 187)	300 (260, 338)	< 0.001
Sensor 5 (lateral ankle)	142 (126, 184)	202 (142, 237)	91 (73, 147)	264 (192, 342)	< 0.001
Sensor 6 (dorsum foot)	97 (61, 177)	152 (82, 208)	63 (44, 151)	163 (136, 287)	< 0.001
$ETCO_2$	33 (32, 35)	32 (30, 33)	34 (28, 36)	32 (31, 33)	0.002

Table 3

Statistically significant difference in $P_{tc}O_2$ post-hoc comparisons using Wilcoxon Sign Rank test with Bonferroni correction; $P < 0.05$ considered significant; NRB – non-rebreather; NRB 10 – NRB at 10 L·min^{-1}; NRB 15 – NRB at 15 L·min^{-1};

Head hood > NRB 10
Head hood > NRB 15
Head hood > Demand valve
NRB 15 > NRB 10
NRB 15 > Demand valve
NRB 10 = Demand valve
(for all sensor sites)

Often, desirable dive sites are far from shore or in remote areas where hospital care, let alone hyperbaric therapy, is not immediately available. The demand valve only delivers O_2 when the diver inspires and, therefore, allows for conservation of O_2 – dependent on the tidal volume of the user. The ease of use, familiarity for divers, potential to deliver high inspired O_2 concentrations[16] as well as the potential for O_2-supply conservation has led to the recommendation of the demand valve as the O_2 delivery method of choice in the first-aid and pre-hospital treatment of DCI.[13] Lower O_2 flow rates with the NRB have been suggested to conserve O_2. However, our study demonstrates lower tissue O_2 levels with both these approaches, questioning the clinical efficacy of these recommendations.

Typically, first-aid oxygen units, such as that marketed by the Divers Alert Network, use a relatively small-sized O_2 cylinder, containing around 490 (Australian C-size cylinder) to 635 litres (US Jumbo D-size cylinder) of oxygen.[6] This finite supply of O_2 is designed to treat the diver for a short time on scene while transporting them back to shore and/or arranging ambulance or air-medical transport.[7,13] At a 15 L·min^{-1} flow rate, the 490 litre C-size cylinder would last for just over 30 minutes and at 10 L·min^{-1} approximately 45 minutes.[17] This is the disadvantage of using an open system.[18] In our study, participants breathing O_2 via the demand valve had a lower median respiratory rate of nine breaths per minute. Thus a C-sized cylinder used with a demand valve might last longer than 45 minutes, but with lower levels of tissue oxygenation. Whether higher tissue O_2 levels for a shorter time period are clinically better than lower tissue oxygenation for a longer period of time in reducing symptoms and signs of DCI remains to be determined through clinical studies.[19]

The findings for the demand valve were unexpected and counter-intuitive; we anticipated $P_{tc}O_2$ readings with the demand valve to approach or exceed those with an NRB at 15 L·min^{-1}. The findings are consistent with earlier findings in a hyperbaric chamber that breathing O_2 via a demand valve achieved adequate inspired O_2 concentrations (F_IO_2) only when coached by trained staff.[20] Other investigators have explored semi-closed-circuit O_2 delivery devices for the delivery of O_2 in DCI.[17,18] None of these devices, however, are commonly used by recreational divers, partly due to increased complexity and training and maintenance requirements.

A potential limitation to our study is that we did not measure the arterial oxygen partial pressure (P_aO_2) but, rather, used $P_{tc}O_2$ as a non-invasive method of measuring tissue oxygenation. Many DCI symptoms are caused by tissue nitrogen bubbles, therefore a measurement estimating tissue oxygenation may be more relevant for this study. Further, any bias associated with using $P_{tc}O_2$ instead of P_aO_2 would be a non-differential bias, consistent across all participants and all devices and would not affect the relative within-subject differences in oxygenation achieved by each device.

We measured F_IO_2 directly via the nasal cannula whilst subjects used the hood. With this apparatus, F_iO_2 levels reached 98% in approximately 6 min. Since $P_{tc}O_2$ levels using the NRB and demand valve were both clinically and statistically less than those obtained while breathing O_2 in a hood, we can confidently say that no first-aid or pre-hospital device provided 100% inspired O_2. However, we remain of the opinion that the gold standard for oxygen administration in first aid for DCI is an F_iO_2 of 100%. This should be achievable using the DAN demand valve, but further work is needed on methods of deploying the demand valve in order to ensure it delivers this F_iO_2.

It is important that NRB masks are in good condition (i.e., not distorted) with all three one-way valves fitted and that a reasonable face seal is achieved. This is too often not the reality in the diving community. In our study, the $ETCO_2$ nasal cannula tubing may have contributed to a compromised mask seal, although we attempted to keep this to a minimum.

We used a single, new demand valve in this study. We did not test the inhalation and exhalation resistances of this valve. If the inhalation resistance was higher than specified by the manufacturer, air may have been entrained via an anti-asphyxia function reducing the inspired O_2 concentration. This is more of a problem when a diver is sitting with their head down or lying on their side.[13] Two subjects were noted to have red marks on their face after breathing from the demand valve. When questioned about this, they stated that they knew they had to hold the mask tightly to decrease the amount of air entrained. However, these two participants did not have higher demand valve $P_{tc}O_2$ levels than other participants. It may be beneficial to educate first aid providers and divers to ensure the diver holds the demand valve mask tightly to their face and breathes sufficiently deeply to trigger the valve. Anecdotally, the subjects felt the demand valve was the most uncomfortable to use.

Conclusion

Based on $P_{tc}O_2$ values, of the commonly available first-aid O_2 delivery devices, the NRB at 15 $L \cdot min^{-1}$ is the device and flow rate that delivers the most O_2 to body tissues and, therefore, should be considered as a first-line treatment in divers with suspected DCI.

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Conflict of interest
John Lippmann is the Chairman and Director of Research, DAN Asia-Pacific, which sells oxygen equipment.

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Cutis marmorata in decompression illness may be cerebrally mediated: a novel hypothesis on the aetiology of *cutis marmorata*

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Abstract

(Kemper TCPM, Rienks R, van Ooij PJAM, van Hulst RA. *Cutis marmorata* in decompression illness may be cerebrally mediated: a novel hypothesis on the aetiology of *cutis marmorata*. *Diving and Hyperbaric Medicine*. 2015 June;45(2):84-88.)

Introduction: Cutaneous decompression sickness (DCS) is often considered to be a mild entity that may be explained by either vascular occlusion of skin vessels by bubbles entering the arterial circulation through a right-to-left shunt or bubble formation due to saturated subcutaneous tissue during decompression. We propose an alternative hypothesis.

Methods: The case is presented of a 30-year-old female diver with skin DCS on three separate occasions following relatively low decompression stress dives. Also presented are the findings of cutaneous appearances in previously reported studies on cerebral arterial air embolism in pigs.

Results: There was a close similarity in appearance between the skin lesions in this woman (and in other divers) and those in the pigs, suggesting a common pathway.

Conclusions: From this, we hypothesize that the cutaneous lesions are cerebrally mediated. Therefore, cutaneous DCS might be a more serious event that should be treated accordingly. This hypothesis may be supported by the fact that *cutis marmorata* is also found in other fields of medicine in a non-diving context, where the rash is referred to as *livedo reticularis* or *livedo racemosa*. These are associated with a wide number of conditions but of particular interest is Sneddon's syndrome, which describes the association of *livedo racemosa* with cerebrovascular events or vascular brain abnormalities. Finally, there is a need for further research on the immunocytochemical pathway of cutaneous DCS.

Key words

Decompression sickness; cerebral arterial gas embolism (CAGE); decompression illness; patent foramen ovale (PFO); case reports; animal model; hypothesis

Introduction

Decompression illness (DCI) describes a range of symptoms and signs caused by a rapid reduction in environmental pressure, which results in the formation of intravascular or extravascular gas bubbles.[1] Symptoms range from skin itching and joint pain to severe neurological signs, cardiac collapse and death.[1] Cutaneous symptoms, also referred to as 'skin bends',[2] may manifest as two very distinct morphological rashes. One is the more common, fine erythematous, itchy rash, often difficult to differentiate from sunburn, and not usually associated with progress to more serious symptoms. The second is the more typical marble-like rash called *cutis marmorata*, also referred to as *livedo reticularis* (Figure 1).[1]

Rapid reduction in environmental pressure can occur during ascent after diving or exposure to a hypobaric environment by flying to high altitudes. DCI comprises two pathophysiological syndromes; arterial gas embolism (AGE) and decompression sickness (DCS). AGE can be caused by rupture of alveolar capillaries as a result of gas expansion in alveoli and result in air bubbles entering the arterial circulation. Also, venous gas emboli may result in AGE by entering the arterial circulation through a right-to-left shunt.[1] Furthermore, AGE can be iatrogenically inflicted and is described in mechanically ventilated patients.[3] Another rare form of AGE is described in airplane passengers with pre-existing lung pathologies, most commonly in the form of intra-pulmonary air-filled cysts.[4,5]

The other pathophysiological phenomenon of DCI is the more common DCS which is caused by in-situ bubble formation of dissolved inert gas, such as nitrogen.[1] DCS has traditionally been classified into two further sub-types: Type 1 with musculoskeletal pain, cutaneous symptoms, including pain, cutaneous manifestations and constitutional symptoms and Type 2, which may include vestibular, neurological and pulmonary symptoms.[1] In cutaneous DCS, the typical *cutis marmorata* is believed to be caused by vascular occlusion of skin vessels by peripheral gas bubbles in the subcutaneous tissues, and is reported to be more likely to be associated with a right-to-left shunt. The hypothesis is that venous gas bubbles enter the arterial circulation through a right-to-left shunt and, in turn, cause vascular occlusion of the peripheral skin vessels.[6] Interestingly, multiple reports of AGE have often described *cutis marmorata* as an associated clinical finding.[3–5]

We propose a new hypothesis for the aetiology of *cutis marmorata*. This is illustrated with a case report of a diver with 'undeserved' DCI, who underwent cardiologic screening for a right-to-left shunt, and an animal study of AGE.

Case report

A 30-year-old, female scuba diver was referred to our hospital for further analysis after suffering DCS. Patient history was suspect for three episodes of cutaneous DCS. The first episode was in 2008 after a dive to 30-metres

Figure 1
Cutis marmorata, in a scuba diver
(courtesy Richard Moon MD, with permission)

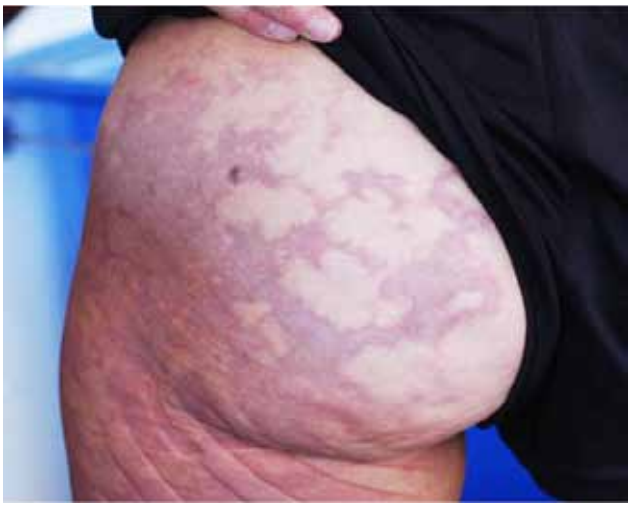
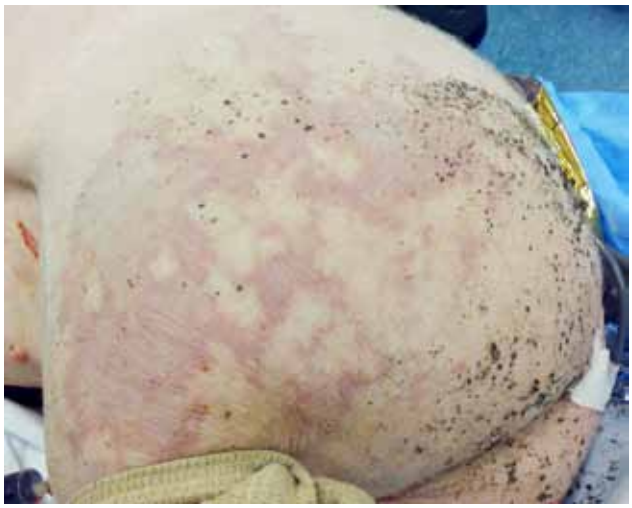


Figure 2
Cutis marmorata in a swine 4 min after introducing an air bubble into the arterial brain circulation



depth. Thirty minutes after the dive, the patient experienced intense itching with the formation of red spots spreading from the shoulder to the chest and the legs; the symptoms completely disappeared after breathing 100% oxygen. All three dives were inconsequential and she was diagnosed as having had 'undeserved' DCS. She exhibited no cardiac risk factors, including no smoking or alcohol consumption. Transoesophageal echocardiography was performed which demonstrated the presence of a type II atrial septum defect (ASD). As this has been associated with DCS,[6] she was advised against diving, and the possibility of closure of the ASD was discussed.

Animal study

Our group has had extensive experience since 2000 with ethical committee-approved studies on cerebral arterial gas embolism (CAGE) and its effects on brain metabolic function in anaesthetised pigs, using air injection into the internal carotid artery and continuous measurement with multiparameter sensors and microdialysis.[7] It was concluded that CAGE has a deleterious effect on intracranial pressure and brain metabolism. An interesting secondary observation has been that within minutes of introducing bubbles into the brain circulation, a typical mottled rash appeared on the skin of the pigs (Figure 2), which bore a striking resemblance to the skin rashes found in human DCS (Figure 1). In a recent study reported in 2013, all 22 pigs suffering CAGE developed this skin rash.[8] The amount of air injected was found to have no additional influence on the development or severity of the skin rash.

Discussion

It is suggested that *cutis marmorata* is caused by the presence of nitrogen bubbles in the subcutaneous tissues and blood vessels as a result of decompression, which causes vascular congestion and an inflammatory response.[9,10]

Our human case report is consistent with the finding of a significant relationship between cutaneous DCI and the presence of a cardiac right-to-left shunt.[6] The authors concluded that cutaneous DCI may be explained by two pathophysiological mechanisms. First, DCI is usually associated with a large right-to-left shunt and it was hypothesised that the marbled appearance of the skin is caused by vascular occlusion of skin vessels. The gas bubbles are thought to enter the arterial circulation via the cardiac shunt causing a paradoxical gas embolism with peripheral amplification when the bubble emboli invade tissues supersaturated with inert gas. However, why such a large area of skin is affected by the occlusion of only a few skin vessels could not be explained. The second possible pathophysiological mechanism focuses on individuals without a shunt, where bubbles pass through an overloaded lung filter or where autochthonous bubbles form in situ is postulated as the most likely mechanism.

We propose an alternative pathophysiological mechanism for developing *cutis marmorata*. Our experiments in swine show that it occurs within minutes after introducing a single gas bolus into the arterial brain circulation. We speculate on a pathway where the presence of an intracranial gas embolism gives rise to the release of neuropeptides, which initiates an inflammatory response. There is evidence that many neuropeptides are localised in the skin, where they are released from sensory nerves, producing several features of acute and chronic inflammation such as vasodilatation, plasma extravasation and production of cytokines.[11,12] However, a weakness of our hypothesis is the lack of immunocytochemical information from our animal studies.

In an investigation of the histopathology and ultrastructure of cutaneous lesions in swine after decompression, the lesions

were biopsied and histological abnormalities were found in 91% of the biopsies.[13] The most common finding was vascular congestion and in 45% of the lesions, focal areas of vasculitis were noted. Perivascular neutrophil infiltrates, oedema and occasional haemorrhage were also found. All biopsied skin lesions showed ultrastructural abnormalities, with acute inflammation affecting the dermal vasculature as the most common finding.

In contrast to the hypothesis of Wilmshurst et al,[6] this pathophysiological mechanism may explain why such a widespread area of the skin is affected, since the skin lesions may be explained by a centrally-mediated inflammatory response. However, we cannot rule out the possibility of the gas bubble migrating through the brain circulation and re-entering the body's arterial system via venous return and through the intra-cardiac right-to-left shunt, resulting in peripheral gas emboli. Nevertheless, the speed at which the skin changes in the pigs occurred is more suggestive of a centrally-mediated response rather than a re-circulating gas embolism. Furthermore, this mechanism supports other studies showing that the presence of *cutis marmorata* may be a prelude to more severe illness involving the central nervous system or cardiovascular system,[13,14] since we believe that *cutis marmorata* may be associated with intracranial gas emboli, most likely accompanied by a congenital heart defect.

Of interest is the fact that *cutis marmorata* is also found in other fields of medicine in a non-diving context, where the typical skin manifestations are referred to as *livedo reticularis* or *livedo racemosa*; these two terms are often used interchangeably and both entities are more often referred to as *livedo reticularis*. Although used interchangeably, it is of clinical importance to differentiate between the two entities.[15] *Livedo reticularis* is a striking, macular, violaceous, net-like, patterned erythema of the skin and can be differentiated into four entities based on the duration of the rash and its association with temperature.[16] The four entities consist of physiologic, primary, idiopathic and amantadine-induced *livedo reticularis*.[16] Physiological *livedo reticularis* most often affects young women and is commonly found on the legs as a result of cold exposure. The mottling of the skin is caused by impairment of the blood flow in cutaneous vessels and usually resolves on re-warming of the skin.[16] Primary *livedo reticularis* (also with a fluctuating course) differs from physiologic *livedo reticularis* in that it is unrelated to ambient temperature. In contrast to physiologic and primary *livedo reticularis*, the idiopathic form is persistent and diagnosed when no other pathological signs are found.[16] This last form is amantadine-induced *livedo reticularis* and (as the name suggests) is caused by the use of the synthetic antiviral agent amantadine, which is used for the treatment of Parkinson's disease and symptoms of multiple sclerosis.[16]

Livedo racemosa is characterised by a striking, violaceous, net-like patterning of the skin, similar to *livedo reticularis*, but is more widespread and generalised. In contrast to *livedo reticularis*, which typically occurs on the limbs, it is also found on the trunk and/or buttocks.[16] *Livedo racemosa* also differs in shape; instead of a regular, net-like patterning as found in *livedo reticularis*, it is characterised by irregular, broken, circular segments.[15] Moreover, *livedo racemosa* is associated with a number of disorders including antiphospholipid syndrome, livedoid vasculopathy, systemic lupus erythematosis, essential thrombocythaemia, thromboangiitis obliterans, polycythaemia rubra vera, polyarteritis nodosa and Sneddon's syndrome.[16] Although *cutis marmorata* is often referred to as *livedo reticularis*, the skin findings in DCI and in our study animals show more similarities with *livedo racemosa* with regard to morphology and localisation.

Of particular interest is Sneddon's syndrome, which is characterised by the combination of cerebrovascular events and widespread *livedo racemosa*.[17] In this syndrome, the *livedo racemosa* may precede the onset of stroke by years and can be located on the limbs, trunk, buttocks, face, or the hands or feet. The trunk and buttocks are involved in nearly all patients and *livedo racemosa* is noticed in more than half of the patients before cerebrovascular incidents.[17] In some patients, the rash is first detected at the time of stroke occurrence and, in rare cases, it appears after neurological symptoms.[17] Since the rash in some patients with Sneddon's syndrome is present for years in the absence of neurologic symptoms, preluding the first cerebrovascular event, it is plausible, considering our hypothesis, that the formation of *cutis marmorata* after suffering DCI is associated with subclinical brain damage in the absence of neurological signs or symptoms.

Sneddon's syndrome was originally considered to be a clinical diagnosis but is now regarded as a manifestation of different disease entities and can be divided into three different forms.[17] The first form is primary Sneddon's syndrome and is considered as Sneddon's syndrome without an identifiable causative factor. The second is an autoimmune form in association with antiphospholipid antibodies or coexisting systemic lupus erythematosus. The third is associated with a thrombophilic form.[17] The pathophysiology of Sneddon's syndrome remains incompletely understood, although the association with antiphospholipid antibodies suggests that the symptoms are secondary to a thrombotic process.[17] Although thrombosis may play a role in the pathogenesis of Sneddon's syndrome it is unclear how it occurs in antiphospholipid negative cases. Since heart valve abnormalities are also a common finding in Sneddon's syndrome, with a total prevalence similar in both antiphospholipid positive and negative cases, it is thought that an embolic mechanism may play an important role in the occurrence of neurologic and even skin manifestations.[17] Because some patients appear to be antiphospholipid-negative and lack other coagulation deficits, it is thought that the primary vasculopathy is the pathophysiologic change in Sneddon's syndrome and that the

non-vasculitic small and medium-sized vessel arteriopathy (as found in brain biopsies) may be the cause of both skin symptoms and cerebrovascular events. However, the type and origin of the arteriopathy remains largely unknown.[17]

The occurrence of *cutis marmorata* after inflicting a cerebral embolic event in our study animals, and the presence of *livedo reticularis* in association with cerebrovascular accidents in other clinical syndromes, may suggest that the typical skin rash has a similar common pathway in the brain. This could also explain why the livedo occurs in patients without coagulation deficits, since the skin rash may be centrally induced. This hypothesis is possibly supported by the case report of a 19-month-old girl who developed *livedo reticularis* during a second cerebrovascular event only a few weeks after a first event.[18] The event presented itself as right-sided hemiparesis and lethargy and was found to be a result of subacute ischaemic changes in the left frontoparietal white matter on MRI scanning. No thrombosis was identified but the vascular pattern was consistent with Moyamoya disease. No primary coagulation deficit could be identified. This latter case also illustrates the development of a livedo rash associated with intracranial vascular changes in the absence of a coagulation deficit.

We hypothesise that a common pathway in the brain may play a role in the development of the typical skin changes found in both DCI and other clinical entities associated with *livedo reticularis*. Although the exact mechanism remains unclear, we postulate a mechanism in which bubbles or bubble-related effects (oedema, inflammation) in the brain give rise to the release of neuropeptides and, in turn, cause an inflammatory response in the skin. We believe that additional experiments in which immunocytochemical measurements are performed may provide additional evidence to support this hypothesis and further explain the pathophysiological mechanism of DCI and, possibly, other clinical entities associated with *livedo reticularis*. Besides this, it is likely that *cutis marmorata* may have multiple causes, including local or systemic effects of bubbles.

The presence of *cutis marmorata* may be a prelude to a more serious clinical DCI syndrome and requires immediate appropriate treatment. These findings also suggest that the classification system traditionally used is insufficient and, therefore, we prefer to use the more inclusive term 'decompression illness' which has largely replaced the earlier three-tiered classification system.[1]

Conclusion

Based on this case report, the findings from our pig CAGE studies and additional literature, we hypothesise that *cutis marmorata* in DCI may be caused by the presence of an intracranial air embolism, most likely associated with the presence of a right-to-left shunt, resulting in an AGE. Although the exact mechanism remains unclear, we postulate that bubbles or bubble-related effects in the brain arteries give rise to the release of neuropeptides and, in turn, cause an inflammatory response. This hypothesis may be supported by the fact that *cutis marmorata* is also found in other non-diving fields of medicine in which intracranial pathology is present, with or without coagulation abnormalities. A weakness of our animal studies is the lack of immunocytochemical information. Additional research in which such measurements are performed may provide additional evidence to support this hypothesis and further explain the pathophysiological mechanism of DCI and, possibly, other clinical entities associated with *livedo reticularis*.

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Comparison of the size of persistent foramen ovale and atrial septal defects in divers with shunt-related decompression illness and in the general population

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Abstract

(Wilmshurst PT, Morrison WL, Walsh KP, Pearson MJ, Nightingale S. Comparison of the size of persistent foramen ovale and atrial septal defects in divers with shunt-related decompression illness and in the general population. *Diving and Hyperbaric Medicine*. 2015 June;45(2):89-93.)

Introduction: Decompression illness (DCI) is associated with a right-to-left shunt, such as persistent foramen ovale (PFO), atrial septal defect (ASD) and pulmonary arteriovenous malformations. About one-quarter of the population have a PFO, but considerably less than one-quarter of divers suffer DCI. Our aim was to determine whether shunt-related DCI occurs mainly or entirely in divers with the largest diameter atrial defects.

Methods: Case control comparison of diameters of atrial defects (PFO and ASD) in 200 consecutive divers who had transcatheter closure of an atrial defect following shunt-related DCI and in an historic group of 263 individuals in whom PFO diameter was measured at post-mortem examination.

Results: In the divers who had experienced DCI, the median atrial defect diameter was 10 mm and the mean (standard deviation) was 9.9 (3.6) mm. Among those in the general population who had a PFO, the median diameter was 5 mm and mean was 4.9 (2.6) mm. The difference between the two groups was highly significant ($P < 0.0001$). Of divers with shunt-related DCI, 101 (50.5%) had an atrial defect 10 mm diameter or larger, but only 1.3% of the general population studied had a PFO that was 10 mm diameter of larger.

Conclusions: The risk of a diver suffering DCI is related to the size of the atrial defect rather than just the presence of a defect.

Key words

Patent foramen ovale (PFO); persistent foramen ovale; right-to-left shunt; decompression illness; venous gas embolism; neurology; migraine

Introduction

About one quarter of adults have a persistent foramen ovale (PFO).[1] The prevalence is greater in individuals with cryptogenic stroke, decompression illness (DCI) and migraine with aura.[2–5] It is postulated that a PFO allows paradoxical thromboembolism in some cases of cryptogenic stroke, paradoxical gas embolism in some cases of DCI and some unidentified migraine-inducing agent to bypass the lungs in some cases of migraine with aura. The higher incidence of stroke and DCI in people with migraine with aura compared with the general population may be because migraine with aura is an indicator of a high prevalence of PFO, particularly large ones.[6–8]

However, there is no absolute concordance between PFO and cryptogenic stroke, DCI or migraine with aura. Therefore, when considering whether a PFO should be closed to prevent recurrence of events such as stroke or DCI, we need to differentiate those PFOs that were causal from those that were coincidental. Only rarely in cases of stroke is there unequivocal evidence of paradoxical embolism, for example, when echocardiography demonstrates a venous thrombus straddling a PFO. There is currently no way of demonstrating in an individual patient whether a PFO has a role in the aetiology of migraine with aura. The situation with DCI is different. Shunt-related DCI usually has characteristic clinical features which distinguish it from DCI caused by pulmonary barotrauma or an unsafe dive profile.[4,9] Analysis of the dive profile allows us not only to rule out an unsafe dive, but also to determine whether the patient's inert gas load at the onset of symptoms was likely to have resulted in venous bubble liberation. Contrast echocardiography then allows us to determine whether there is a right-to-left shunt that would allow significant numbers of these venous bubbles to bypass the lung filter.

Contrast echocardiography provides a semi-quantitative assessment of functional shunt size. A right-to-left shunt graded "*large at rest*" on contrast echocardiography is found 8–10 times more frequently in divers with cutaneous DCI (49.2%) and with neurological DCI (41%) than in controls (4.9%, $P < 0.001$).[10,11] Large shunts demonstrated with a Valsalva manoeuvre and medium shunts at rest are 2–4 times more frequent in divers with DCI than controls, but small shunts are no more frequent in divers with DCI than controls.[10,11] These data suggest that the risk of shunt-related DCI is related to the size of the shunt rather than simply the presence or absence of a PFO.

Shunt size is also likely to be important in the role of PFO in stroke and migraine with aura. Certainly in patients with severe migraine the high prevalence of right-to-left shunts is related to an excess of large shunts and not small

shunts and similarly the prevalence of migraine with aura is related to shunt size on contrast echocardiography.[12–14] It is also intuitively probable that risk of paradoxical thromboembolism is greater with a large shunt than with a small shunt.

Functional shunt size assessed by contrast echocardiography is governed by variable factors, such as inter-atrial pressure gradient and atrial blood-flow patterns, and constant factors, such as the dimensions of the foramen ovale. Of these factors governing shunt size, the PFO diameter should be easiest to measure reproducibly. We compared the anatomical diameter of PFO and atrial septal defects (ASD) in 200 consecutive divers who had balloon-size measurement at the time of transcatheter closure of atrial shunts after shunt-related DCI with PFO sizes reported in a large population study.[1]

Methods

INVESTIGATION OF DIVERS

The divers had attended our clinic for investigation of divers who have suffered DCI. Investigations included chest X-ray and dynamic spirometry in all and high resolution computer tomogram scans of the chest in some when there was rapid onset of neurological symptoms but chest X-ray and lung function tests were normal to exclude lung disease capable of causing pulmonary barotrauma. Contrast echocardiography was done to determine the presence and functional size of any right-to-left shunt. The heart was imaged (apical, four-chamber view) with a Hewlett Packard Sonos machine. Bubble contrast was produced by pushing 6–8 ml sterile saline (0.9% NaCl), 0.5–1 ml of the patient's blood and 0.5–1 ml air back and forth between two syringes connected by a three-way tap until there were no visible bubbles. This mixture was then injected through a 21-gauge butterfly needle into a left antecubital vein with the arm slightly elevated to ensure rapid contrast arrival in the right atrium. The first contrast injection was performed with the patient resting and breathing normally. If no shunt was seen with the first contrast injection, up to five subsequent injections were performed with Valsalva manoeuvres, with the operator causing sudden release of the manoeuvre, as described previously.[15] Shunts were graded according to the maximum number of bubbles seen in the left heart on frame-by-frame analysis: small shunts – fewer than six bubbles, medium shunts – six to 20 bubbles and large shunts – more than 20 bubbles.[2]

Divers with clinical features of one or more episodes of shunt-related DCI, using criteria described previously,[9] are counselled on three possible ways to reduce their risk of DCI in the future – namely to stop diving, to modify their diving to prevent venous bubble formation or to have transcatheter closure of their atrial shunt. Patients are advised to go home and think about the options carefully. The decision on which option to choose is left entirely to the patients.

CLOSURE OF ATRIAL DEFECTS

In a series of 207 consecutive divers who decided to have transcatheter closure of their inter-atrial defect following shunt-related DCI, a 25 mm Amplatzer™ PFO device (AGA Medical Corporation, Minnesota, USA) was inserted in seven without measuring the PFO diameter. It is generally believed that insertion of this device does not require balloon sizing of a PFO. Between 11 December 1996 and 22 November 2007 the remaining 200 divers had balloon sizing of the atrial defect at the time of the procedure to aid selection of an appropriate diameter Amplatzer Septal Occluder™ (AGA Medical Corporation, Minnesota, USA). For the purposes of this report, the consecutive series was terminated at 207 to provide a large and convenient sample size of 200 divers who had undergone balloon sizing to compare with the historic control group. Since then more than 100 further divers seen at our centre after they suffered DCI have had closure of a PFO or an ASD.

COMPARISON OF DEFECT SIZE IN DIVERS AND A GENERAL POPULATION

We compared retrospectively the diameter of the atrial defect in the 200 divers who had a closure procedure with the PFO diameter data reported in 263 (27.3%) people who had a PFO in a series of 965 post-mortem examinations in the general population using a Student's *t*-test.[1] Diameters are expressed as mean (standard deviation) and median. Permission to incorporate in our paper the post-mortem data from the earlier report was granted by the authors and Mayo Clinic Proceedings, which published that paper.[1] In their study, the PFO diameters were measured post mortem in formalin-fixed hearts using calibrated probes.

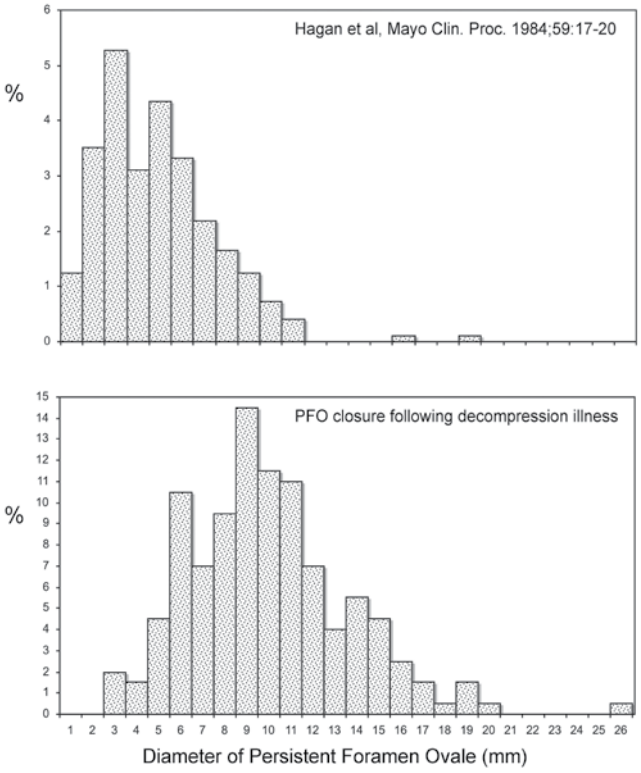
In the divers, PFO diameter was measured using an Amplatzer™ sizing balloon (AGA Medical Corporation, Minnesota, USA), which has calibration markers. The balloon was inserted across the atrial defect over a wire. It was inflated gently at low pressure until a waist was seen in the balloon and there was cessation of colour flow across the atrial septum using transoesophageal echocardiography. The diameter of the waist was measured using quantitative X-ray fluoroscopy in a view orthogonal to both the long axis of the balloon and to the plane of the interatrial septum.

All information reported in this paper was obtained as part of normal patient care. In particular, we routinely measure PFO diameter as part of the closure procedure. Therefore, no additional research consent was obtained for this retrospective data analysis.

Results

The patients in this report were in a consecutive series of 636 divers who attended our clinic for investigation of divers with DCI. Of these, 370 (58.2%) had features of

Figure 1
Histograms showing the distribution of diameters of persistent foramen ovale (PFO) in the general population[1] (with permission) (upper panel) and the distribution of the diameters of PFO and atrial septal defects in divers with shunt-related DCI (lower panel)



shunt-related DCI and had a significant right-to-left shunt (large or medium shunt at rest or large shunt with a Valsalva manoeuvre). The remaining 266 (41.8%) were diagnosed as having DCI as a result of an unsafe dive profile or arterial gas embolism secondary to pulmonary barotrauma as a result of an uncontrolled ascent or lung disease. Of the 266, 185 (69.5%) had no shunt. The remaining 81 (30.5%) had a shunt, which in 80 was a small atrial or small pulmonary shunt. In one there was a large shunt at rest, but the onset of neurological symptoms was during ascent from a dive to 15 metres' depth and a CT scan of her chest showed pulmonary bullae.

Of the 370 who had shunt-related DCI, 346 (93.5%) were considered to have an atrial shunt and 24 (6.5%) had features of a pulmonary shunt. One of those with a significant pulmonary shunt returned to diving after coil occlusion of a single large pulmonary arteriovenous malformation. Two-hundred-and-seven (59.9%) of the 346 with an atrial shunt (or 32.5% of divers attending the clinic) chose to have transcatheter closure of their atrial defect, but in seven cases the diameter of the defect was not measured.

In the 200 divers (140 men and 60 women) who had balloon sizing of their atrial defect, 11 (5.5%) had a secundum ASD and 189 (94.5%) had a PFO. On one or more occasions, 150 of the 200 divers (75%) had suffered neurological, 12 (6%) cardiorespiratory and 99 (49.5%) cutaneous DCI. Some divers had more than one manifestation of DCI at a time. Others had different manifestations on separate occasions. On one or more occasion, 63 divers (31.5%) had post-dive migraine with aura or aura without headache. According to the criteria of the International Classification of Headache, 15 divers (7.5%) had migraine without aura and 104 (52%) had migraine with aura unconnected with diving.[16] Three divers had a cryptogenic stroke, confirmed on computerised tomography brain scans at ages 18, 37 and 58 years. Their strokes were unrelated to diving and none of the three had migraine.

Figure 1 shows the distributions of diameters of atrial defects (PFO or secundum ASD) in the divers with DCI and the distribution of PFO diameters in the general population. The overall prevalence of PFO in the general population was 27.3%. Of those in the general population with a PFO, the median PFO diameter was 5 mm and mean was 4.9 (SD 2.6) mm. In the divers who had suffered shunt-related DCI the median atrial defect diameter was 10 mm and the mean was 9.9 (SD 3.6) mm. The difference between the two populations is highly significant ($P < 0.0001$). Of divers with shunt-related DCI, 101 (50.5%) had an atrial defect that was10 mm diameter or larger, but only 1.3% of the general population had a PFO that was 10 mm diameter or larger.

Discussion

A criticism of this study is that the PFO diameters in the two groups (divers and controls) were measured using different techniques, but there is currently no other ethically justifiable method of measuring PFO diameter in normal controls. In this analysis we wished to compare PFO and ASD diameters obtained during closure procedures in divers who had had shunt-mediated DCI with the only available information we have on PFO diameter in normal hearts – namely the post-mortem data from Hagen et al.[1] There are no data for the general population comparable to ours in divers. Given the large magnitude of the differences in PFO diameters between the groups, any small difference caused by differences in measurement techniques would not have significantly affected the conclusions. The post-mortem study showed that the PFO rates in males and females were not different (26.8% and 27.6% respectively overall), and did not differ in each of the 10 decade subgroups. Neither did PFO size differ between males and females.

The seven divers who did not have balloon sizing of their defects did not differ clinically from the 200 that did have balloon sizing and their contrast echocardiogram appearances were comparable to those who had balloon sizing. Their PFOs were considered to be similar to those who had balloon sizing, so omission of their defect diameters is unlikely to have had a significant effect on the findings in this study.

Many of the divers with a significant shunt and who had no closure procedure have returned to diving using breathing gases and dive profiles that are unlikely to liberate venous bubbles on decompression. The decision to undergo closure was not influenced by whether the shunt was graded on contrast echocardiography as large or medium at rest or large with a Valsalva manoeuvre, so PFO diameter results of those who underwent closure are likely to be representative of all 346 divers who had shunt-related DCI with an atrial shunt.

It has already been shown, using contrast echocardiography, that a right-to-left shunt is found in a significantly greater proportion of divers with cutaneous DCI (77%) and with neurological DCI (58%) than in controls (27.6%, $P < 0.001$).[10,11] It has been concluded that a PFO increases the risk of DCI by a factor of approximately 2.5.[17] However, this risk assessment does not take into account the fact that the excess of shunts in affected divers is comprised of large shunts. Our data suggest that the risk of DCI is greatest in divers with the largest right-to-left shunts, as determined by PFO diameter. Comparably sized PFOs are found in a very small proportion of the general population. When considering pathogenesis of paradoxical embolism through a septal defect, it should be remembered that the risk is probably related to defect area rather than diameter. A doubling of a diameter will increase the area four-fold and may have a similar exponential effect on risk.

These observations may provide insight into the relationship of migraine with aura and DCI.[7] Contrast echocardiography in 432 patients with severe migraine with aura in the MIST (Migraine Intervention with STARFlex Technology) Trial, showed that 260 (60.2%) had a right-to-left shunt.[12] The large number of right-to-left shunts compared with population studies was the result of an excess of large shunts, which were usually across a large PFO. There was no excess of small shunts. In keeping with other studies showing a strong association between migraine with aura and large right-to-left shunts, 52% of our divers had migraine with aura, a rate approximately 12–15 times higher than in the general population.[12-14,18] As in other studies, there was no increase in prevalence of migraine without aura. These data support the evidence that the link between DCI and migraine with aura is shunt size, which is a reflection of PFO diameter.[13,14]

These observations may also provide insight into the relationship of stroke and DCI. Three divers in the study (1.5%) had a history of cryptogenic stroke at relatively young ages. It is difficult to draw conclusions from observations in just a few individuals, but this is a high rate of premature stroke. We have previously reported another man who had a cryptogenic stroke when straining at stool at age 23 and who subsequently had two episodes of shunt-related DCI.[19] These anecdotal observations suggest that if a PFO is large enough to permit paradoxical gas embolism then in some cases it may be large enough to also permit paradoxical thromboembolism.

Others have reported, using transoesophageal echocardiography, that the magnitude of the right-to-left shunt across a PFO, shunting at rest and opening dimension of a PFO are all greater in patients who have had an ischaemic arterial event considered to be the result of paradoxical embolism than in patients with an ischaemic event without features of paradoxical embolism or in patients without an ischaemic event.[20–22] Because the excess right-to-left shunts in patients with migraine with aura are mainly large PFOs and to a lesser extent pulmonary arteriovenous shunts,[12] these data support the hypothesis that the increased incidence of stroke in patients with migraine compared with the general population is because patients with migraine have a high prevalence of large atrial shunts and hence an increased risk of paradoxical embolism.[8]

Conclusions

The risk of a diver suffering shunt-related DCI is related to the size of the right-to-left shunt. When shunting is across an atrial defect, the dimensions of the defect are important rather than just the presence of the defect.

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Contributions

PTW had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors were involved in clinical care of patients, conception of the study and writing the paper.

Conflict of interest

KPW has acted as a proctor for AGA Medical. No other author has any conflicts of interest.

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An audit of persistent foramen ovale closure in 105 divers

Alex Pearman, Luc Bugeja, Martin Nelson, Gergely V Szantho and Mark S Turner

Abstract

(Pearman A, Bugeja L, Nelson M, Szantho GV, Turner MS. An audit of persistent foramen ovale closure in 105 divers. *Diving and Hyperbaric Medicine*. 2015 June;45(2):94-97.)

Introduction: Right-to-left shunt across a persistent foramen ovale (PFO) has been associated with cutaneous, neurological and vestibular decompression illness (DCI). Percutaneous closure of a PFO has been used to reduce the risk of DCI. There are no randomised controlled trial data to support PFO closure for the prevention of decompression illness (DCI), so the need for audit data on the safety and efficacy of this technique has been recognised by the National Institute of Health and Clinical Excellence in the UK.

Method: Retrospective audit of all transcatheter PFO closures to reduce the risk of DCI performed by a single cardiologist with an interest in diving medicine.

Results: A total of 105 eligible divers undergoing 107 procedures was identified. There was a low rate of procedural complications; a rate lower than a recent randomised trial of PFO closure for stroke. Atrial fibrillation required treatment in two patients. One patient with a previously repaired mitral valve had a stroke that was thought to be unrelated to the PFO closure. Sixteen divers had minor post-procedure symptoms not requiring any treatment. Two divers required a second procedure because of residual shunt; both subsequently returned to unrestricted diving. Eighty-one of 95 divers in whom follow-up bubble contrast echocardiography was available returned to unrestricted diving.

Conclusions: The PFO closure procedure appeared to be safe and was associated with the majority of divers being able to successfully return to unrestricted diving.

Key words

Patent foramen ovale (PFO); persistent foramen ovale; echocardiography; right-to-left shunt; transcatheter closure; clinical audit

Introduction

The association between right-to-left shunts across a persistent foramen ovale (PFO), and some types of decompression illness (DCI) was first described in 1989.[1] Subsequent studies have added further supportive evidence of this link, such that closing a PFO to prevent DCI has become widely accepted in the diving community.[2–6] Whilst a randomised controlled trial has not been undertaken, the observational evidence on transcatheter closure of PFO is highly supportive of the technique and the proposed mechanism is biologically plausible. As there appears to be excess risk of diving without additional restriction of nitrogen load for those with a large right-to-left shunt, one would question whether a randomized trial of diving with or without PFO closure is ethical.

PFO closure appears safe; however, potentially important complications can occur.[7] The National Institute for Health and Clinical Excellence (NICE) has reported on PFO closure for preventing paradoxical embolus in divers and one of their recommendations is that audits should be undertaken, hence this report.[8] An issue with PFO closure for divers is the potential for residual leaks across the septum. We have reported previously that residual right-to-left shunts can be seen on bubble contrast echocardiography, and these are of particular relevance to divers.[9] In order to follow the recommendations of NICE and to help to inform divers considering PFO closure to prevent DCI, we audited the practice of one cardiologist (MST) at the Bristol Heart Institute, Spire Hospital, Bristol and the Manor Hospital, Oxford.

The aims of the study were to confirm the safety of our management of PFOs among divers and to satisfy the recommendation of the NICE guidelines (Table 1). Four specific objectives were assessed:

- To demonstrate the efficacy of PFO closure;
- To identify complications that have arisen as a result of the procedure;
- To identify the likelihood of being able to return to diving;
- To better inform divers who have a PFO and are considering a closure procedure.

Table 1
Audit standards used in this study

Criteria	Source	Target
Complications		
Serious procedural and device	RESPECT[10]	< 4%
General procedural and device	NICE guidelines[8]	<10%
Successful implantation	NICE guidelines	100%
Reduction in shunt at follow up (minor or no shunt)	Previous studies[9]	>80%
Unrestricted return to diving	NICE guidelines	>80%

Methods

This audit was approved and registered by the University Hospitals Bristol NHS Foundation Trust Audit Department (audit number 3820). The audit standards that were used are listed in Table 1. A retrospective audit of the Bristol Heart Institute cardiology databases was used to identify all patients who had had percutaneous PFO closure between 28 February 2005 and 10 May 2014. As this showed PFO closures for all indications, the patients presenting with DCI had to be identified.

The audit also included patients who were found to have a large right-to-left shunt without DCI but who were offered closure owing to their desire to dive in an unrestricted way. Patients who had the procedure undertaken privately were also included. Two patients were excluded as they had their original procedures performed at different centres and were referred to the Bristol Heart Institute for a second opinion. Other sources of information used included the patients' clinical notes, a congenital heart disease database, a private patient database and the PACS imaging database. The data were transferred to an Excel spreadsheet for analysis.

As the evidence in the NICE guidelines on the expected rates of complications is limited, the decision was made to benchmark against the RESPECT study,[7] which looked at PFO closure after cryptogenic stroke in 980 patients and included 460 PFO closure procedures. It is recognized that this represents a population who have had stroke or transient ischaemic attack rather than DCI; however, the RESPECT study patients were screened for vascular disease or other embolic causes for stroke. Thus, the RESPECT study population did not have overt vascular disease or atrial fibrillation, so may not be so different to a population of divers as might first be considered and represents the largest group of patients described in the medical literature who have undergone PFO closure and the device used was the most prevalent in our patients.

Follow-up bubble contrast echocardiography was usually performed at six months after the procedure. The size of shunt is defined as the largest number of bubbles seen in a single still frame of the bubble contrast echo imaging. Shunts less than 15 bubbles in a single frame have not been associated with DCI, so are considered safe for unrestricted diving. Those with residual leaks of greater than 15 bubbles at six months had a repeat bubble contrast echo usually at one year after the procedure. A negative bubble contrast echo also excludes a pulmonary shunt, which could theoretically be unmasked after closure of a PFO-related shunt.

Results

A group of 105 divers was identified, two of whom had two procedures. One patient who did not have a device implanted because the PFO was too small to justify occlusion was excluded from the analysis, leaving 106 procedures in 104 divers. Sixty-seven were male and 37 female, with a mean age at procedure of 40.8 (range 16–63) years. The balloon size showed a mean diameter of 6.95 mm. The average balloon size in the 16 patients whose pre-procedural shunt was not reported is 6.21 mm, confirming that these patients also had a reasonably sized PFO. The median procedure time was 27 (range 17–130) minutes and median screening time 5 (range 2–17) minutes. All patients had either a transoesophageal echo or intracardiac echocardiographic guidance.

Table 2
Symptoms and signs of decompression illness in order of frequency of presentation in 105 divers presenting for persistant foramen ovale closure procedures

Presenting complaint	Number of divers
Cutaneous	33
Neurological	23
Inner ear	15
Multiple complaints	8
Joint pain only	2
No DCI	16
Not reported	8

DECOMPRESSION ILLNESS

Cutaneous DCI was the most common presentation of DCI followed by neurological and inner-ear symptoms and signs. Presentations are summarised in Table 2. The 16 patients who did not present with DCI wished to continue diving after having been recognised as having a PFO.

PROCEDURES AND COMPLICATIONS

The devices implanted were 89 Amplatzer™ (StJude Medical, USA), seven Gore Septal Occluder™ (Gore Medical, USA), six Premere™ (St Jude Medical, USA), three Helex™ (Gore Medical, USA) and one Starflex™ (NMT Medical, USA). All 106 procedures were considered to have been successful at the time. Major complications occurred in three patients (< 3%), all of which were also reported in the RESPECT study, and three (< 3%) displayed minor complications during the procedure. Sixteen other patients reported a range of minor symptoms. These were not discussed in the RESPECT study nor in the NICE guidelines, and most research does not classify these symptoms as complications. Table 3 lists all the complications that arose.

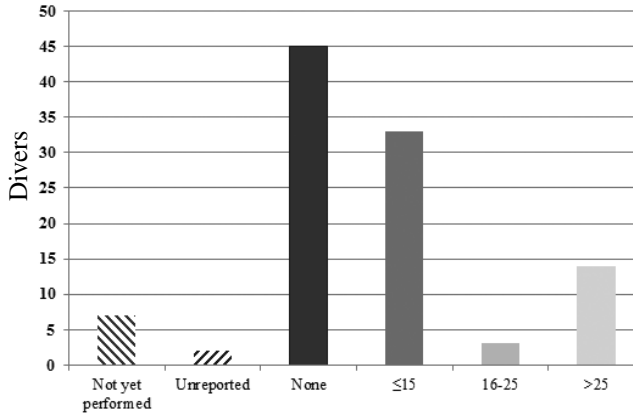
RESIDUAL SHUNT

Post-procedural shunt is displayed in Figure 1. Ninety-eight bubble contrast echocardiography follow-up results were available at the time of writing. No shunt was found after 45 procedures and mild shunt (< 15 bubbles) after

Table 3
Complications documented in individuals who underwent transcutaneous closure of an atrial septal defect

Complication	Occurrence	Number of patients	Treatment
Major			
Atrial fibrillation	> 6 month follow up	1	Ablation
Atrial flutter	6 weeks post procedure	1	Cardioversion
Stroke	> 6 month follow up	1	N/A
Minor			
Transient inferior ST segment elevation	Procedure	1	None
Retroperitoneal haematoma	Procedure	1	None
Vagal symptoms	Procedure	1	Atropine
Other symptoms			
Palpitations	≤ 6 months post procedure	10	None
Chest pain	6 week follow up	3	None
Chest pain and palpitations	6 week follow up	2	None
Nausea and dizziness	6 week follow up	1	None

Figure 1
Post-procedural shunt present at 6 month follow up on bubble contrast echocardiography



33 procedures. Thus 78/98 (80%) were considered fit for unrestricted diving. All patients who received an occluder had reduced shunts compared to pre-procedure but the shunt reduction standard we applied was rigorous.

RETURN TO DIVING

Eighty-one of the 98 divers followed up at the time of writing were cleared to resume unrestricted diving, as the additional three patients had shunts between 15 and 25 bubbles, present only on vigorous Valsalva release. A further 14 were given restrictions on their diving depths and were offered further follow-ups to monitor whether the endothelialisation had progressed and that the shunt had regressed. Two patients who were initially advised to restrict their diving had a repeat procedure which then allowed them to recommence unrestricted diving. An Amplatzer Vascular Plug 4™ (St Jude Medical, USA) was used to occlude the residual shunt in both cases. All divers with residual shunts were advised to minimise lifting and straining for an hour after surfacing, as well as being advised to manage their inert gas load.

MIGRAINE

Thirty-eight of 78 patients, in whom it was recorded, suffered pre-procedural migraine. At follow up, only seven of 45 patients, in whom this was documented, had suffered post-procedural migraine.

Discussion

We have confirmed that closure of an atrial septal defect in a group of divers is safe and effective, achieving our audit standards, and allowing a high proportion of divers to return to diving. The one most serious adverse event (stroke) appears to have been due to a pre-existing mitral valve repair, with implanted prosthetic valve ring and other material in the heart (which would have excluded the patient from the RESPECT trial against which we have benchmarked), or atrial fibrillation. The mitral valve repair had been undertaken using a minimally invasive surgical technique in another hospital (the PFO was not identified at the time). Following the stroke, the patient was assessed in a different hospital independently as he lived in another part of the UK. It was concluded that there was no complication of the PFO device closure itself and we had previously assessed the PFO as being completely closed. Whilst it is possible that the PFO procedure could have increased the chance of atrial fibrillation (AF), previous mitral valve surgery is a potent cause of this arrhythmia.

One episode of DCI occurred in the one diver who had problems with atrial fibrillation, and required a pulmonary vein isolation/AF ablation, which included two punctures in the atrial septum. The recurrent DCI occurred two months after the ablation and after the data collection for this study was completed. The onset of symptoms was soon after

surfacing. He had previously had normal lung function tests and a normal thoracic CT scan to exclude bullae, but it remains possible that he suffered pulmonary barotrauma or that the defects created in the atrial septum for the ablation had not closed at the time of the recurrent DCI. The diver had not followed our usual protocol of having repeat bubble contrast echocardiography after puncture of the atrial septum.

The majority of procedures over the time period audited used the Amplatzer device, primarily because our previous study showed a better closure rate with this device, rather than the Gore Helex device. However, recently the Gore Septal Occluder has been used for some patients as our anecdotal experience is that this device has a good occlusion rate as well.

Whilst some patients have residual shunt at 6 months after the procedure, progressive closure of the PFO is frequently observed.[10] In this audit, a few patients who still had a residual shunt at 6 months returned to unrestricted diving after subsequent bubble contrast echo or repeat procedures. Divers should be aware that, despite complete closure of a PFO, it is still possible to suffer DCI that is not PFO-related. One diver with a residual bubble leak of > 25 (that he was aware of) had an episode of itching suggestive of cutaneous DCI during a deep trimix dive, but treated it himself with an enriched oxygen mixture and so no formal diagnosis was made. He has not had any further episodes and his residual leak has since diminished to around 25 bubbles.

The observed reduction in the recorded prevalence of migraine after PFO closure is in keeping with previous observational studies.[11]

The patients in this audit were highly selected. A careful history was taken and any patients with early onset of DCI were assessed for causes of pulmonary barotrauma and, during the time of this audit, several patients were identified as having bullae on CT scans and did not progress to PFO closure. Only patients with a bubble contrast echo suggesting a moderate or large shunt were offered PFO closure.

Conclusions

In this population of divers, treated with PFO closure after careful assessment by a cardiologist with an interest in diving medicine, PFO closure was associated with a low complication rate and a high rate of return to unrestricted diving.

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Conflicts of interest

MT acts as a consultant and proctor for St Jude Medical, Medtronic and Edwards Lifesciences, as a consultant and lecturer for Gore Medical and performs PFO closures on private patients.

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Review articles

The role of persistent foramen ovale and other shunts in decompression illness

Peter T Wilmshurst

Abstract

(Wilmshurst PT. The role of persistent foramen ovale and other shunts in decompression illness. *Diving and Hyperbaric Medicine*. 2015 June:45(2);98-104.)

A persistent foramen ovale (PFO) and other types of right-to-left shunts are associated with neurological, cutaneous and cardiovascular decompression illness (DCI). A right-to-left shunt is particularly likely to be implicated in causation when these types of DCI occur after dives that are not provocative. It is believed that venous nitrogen bubbles that form after decompression pass through the shunt to circumvent the lung filter and invade systemic tissues supersaturated with nitrogen (or other inert gas) and as a result there is peripheral amplification of bubble emboli in those tissues. Approximately a quarter of the population have a PFO, but only a small proportion of the population with the largest right-to-left shunts are at high risk of shunt-mediated DCI. The increased risk of DCI in people with migraine with aura is because migraine with aura is also associated with right-to-left shunts and this increased risk of DCI appears to be confined to those with a large PFO or other large shunt. Various ultrasound techniques can be used to detect and assess the size of right-to-left shunts by imaging the appearance of bubble contrast in the systemic circulation after intravenous injection. In divers with a history of shunt-mediated DCI, methods to reduce the risk of recurrence include cessation of diving, modification of future dives to prevent venous bubble liberation and transcatheter closure of a PFO.

Key words

Right-to-left shunt; persistent foramen ovale (PFO); arterial gas embolism; decompression illness; bubbles; percutaneous closure; review article

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Introduction

Paradoxical thromboembolism across a persistent foramen ovale (PFO) as a cause of stroke was first postulated in 1877,[1] but it was believed to be a rare event until 1988 when two case control studies showed that this mechanism may be numerically important, particularly in young stroke patients.[2,3] It was around that time that the role of paradoxical gas (nitrogen) embolism as a cause of decompression illness (DCI) in divers was first proposed.[4]

Until then, the prevailing hypothesis was that what we now call decompression illness in divers had two distinct mechanisms. One mechanism is arterial gas embolism (AGE), which is caused by pulmonary barotrauma on ascent, so that alveolar gas invades the pulmonary veins and is carried to the systemic circulation. The onset of symptoms should be during or immediately after ascent and should affect tissues with the greatest blood flow, particularly the brain. The second mechanism is decompression sickness (DCS) resulting from excessive amounts of bubble liberation from solution in solid tissues and venous blood.

Some venous bubbles are liberated after many dives that are not provocative, but as the bubbles pass through alveolar capillaries, the gas diffuses out of the bubbles into the alveoli down the concentration gradient. Therefore, venous bubbles liberated after dives generally should not reach the systemic circulation, unless massive amounts of bubbles are liberated and overwhelm the alveolar filter. In theory, there should be a delay in liberation of bubbles and hence of onset of DCS after surfacing unless the dive profile is extremely provocative, when there can be a very rapid onset, similar to that in AGE secondary to pulmonary barotrauma. According to this hypothesis cutaneous manifestations and joint pain could not be the result of gas embolism.

A difficulty with this hypothesis was that many divers who have had DCS with some latency in onset of symptoms and, therefore, not the result of pulmonary barotrauma of ascent, are certain that their dive profiles were conservative. The later advent of decompression computers confirmed that the majority of episodes of DCS follow a dive with a profile generally considered to be conservative.

The possibility that DCS in divers might result from paradoxical gas embolism was proposed in 1986: A diver who had cerebral and spinal DCS after an air dive with a profile that had a risk of causing venous gas nucleation but was of a low risk of causing DCS was discovered to have an atrial septal defect (ASD).[4] It was proposed that even when there is relatively little venous bubble formation during decompression, a right-to-left shunt may allow paradoxical gas embolism. In that way the venous bubbles evade the pulmonary filter and pass into the systemic circulation where bubble emboli invade critical tissues and cause DCI.[4] This

mechanism requires that the gas emboli pass into tissues that are supersaturated with nitrogen, so that the embolic bubbles are amplified as nitrogen passes out of the supersaturated tissue into the bubble.[5] This amplification of embolic bubbles is critical to the postulated pathophysiological mechanism of manifestations of DCI.

Echocardiography with bubble contrast is a common procedure in hospitals when testing for a right-to-left shunt, but patients do not suffer symptoms and signs of DCS, even when large numbers of bubbles cross the communication. That is because, in that situation, their tissues are not supersaturated with inert gas. During contrast echocardiography, the injected air bubble emboli have a higher partial pressure of nitrogen than the tissues they invade, so the nitrogen rapidly diffuses out of the bubble down the concentration gradient.[5]

If a diver with a large right-to-left shunt performs a dive such that many bubbles are liberated and, as a result, many small bubbles cross the communication, the bubbles will be distributed widely according to tissue blood flow. In that situation, the manifestations of DCI will be determined largely by whether the tissues invaded by bubble emboli are still supersaturated and hence able to amplify embolic bubbles. This may explain the fact that shunt-mediated DCI can manifest both in tissues with high blood flow and hence high emboli load, such as the brain, but also in tissues with low blood flow, such as skin and subcutaneous tissues.

Neurological decompression illness

In 1989, Moon and colleagues reported that 11 of 18 patients with a history of serious neurological DCS had a right-to-left shunt consistent with the presence of a PFO on transthoracic contrast echocardiography (TTE) compared with a shunt in only nine of 176 (5%) historic controls (reported by different investigators using a different technique) ($P = 0.0001$).[6] No shunt was detected in 12 divers with mild DCS, defined as joint pain or sensory symptoms only.

The same year, a blind case controlled study compared the findings on contrast echocardiography in 61 divers with DCS divided into pre-defined sub-groups with 63 control divers.[7] Shunts were detected in 15 of 63 controls compared with 19 of 29 divers with neurological symptoms of DCI with onset within 30 minutes of surfacing ($P < 0.01$). Of the remaining 10 divers in this sub-group, four had lung disease. When latency of neurological symptoms exceeded 30 minutes, four of 24 had a shunt. Shunts were present in one of six with joint pain but in three of five with cutaneous DCS (three of those with skin bends also had neurological symptoms). Shunts were present in significantly more divers (16 out of 25) who had DCS after dives that were not provocative than in divers who had symptoms after provocative dives (nine of 36). Provocative dive profiles were significantly more often associated with late onset neurological DCS (22 of 26, $P < 0.001$) and joint DCS (seven of eight, $P < 0.01$) than with neurological DCS with latency less than 30 minutes (nine of 31). Spinal manifestations appeared to be related to having a shunt.

The findings in the study were extended by increasing the number of affected divers to 97 and control divers to 109.[8] Shunts were present in 26 of 109 (24%) of controls, but in significantly more divers with neurological DCS with latency within 30 minutes (33 of 50), cutaneous DCS (12 of 14) and cardiorespiratory DCS (seven of 12). The prevalence of shunts in divers with neurological DCS with latency greater than 30 minutes (nine of 35) and joint pain (three of 20) did not differ significantly from the control group.

Risk factors for DCS were present in 29 of 38 dives (not divers) preceding neurological DCS with latency more than 30 minutes and 20 of 23 of dives followed by musculoskeletal DCS. The proportions of provocative dives preceding neurological manifestations with onset within 30 minutes (21 of 58), cutaneous rashes (seven of 29) and cardiovascular manifestations (four of 12) were significantly fewer.

At the time, these findings were controversial. So a replication study was performed under the supervision of the Medical Research Council and the MRC Decompression Sickness Panel, which supported the reported findings.[9] Since then, many studies in divers with DCI have provided more information about the types of DCI associated with shunts and the type and size of shunts responsible.

A blind case control study to determine the relationship between different manifestations of neurological DCI and its causes in 100 consecutive divers with 115 episodes of neurological DCI and 123 historical control divers found that the size of right-to-left shunts was critical to the development of DCI.[10] A large shunt was seen after a single injection of bubble contrast at rest in 41 of 100 (41%) cases compared with six of 123 (4.9%) controls ($P < 0.001$). A Valsalva manoeuvre increased the rates of large shunts detected to 51% of cases and 7.3% of controls ($P < 0.001$). Shunts graded large or medium in size were present in 52% of affected divers and 12.2% of controls ($P < 0.001$). Spinal decompression illness occurred in 26 of 52 affected divers with large or medium size shunts and in 12 of 48 without a significant shunt ($P < 0.02$). Five of the 52 large or medium shunts were pulmonary, not intracardiac shunts and three of these five divers had spinal DCI.

The distribution of latencies of DCI symptoms and signs differed markedly between the 52 divers with a large or medium shunt (63 episodes with median latency 20 minutes, of which 10 episodes had a latency of five minutes or less), and the 30 divers who had either lung disease (on chest X-ray and/or pulmonary flow-volume loops) or had performed a provocative dive (31 episodes, of which 20 had a latency

of 5 minutes or less). In the 18 divers who had 21 episodes of neurological DCI after non-provocative dives but had no significant shunt or lung disease on the tests performed, a short latency was associated with a significantly higher prevalence of smoking than in other groups of divers.

Since then, other studies have consistently confirmed that a right-to-left shunt and, in particular, a large shunt is strongly associated with cerebral and cochleovestibular DCI.[11,12] A transcranial Doppler study comparing 101 divers with DCI and 101 controls found that "*major shunts*" were present in 11.9% of controls, but in significantly more divers with cochleovestibular (24 of 34), cerebral (13 of 21) and spinal bends (10 of 31). Only two of 15 with joint pains had major shunts.[12]

Thromboembolic events frequently affect the brain and rarely affect the spinal cord. This predilection for affecting the brain is attributed to the considerably greater blood flow to the brain compared with the spinal cord. But the frequencies with which neurological DCI affects the spinal cord and brain are much more comparable. So, the possibility that spinal DCI might result from an embolic process was controversial. However, a number studies have found a significant relationship between spinal DCI and large right-to-left shunts.[7,10,12–14] In a study of 49 divers with spinal DCS (17 cervical and 32 thoraco-lumbar) and 49 controls, the prevalence of right-to left shunts was reported to be significantly greater in divers with spinal DCS than controls, and particularly so for thoraco-lumbar spinal DCS.[14]

However a study using transoesophageal echocardiography (TOE) with bubble contrast reported that the prevalence of PFO in divers with neurological DCS (22 of 37) did not differ from in control divers (13 of 36).[11] In a sub-group analysis, 20 divers with a history of "*cerebral DCS (cerebral, cerebellar, high-spinal, vestibular or cochlear symptoms)*" were compared to 20 controls and 17 divers with "*spinal DCS*" were compared to 16 controls. The level that differentiated spinal DCS from high spinal and the number of high spinal cases that were in the "*cerebral DCS*" group are not stated. One quarter of the controls for the cerebral DCS group but half of the controls for the spinal DCS group had a PFO. The authors stated that "*in the sub-group of divers with cerebral DCS, the prevalence of PFO (16 of 20) was significantly higher than in control divers (five of 20). In contrast, for the subgroup of divers with spinal DCS, PFO prevalence (six of 17) was comparable to the prevalence in their control group (eight of 16)".*[11]

At first sight it may seem surprising that spinal injury is a common manifestation of DCI that appears to be the result of paradoxical gas embolism across a right-to-left shunt. An explanation is provided by experiments performed on pigs which were compressed to 507 kPa for 30 minutes breathing air and then rapidly decompressed.[15] Immediately after decompression, there were few bubbles detected in venous blood, but the numbers increased and peaked between 5 and 30 minutes after decompression. Arterial bubbles were detected in all six pigs that were found to have a PFO but only two of eight pigs without a PFO. In both groups the peak arterial bubble count was detected between 15 and 30 minutes after surfacing, and only one pig had arterial bubbles detected less than seven minutes after surfacing. These data in pigs may explain the observation in divers that the incidence of spinal DCI is frequent and also that the median latency of onset of cerebral DCI is 3 minutes compared with median latency of 10 minutes for spinal DCI.[16]

Most bubbles crossing a shunt into the systemic circulation will pass to the tissues with the greatest blood flow, such as the brain, but because of the brain's rapid nitrogen elimination half-life, there are few bubbles present in venous blood and even fewer in arterial blood during the brief period after a dive when the brain is supersaturated with dissolved nitrogen and thus able to amplify embolic bubbles. Any bubbles that do enter the brain at that early stage will be amplified because the brain is supersaturated and cause cerebral DCI. Later, larger numbers of venous bubbles are liberated and larger numbers can cross a PFO or other shunt. At that time, large numbers of bubbles invade the brain, but it is no longer supersaturated, so the gas passes out of the bubble down the concentration gradient and dissolves. Far fewer bubble emboli enter the spinal cord, but those that do invade the spinal cord arrive at a time when, because of its slower nitrogen elimination half-life, it is still supersaturated and able to amplify bubble emboli. Dive profiles that result in even later peaks in venous bubble liberation and hence later paradoxical embolism in divers with a right-to-left shunt are likely to account for non-neurological shunt-mediated DCI.

Cutaneous decompression illness

The unexpected observation in a small number of early reports,[7,8] that cutaneous decompression illness occurred in individuals with a right-to-left shunt has been confirmed in a larger study.[17] This case control study compared the prevalence and sizes of right-to-left shunts determined by contrast echocardiography performed blind to history in 61 divers (including one caisson worker), who had a history of cutaneous DCI and 123 historical control divers. Twenty-nine divers had had a single skin bend, and 32 had had multiple episodes. It was found that 47 of the 61 cases had a shunt compared with 34 of 123 (27.6%) control divers ($P < 0.001$).[17] The size of the shunts in those with cutaneous lesions was significantly larger than in the controls. Of 61 cases with cutaneous DCI, 30 had a large shunt at rest compared with six of 123 (4.9%) of the controls ($P < 0.001$). Five of the 47 shunts in those with cutaneous DCI were pulmonary. During transcatheter closure procedures, 17 of these divers had a significant inter-atrial shunt; the mean diameter of the PFO being 10.9 mm. Cutaneous DCI occurred after dives that were provocative in those without shunts and after shallower dives that were not provocative

in those with shunts. These findings strongly support the hypothesis that cutaneous DCI is usually due to paradoxical gas embolism with peripheral amplification of bubble emboli in skin and subcutaneous fat that is supersaturated with nitrogen. When cutaneous decompression illness occurs in divers who do not have a shunt it nearly always occurs after deep and provocative dives. It is possible that in those cases the mechanisms include the lung filter being overwhelmed by massive amounts of venous bubbles or of autochthonous bubble formation (i.e., bubble nucleation in the skin rather than bubble embolism).[15,17]

In this study some divers with significant right-to-left shunts had pain in a shoulder associated with an overlying rash.[17] We have observed this in a number of other cases since then. This appears to be the exception to the rule that joint DCI is not associated with a shunt.

Sub-atmospheric decompression illness

Decompression illness can also occur during sub-atmospheric decompression in high altitude aviators and in astronauts on space walks. Human terrestrial hypobaric chamber experiments indicate that gas nucleation occurs in body tissues with all decompression protocols studied.[18] Monitoring the pulmonary artery with Doppler ultrasound reveals that heavy burdens of circulating gaseous emboli are present in between 6% and 39% of those subjected to subatmospheric decompression.[18] In these hypobaric chamber studies serious DCI has been encountered, including massive cutaneous 'marbling' (characteristic of cutaneous DCI), severe cerebral dysfunction and circulatory shock.[19] The National Aeronautics and Space Administration tested four individuals who had serious DCI resulting from space-walk simulations, in three of whom contrast TTE detected a PFO at rest.[18]

The link between decompression illness and migraine

It has been recognised for 70 years that individuals who have migraine with aura have an increased risk of neurological DCI and often experience migraine symptoms, particularly migraine visual aura, during sub-atmospheric decompression.[20] The relationship between shunts and migraine with aura were reported more recently.[21,22] Divers who have migraine with aura (typically visual aura but sometimes with hemiplegia, hemisensory abnormalities, dysphasia or cognitive features) also often experience an identical migraine aura with or without headache following dives.[23] This nearly always occurs in divers who have a clinically significant right-to-left shunt (usually a large PFO but sometimes a pulmonary shunt) and in them it occurs after dives with profiles that are expected to liberate venous bubbles.[23] In some cases a similar migraine aura is experienced after right-to-left shunting of bubbles during contrast echocardiography.[23] Therefore, it appears that the association between a history of migraine with aura and the increased risk of DCI is because migraine with aura is an indicator of an increased prevalence of large right-to-left shunts.

In a study of 400 divers who had contrast echocardiography following DCI, there was a relationship between the size of right-to-left shunts and prevalence of migraine with aura.[24] A large shunt at rest was present in 170 (42.5%). A further 33 (8.25%) had a large shunt with a Valsalva manoeuvre. Twelve (3%) had a medium shunt, 24 (6%) had a small shunt and 161 (40.25%) had no shunt. Small shunts are not considered to have clinical significance and, in those divers as well as in those with no shunt, DCI was thought usually to be the result of a provocative dive profile or pulmonary barotrauma as a result of lung disease. In those with no shunt or only a small shunt, the lifetime prevalence of migraine with aura was similar to that in the general population (11%). Ninety of the 170 (53%) with large shunts at rest had migraine with aura. In those with large shunts with a Valsalva manoeuvre or a medium shunt, the lifetime prevalence of migraine with aura was intermediate at 21% and 25% respectively.

Detection and estimation of the size of a shunt

The amount of shunting across a PFO is dynamic; it varies from beat to beat of the heart and with respiration. The factors affecting shunting include the dimensions of the PFO, the size of the flap covering the left atrial side of the PFO, the mobility and compliance of the flap, the pressure gradient between the atria and the atrial flow characteristics. The last two are variable.

The main reason for testing a diver to determine whether they have a PFO or other right-to-left shunt is to advise about the risks of future diving. If a shunt is present, the diver should be counselled on the options.[25] These are to stop diving; to modify diving to reduce the chances of venous bubbles forming and to reduce tissue nitrogen loading after dives; or to have transcatheter closure of their PFO. It has been estimated that the presence of a PFO possibly increases the risk of DCI in a diver by 2.5 times, namely to approximately 5/10,000.[26] However, it is clear that risk is related to the size of the shunt rather than the presence or absence of a PFO.[10,17,27]

There are three ultrasound techniques used commonly for detecting a PFO – transcranial Doppler, transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE). Each technique requires confirmation of a right-to-left shunt by detecting contrast in the arterial circulation following intravenous injection. There are proponents of each technique, and this is probably because the techniques are operator dependent. Therefore, operators favour the technique that they judge gives them the best results. One thing is certain, one must use bubble contrast because other types of intravenous contrast give false positive results. In addition, if one wishes to determine

whether venous nitrogen bubbles pass through a shunt into the arterial circulation, it is logical to test that using intravenous bubbles of air, which is predominantly nitrogen.

Transcranial Doppler with bubble contrast is quick, simple and is probably the most sensitive technique for detecting a right-to-left shunt but, because it does not image the heart, it does not differentiate inter-atrial from pulmonary shunts.

Cardiologists often consider TOE to be the 'gold standard' for detecting a PFO but that view is based on poor evidence. About one-quarter of the general population have a PFO and in high-risk groups, such as patients with stroke, the proportion of patients with a PFO should be greater. Yet some studies using TOE have reported prevalence rates of PFO as low as 3.2% in groups who might be expected to have prevalence rates of around 25% or greater.[28] This low prevalence came from a group that reported that TOE with contrast and colour-flow mapping were the "*methods of choice for the detection of atrial level shunts*".[29] One presumes some PFOs must have been missed by their technique. My colleagues and I have closed a large number of sizable PFOs after other cardiologists had reported that their TOE assessment had excluded the presence of a PFO (unpublished obseervations). Clearly TOE often fails to detect a large PFO in some patients and part of the reason may be that performance of Valsalva manoeuvres and sniffing to promote right-to-left shunting are difficult to perform during transoesophageal echocardiography.

In a study describing repeat TOE assessments for PFO in 40 divers with the second assessment six to eight years after the first, shunt size was graded as 0 (none), 1 (less than 20 bubbles in the left heart) or 2 (more than 20 bubbles in the left heart).[30] Twenty divers had no shunt on the first assessment, but on the second assessment three of the 20 had a grade-1 shunt and one had a grade-2 shunt. Of nine that had a grade-1 shunt at the first assessment, three had no shunt and five had a grade-2 shunt at the second assessment. The 11 grade-2 shunts at the first assessment remained grade-2 at the second assessment. The authors reported that during seven years "*significant increases in prevalence and size of PFO were found*" which they attributed to "*de novo opening or increasing permeability of PFOs*". A more plausible explanation is probably that TOE with contrast assessment for the presence and size of a PFO is not reproducible from one test to another. My own unpublished experience using TTE with contrast is that PFO size does not change significantly over 20 years of follow up.

One reason why TOE may miss a large PFO is that performance of a Valsalva manoeuvre and other manoeuvres designed to promote shunting are difficult for patients who are sedated and have a probe in their oesophagus. The use of sedation and passage of the probe also involve risk to the patient and increase the time taken for the procedure and the recovery of the patient.

My preference is for TTE with bubble contrast.[10] It can be performed quickly, without sedation and allows visualisation of the heart including the inter-atrial septum. Also, one can see whether provocative manoeuvres are being performed correctly. In addition, one can also distinguish between atrial and pulmonary shunts.[31] We consistently find that about one-quarter of normal controls have a shunt, but most of their shunts are small.[7,10,24] We consistently find higher rates of shunts and larger-sized shunts in high risk groups, such as divers with DCI and patients with paradoxical thromboembolism and migraine with aura.[7,10,17,24,32] We also detect very high rates of pulmonary shunts in patients with hereditary haemorrhagic telangiectasia, in whom there is a very high prevalence of large pulmonary arteriovenous malformations.[31] Our clinical assessments are consistently confirmed at closure procedures.

As stated, divers with the largest shunts have the greatest risk of DCI, as a result of paradoxical gas embolism, but other critical factors, including a dive profile that results in venous bubble formation and that loads critical tissues with inert gas (nitrogen) at the time of paradoxical embolism, are important.

Transcatheter closure of atrial shunts to prevent recurrence of DCI in divers was first reported in 1996.[33] Initially the procedure was restricted to commercial divers, for whom inability to return to unrestricted diving had serious financial consequences. Increasingly amateur divers who have had shunt-mediated DCI request PFO closure to permit unrestricted diving.[34–36] My colleagues and I have closed atrial shunts in about 300 divers with a history of shunt-mediated DCI. At the time of PFO closure in 200 of these, the median diameter of defects was 10 mm as reported in another paper in this issue.[35] A post-mortem study of 965 individuals showed that although 27.3% of the populations have a PFO, only 1.3% have a PFO that is 10 mm diameter or greater.[37] Extrapolating from this it seems that the 1 to 2% of divers with the largest right-to-left shunts experience half of the episodes of shunt-mediated DCI, which accounts for the majority of episodes of neurological and cutaneous DCI. Therefore, the available evidence suggests that the risk of a diver having shunt-mediated DCI is related to the size of their shunt, which in the case of shunting across a PFO, is largely determined by the diameter of their PFO.

However, it is also clear that shunting across a PFO is increased by some manoeuvres, such as release of a Valsalva manoeuvre. The amount of shunting across a significant PFO varies during the respiratory cycle, being maximal during inspiration. One typically sees a bolus of bubbles crossing to the left atrium during inspiration, with lesser amounts and sometimes no shunting during other phases of respiration.

The appearance with a pulmonary shunt is different, with the amount of shunting affected little at different phases of the respiratory cycle.[31] As a result, a more significant

pulmonary shunt may appear visually less impressive than a smaller atrial shunt, because a moderate degree of pulmonary shunting on every heart beat may result in more bubbles shunting to the arterial circulation than a larger number of bubbles shunting across a PFO on, say, every fourth heart beat that corresponds with peak inspiration or even less frequently if shunting only occurs when the diver releases a strain or Valsalva manoeuvre.

We also need to realise that our assessments are usually performed at rest. Shunting can be affected by the activities of an individual at the time of appearance of bubbles in the right heart. Shunting across a PFO may be increased in some individuals by exertion.[38] Pulmonary shunting is much more likely to increase with exertion.[39,40] As a result, some authorities recommend that the counselling of divers with DCI and their assessment for a shunt should be performed by a combination of a cardiologist and a doctor with knowledge of diving medicine.[41]

Before referring a diver for transcatheter closure of a PFO, I recommend that all five of the following criteria below should be satisfied:

- There is no other potential cause for DCI; therefore, a provocative dive profile and lung disease that could cause gas trapping should be excluded.
- The dive profile was likely to have liberated some venous bubbles.
- The symptoms and latency of symptom onset are consistent with shunt-mediated DCI.
- Investigations demonstrate a significant right-to-left shunt with features consistent with an atrial shunt.
- The patient understands the risks of the procedure including the possibility that transcatheter closure of a PFO is not always successful.

We anticipate successful complete closure of a PFO in more than 90% of cases, but it must be realised that there are considerable differences in the successful rate of PFO closure with different devices.[42] Therefore, the device used should be one with the best record of successful closure when the patient's anatomy is taken into consideration. It is essential that, before return to diving after PFO closure, contrast echocardiography should confirm that there is no significant residual shunt.[25]

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Pathophysiology of inner ear decompression sickness: potential role of the persistent foramen ovale

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Abstract

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Inner ear decompression sickness (inner ear DCS) may occur in isolation ('pure' inner ear DCS), or as part of a multisystem DCS presentation. Symptoms may develop during decompression from deep, mixed-gas dives or after surfacing from recreational air dives. Modelling of inner-ear inert gas kinetics suggests that onset during decompression results from supersaturation of the inner-ear tissue and in-situ bubble formation. This supersaturation may be augmented by inert gas counterdiffusion following helium to nitrogen gas switches, but such switches are unlikely, of themselves, to precipitate inner-ear DCS. Presentations after surfacing from air dives are frequently the 'pure' form of inner ear DCS with short symptom latency following dives to moderate depth, and the vestibular end organ appears more vulnerable than is the cochlea. A large right-to-left shunt (usually a persistent foramen ovale) is found in a disproportionate number of cases, suggesting that shunted venous gas emboli (VGE) cause injury to the inner ear. However, this seems an incomplete explanation for the relationship between inner-ear DCS and right-to-left shunt. The brain must concomitantly be exposed to larger numbers of VGE, yet inner ear DCS frequently occurs in the absence of cerebral symptoms. This may be explained by slower inert gas washout in the inner ear than in the brain. Thus, there is a window after surfacing within which VGE arriving in the inner ear (but not the brain) would grow due to inward diffusion of supersaturated inert gas. A similar difference in gas kinetics may explain the different susceptibilities of cochlear and vestibular tissue within the inner ear itself. The cochlea has greater perfusion and a smaller tissue volume, implying faster inert gas washout. It may be susceptible to injury by incoming arterial bubbles for a shorter time after surfacing than the vestibular organ.

Key words

Diving; decompression illness; inner ear; right-to-left shunt; patent foramen ovale (PFO); persistent foramen ovale; review article

Introduction

Decompression sickness (DCS) is caused by bubble formation from dissolved inert gas during or early after ascent from a compressed gas dive.[1] These bubbles may form if the sum of dissolved gas pressures in a tissue or its microcirculation exceeds ambient pressure (a state referred to as 'supersaturation').[2] Decompressions from pressures as low as 1.35 ATA (3.5 m depth) have resulted in detection of venous gas emboli (VGE).[1] Bubble formation in blood and/or tissues may occur sub-clinically but, depending on factors that are presumed to include their size, number and location, these bubbles may produce mild to serious symptoms reflecting involvement of one to many organ systems.[3] Inner ear involvement in DCS may manifest as vestibular symptoms and signs (vertigo, nausea, vomiting, ataxia) or cochlear symptoms (deafness, tinnitus) or both.[4] Vestibular manifestations are the commoner.[4,5] Inner ear involvement may be part of a multi-system presentation, but inner-ear DCS may also occur as an isolated or 'pure' event.

Early case series of inner-ear DCS associated the injury with deep mixed gas diving, and commonly symptoms arose during decompression (that is, whilst the diver was still ascending).[6] Not surprisingly, inner-ear DCS has been reported to occur during decompression from deep technical dives.[7] Although pure inner-ear DCS was originally associated with mixed gas diving, it has since become clear that this injury may follow typical recreational dives using air though, as will be discussed, these dives are usually in the deeper range of air diving.[5] In these cases, symptoms typically develop within the first hour of surfacing. Several case series have demonstrated an unexpectedly high proportion of inner-ear DCS cases are subsequently demonstrated to have a large persistent (patent) foramen ovale (PFO).[4,8–10] This article does not purport to be a systematic review of all relevant literature and, therefore, we do not describe a search methodology. However, these authors have maintained a strong focus on this particular form of DCS since 2002, and this article refers to those publications that we believe are key to characterising and explaining its presentation and pathophysiology.

Inner-ear DCS during decompression from deep dives

As mentioned above, a subset of inner-ear DCS cases occurs during decompression from deep dives whilst the diver is still immersed and completing the stops prescribed by their decompression algorithm. The onset of vertigo and intractable vomiting during immersion presents obvious hazards and a challenging 'Catch 22'. Thus, if a vertiginous, vomiting diver remains underwater there is a possibility of an

airway accident leading to drowning. However, if the diver omits significant periods of decompression by surfacing not only may the inner-ear DCS symptoms worsen, but the inevitable excessive supersaturation in other tissues may also provoke life-threatening, multi-organ DCS.

Not surprisingly, inner-ear DCS and its avoidance is of significant interest to deep technical divers. Their dives typically involve the use of 'mixed gases' containing helium for its low density and non-narcotic properties, with 'gas switches' to mixes containing less helium, more nitrogen and more oxygen at shallower decompression stops.[11] These switches are made in the belief that they accelerate decompression and to save money on the cost of helium. Prevalent anecdotes arising from commercial and military deep, bounce-diving programmes in the 1970s and 1980s temporally related the onset of inner-ear DCS symptoms to these gas switches in a noticeable proportion of cases.[6] This fostered a widespread belief that inner-ear DCS was, at least in some cases, caused by an inert-gas counterdiffusion phenomenon following such switches.

Counterdiffusion of inert gases as a cause of bubble formation in the skin and inner ear was investigated in the 1970s after pruritus and vestibular symptoms were seen when humans breathing (and surrounded by) an oxygen-helium chamber atmosphere were switched to breathing gas mixes containing nitrogen or neon.[12,13] In explanation, the inward diffusion of helium across the skin (towards blood and tissue containing less dissolved helium) was assumed to be faster than diffusion of nitrogen towards the chamber atmosphere in the opposite direction, and this was assumed to cause inert gas supersaturation and bubble formation in the skin, with consequent development of pruritus. This process was referred to as "*isobaric gas counterdiffusion*" given that it occurred without any change in the chamber pressure itself.[13]

It was much less obvious why bubbles would form in the vestibular organ under the same experimental conditions because, with the possible exception of the middle ear, there was no obvious source of exogenous helium that would exchange with nitrogen in blood across the inner ear to cause inner ear supersaturation in a manner analogous to the skin. Indeed, authors of much of the related work acknowledged that provided a diver was not surrounded by helium, a switch from breathing a helium-based mix to breathing a nitrogen-based mix should produce a transient (and advantageous) under-saturation in body tissues because helium was predicted to diffuse more quickly from tissue to blood than nitrogen would diffuse from blood to tissue.[13]

This issue received a contemporary re-evaluation with the 2003 publication of a kinetic model to predict inert gas partial pressures in three compartments representing the membranous labyrinth, perilymph and endolymph of the inner ear.[7] It is important to appreciate that the membranous labyrinth is the site of the functionally important receptors of the cochlea and vestibular end organs, and it is the only one of the three compartments that is perfused. The model was used to predict the effect of an isobaric helium-to-nitrogen breathing gas switch which produced vestibular symptoms in the chamber experiments discussed above.[13] This revealed a fascinating consequence of the unique anatomy of the inner ear in which the perilymph and endolymph are non-perfused compartments that take up and eliminate inert gas through the perfused membranous labyrinth. After a period of heliox breathing, the perilymph, in particular, accumulates a substantial reservoir of helium. Following a switch to nitrox breathing, owing to a higher diffusivity of helium than of nitrogen, diffusion of helium from the perilymph and endolymph to the membranous labyrinth exceeds the diffusion of nitrogen in the opposite direction. At the same time, owing to higher solubility of nitrogen than of helium in blood, delivery of nitrogen to the membranous labyrinth in the arterial blood exceeds the removal of helium in the venous outflow. Together these could cause a transient supersaturation of the membranous labyrinth without decompression.

With respect to the Lambertsen and Idicula experiment, in which vertigo occurred after a switch from breathing heliox to breathing a mixture of oxygen, helium and 10 ATA (1.01 mPa) of nitrogen at an absolute pressure of 37.4 ATA (3.79 mPa),[13] the model predicted isobaric supersaturation of 0.4 ATA (40 kPa) which exceeded previously reported thresholds for bubble formation in vivo,[14] and this was, therefore, a plausible explanation for the vestibular symptoms reported in that study. In this regard, the perilymph/endolymph 'helium reservoir' can be seen as acting in an analogous (albeit transient) role to the helium chamber atmosphere in the experiments which caused skin symptoms.

The model was developed primarily in an attempt to explain pure inner-ear DCS arising during decompression from deep, mixed-gas technical dives, and the modelling of one such event (a decompression dive to 110 metres' sea water (msw) for 25 minutes) showed that even prior to any gas switches the membranous labyrinth had become substantially supersaturated (1.7 ATA, 172 kPa peak) during the ascent.[7] Thus, one explanation for the onset of inner-ear DCS during decompression from deep dives was simply that the inner ear was allowed to become excessively supersaturated, which could provoke bubble formation in situ. In this case report, the helium-to-nitrogen gas switch resulted in a much smaller effect on membranous labyrinth supersaturation than in the Lambertsen experiment, mainly because the partial pressure of nitrogen substituted for helium was comparatively small.[7] Indeed, the counterdiffusion effect was manifest only as a transient slowing of membranous labyrinth gas washout.

We suspect that the isobaric counterdiffusion effects of typical gas switches in technical diving would rarely, if

Table 1
Numbers of inner-ear DCS cases presenting with isolated inner ear symptoms and within the latency categories specified in those series reporting compatible data; only one diver (in the Ignatescu study[8]) developed symptoms during ascent
* % out of 211; † combined numbers and % for latency >30 min

Study	*n*	'Pure' inner ear DCS	Latency of symptoms after surfacing (min)		
			0–30	31–60	>60
Ignatescu[8]	33	16	22	7	3
Klingmann[4]	34	28	20	9	5
Nachum[5]	29	15	18	6	5
Smerz[18]	28	Unknown	21	3	4
Gempp[9]	115	98	98	17†	
Totals (%)	239	157 (74)*	179 (75)	59 (25 †)	

ever, be sufficient to produce inner-ear bubble formation in their own right, and inner-ear DCS occurring during decompression from deep, mixed-gas dives may be explained primarily by inadequate decompression. However, if a switch takes place when there is substantial pre-existing supersaturation of the membranous labyrinth, it is plausible that the resulting counter-diffusion effect could transiently augment this supersaturation and increase the probability of symptomatic bubble formation. In this regard, it is germane to mention that the basis for using nitrogen switches to accelerate decompression from helium dives has recently been challenged,[15] and in the absence of gas cost as a factor (e.g., when using a rebreather), the advantages of performing gas switches are now open to substantial debate.

Finally, for completeness, we cannot exclude the possibility that the right-to-left shunt of VGE, for instance across a PFO, as discussed below, might be relevant to isobaric inner-ear DCS and in some inner-ear DCS cases arising during decompression, because VGE formation occurs both during isobaric counterdiffusion of helium and nitrogen across the skin and during decompression.[16,17]

Inner ear DCS arising after diving

The second subset of inner-ear DCS cases arises after diving. There are now five substantial series of inner-ear DCS cases (Table 1).[4,5,8,9,18] For completeness, we note that two other series[19,20] were considered but not included in this review because of case overlap with Klingmann (2012).[4] Of the total 239 divers presented, only one developed symptoms during decompression.The vast majority arose after air diving to moderate depths. Pooled maximum depth data for the incident dives in the 96 cases from three of the series show a median maximum depth of 34.5 msw (range 15–122 msw).[4,5,8] Neither of the other two series[9,18] reported individual dive depths to allow data pooling but the mean depth maxima in these series were 32 msw and 41 msw respectively. Many cases (74.4% in series reporting relevant

Table 2
Numbers of inner-ear DCS cases presenting with vestibular only, cochlear only and combined presentations in those series reporting compatible data

Study	*n*	Vestibular	Cochlea	Vestibular and cochlear
Klingmann[5]	34	19	0	15
Nachum[4]	29	10	4	15
Smerz[18]	28	19	0	9
Gempp[9]	115	88	7	20
Totals (%)	206	136 (66)	11 (5)	59 (29)

Table 3
Methods and outcomes of testing for right-to-left shunt (RLS) in inner-ear DCS cases from those series reporting compatible data; all four studies used bubble contrast; TTE – transthoracic echocardiology; TCD – transcranial Doppler; * % out of 179

Study	*n*	Test	RLS +ve	Large RLS
Ignatescu[8]	30	TTE	24	24
Klingmann[4]	34	TCD	25	Not specified
Cantais[10]	34	TCD	28	24
Gempp[9]	115	TCD	95	89
Totals (%)	213		172 (81)	137 (77*)

data) exhibited 'pure' inner-ear symptoms (that is, there were no other DCS manifestations) and in most cases these symptoms developed with relatively short latency; 85.4% presented within 60 minutes of surfacing. The proportion of divers presenting with inner-ear symptoms classified as vestibular only, cochlear only, or both vestibular and cochlear are shown in Table 2 for those series with compatible data. The vestibular organ appears affected both more often and more often in isolation than the cochlear organ. In summary, inner-ear DCS occurring after surfacing can be characterised as a frequently isolated or 'pure' clinical syndrome with short symptom latency following dives to moderate depths, and to which the vestibular end-organ appears more vulnerable than the cochlea.

A striking feature of inner-ear DCS occurring after surfacing is strong association with the presence of a right-to-left shunt. Data from relevant studies are summarised in Table 3.[4,8–10] Three studies used transcranial Doppler (TCD) (or occasionally carotid Doppler) to detect a right-to-left shunt after injection of bubble contrast solution into a peripheral vein.[4,9,10] These tests can detect shunting but do not delineate the anatomical source of the shunt, though it was presumed in most cases to be via a PFO in a study using transthoracic echocardiography with bubble contrast.[8] Studies of right-to-left shunt (or specifically PFO) in control groups of divers who have not reported DCS, find an approximately 25% incidence of any right-to-left shunt and a 12% incidence of

large right-to-left shunt (where 'large' is usually defined as spontaneous shunting of bubble contrast).[10,21] Comparison of these values to those reported for the case series in Table 3 suggests that right-to-left shunt (and particularly large shunts) are significantly over-represented amongst divers suffering inner-ear DCS. A similar, although somewhat weaker association exists between right-to-left shunt and cerebral, spinal and cutaneous DCS.[22–25]

The most obvious interpretation of the association between right-to-left shunt and some forms of DCS is that a shunt allows VGE to bypass the pulmonary capillaries which normally act as a filter and prevent most VGE from reaching the arterial circulation.[26] Arterialised bubbles then impact organs where they cause harm. This pathophysiological mechanism requires that VGE occur at or before the time of symptom onset and that arterialised bubbles have sufficient lifetimes to reach the affected organ; both of these conditions are plausible for inner-ear DCS. To accommodate the typically short symptom latencies for inner-ear DCS (Table 1), VGE must form very early after surfacing from recreational air dives. Indeed, VGE are commonly detected less than 30 minutes, and as soon as two minutes, after decompression from no-stop chamber dives.[27]

There is a paucity of related data following recreational dives in the field, because many relevant studies do not begin VGE monitoring within the first 30 minutes after surfacing, and those that do frequently report the peak bubble count or grade over multiple sequential observations without providing data for each observation. Nevertheless, one study showed that 26% and 45% of unrestricted first and repetitive (respectively) recreational scuba air dives resulted in Spencer VGE Grades 2–4 around 30 minutes post dive.[28] The unsurprising finding in the same study that dives with a higher predicted probability of DCS produced more VGE may explain the moderately deep (and, therefore, provocative) nature of most incident dives in the inner-ear DCS series cited here. There is ample evidence that even small arterialised VGE are able to reach the cerebral circulation. For instance, TCD detection of arterialised agitated saline (in which air bubbles are of similar size[29] to decompression VGE[30]) has demonstrated this on many occasions (Table 3).

Thus, the intuitively obvious relevance of a right-to-left shunt is that small VGE that become 'arterialised' across the shunt could embolize the inner ear vascular supply and produce vestibulo-cochlear dysfunction. A clinical observation that lends circumstantial weight to this hypothesis is the occasional onset of symptoms in temporal relation to lifting or straining early after surfacing;[8] such manoeuvres would be expected to increase right heart pressures and promote flow across a right-to-left shunt. However, the commonality of the blood supply to both inner ear and the brain, another 'at-risk' organ, raises questions about the provenance of this relatively simple explanation.

The arterial supply to the inner ear is a branch of either the basilar artery or the anterior inferior cerebellar artery (itself a branch of the basilar artery) and flow through these cerebral vessels is vastly greater than through the labyrinthine artery. Since tiny bubbles will tend to distribute with flow,[31] the posterior circulation of the brain will be exposed to a substantially greater proportion of any arterialised VGE passing up the basilar artery. Despite this, inner-ear DCS commonly occurs in the absence of any symptoms of other organ involvement (Table 1) begging the question "*how can there be only inner-ear manifestations when the brain must simultaneously be exposed to much greater numbers of emboli*"?

It could be argued that the inner ear represents a functionally important and sensitive end-arterial territory that might be particularly vulnerable to injury by arterial micro-bubbles. However, the brain also contains functionally important end-arterial loci.[32] Moreover, there are other clinical situations in which patients are exposed to many small arterial bubbles but in which it is the brain that appears more vulnerable to injury than the inner ear. A contextually relevant example is the introduction of microbubbles to the arterial circulation in a strongly positive PFO test using bubble contrast. These bubbles are of similar size to VGE produced in decompression,[29,30] and they occasionally produce symptoms suggestive of evanescent cerebral injury,[21,33–35] but there are no reports of inner-ear injury following PFO tests. Similarly, microbubbles may contribute to post-operative cognitive impairment following cardiac surgery,[36] but (to our knowledge) peri-operative exposure to these bubbles has never been associated with inner-ear injury.

An explanation for the almost paradoxical selective vulnerability of the inner-ear to injury by arterial microbubbles after diving was first proposed by the present authors.[37] Using published models for predicting inert gas tensions in brain and inner ear, comparison was made of supersaturation in the membranous labyrinth and brain over the first hour after surfacing from a no-decompression-limit air dive to 30 msw.[7,15,38] This depth corresponded to the typical depth of incident dives in inner-ear DCS series reported at that time. The models predicted nitrogen wash out from the brain and inner ear with approximate half times of 1.2 and 8.8 minutes respectively. Consequently, on the simulated dive where ascent was conducted at the prescribed rate, the brain would develop a small and transient supersaturation whereas the inner ear would become significantly supersaturated during ascent, and this would decay over approximately 30 minutes after surfacing.[37]

We proposed that any small arterial bubbles arriving in the inner ear during this 'supersaturation window' would tend to grow from inward diffusion of supersaturated gas (as has been demonstrated in other tissues)[39] whereas similar bubbles entering the brain microcirculation would not grow, and would tend to redistribute through to the venous side.

On this basis, bubbles arriving in the inner ear early after a dive could be expected to produce greater harm. However, notwithstanding its rapid inert gas elimination kinetics and consequent resilience in comparison to the inner ear, it is plausible that the brain can still be injured by large numbers of small arterial bubbles, as is believed the case in cardiac surgery.[36] This would explain the previously reported over-representation of large right-to-left shunts among divers suffering cerebral DCS.[22]

Two recent studies extended our hypothesis to an explanation for the apparent vulnerability of the vestibular apparatus in comparison to the cochlea.[4,8] The authors cited data demonstrating that blood flow to the cochlea exceeds blood flow to vestibular organ by a factor up to times four,[40,41] and that cochlea tissue volume is smaller than that of the vestibular organ.[42] These characteristics would result in a shorter perfusion half-time for inert gas exchange in the cochlea than in the vestibular organ. Thus, the greater susceptibility of the vestibular organ than the cochlea to injury (Table 2) may be explained by slower gas washout and, therefore, more prolonged supersaturation in the vestibular organ than in the cochlea. As a result there will be a longer period during which bubbles can grow in the vestibular organ than in the cochlea.

Thus, in summary, it seems plausible that a large PFO predisposes to inner ear DCS by allowing VGE to enter the arterial circulation. This is more likely to occur following dives which are more provocative for VGE formation, and right-to-left shunting of VGE may be promoted by lifting, straining, or exercising early after diving. In respect of inner-ear DCS, shunting of VGE is maximally hazardous early after a dive when the inner ear remains supersaturated with inert gas. Although not investigated formally, it is plausible that a similar mechanism involving residual tissue supersaturation may explain the unexpectedly high prevalence of RLS among divers suffering spinal and cutaneous DCS. Shunted VGE are less likely to injure the brain because it eliminates inert gas very quickly. However, cerebral symptoms could occur if large numbers of VGE are shunted.

The implications of these pathophysiological mechanisms to treatment of relevant DCS cases and to decision making around investigation and management of right-to-left shunts after a relevant DCS episode are beyond the scope of this summary, and are considered in other papers in this issue.

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Assessing potential divers with a history of congenital heart disease

Mark S Turner

Abstract

(Turner MS. Assessing potential divers with a history of congenital heart disease. 2015 June;44(2):111-115.)
This article describes a structured approach to assessing the medical fitness of potential divers who have a history of congenital heart disease. The importance of a complete and accurate cardiac history, including details of surgery and other interventions is emphasised. Specific assessment of intracardiac shunts, exercise capacity and ability to deal with the physical challenge of diving, risk of diving-induced pulmonary oedema, of arrhythmia and of incapacity in case of arrhythmia and the consequences of surgical and catheter treatment are discussed, including the risks associated with lung injury and the pressure limitations of implanted devices like pacemakers. Clinical assessment will usually include echocardiography and exercise testing with additional investigations such as MRI scanning, CT of heart or lungs, cardiopulmonary exercise testing and ECG monitoring, as required. Examples of different congenital lesions are given applying this approach (atrial septal defect, tetralogy of Fallot, bicuspid aortic valve and the Fontan circulation). The approach is based on an individual cardiologist's opinion and is not specifically evidence-based, but seeks to apply what is known in other areas of diving medicine to this potentially complex group of patients.

Key words
Fitness to dive; cardiovascular; pathology; physiology; children; right-to-left shunt; review article

Introduction

Due to the success of congenital cardiac surgery, interventional cardiology and paediatric intensive care, more than 85% of children with congenital heart disease reach adulthood. Furthermore, there are individuals who present in adulthood with congenital lesions.[1] There are now potential divers with congenital heart disease, some having had surgery or interventional treatment. There are no randomised controlled trials to guide us in this area, so this article is based on personal opinion and on an understanding of the mechanisms of diving illnesses and is influenced by the UK Sports Diving Medical Committee Guidelines.[2]

We aim to treat our patients so they can lead as normal a life as possible and there is good evidence that exercise improves patients with all forms of heart disease. Diving, however, carries specific risks that do not apply to most other sports, so special consideration of divers is justified. This article cannot be comprehensive and is not a replacement for an individualised specialist assessment; an accurate assessment of the 'patient' is needed, before the 'patient' can become a 'diver'. Table 1 summarises the key areas to consider when assessing potential divers.

Intracardiac shunts

'Hole in the heart' is a well-known form of congenital heart disease, such as atrial septal defect (ASD) or ventricular septal defect (VSD). ASD and VSD can be part of other types of congenital heart disease. VSD is part of Tetralogy of Fallot, but less well-known is that Ebstein's anomaly of the tricuspid valve is associated with an ASD or a large persistent foramen ovale (PFO) in 80% of patients.

In normal life, ASD will cause enlargement of the right ventricle, atrial arrhythmias, breathlessness and a small risk of stroke by paradoxical embolus (although the left atrial pressure is usually higher than the right). For divers, breathlessness and arrhythmia may be precipitated underwater, but perhaps more importantly paradoxical embolization of nitrogen bubbles during decompression causes some types of decompression illness (DCI). In a normal heart with PFO, the left atrial pressure is higher than the right, so the 'flap' is held down. The patient with Ebstein's anomaly, ASD, or tetralogy of Fallot is more likely to have a higher right atrial pressure, with a higher chance of right-to-left shunt, increasing the risks of DCI.

Obligate right-to-left shunts mean patients are desaturated at rest. These are patients with complex circulations with mixing of the systemic venous (blue) blood with the pulmonary venous (red, oxygenated) blood. Therefore, measuring oxygen saturation is important for congenital heart disease patients. Other lesions can cause desaturation, such as a left superior vena cava draining straight to the left atrium, where bubble contrast echocardiography (echo)

Table 1
Issues for assessment in patients with congenital heart disease

- Potential for right-to-left shunt;
- Ability to deal with the physical challenges of diving;
- Risk of diving-induced pulmonary oedema;
- Risk of arrhythmia/sudden loss of capacity;
- Risk of non-cardiac issues/associations; e.g., lung damage post thoracotomy, bullae in Marfan syndrome;
- Drug therapy/pacemaker.

performed from the left arm, will cause the left atrium to fill with many bubbles, whereas a bubble echo from the right arm, could be falsely negative. This underlines the need to understand the cardiac anatomy.

Assessment of right-to-left shunt

Given the high prevalence of right-to-left shunt in patients with congenital heart disease, bubble contrast echocardiography, according to the protocol developed by Wilmshurst et al,[3] should be performed in all potential divers to assess the risk of DCI; and the magnitude of the shunt determines the risk.[3] The bubble echo must be performed in accordance with this protocol and the images should be quality controlled. The bubble images must show excellent opacification of the right heart, with complete filling with microbubbles. If gaps exist between the bubbles, then opacification is inadequate and can underestimate the shunt. Furthermore the quality of the provocative manoeuvres must be assessed. With a good Valsalva, it should be possible to see the left-sided heart chambers become smaller during the Valsalva, and recover their size after release. The image must not be interrupted at the time of Valsalva release, maintaining a view of the left ventricle, as the bubble shunt can sometimes only be seen for a few beats. No medical test is perfect, but bubble contrast echo is very operator-dependent, and sadly many studies sent to us from elsewhere fail our quality control criteria and can be falsely negative.

For those with moderate or large shunts, diving may still be possible but with very careful management of gas load. If the gas load is low, venous bubbles do not form, and the tissues do not build up a significant partial pressure of inert gas. As the pathophysiology of shunt-related DCI relies on venous bubbles being present to cross the PFO, or other defect, and then to embolise to tissues where there is already a significant inert gas burden, modification of gas load, and avoiding lifting or straining after surfacing should effectively reduce the risk. The UKSDMC recommends 15 metres, or equivalent air depth or the use of the DCIEM tables as suitable risk-reduction measures (although this may not be applicable to less fit or older individuals with underlying cardiac pathology).

For individuals with very large or resting shunts, and especially those with desaturation, my view is that they must be at higher risk of DCI and may not be fit to dive, or may need more rigorous limitation of gas load. If the desaturation is because of complex pathology, there may be other reasons to be unfit for diving.

Ability to deal with the physical challenges of diving

Some patients with congenital heart disease can achieve normal cardiopulmonary performance on exercise testing, whereas others will always be limited. Increasingly we use cardiopulmonary testing clinically, so this information may be available. During diving the cardiac output may need to increase to deal with exercise or anxiety, or to undertake safety-critical tasks. Good ventricular function and well-functioning valves on echocardiography or cardiac MRI scanning is reassuring, especially if accompanied by a normal cardiopulmonary exercise test.

Patients with common lesions such as repaired tetralogy of Fallot have a wide spectrum of exercise capacity and symptoms. Some will have severe pulmonary regurgitation and require early pulmonary valve replacement, whereas others can survive after primary repair with good function and do not require repeat surgery.[4] Thus, careful clinical assessment of the individual coupled with MRI and cardiopulmonary exercise testing is usually needed.

Immersion pulmonary oedema (IPE)

Ventricular function, valve function and exercise capacity are also relevant to diving-induced IPE. In IPE's 'purest' form, the systemic vascular resistance increases pathologically during immersion, due to an exuberant vasoconstriction, making the heart pump against a greater resistance. This in turn increases the left atrial pressure, such that the pulmonary capillaries leak and pulmonary oedema commences.[5] If the left atrial pressure starts high due to impaired ventricular or valve function, or hypertension, left atrial pressure has less to rise before the onset of pulmonary oedema. As some vasoconstriction to cold and immersion is normal, and the compression of abdomen and legs may also increase atrial pressures, a high starting left atrial pressure is likely to put the diver at higher risk of IPE. Furthermore, a diseased ventricle will need to increase the left atrial pressure more than usual in order to increase cardiac output, as increasing contractility may be limited by the underlying ventricular disease. Tissue Doppler measurements may estimate left atrial pressure, and should be performed during a transthoracic echocardiogram. Severe limitation to exercise capacity, significant ventricular impairment, evidence of elevated left atrial pressure, or significant valve disease are probably barriers to diving, but may be an indication for corrective surgery or intervention.

Conditions severely limiting the increase in cardiac output with exercise

Aortic stenosis, pulmonary stenosis, pulmonary vascular disease and hypertrophic obstructive cardiomyopathy can cause an inability to increase the cardiac output that is so profound that collapse can occur on exercise. Any potential diver with a history of exercise-related collapse is at markedly increased risk and should not dive until the underlying cause is treated, and they are reassessed. Symptomatic patients with hypertrophic cardiomyopathy are unlikely to be candidates for diving and our knowledge of diving risk in asymptomatic patients with hypertrophic cardiomyopathy is inadequate to make any recommendation.

Arrhythmias

Arrhythmias are the commonest reason for emergency admission in adult congenital heart patients, atrial arrhythmia being the most common; however, ventricular arrhythmia is more likely to be incapacitating and life threatening.[1] For this reason, any patient who has had ventricular arrhythmia without a definite and reversible cause, is likely to be at greater risk and is unlikely to be fit to dive.

Atrial arrhythmias can cause haemodynamic compromise, if the rate is very fast, or if the underlying heart or valve function is poor. Thus, if the diver is on rate-controlling medication and the heart function and exercise capacity are good, the diver is unlikely to come to harm if they suffer an atrial arrhythmia, so long as they can surface immediately (without obligatory decompression stops). How the diver feels when they get atrial arrhythmia on the surface is a key part of the history in this situation.

Consequences of treatment/associations

To survive, many patients will have had surgery or catheter-based interventions which could have an impact on diving fitness. Previously arterial shunts (e.g., Blalock-Taussig) were often used to increase pulmonary blood flow for cyanotic patients, e.g., tetralogy of Fallot. Modern surgery aims for a primary repair at a younger age, but potential divers may have been treated with shunts, which are usually performed through a thoracotomy. Thoracotomy has a potential to cause lung damage and scoliosis. A further risk to lung function is that phrenic nerve palsy can occur during complex congenital heart repairs. These lesions may be risk factors for pulmonary barotrauma, may compromise lung function and potentially limit exercise capacity.

Catheter interventions should not damage the lungs, but pneumothorax at the time of subclavian puncture (such as for pacemaker implantation or lines for intensive care or dialysis) could occur and the potential diver's history needs to be scrutinised for this type of complication. A traumatic pneumothorax from needle injury may not increase the risk of pulmonary barotrauma, but lung or pleural scars from infections or pleural adhesions may have an impact.

Pacemakers are no longer just used to treat bradycardia and so the mere presence of a pacemaker is not enough information to inform decisions about fitness to dive. Patients with cardiac resynchronisation therapy (CRT) will have had an impaired left ventricle and heart failure symptoms – they will, therefore, have reduced exercise capacity and increased risk of IPE unless they have responded dramatically to the therapy. Implantable defibrillators are used for those at very high risk of ventricular arrhythmia, so are unlikely to be fit to dive. Some defibrillators still function normally at 709 kPa (St Jude Medical USA),[6] but it is the underlying heart disease that is the contraindication to diving. If the risk of arrhythmia is not as high, e.g., if the ICD was implanted for primary prevention, or if there was a clear precipitant, one may make an individual decision about diving fitness. In these cases, mitigation of the risk of arrhythmia, or ICD discharge may be appropriate, such as the use of a full-face mask that would prevent inhalation of sea water in case of blackout, diving with an experienced buddy and avoiding obligatory decompression stops. Furthermore, different ICDs and pacemakers are tested to different pressures, so the device must be precisely identified.[7] For example, most St Jude Medical devices are tested to 7 ATA (709 kPa), whereas Medtronic are tested to 2.5 ATA (253 kPa), and devices may malfunction if taken beyond their tested depths.

Clinical assessment

PAST HISTORY

It is essential to obtain a detailed past medical history, including the nature of surgical and/or other interventions, their complications, other medical problems and a full drug history. Understanding the detail, such as thoracotomy or sternotomy, is important when assessing risk and potential lung damage. Remember to discuss other congenital abnormalities and whether the cardiac lesion is part of a syndrome. Ask about exercise capacity and exercise-related symptoms, palpitations, migraine with or without aura, blackouts and collapse.

EXAMINATION and ECG

Examine for blood pressure, murmurs, scars (thoracotomy, sternotomy and groin scars) and for the presence of a pacemaker, which may be in a pectoral position or could be in the abdomen. The morphology of the QRS complexes and T-waves may be abnormal, so an abnormal ECG in itself may not exclude the potential candidate. However, recording an ECG is important to assess the cardiac rhythm and to assess conduction abnormalities. Ambulatory ECG monitoring may be needed if there is an increased risk of arrhythmia or heart block.

ECHOCARDIOGRAPHY

Echocardiography is important to identify and quantify valve lesions, assess ventricular function and look for other congenital cardiac abnormalities such as coarctation of the aorta. So, a supra-sternal view is needed, which is not performed by all echocardiographers, even though it is part of a standard examination performed in high-quality departments. Bubble contrast echocardiography will often be needed, and should include the use of provocation manoeuvres to promote right-to-left shunt such as Valsalva release and sniffing.[3] Many departments perform bubble contrast echocardiography in a way that does not satisfy our quality control criteria, so the rigour with which this test is performed is extremely important if false negative tests are to be avoided.

As described earlier, bubble contrast should totally opacify the right heart so, if any 'black', unopacified space can be seen in the right heart, the contrast is inadequate (bubbles are white and should not be separated by any blackness at all). The bubbles in the right heart need to be present at the time of a sniff or Valsalva release, the left heart should get noticeably smaller with the Valsalva (as the venous return is restricted), the septum should bulge to the left on Valsalva release and bubbles should be seen along the entire length of the septum as it bulges. The echo pictures need to be recorded for many beats – I usually record at least 10 beats – so that the pattern and timing of bubbles entering the left heart can be seen. Any scans not satisfying these criteria cannot be used for risk assessment, and need to be repeated. Transoesophageal echo is very rarely needed and is less sensitive for shunts, although many echocardiologists who are not PFO specialists will disagree with this.

EXERCISE TESTING

Exercise testing can be used to confirm that there are no exercise-induced arrhythmias, can give some reassurance about ischaemia (but more sensitive ischaemia tests are now available if ischaemia is a specific issue, e.g., for patients after the arterial switch operation where the coronaries are moved) and gives reassurance that the cardiac output can be increased. Tests such as cardiopulmonary testing or the Chester step test[8] can give reassurance about exercise performance and provide some reassurance about IPE, although IPE can occur even in very fit individuals if the pathophysiology is solely extreme vasoconstriction. ECG monitoring may be appropriate if there is concern over arrhythmia or intermittent heart block.

OTHER TESTS

Spirometry and chest radiography are indicated in all potential divers who have had chest surgery (thoracotomy or sternotomy) to help to determine if there is any lung damage that could increase the risk of pulmonary barotrauma, although normal lung function and chest radiography cannot exclude this risk. Some cardiac abnormalities may be associated with lung abnormalities, and if there is a high index of suspicion, chest CT scanning may be needed to identify bullae, scarring or other abnormalities.

Four clinical examples of the systematic approach to assessment are presented in Table 2.

Summary

This article has attempted to provide a framework for assessing potential divers with a history of congenital heart disease. It does not replace a full assessment by a (congenitally-trained) cardiologist with experience in diving medicine, but seeks to illustrate some of the issues and complexities that need to be evaluated. The overwhelming

Table 2

Four case examples of the systematic approach to assessing potential divers with a history of congenital heart disease

1. Secundum ASD

Intracardiac shunt
Untreated: increased risk of DCI;
Treated: bubble echo for residual shunts;
Cardiac function and exercise capacity
Untreated or treated: assess ventricular size and function, right ventricular size, right ventricular pressure and exercise capacity;
Risk of IPE: likely to be low if ventricular function and exercise capacity are okay;
Arrhythmia risk: age and pathology dependent; risk of atrial fibrillation (usually well tolerated).

2. Tetralogy of Fallot

Unoperated ToF
Patient should not dive as they have obligate right-to-left shunts, poor cardiopulmonary exercise performance and systemic right ventricular pressures.
Operated ToF patients
Right to left shunt: assume PFO or ASD; undertake bubble contrast echo; residual ventricular septal defect (VSD) may be present, and if the right ventricular pressure is elevated (as it commonly is) then right to left shunt across the VSD may be seen, but should also be identified with bubble contrast echocardiography.
Cardiac function and exercise capacity: pulmonary regurgitation (PR) and right ventricular dilatation common; exercise capacity should be normal or nearly normal.
Risk of IPE: likely to be low if ventricular function and exercise capacity are okay;
Consequences of surgery: impaired lung function common (previous thoracotomy, scoliosis, potential for lung hypoplasia due to poor pulmonary flow in early life);
Arrhythmia risk: both atrial fibrillation and flutter can occur, but also ventricular tachycardia (most likely to cause collapse).

3. Bicuspid aortic valve

Right to left shunt: association with PFO, so bubble contrast echo indicated;
Ability to exercise: depends on severity of valve dysfunction and ventricular function;
IPE risk: depends on severity of valve lesions, ventricular function, coexistent coarctation of the aorta;
Arrhyhmia risk: atrial fibrillation risk, which can cause collapse if valve lesions severe or ventricular function impaired;
Associations: aortic enlargement (aortopathy) and dissection risk present.

4. Fontan circulation

This is a single ventricle repair, with non-pulsatile flow to the lungs, and is used only for severe forms of heart disease where a two ventricle repair is not possible.
Right to left shunt: very common, can be at atrial level or via venous collaterals;
Exercise capacity: low fitness levels and poor cardiopulmonary exercise tests;
IPE: the risk of IPE hard to predict, but vasoconstriction would cause low cardiac output;
Arrhythmia: atrial arrhythmia is common in Fontan patients, often causing haemodynamic compromise on the surface.

principle is that the underlying cardiac condition needs to be defined as accurately as possible to allow a meaningful risk assessment. Once additional risks are understood, the diver can mitigate the risks such as by avoiding decompression obligations, diving with experienced buddies and avoiding remote or extreme diving.

Furthermore, while some of the recommended testing may reassure us that there is not an excessive risk associated with diving, any patient with a congenital heart disease history is likely to be at a slightly greater risk than a similarly aged diver without any cardiac history. Therefore, a discussion with the individual is needed to ensure that they are fully informed of additional risks that diving may pose. For this reason, I would be reluctant to assess a child with congenital heart disease for diving, as my personal view is that the individual needs to 'own' this unquantifiable risk themselves, rather than their parents taking responsibility for it.

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Conflicts of interest

Dr Turner is a Consultant and Proctor for St Jude Medical (structural heart division), Medtronic Inc and Edwards Lifesciences (heart valve divisions) and a Consultant and Lecturer for Gore Medical.

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

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

PFO and ASD case reports

Delayed blood-brain barrier disruption after shallow-water diving demonstrated by magnetic resonance imaging

Amir Hadanny, Sigal Tal, Gregori Fishlev, Yair Bechor and Shai Efrati

Abstract

(Hadanny A, Tal S, Fishlev G, Bechor Y, Efrati S. Delayed blood-brain barrier disruption after shallow water diving demonstrated by magnetic resonance imaging. *Diving and Hyperbaric Medicine*. 2015 June;45:116-120.)
A 22-year-old diver presented to our emergency room complaining of headaches and left side numbness three days after diving to a depth of 6 metres for 25 minutes. On examination, he had left-sided hypaesthesia, and a post-contrast FLAIR brain MRI sequence revealed significant diffuse meningeal enhancement, indicating blood-brain-barrier (BBB) disruption. The patient was treated with hyperbaric oxygen; the initial four sessions resulted in only partial symptom improvement correlating with partial improvement in the MRI findings. Ten additional hyperbaric treatments resulted in complete resolution of the symptoms and normalization of MRI findings. The main aim of this case report is to present a probable, atypical, delayed-onset case of shallow-water decompression sickness culminating in significant BBB damage, which was demonstrated by special MRI techniques.

Key words
Decompression sickness; persistent foramen ovale; radiological imaging; brain; hyperbaric oxygen therapy; case report

Introduction

Decompression sickness (DCS) occurs rarely after a single dive to depths less than 10 metres' sea water (msw).[1] We present a patient who developed neurological symptoms after a single dive to 6 msw and in whom there was radiological evidence of endothelial injury to the blood-brain barrier (BBB).

Case report

A healthy, experienced, 22-year-old, male diving instructor developed headaches and left-sided numbness three days after diving to 6 metres' sea water (msw) for 25 minutes with no decompression violations. There were no preceding, provocative dives, his last dive being a no-decompression dive to 30 msw a week earlier, or unusual ascents during the dive. The dive profile was confirmed from his computer. His headaches were described as non-localized, fluctuating, pressure-like pain partially relieved with paracetamol and associated with nausea. His symptoms started gradually 24 hours after surfacing and he presented to the nearest emergency medicine department (ER) from where he was discharged after neurological examination and brain contrast induced CT scan were all normal. He presented to our ER three days later as the symptoms had worsened. On arrival, he was apyrexial and had normal vital signs, blood count and basic metabolic panel. However, neurological evaluation revealed left leg hypaesthesia. A brain MRI with FLAIR post-gadolinium injection sequence revealed marked diffuse meningeal enhancement indicating significant blood-brain barrier (BBB) disruption (Figure 1). Normobaric oxygen had not been given and lumbar puncture was not performed prior to the MRI.

Despite the unusual presentation and long delay, a diagnosis of DCS was considered the most likely. The patient was treated with four daily hyperbaric oxygen treatments (HBOT) at 203 kPa for 90 minutes, resulting in significant clinical improvement though a mild headache persisted. Follow-up MRI revealed partial improvement in meningeal enhancement. The patient continued with 10 additional daily HBOTs with complete symptom relief. A second follow-up MRI demonstrated complete resolution of the BBB disruption with normal FLAIR sequence (Figure 1). A transoesophageal echocardiogram evaluation revealed a 2–3mm persistent foramen ovale (PFO), and a contrast echocardiogram revealed a right-to-left shunt of gas bubbles during coughing.

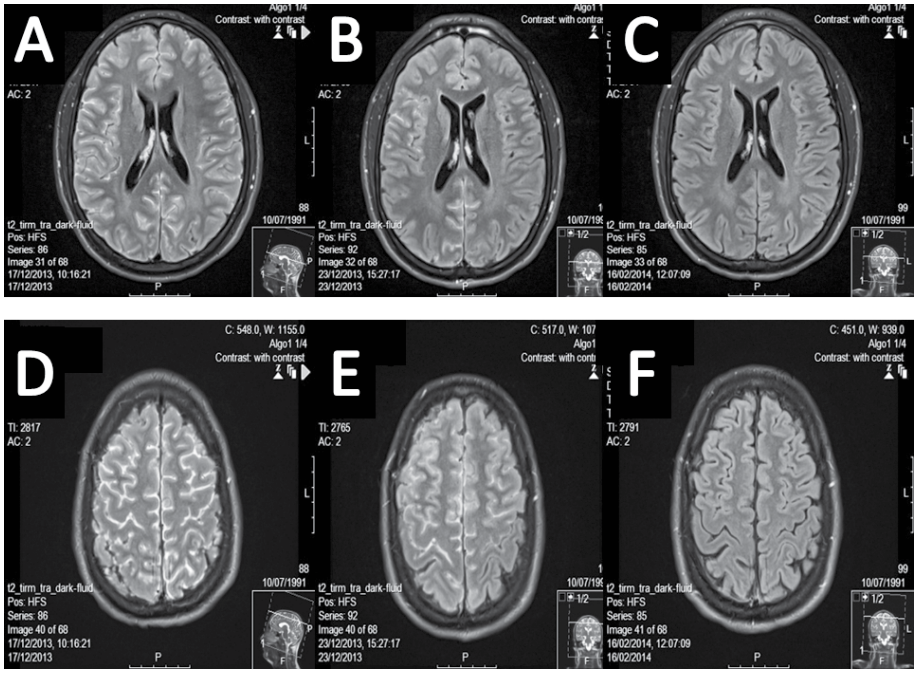
Discussion

DCS AND BBB DAMAGE

Brain MRI scans are considered to have a low sensitivity for the diagnosis of cerebral DCS, often being normal or infrequently revealing T2-weighted high signal intensity lesions in the subcortical white matter, which represent ischaemic changes.[2,3] The hyperintensity changes usually do not correlate with the clinical presentation. Recently a case report of cerebral DCS demonstrated hyperintense areas in the bilateral occipito-parietal lobes mimicking posterior reversible encephalopathy.[4] In our patient, there was a unique pattern of diffuse meningeal enhancement in the FLAIR post-contrast sequence, indicating BBB disruption. Bubble-related injury may be the result of direct mechanical distortion of tissues by extravascular bubbles, tissue hypoxia due to vascular obstruction and secondary effects related to intravascular bubble-induced endothelial

Figure 1

FLAIR post-gadolinium images on presentation (A, D) show massive diffuse hyperintensity signal in CSF spaces representing meningeal enhancement; no focal lesions, gray matter or white matter changes were observed. One week later after four hyperbaric oxygen treatments (HBOT) (B, E) images show decreased meningeal enhancement, and one month later the images (C, F) show normal brain MRI



damage.[5–7] Several animal models have shown induced BBB endothelial damage;[8,9] however, in humans, we are aware of only a single, recent case report of impaired endothelial dysfunction of a scuba diver with inner-ear DCS.[10]

The BBB is a neurovascular unit consisting of endothelial cells and the foot processes of astrocytes, and has the ability to control the exchange of humoral factors and cells between the circulation and the brain, thus playing a crucial role in maintaining cerebral homeostasis. The mechanisms of BBB disruption involve endothelial cell activation and endothelial basement membrane degradation by matrix metalloproteinases.[11]

RADIOLOGICAL IMAGING IN DCS

Imaging studies generally are not considered to be part of the standard assessment of DCS. However, in the current unusual presentation, brain imaging was important for establishing a diagnosis and for follow up. The findings correlated with the clinical presentation. A post-contrast FLAIR sequence MRI, which is not commonly performed, was used in the current evaluation. Under normal conditions, the gadolinium contrast particles do not cross the BBB. When the BBB is disrupted, it allows diffusion of particles into the cerebrospinal fluid (CSF).[15] The gadolinium shortens the T1 signal and, therefore, disrupts the CSF signal suppression of FLAIR sequence; hence the CSF spaces appear hyperintense.[16,17] The sensitivity of FLAIR for lower concentrations of contrast is ten-fold higher than T1WI.[17] This enhancement of CSF serves as an excellent imaging biomarker for BBB disruption called 'hyperintensity reperfusion marker' (HARM).[18] Recently BBB dysfunction was demonstrated in reversible encephalopathy, using the same MRI sequence.[19]

The unique pattern of the imaging in the current case enables analysis of dynamic contrast enhanced MRI (DCE MRI) and diffusion tensor imaging (DTI). DCE MRI is used to interrogate BBB permeability as part of microvascular permeability studies of human brain tumors.[20,21] Under normal cerebral blood flow, the kinetic parameter K^{trans} reflects BBB leakage into the CSF. Thus, high values of K^{trans} indicate high permeability. As seen in Figure 2, on presentation, the DCE MRI revealed diffuse high K^{trans} values, which had normalized at one month. This advanced imaging supports the BBB disruption induced by DCS as discussed above.

By using DTI in MRI scanning, gray and white matter microstructural integrity can be evaluated based on the directionality of diffusion in the brain. Mean diffusivity (MD) provides a measure of the average of total diffusion within a voxel. Damage to brain matter increases the MD through loss of barriers to free diffusion.[22,23] Recently, an animal model demonstrated decreased MD values even in spinal gray matter.[24] In the current case, the cortical (gray matter) MD values at presentation and after completion of HBOT sessions were compared. MD measurement was in exactly the same areas of interests. At the end of the treatment MD values had decreased significantly. Moreover, the most significant decrease/improvement was

Figure 2

K^{trans} values in a region of interest within the right post central gyrus; K^{trans} imaging reflects diffusion of gadolinium across the capillary endothelium; red colours mean high permeability, whereas blue represents normal permeability; at presentation, K^{trans} values are diffusely high (A; mean 0.027 min^{-1}); lower one week later (B; mean 0.023 min^{-1}) and normal at one month post presentation (D; mean 0.014 min^{-1})

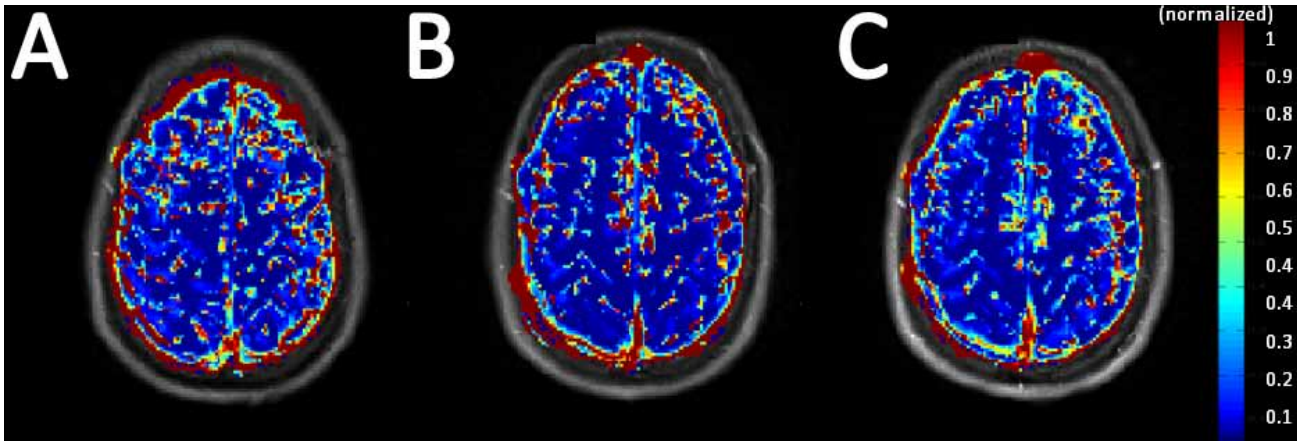


Figure 3

Mean diffusivity (MD) of grey matter/cortex using DTI imaging; red colours mean high diffusion and blue low diffusion; Post HBOT (B) compared to presentation imaging (A) shows lower values of MD (darker blue), in particular, the right post-central gyrus (responsible for left-sided sensation, shows the most improvement (shown in black rectangle), correlating with the diver's left-sided hypaesthesia

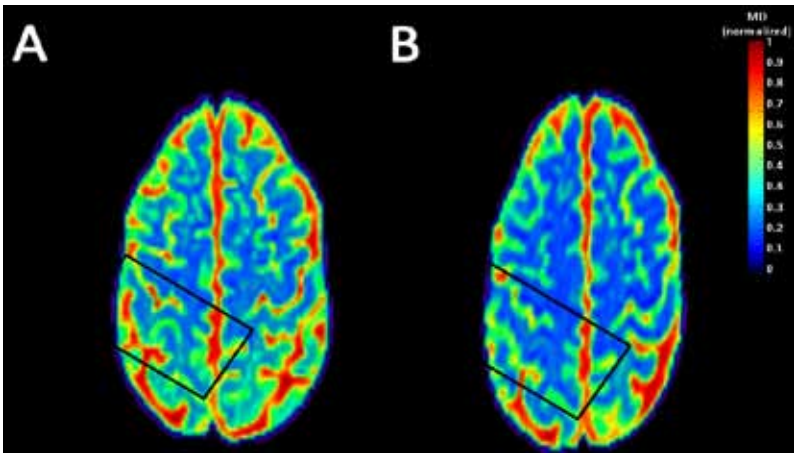
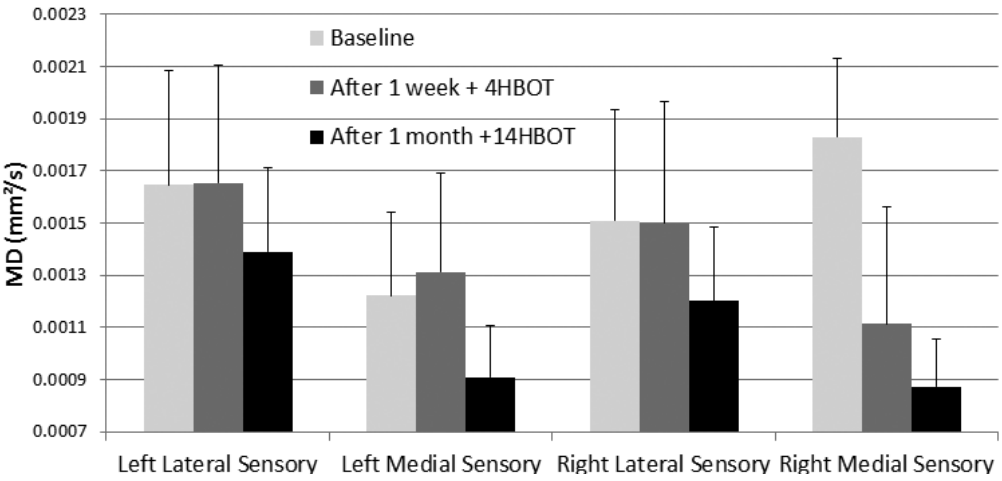


Figure 4

Mean diffusivity (MD) of grey matter/cortex using DTI imaging values; the right medial post-central gyrus, which is responsible for left leg sensation, showed the greatest change in MD, correlating with the diver's left-sided hypaesthesia



seen in the right medial post central area, which correlates anatomically with the patient's left-sided numbness (Figures 3 and 4).This is the first case in which DTI provides analysis of microstructural damage in DCS. With the increasing availability of this technology, DTI may add important information on the pathophysiology of DCS.

UNUSUAL FEATURES IN THIS CASE

Despite its unusual features, we believe this case represents atypical, shallow-water DCS, with delayed onset of neurological symptoms and signs, and associated with significant BBB damage on MRI.

Shallow water DCS

DCS is rare at depths of less than 10 msw, but neurological involvement is more likely in the presence of a PFO, as was demonstrated post injury in this diver.[12]

Delayed presentation

Most cases of DCS occur soon after surfacing, especially when the central nervous system (CNS) is involved. In a cohort of 1,070 CNS decompression patients, 56% of divers developed symptoms within 10 minutes and 90% within 4 hours after surfacing.[13] In the present case, the symptoms started 24 hours after surfacing, which is rare. Recently, the lymphatic system has been suggested as a slow carrier of micro-bubbles resulting in delayed presentation;[14] however, this delay could be related also to the time needed for endothelial dysfunction to develop.

DIFFERENTIAL DIAGNOSIS

Due to the unusual presentation, other neurological diagnoses should be considered. Subarachnoid haemorrhage commonly presents with acute, severe headaches and may be associated with nausea, vomiting and loss of consciousness. However, localizing signs, such as the hypaesthesia seen in our patient, are usually absent. Non-contrast CT performed within 6 hours of symptom onset, approaches 100% sensitivity.[25] Our patient had a negative CT scan in the first few hours from symptoms. A T2* MR sequence is more sensitive than CT in the subacute phase for detecting haemorrhage, which is seen as a low-intensity signal.[26,27] In our patient, the T2* sequence after three days did not demonstrate low signal intensities. Considering the extensive enhancement in our case, small and undetected subarachnoid haemorrhage is unlikely. Lumbar puncture should be considered with negative CT scan and high suspicion for haemorrhage, but was not considered to be indicated in this case.

Infectious meningitis commonly presents with fever and meningeal signs associated with signs of increased intracranial pressure such as headaches, nausea, vomiting, papilloedema, loss of consciousness and focal deficits. CT is usually normal in the early disease process. Of patients with meningitis, 90% may show post-contrast FLAIR hyperintensities in different locations; 70% of these also show post-contrast T1W hyperintensities.[28] Bacterial and viral meningitis exhibit enhancement that is typically thin and linear.[29] In our case, there were no post-contrast T1W changes, and post-contrast FLAIR showed diffuse and thick hyperintensities. Also, our patient did not have fever or meningeal signs, as well as normal blood tests. Again, owing to a low suspicion for an infectious cause, lumbar puncture was not performed. Moreover, the patient had clinical improvement after the first HBOT, which would not be expected in an infectious aetiology without concomitant antibacterial or antiviral agent administration.

Primary headaches syndromes (e.g., migraine, thunderclap headache) present with characteristic patterns of headache and have normal neurologic examination. In most cases, brain imaging is normal, yet in 12–46% of migraine patients, MR studies show white matter abnormalities,[30] which were not seen in our patient. Other iatrogenic causes for meningeal enhancement, such as oxygen administration or lumbar puncture were not done before the MR imaging.

HBOT FOR BRAIN RELATED INJURIES

Due to the delayed atypical symptoms, the shallow water diving profile and the fact that all bubbles would be dissolved by day three after surfacing, it was decided to use a 203 kPa, 90 minutes HBOT protocol rather than a US Navy Treatment Table 6 (USN TT6). In an animal model, HBOT has been shown to stabilize the BBB following a global cerebral injury.[31] However, in a recent study, we reported that divers with delayed decompression had better clinical outcomes when treated with USN TT6 compared to 203 kPa HBOT.[32]

In conclusion, we report a case of probable DCS-induced BBB disruption (demonstrated with special MRI techniques) in a diver with a PFO following a shallow scuba dive, treated with HBOT and resulting in full recovery, symptomatically and radiologically.

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Atrial septal defect: a coincidental finding on a screening medical

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Abstract

(Elliott EJ. Atrial septal defect: a coincidental finding on a screening medical. *Diving and Hyperbaric Medicine*. 2015 June;45(2):121-3.)
An otherwise fit, healthy medical practitioner who was a recreational diver underwent a medical assessment for a remote posting as an Antarctic Medical Practitioner at which a coincidental finding of an atrial septal defect (ASD) was made. ASDs can have health implications in extreme environments such as high altitude and is contraindicated in scuba diving. ASDs are common, being present in 1:1,500 live births and comprise 10% of all cardiac abnormalities. In this case, a percutaneous occlusive device was inserted under general anaesthetic with subsequent improvements in the practitioner's exercise capacity, return to diving and full employment, including Antarctic deployment, and right-sided heart remodelling 18 months post closure.

Key words
Right-to-left shunt; cardiovascular; radiological imaging; treatment; occupational health; case reports

Introduction

Atrial septal defect (ASD) is generally regarded as a contraindication for scuba diving because of the associated potential increased risk of decompression illness (DCI). It may also impact on occupational activities in other extreme environments such as deployment to altitude. Here, a medical practitioner reports her experience with the discovery at a routine pre-deployment medical of an ASD and its impact on her recreational and professional life.

Case report

An otherwise fit, healthy 33-year-old female medical practitioner who was a recreational diver underwent a medical assessment for a remote posting as an Antarctic Medical Practitioner (AMP). The screening included an exercise stress test (EST) because the deployment included high-altitude exposure. This EST resulted in a cascade of events that lead to a diagnosis of an ASD.

The diver recalled infrequent, brief attacks of palpitations lasting a few seconds that had begun the previous year, blamed on stress and caffeine. While she had always enjoyed an active lifestyle with regular aerobics, middle distance running and competitive Irish dancing to National levels, she expressed difficulty maintaining cadence with running owing to fatigue and shortness of breath on exertion. Past history was significant for pertussis in early infancy and mumps as a child despite immunisation, plus childhood asthma with several infective exacerbations annually. An Open Water diving certification was obtained in 2011 (with a negative bronchial provocation test in an earlier Antarctic medical). However, she had undertaken only a limited number of dives without event. Numerous extended overseas trips and several altitude exposures to 4,700 m in South America and 2,500 m in Greenland had ended otherwise uneventfully from a health viewpoint.

An ECG in 2008 for an expedition to Greenland showed P-wave inversion but no further assessment was recommended at that time, as she was otherwise asymptomatic, fit and well. The 2013 EST showed that, with exercise provocation, the P-waves reverted and the EST was completed routinely. No clinical signs were elicited on examination, and chest X-ray did not reveal cardiomegaly or prominent pulmonary vasculature. Transthoracic echocardiography (TTE) showed a secundum ASD measuring 12 mm with a shunt calculated at 1.8 (pulmonary flow/systemic flow ratio). Also of note was a mildly dilated right atrium (RA) and ventricle with an enlarged inferior vena cava to the upper limit of normal and mild pulmonary artery (PA) dilatation. Considering the size of the shunt, closure of the ASD was recommended. This diagnosis precluded medical fitness for her proposed Australian Antarctic service.

The diver travelled interstate to have an Occluotech Figulla® device inserted percutaneously under general anaesthesia with transoesophageal echocardiogram (TOE) and fluoroscopic guidance. Intraoperatively a balloon catheter was used to measure an appropriately sized device, and revealed a much larger defect, requiring a 33 mm occlusive device. There were no post-operative complications and aspirin and clopidogrel were prescribed for three months, with a subsequent three months at a twice weekly dose, then cessation. A secondary recommendation was to encourage screening for the extended family, with an older sibling also having a small ASD discovered. Coincidentally, a nephew has a congenital ventricular septal defect, which had been detected at birth.

Follow-up TTE at six weeks, three months, and a bubble contrast TTE at six months indicated no residual inter-atrial defect, which leant a green light to undertaking a dive medical and an uneventful resumption of scuba diving in mid-2014. From diagnosis until the six-week check-up, risk

Table 1
Current management recommendations for atrial septal defects

Medical Therapy
- Small ASD < 5mm[4]
- Normal RV size[4]
- No pulmonary arterial hypertension[4]

Interventional (occlusion device) and surgical closure
- Significant shunt Qp/Qs ratio > 1.5 + presence of:
  - ° Recurrent respiratory tract infections (paediatrics)[2]
  - ° Failure to thrive (paediatrics)[2]
  - ° Exercise intolerance[5,6,8]
  - ° Dyspnoea[5,6,8]
  - ° Fatigue[5,6]
  - ° Palpitations[6]
  - ° Heart failure[5,6,8]
  - ° Atrial arrhythmias[5,6,8]
- Right-sided heart enlargement ± symptoms[4]
- Paradoxical embolism[4]
- Orthodeoxia-platypnoea[4]
- Pulmonary arterial hypertension (not severe)[2]

Device closure
- < 40 mm[2,9]
- adequate rims of tissue (> 5 mm) from the defect to surrounding structures[2]

Table 2
Post-operative complications of percutaneous atrial septal defect closure; SVT – supraventricular tachycardia

Minor

Early
- Arrhythmia (atrial fibrillation/flutter; SVT)[5,11,13]
- Heart block[5]
- Femoral access site complications[5]
- Blood transfusion (rare)[13]

Late
- Nickel allergy[11]

Major

Early
- Device malpositioning/embolisation (rare)[3,5,7,11]
- Air embolism[12]
- Device thrombus[5,7]
- Pericardial effusion with tamponade[5,7]
- Mitral valve dysfunction[3,5]
- Venous obstruction[3,5]
- Cardiac perforation (rare)[3,5]
- Stroke[7]

Late
- Device erosion[3,5,7]
- Endocarditis[7,11]
- Thromboembolism[5,11]

mitigation for working as a medical officer in a hyperbaric medicine unit included having another doctor present to undertake in-chamber duties. After the six-week check to the six-month bubble contrast echo, restricted clearance was granted to undertake quick 'dips' in the chamber to provide acute patient care. Long-term follow up plans include an annual TTE, the first of which showed resolution of RA and PA dilation, and all previous activities, including scuba diving and employment with no restrictions have been resumed, including middle distance running at 30 seconds less per kilometre with little training and she has recently returned from Antarctic deployment.

Discussion

ASDs are one of the most common congenital cardiac defects (10% of all heart abnormalities and approximately 1 in 1,500 live births, with a 2:1 female to male ratio for secundum defects).[2,3] There are four anatomical subsets of ASD: secundum (75%), primum (15%–20%), sinus venosus (5%–10%), and coronary sinus ASD (< 1%).[4] The latter three are not conducive to percutaneous device repair due to their anatomical locations.[2,4] An ASD can co-exist with a persistent patent ovale (PFO).[4] Most cases are sporadic; however, there are genetic markers for familial ASD including Holt-Oram syndrome and Ellis van Creveld syndrome (associated skeletal abnormalities), and mutations of GATA4 and NKX2.5 (associated conduction abnormalities).[3,5–7]

ASDs, regardless of size, often remain undiagnosed until later life. Generally a defect of less than < 8 mm diameter will close during infancy (approximately 4%), with spontaneous occlusion unlikely beyond early childhood.[6,8] If left untreated, defects tend to increase in size owing to left-to-right shunting across the atrial communication, causing symptoms of right heart and pulmonary vascular volume overload, which may become apparent from the third decade, with almost all lesions symptomatic by the sixth decade.[4,6,8] Symptoms include exertional dyspnoea, fatigue, syncope, and palpitations and are not correlated with shunt size.

Examination findings depend on the extent of the left-to-right shunt and its effect on the architecture of involved structures. An ASD itself does not produce an adventitious sound as there is no pressure gradient, and it is an acyanotic condition.[5,6] Only when the shunt is reversed due to increased pulmonary vascular resistance (Eisenmenger syndrome), may cyanosis and clubbing present.[6] ECG may show sinus rhythm, atrial flutter or fibrillation, with inverted P-waves indicating an absent sinus node, and potentially an incomplete right bundle branch block if right ventricular dilation is present. Chest X-ray may show cardiomegaly with prominent pulmonary vasculature, and low left heart output is evident with a small aortic notch.[3,4,6] ASDs are investigated with TTE and further detailed information achieved with TOE or contrast TTE with agitated saline.[7]

Current management recommendations for ASD are summarised in Table 1.

The first successful ASD closure was done via median thoracotomy on cardiac bypass in 1952, with the first device closure done surgically in 1974, and the first percutaneous device closure in 1991.[10,11] This has resulted in better cosmesis, cost reduction, reduced post-operative complications, and reduced hospital stay. Percutaneous closure with an endoluminal device is a safe and effective intervention for secundum ASDs < 40 mm, with low risk of intraoperative complications under expert proceduralist care (Table 2).[8]

There are currently three occluder devices on the Australian market, made of a nickel/titanium alloy (nitinol), the Amplatzer Septal Occluder (ASO), Helex Septal Occluder, and Figulla Septal Occluder (FSO).[8,9,11,12] Right-sided heart and pulmonary vasculature remodelling occurs post closure, with best overall morbidity and mortality favouring closure prior to 25 years of age.[3,6] Regardless of age at closure, patients will experience a degree of improved exercise capacity due to right ventricular remodelling, improvement in left ventricular function and decrease in pulmonary arterial pressures.[8]

Post-operative recommendations are to have a TTE at least every two years initially to ensure maintenance of device placement and evaluation of improvement in right heart size and pulmonary pressures.[5] Anticoagulation (i.e., aspirin and clopidogril) is given for several months up to a year post device closure owing to the risk of formation of thrombus until the device is epithelialized and a potential for atrial fibrillation.[3,5] There are conflicting recommendations for post-operative endocarditis antibiotic prophylaxis (risk approx. 0.8%).[4,5,7,11]

Persistence of a shunt may also occur; however, these are often small and close within 12 months post-operatively and are best assessed with a contrast TTE.[3] Recommendation for returning to normal sporting activities, including scuba diving, is within three to six months post-operatively provided that there is no evidence of right heart failure pulmonary arterial hypertension or arrhythmias.[5] Owing to a low risk profile, feasibility, and substantial symptomatic improvement due to post-operative cardiovascular remodelling, percutaneous device closure of secundum ASDs should be considered for all haemodynamically significant lesions, regardless of age.

Lessons learned by the author include a lower threshold as a doctor for discounting difficult to interpret symptoms or investigations in respect to cardiac anomalies, an appreciation for the public health system and exemplary collegiate support in times of need.

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Cerebral arterial gas embolism in a professional diver with a persistent foramen ovale

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Abstract

(Wilson C, Sayer MDJ. Cerebral arterial gas embolism in a professional diver with a persistent foramen ovale. *Diving and Hyperbaric Medicine*. 2015 June;45(2):124-126.)
A 33-year-old, male professional scallop diver diving on the Outer Hebrides in Scotland rapidly developed symptoms of cerebral arterial gas embolism following a provocative dive with possibly a fast ascent. During transfer by helicopter to the mainland for treatment, his symptoms improved on surface oxygen. He was recompressed on a Royal Navy Treatment Table 62 (RN TT62) with complete resolution. Just over six weeks later, again diving on the Outer Hebrides and after adopting more conservative diving practices, he developed symptoms and signs of vestibular decompression sickness after a problem-free dive, with dizziness, poor co-ordination and gait, nausea and vomiting, and rotational vertigo. He was again transported to the mainland for recompression treatment. He received an extended RN TT62 and required five further Comex 12 (223 kPa) hyperbaric oxygen treatments over the following three days before he was symptom free. A 4 mm persistent foramen ovale (PFO) was subsequently diagnosed and he underwent successful closure of the defect with Amplatzer device and returned to commercial diving a year later.

Key words
Patent foramen ovale (PFO); persistent foramen ovale; cerebral arterial gas embolism (CAGE); inner ear; hyperbaric oxygen therapy; transcatheter closure; case reports

Introduction

The "*king scallop*" (*Pecten maximus* (L.)) is an edible marine bivalve mollusc; its meat is considered excellent and a luxury product. It occurs and is fished for in large numbers in the eastern Atlantic Ocean.[1] The largest fishery is in the UK with a significant proportion based in Scotland.[1,2] Of all scallops landed in the UK, approximately 2% are fished for by diving, the rest by use of dredges.[2] Scallops caught by diving attract a premium price as real-time selection produces a high-quality catch in terms of size and comes from a sustainable fishery that causes insignificant environmental impact.[3] All commercial diving for shellfish in the UK must adhere to the 1997 Diving at Work Regulations[4] as detailed by the inland/inshore Approved Code of Practice.[5,6] We present the case of a commercial scallop diver who suffered severe decompression illness (DCI) that threatened his livelihood.

Case history

INCIDENT ONE

A fit, 33-year-old male had been a commercial diver for about six years, running his own diving company based on the Outer Hebrides mainly involved in diving for scallops. He had an in-date (less than 12 months old) UK Health and Safety Executive (HSE) commercial diving medical. Past medical history included migraine with aura. Prior to these events he had not had any previous diving-related medical problems.

On the day of the first incident, this was his first dive for four days. He was supposedly diving on nitrox to a maximum depth of 35 metres' sea water (msw) using a *Suunto Gekko* dive computer set to 34% oxygen (estimated pO_2 1.53 bar). Although the computer recorded an ascent warning, the diver reported the dive as problem-free; he surfaced at approximately 10:00 h with a total bottom time of 25 min.

Ten minutes after surfacing he felt increasingly unwell and developed a severe headache and right-sided weakness. This progressed to collapse and probable loss of consciousness; he was subsequently reported by his partner to have had slurred speech on regaining consciousness. At this point he also complained of "*pins and needles*" in his right side. He commenced breathing on oxygen on his dive boat and at about 10:30 h contact was made with the emergency coastguard services. On retrieval by rescue helicopter, he was continued on high-flow oxygen and transferred to the recompression chamber near Oban, arriving at about 12:00 h accompanied by a diver from a neighbouring vessel, though not his diving buddy.

On arrival, he was in a good condition being able to self-transfer, and to provide a history of events; he felt "*almost normal*". He was fully orientated in time and place, speech was normal and he had no nausea or dizziness; he was able to take oral fluids and pass urine. Neurological examination was completely normal. He was recompressed on a Royal Navy Treatment Table 62 (RN TT62) during which he remained comfortable and symptom-free. Prior to discharge the following day after overnight observation in hospital he was advised that as he had had an unprovoked incident of gas embolism he should be assessed for a persistent foramen ovale (PFO) before returning to diving.

INCIDENT TWO

He returned to diving before investigations for a PFO had occurred and had a second incident six weeks later whilst, again, shellfish diving in a North Uist sea loch. He was using nitrox35 (own-blended and tested by himself), though his computer was set at 33%. He did two dives: the first for 40 min to a maximum depth of 24 msw and a second to a maximum depth of 27 msw for 37 min with a surface interval of 113 min, surfacing from the second dive at about 13:30 h; his computer did not show any problems with either dive.

Thirty minutes after surfacing he developed marked dizziness with associated nausea and vomiting. He had difficulty walking and lacked co-ordination. He commenced breathing on his own oxygen and was retrieved by ambulance to a local cottage hospital. Examination on arrival demonstrated gross rotational nystagmus, normal pulse and blood pressure and mild hypothermia at 35°C. He was continued on oxygen, given intravenous fluids and an anti-emetic, cyclizine, and transported to the Oban chamber by rescue helicopter, arriving at 17:50 h.

On arrival, there had been some improvement, though he was still dizzy but with reduced nausea. He had bilateral gaze nystagmus, full power and sensation, finger to nose pointing was normal but he had poor gait and was unable to perform the sharpened Romberg test. During Romberg testing and heel-toe walking he would fall to his right. He was recompressed on a RN TT62, just over four hours after onset of symptoms. During treatment, he showed only partial improvement so the treatment was extended twice at 18 msw and once at 9 msw, surfacing at 01:05 h. He was still dizzy with unsteady gait and abnormal heel-toe walking and Romberg test (falling to the right) and he still had nystagmus on right gaze. He had received five litres of saline from his initial management; he was transferred to the Oban hospital for post-treatment monitoring.

With residual symptoms, he received further recompressions on a Comex 12 (223 kPa) twice daily. By the third day after five additional treatments, he had complete resolution of his symptoms and signs and felt well. He was discharged with advice not to dive until he had been assessed for a vascular right-to-left shunt. He returned to work as a labourer while awaiting investigations. These subsequently demonstrated a 4 mm PFO which was closed by a Amplatzer™ device. A repeat echo demonstrated no intracardiac shunting a year following closure so he returned to diving and has reported no further episodes of diving-related complications.

Discussion

This patient's past medical history stated that he suffered migraine with aura. Migraine with aura is over four times more prevalent in individuals with a PFO than in those without [6,7] and PFOs, or right-to-left shunts, account for large proportions of decompression illness (DCI) cases.[8,9]

This current case study is presented as an example of a commercial diver who may have benefitted from earlier PFO-screening based on past medical history. At present in the UK, guidance provided to Approved Medical Examiners of Divers by the Health and Safety Executive states that: "*Examination for the presence of an intracardiac shunt is not a requirement of either the initial or annual examinations*" and "*However, examination for a patent foramen ovale should be undertaken in a diver who has suffered neurological, cutaneous or cardiorespiratory decompression illness. This is particularly important where there is a history of migraine with aura or where the dive profile was not obviously contributory, since it may be pertinent to an assessment of the overall risk to the diver of continuing to dive. A positive finding is not necessarily a reason for a declaration of unfitness. However, the opinion of a cardiologist with an interest in diving medicine is recommended*".[10]

Even with the heightened risk of DCI in individuals with PFOs, and the increased incidence of PFOs in people experiencing migraines with aura, other recommendations also suggest only screening for a PFO in divers with migraines with aura following at least one episode of DCI.[11] Commercial divers who do screen positive for a PFO may wish to continue diving for reasons of continued employment and may not be able to adopt more conservative diving options open to the recreational diver.[11] In such circumstances, including the present case, referral to a cardiologist to examine the possibility of PFO closure is probably the only available option.[10,11]

The Scottish National Health Service now administers an emergency recompression service based on three facilities: one each for the east and west coasts, and one for the north of Scotland.[12] Since December 2014, guidance provided to commercial divers employing the Inland/Inshore Approved Code of Practice permits contractors of diving operations that are shallower than 50 msw with no more than 20 min of in-water staged decompression to plan for transfer times to a recompression facility of no more than 6 h while making use of emergency services.[13] The present account, with evacuation times of 2 h 15 min and 4 h, demonstrates the goals set by this new guidance to be achievable even in the remotest areas of the UK.

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Diving and percutaneous closure of persistent (patent) foramen ovale

Efrén Martinez-Quintana, Silvia Gopar-Gopar and Fayna Rodriguez-González

Abstract

(Martinex-Quintana E, Gopar-Gopar S, Rodriguez-González F. Diving and percutaneous closure of patent foramen ovale. *Diving and Hyperbaric Medicine*. 2015 June;45(2):126-128.)
Paradoxical arterial gas embolism after diving, in patients with a persistent foramen ovale (PFO) is a potentially catastrophic complication that occurs when gas bubbles occlude blood flow at cardiac or cerebral level. Because the relationship between PFO and decompression illness is currently not clear, we should ensure that patients understand the uncertainties about the efficacy of transcatheter closure of a PFO and the possibility of complications if closure is decided upon. We report a female diver who developed temporary bradycardia, hypotension and evidence of myocardial ischaemia during a closure procedure.

Key words
Scuba diving; persistent foramen ovale; transcatheter closure; side effects; case reports

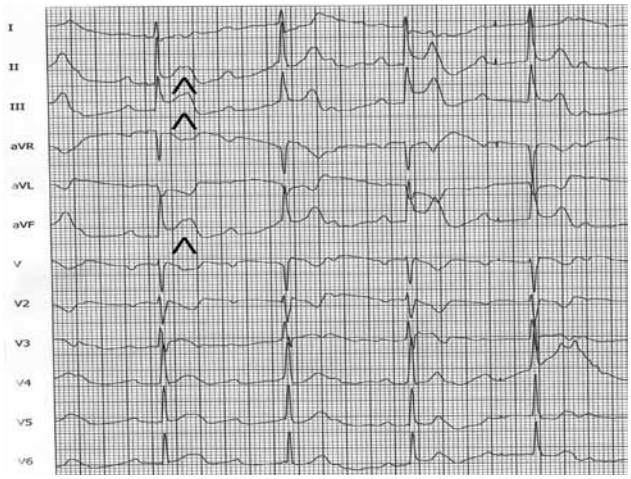
Introduction

Persistent foramen ovale (PFO) is an incomplete closure of the atrial septum that results in the creation of a flap or a valve-like opening in the atrial septal wall. In approximately 25% of the adult population the PFO remains open although symptoms are uncommon. However, in patients who have a PFO and a history of cryptogenic stroke, either aspirin or warfarin therapy is the first therapeutic choice. Meanwhile, percutaneous PFO closure is an acceptable alternative to medical therapy in those patients who have recurrent cryptogenic stroke despite optimal medical therapy.[1] In contrast, guidelines for screening for PFO in divers are difficult to create because the relationship between PFO and decompression illness (DCI) remains unclear and also because DCI is rare and percutaneous closure of PFO or atrial septal defects to prevent recurrent cerebral embolic events may have occasionally serious complications.[2,3]

Case report

A 37-year-old, female professional diver, without cardiovascular risk factors, was referred to our adult congenital heart disease unit for evaluation. The patient had a New York Heart Association functional class I/IV and a history of migraine with aura and tingling in the fingers and

Figure 1
12-lead electrocardiogram showing ST elevation in the inferior leads (arrow heads)



around the mouth in relation to diving. Physical examination revealed normal heart sounds, the extremities were normal with no oedema or venous thrombosis and respiratory and abdominal examination were unremarkable. Because DCI was suspected, transthoracic and transoephageal echocardiography were performed, showing normal left and right ventricular function, normal atria, no valvular heart disease and a PFO with a moderately positive bubble test when agitated saline contrast was administered and Valsalva manoeuvres were done.

For this reason, PFO closure was performed under fluoroscopic guidance with a 30-mm Amplatzer™ multi-fenestrated Septal Occluder ('Cribriform') (St Jude Medical, Inc.; St Paul, MN). However, following the release of the device, the patient developed chest pain, electrocardiographic inferior ST elevation (Figure 1), bradycardia and hypotension. This resolved with volume expansion and narcotic analgesia. Because of this event, coronary angiography was performed, which showed normal coronary arteries and an apparently correctly positioned device (Figures 2 and 3). Transthoracic echocardiography done during the procedure and the following day confirmed correct positioning of the device, with no residual right-to-left shunt.

Discussion

DCI includes both decompression sickness (DCS) and arterial gas embolism (AGE). DCS refers to the clinical syndrome of neurological deficits, pain or other clinical disorders resulting from the body tissues being supersaturated with inert gas after a reduction in the ambient pressure. Meanwhile, AGE describes the penetration of gas bubbles into the systemic circulation, from ruptured alveoli after lung barotrauma or migration from the venous circulation (venous gas embolism) either via a right-to-left

Figure 2
Left coronary artery in the right anterior oblique cranial projection with no significant coronary lesions (LDA – left descending artery; Cx- circumflex artery)

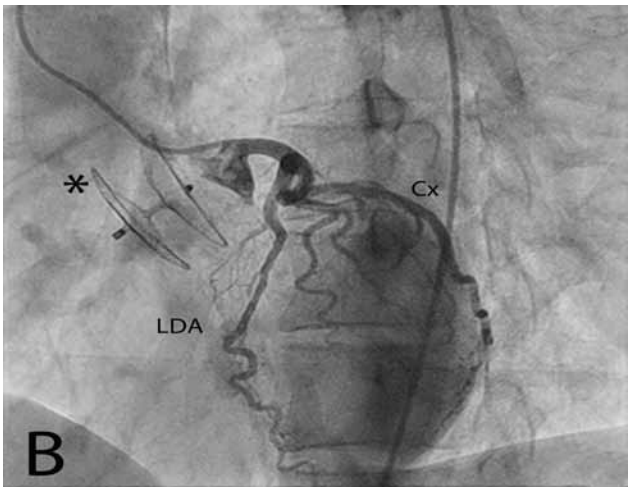
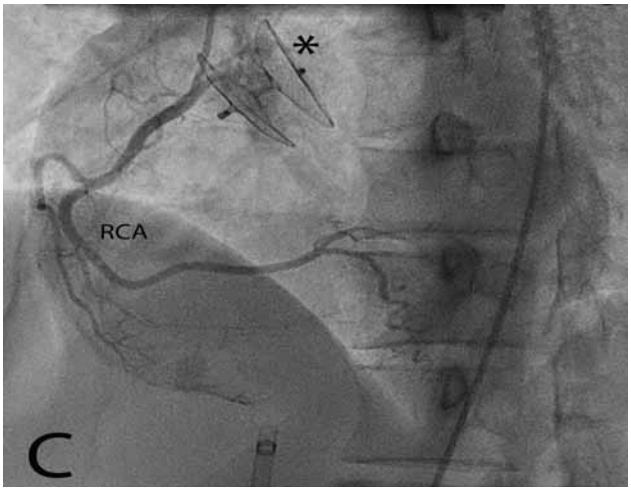


Figure 3
Dominant right coronary artery in the left anterior oblique projection (RCA- right coronary artery) without significant coronary lesions; * shows the position of the Amplatzer™ in Figures 2 and 3



shunt such as a PFO, atrial septal defect (ASD), extra-cardiac shunts or by overwhelming the filtering capacity of the lungs or from within the arterial circulation itself in severe DCS.

Diving often causes the formation of 'silent' bubbles upon decompression. A minor AGE may cause very mild symptoms or none at all. Nonetheless, if the bubble load is high, then the risks of DCS and the number of bubbles that could cross to the arterial circulation via a pulmonary shunt or PFO increase.[4] The symptoms of AGE usually occur during ascent or within a few minutes of surfacing and include mainly neurological and cardiovascular events. Neurological problems are protean, including sudden unconsciousness, motor deficits, seizures, visual

disturbances, aphasia and paraesthesiae. Meanwhile, cardiac problems include myocardial infarction, arrhythmias and sudden death.[5–7] In cases of myocardial infarction, micro-embolic gas bubbles most likely affect the terminal coronary arteries owing to their small size.[5] However, symptoms can sometimes develop more than 48 hours after diving, especially when the patient has travelled to altitude or flown after diving. In this context, paradoxical AGE of the myocardium may be seen as a result of delayed DCS.

Whilst approximately one quarter of the population have a PFO or a small ASD, the risk of paradoxical embolism in the overall sports diving population is very low. Moreover, specific DCS incidents cannot be linked to the presence of a PFO with any degree of certainty. In fact, there is no consensus on the optimal management of divers with a PFO and a history of neurological DCS. Current evidence on the efficacy of percutaneous closure of PFO for the secondary prevention of recurrent paradoxical embolism in divers is inadequate in quality and quantity, and the evidence on safety shows that there is a possibility of serious complications,[8] such as thrombus formation (mostly within the first month after device implantation), device embolization, erosion of cardiac structures leading to aorto-atrial fistula or pericardial tamponade and post- or peri-procedural arrhythmias. Notwithstanding, evaluation for PFO using echocardiography must be considered in divers with severe or repetitive neurological, cutaneous or cardiorespiratory DCS (especially with a history of migraine with aura).[9,10] If it is believed that a diver's repetitive DCS is related to a PFO, reduction of decompression stress in future diving activities by more conservative diving practice may be a better approach than PFO closure in many divers.[9] If closure is proposed for a diver, they should be advised not to dive until the closure has been performed and adequate follow up with repeat bubble contrast echocardiography demonstrates a satisfactory complete closure or only a small residual shunt.

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Joint position statement on persistent foramen ovale (PFO) and diving

South Pacific Underwater Medicine Society (SPUMS) and the United Kingdom Sports Diving Medical Committee (UKSDMC)
David Smart, Simon Mitchell, Peter Wilmshurst, Mark Turner and Neil Banham

Abstract

(Smart D, Mitchell S, Wilmshurst P, Turner M, Banham N. Joint position statement on persistent foramen ovale (PFO) and diving. South Pacific Underwater Medicine Society (SPUMS) and the United Kingdom Sports Diving Medical Committee (UKSDMC). *Diving and Hyperbaric Medicine*. 2015 June;45(2):129-131.)
This consensus statement is the result of a workshop at the SPUMS Annual Scientific Meeting 2014 with representatives of the UK Sports Diving Medical Committee (UKSDMC) present, and subsequent discussions including the entire UKSDMC. Right-to-left shunt across a persistent or patent foramen ovale (PFO) is a risk factor for some types of decompression illness. It was agreed that routine screening for PFO is not currently justifiable, but certain high risk sub-groups can be identified. Divers with a history of cerebral, spinal, inner-ear or cutaneous decompression illness, migraine with aura, a family history of PFO or atrial septal defect and those with other forms of congenital heart disease are considered to be at higher risk. For these individuals, screening should be considered. If screening is undertaken it should be by bubble contrast transthoracic echocardiography with provocative manoeuvres, including Valsalva release and sniffing. Appropriate quality control is important. If a shunt is present, advice should be provided by an experienced diving physician taking into account the clinical context and the size of shunt. Reduction in gas load by limiting depth, repetitive dives and avoiding lifting and straining may all be appropriate. Divers may consider transcatheter device closure of the PFO in order to return to normal diving. If transcatheter PFO closure is undertaken, repeat bubble contrast echocardiography must be performed to confirm adequate reduction or abolition of the right-to-left shunt, and the diver should have stopped taking potent anti-platelet therapy (aspirin is acceptable).

Key words
Patent foramen ovale (PFO); persistent foramen ovale; fitness to dive; decompression illness; transcatheter closure; cardiovascular; health surveillance; medical society

Introduction

This statement was produced from a workshop held at the 43rd Annual Scientific Meeting of the South Pacific Underwater Medicine Society (SPUMS) on 23 May 2014, and following consultation with the United Kingdom Sport Diving Medical Committee (UKSDMC), two members of which attended the meeting (PW and MT). The statement must be interpreted in consultation with a medical practitioner experienced in diving medicine and will be subject to review based on new evidence becoming available.

The levels of evidence defined for the position statement are those promulgated in the 2015 ACCF/AHA Clinical Practice Guideline Methodology Summit Report:[1]

Ia – Evidence from meta-analysis of randomized controlled trials;
Ib – Evidence from at least one randomized controlled trial;
IIa – Evidence from at least one well designed controlled trial which is not randomized;
IIb – Evidence from at least one well designed experimental trial;
III – Evidence from case, correlation, and comparative studies;
IV – Evidence from a panel of experts.

Each statement is followed by identification of the level of evidence in the literature for that statement and the supporting references.

Statement 1

Routine screening for persistent foramen ovale (PFO) (also referred to as 'patent' foramen ovale) at the time of dive medical fitness assessment (either initial or periodic) is not indicated (IV – consensus of SPUMS/UKSDMC).

Statement 2

Consideration should be given to investigating for PFO under any of the following circumstances:

- A history of decompression illness (DCI) with cerebral, spinal, vestibulocochlear or cutaneous manifestations (IIa);[2–8]
- A current or past history of migraine with aura (IIa);[9–15]
- A history of cryptogenic stroke (IIa); [16,17]
- A history of PFO or atrial septal defect (ASD) in a first degree relative (IIa). [18,19]

Statement 3

If screening for PFO is performed, then the following is recommended:

- That testing is undertaken by centres well practiced in the technique (IV – consensus of SPUMS/UKSDMC);
- The screening must include bubble contrast, ideally combined with trans-thoracic echocardiogram (TTE) because this best facilitates cooperation with provocation manoeuvres. Use of two-dimensional and colour-flow echocardiography without bubble contrast is not adequate (IIa);[6,7,20]
- The screening must include the use of provocation manoeuvres to promote right-to-left shunt including Valsalva release and sniffing as described in the supporting references (both undertaken when the right atrium is densely opacified by bubble contrast) (IIa).[6,7]

Statement 4

Interpreting a positive PFO screening result:

- A spontaneous shunt without provocation or a large, provoked shunt is recognized as an unequivocal risk factor for those forms of DCI listed in statement 2 (IIa);[6–8]
- Smaller shunts are associated with a lower but poorly defined risk of DCI. The significance of minor degrees of shunting needs to be interpreted in the clinical setting that led to testing (IIa).[6–8]

Statement 5

Following diagnosis of a PFO considered likely to be associated with increased DCI risk, the diver may consider the following options in consultation with a diving physician:

- Stop diving (IV – consensus of SPUMS/UKSDMC);
- Dive more conservatively: There are various strategies that might be employed to reduce the risk of significant venous bubble formation after diving, or the subsequent right-to-left shunting of such bubbles across a PFO.
  The appropriateness of this approach, and the strategies chosen, need to be considered on an individual basis, and in discussion with a diving medicine expert.
  Examples include: reducing dive times to well inside accepted no-decompression limits; restricting dive depths to less than 15 metres; performing only one dive per day; use of nitrox with air dive planning tools; intentional lengthening of a safety stop or decompression time at shallow stops; avoidance of heavy exercise and unnecessary lifting or straining for at least three hours after diving (IV – consensus of SPUMS/UKSDMC).
- Close the PFO (III).[7,11,21–24]

Statement 6

The options outlined in statement 5 require careful consideration of the risks and benefits and the clinical setting that led to screening (IV – consensus of SPUMS/UKSDMC).[24]

Statement 7

Following closure of a PFO and before returning to diving, the diver requires a repeat bubble contrast echocardiogram demonstrating shunt closure, a minimum of three months after the closure (III).[11,21,22,24]

Statement 8

Diving should not be resumed until satisfactory closure of the PFO is confirmed, and the diver has ceased potent antiplatelet medication (aspirin is acceptable) (III).[11,21,22,24]

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Conflicts of interest

MT acts as a consultant and proctor for St Jude Medical, Medtronic and Edwards Lifesciences, as a consultant and lecturer for Gore Medical and performs PFO closures on private patients. The other authors declare that they have no conflicts of interest.

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Other case reports

Severe methaemoglobinaemia treated with adjunctive hyperbaric oxygenation

Jörg Lindenmann, Nicole Fink-Neuboeck, Gernot Schilcher and Freyja M Smolle-Juettner

Abstract

(Lindenmann J, Fink-Neuboeck N, Schilcher G, Smolle-Juettner FM. Severe methaemoglobinaemia treated with adjunctive hyperbaric oxygenation. *Diving and Hyperbaric Medicine*. 2015June;45(2):132-134.)
Methaemoglobinaemia results from exposure to oxidizing substances such as nitrates or nitrites. Iron within haemoglobin is oxidized from the ferrous to the ferric state, which blocks the transport of oxygen and carbon dioxide, with subsequent inhibition of the respiratory chain. We describe the case of a 23-year-old male suffering from severe methaemoglobinaemia of 68% after consumption of nitrites ('poppers') in association with considerable ethanol consumption. Toluidine-blue was administered as first-line antidotal therapy immediately followed by hyperbaric oxygenation (HBOT). HBOT resulted in enhanced reduction of methaemoglobin, and rapid tissue re-oxygenation by the oxygen dissolved in plasma was provided, independent of the degree of methaemoglobinaemia. The patient recovered uneventfully and was discharged three days later. This case illustrates the potential of supportive HBOT as a time-saving therapeutic tool in this unusual situation, enabling a quick and sustained reduction in methaemoglobinaemia.

Key words
Hyperbaric oxygen therapy; drugs; toxicity; hypoxia; neuroprotection; case reports

Introduction

Acquired methaemoglobinaemia results from exposure to oxidizing substances such as nitrates or nitrites. Iron within the haemoglobin molecule is oxidized from the ferrous state (Fe^{2+}) to the ferric state (Fe^{3+}). This converts haemoglobin to methaemoglobin which blocks the transport of oxygen and carbon dioxide. Due to the subsequent inhibition of the respiratory chain, cellular hypoxia develops, resulting in generalized mitochondrial respiratory insufficiency. Coma occurs rapidly once methaemoglobin levels of 60% of total haemoglobin are reached; death is usually associated with levels of more than 70%.[1,2]

The efficient management of patients suffering from methaemoglobinaemia remains a therapeutic challenge. The gold standard of treatment comprises 100% oxygen and intravenous administration of antidotes, i.e., methylene blue or toluidine blue. Hyperbaric oxygen treatment (HBOT) for severe methaemoglobinaemia is not standard clinical practice and its use remains controversial.[2] We report the case of a young male suffering from severe methaemoglobinaemia, treated with HBOT.

Case report

A 23-year-old male presented suffering from severe methaemoglobinaemia after oral ingestion of nitrites ('poppers') in combination with excessive alcohol consumption whilst at a party. Before the patient was picked up at the scene by the local emergency physician on duty, syncope had developed, followed by vomiting after he regained consciousness. After a brief stop at the nearest peripheral hospital for medical assessment confirming the suspected diagnosis, the patient was transferred to the university hospital because of the presence of a hyperbaric chamber there.

On admission, the patient was fully conscious (Glasgow coma scale 15) and deeply cyanosed, with a dark grey tinge and pronounced blue lips and fingers (Figure 1). Respiratory, cardiovascular and neurological examination was unremarkable. Continuous oxygen was provided

Figure 1
Clinical appearance of the patient's severely cyanotic hand on admission, compared to a normal person's

by mask as intubation and artificial ventilation were not considered to be indicated clinically. Arterial blood pressure was 110/80 mmHg, heart rate 137 beats per minute and temperature 37.1°C. Electrocardiogram revealed sinus tachycardia with no evidence of myocardial ischaemia; cardiac ultrasound confirmed normal function. Chest radiograph was normal.

Blood samples were drawn immediately on admission, before any diagnostic or therapeutic interventions. These revealed a methaemoglobinaemia level of 68% (normal range 0.4–1.0%), lactate 4.1 mmol·L^{-1} (normal range 0.5–2.2 mmol·L^{-1}), haemoglobin 15.7 g·L^{-1} (normal range 13–17.5 g·L^{-1}), haematocrit 45% and a mild leukocytosis. Blood alcohol level was 2.48% (53.9 mmol·L^{-1}) but further drug screening was negative. Samples were analysed according to international laboratory quality standards using the ABL800 FLEX analyzer to the manufacturer's instructions (Radiometer, Bronshoj, Denmark).

Following initial emergency department evaluation, 100 mg intravenous toluidine blue was administered. Immediately thereafter, HBOT (60 minutes 100% oxygen breathing at 303 kPa pressure and 30 minutes at 223 kPa) was initiated. After the first HBOT, the patient was transferred to the intensive care unit for further continuous oxygen administration combined with haemodynamic and respiratory monitoring. At this time, his cyanosis had reduced considerably, and laboratory values, apart from an increased leukocytosis, were improved (Table 1). After the second HBOT, the patient was transferred to the regular ward. The patient remained in a stable condition, and after a third HBOT, laboratory values had normalised (Table 1). His further course was uneventful, and he was discharged on the third day.

Discussion

A variety of different chemicals are capable of producing elevated levels of methaemoglobin, although nitrites or nitrobenzenes represent the most common causative substances. Inhalation of nitrous oxide or oral intake of nitrites ('poppers') is observed commonly amongst young adult party-goers. The rare but sometimes harmful consequences of these compounds are not well recognised and, therefore, underestimated in many cases.[3] Methaemoglobinaemia results in considerable cellular hypoxia and respiratory insufficiency. The clinical course in the present case, without any neurological sequelae, is noteworthy considering the fact that levels of methaemoglobinaemia exceeding 60–70% of total haemoglobin are usually associated with sudden coma and death.[1,2]

Up to now, intravenous administration of toluidine blue is the first-line antidote in the emergency treatment of patients with methaemoglobinaemia.[4,5] Toluidine blue (or methylene blue) accelerates the enzymatic reduction of methaemoglobin by NADPH-methaemoglobin reductase resulting in increasingly unblocking the respiratory chain. This vital process can be speeded up by adjunctive HBOT because the half-life of methaemoglobin is reduced by the higher oxygen partial pressures under hyperbaric conditions due to its competitive binding to the haemoglobin molecule. An additional rationale for using HBOT is based on the increased oxygen physically dissolved in the plasma while the patient is breathing 100% oxygen under elevated ambient pressure. At 283 kPa, the solubility of oxygen in whole blood is increased by approximately 6 vol%, approximately 300 ml of oxygen in a 5 L blood volume, which is sufficient for human basal metabolism, temporarily obviating the need for haemoglobin-bound oxygen transport under these conditions.[2,4,6,7]

To our best knowledge, this is the first report of HBOT in a case of severe methaemoglobinaemia, where the affected patient remained completely stable without deep unconsciousness throughout his entire course, although he also had excessive alcohol consumption. Notwithstanding that he was conscious and in a stable condition, this was a life-threatening situation. The loss of consciousness before admission, the concomitant ethanol poisoning and a methaemoglobinaemia of 68% represent three unpredictable components which might have resulted in sudden deterioration of the patient´s general condition resulting in possible cardiac arrest. Considering these factors and the clinical outcomes reported in the recent literature, HBOT appears to have served as an important supportive treatment option in this case.[2,4]

Table 1

Methaemoglobin levels, lactate and arterial blood gases before and after treatment

HBOT – hyperbaric oxygen treatment; MetHb – methaemoglobin; O_2Hb – oxyhaemoglobin; COHb – carboxyhaemoglobin; HHb – deoxyhaemoglobin; pO_2 – oxygen partial pressure; pCO_2 – carbon dioxide partial pressure; SO_2 – oxygen saturation; n/a – not applicable

	MetHb (%)	O_2Hb (%)	COHb (%)	HHb (%)	pO_2 (mmHg)	pCO_2 (mmHg)	pH	SO_2 (%)	Lactate (mmol·L^{-1})
On admission	68	30	1.6	2.3	135	34	7.39	99	4.1
After 1st HBOT	26	74	1.2	1.2	270	36	7.44	98	2.6
After 2nd HBOT	0.9	97	2.5	1	98	40	7.43	97	1.3
After 3rd HBOT	0.9	n/a	2.7	n/a	n/a	n/a	n/a	n/a	1.1

HBOT may be used as a sole treatment or combined with systemic administration of methylene blue.[2,4,8–10] When used, HBOT has been found to decrease the methaemoglobin level at a rate of about 8% per hour of exposure.[11] Due to the lack of a standardized treatment algorithm for HBOT in severe methaemoglobinaemia, and regarding the somewhat similar toxic mechanisms to that of carbon monoxide (CO) poisoning, we modified the HBOT protocol used for CO poisoning.[12] HBOT was initiated at a pressure of 303 kPa and daily treatments were given over three days.

In conclusion, the combination of toluidine blue or methylene blue administration and adjunctive HBOT enables a rapid and sustained reduction of methaemoglobinaemia in a severe poisoning. HBOT is a time-saving therapeutic tool that not only accelerates the elimination of methaemoglobin but may also have a protective effect against neurological sequelae from hypoxia by enhancing oxygen delivery to vital organs at a critical time.

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Acknowledgement

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Letters to the Editor

Inner-ear decompression sickness: 'hubble-bubble' without brain trouble?

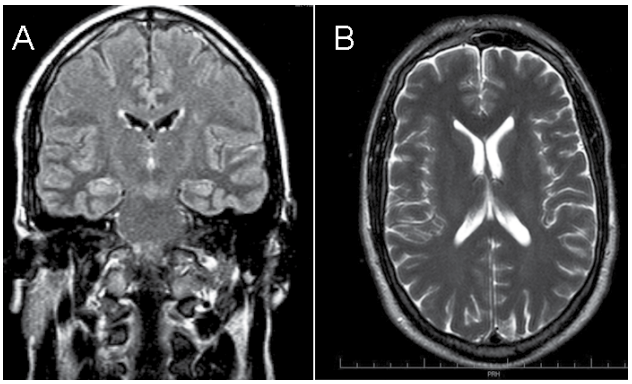
Inner-ear decompression sickness (DCS) is an incompletely understood and increasingly recognized condition in compressed-air divers. Previous reports show a high association of inner-ear DCS with persistent foramen ovale (PFO),[1,2] suggesting that a moderate-to-severe right-to-left shunt might represent a major predisposing factor, and more properly defining it as an event from arterial gas embolism (AGE). However, other conditions characterized by bubbles entering the arterial circulation, such as open-chamber cardiac surgery, do not produce inner-ear involvement, while sometimes damaging the brain extensively.[3] Moreover, in other sites, such as the spinal cord, the prevailing mechanism for DCS is not AGE, but more likely local bubble formation with subsequent compression of venules and capillaries. Thus, AGE might be, more properly, a predisposing condition, neither sufficient, nor possibly even strictly necessary for inner-ear DCS.[2]

A 'two-hit hypothesis' has been proposed, implying a locally selective vulnerability of the inner ear to AGE.[3] Modelled kinetics for gas removal are slower in the inner ear compared to the brain, leading to a supersaturated environment which allows bubbles to grow until they eventually obstruct the labyrinthine artery.[3] Since this artery is relatively small, there is a low probability for a bubble to enter it; this might explain the disproportion between the high prevalence of PFO in the general population (25–30%) and the very low incidence of inner-ear DCS in compressed-air diving (approximately 0.005%).[1,4]

Furthermore, given that the labyrinthine artery usually originates either from the anterior inferior cerebellar artery, or directly from the basilar artery, shunting bubbles will more frequently swarm through the entire brain.[3] In this case, however, the brain's much faster gas removal kinetics might allow for them to be reabsorbed without damaging brain tissue. In line with this scenario is the low probability (approx. 15%) of inner-ear DCS presenting with concomitant symptoms suggestive of brain involvement.[1] Interestingly, PFO is a putative risk factor not only for DCS but also for ischaemic stroke, and it has been hypothesized that a predominantly silent ischaemic cerebral burden might represent a meaningful surrogate of end-organ damage in divers with PFO, with implications for stroke or cognitive decline.[5,6]

Here we report the case of a 44-year-old diving instructor (> 350 dives) who suffered from inner-ear DCS about 10 min after a routine dive (5 min/40 metres' fresh water (mfw), ascent 7.5 mfw·min^{-1}, stop 10 min/5 mfw), resulting in severe left cochlear/vestibular impairment (complete deafness and marked vertigo, only the latter slowly receding after a few hours). The patient was not recompressed. A few months later, transcranial Doppler ultrasonography demonstrated a moderate-to-severe shunt (> 30 bubbles), presumably due to a PFO (he refused confirmatory echocardiography), while a brain MRI (1.5 T) was reported as negative for both recent and remote lacunar infarcts (Figure 1).

Figure 1
(A) Coronal FLAIR and (B) axial T2W brain MR images



We believe this may be evidence that inner-ear DCS could occur while the brain is completely spared, not only clinically, but also at neuroimaging. This would support either of two hypotheses: (a) that the brain is indeed relatively protected from arterial bubbles that preferentially harm the inner ear where, however, they only rarely infiltrate, or (b) that direct bubble formation within the inner ear cannot be completely discarded, and that the elevated PFO/inner-ear DCS association might be, in this latter case, merely circumstantial. We favour the hypothesis that inner-earDCS might be related to AGE in an anatomically vulnerable region. More precise data regarding the exact incidence of inner-ear involvement, isolating those subjects with moderate-to-severe shunt should be obtained before exploring the risk-to-benefit ratio given by transcatheter occlusion of a PFO for prevention of inner-ear DCS; odds that could end up to be sensibly different with respect to other types of DCS presentation.[7]

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Key words
Inner ear; decompression illness; persistent foramen ovale; case reports; letter (to the Editor)

Grommets in HBOT patients: GA vs LA, unanswered questions

We read with interest the article on grommet procedures for patients undergoing hyperbaric oxygen therapy (HBOT),[1] and have a number of comments. It appears the authors may have missed a number of cases. In a previous paper from The Townsville Hospital Hyperbaric Unit (TTH HMU), Commons et al presented 14 of 106 patients (13%) who required grommets over the period between June 2009 and May 2010.[2] These patients are included in the Lamprell et al data set. Figure 1 shows an apparent spike in their cases in 2010 (n = 13, part of the period covered in the previous paper) when compared to the remaining four years of their study (mean number of cases 4.5 per year, for an incidence of 3%). This difference in incidence is statistically significant ($\chi^2 = 8.336$, df = 1, $P = 0.004$).

We suspect the difference may be the result of missed cases rather than a true spike; however, it is not possible to determine this from the paper. Lamprell et al describe identifying cases using the TTH HMU patient database. Did the authors also consider using the operating theatre database and/or ENT clinic records to ensure all cases were captured?

We also have concerns regarding Lamprell's primary outcome measure: time from ENT referral to date of re/commencement of HBOT. These data are presented as median values with the associated ranges, rather than an interquartile range (IQR), the traditional measure of dispersion in non-parametric data. We believe the data sets contain a number of outliers that should be excluded, e.g., 98 days. We ask to see the IQRs and box-and-whisker plots for both data sets, and suspect the statistically significant difference in medians might not remain with outliers excluded from the analysis. There is also no discussion about the clinical relevance of this difference of seven days. Based on the most common indications for HBOT listed, most patients would have received at least 30 daily sessions of HBOT. What impact does a delay of seven days have on their treatment?

As doctors who have worked at this HMU, we know patients preferentially received their grommets under GA prior to 2012 at the request of the ENT surgeon, who believed that insertion under LA was poorly tolerated. The authors do not describe whether the insertion of grommets under LA was associated with patient discomfort; a limitation of this retrospective paper, but a clinically relevant factor in the decision-making process of which form of anaesthesia to use.

The paper by Lamprell et al has shown us that patients may experience a more rapid insertion of grommets and return to HBOT, if inserted under LA versus GA, but this difference may not be important clinically. We believe the authors may have failed to collect all cases and exclude outliers and this, coupled with the lack of documentation about patient satisfaction with insertion under LA, leaves us with more questions than answers.

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Key words
Ear barotrauma; middle ear; ENT; hyperbaric oxygen therapy; letters (to the Editor)

Correction

Correction and response to: Grommets in HBOT patients: GA vs. LA, unanswered questions

We thank Gibbs and Commons for their interest in our paper.[1] There is a key difference between the datasets for Commons et al and our study.[2] Our data set, has grouped five years of data according to the calendar year. This is different from Commons et al's study population recruited between 01 June 2009 and 31 May 2010. We feel this may explain the difference of one case between the two papers in 2010.

Our data collection used the standard clinic and operating theatre databases, and we were advised that there was no searchable clinical code for grommet procedures undertaken with local anaesthetic (LA) in the outpatient clinic. The alternative, to review many hundreds of patients, was considered beyond the study's scope. Instead, the TTH Hyperbaric Medicine Unit (HMU) database was used to recruit cases and cross checked with operating theatre data.

We have since re-investigated the operating theatre database to identify any additional bilateral grommet procedures during 2008 to 2012 and cross checked these with the HMU database. This has identified one to four additional patients per year in the general anaesthesia (GA) group and one additional LA patient that meet the criteria for recruitment into the study. There was one further unconfirmed patient from each of 2008 and 2010, whose charts were unavailable for this response, and have not been included in this amendment. The corrected Figure 1 reflects these changes.

Despite the additional cases, the frequency spike during 2010 remains. A published audit of the number of middle ear barotrauma (MEBT) cases between 2007-2010 also reports an increased incidence of MEBT in 2009–2010 compared with previous years at our unit.[3] Possible reasons for this may be the introduction of new technology at the unit, in the form of the digital Macro View™ otoscope during this period, leading to a possible change in clinical practice and an increased detection of MEBT, or a lower threshold for ENT referral for grommet placement. Alternatively, a 'Hawthorne effect' from the conduct of a prospective study within the TTH HMU, during 2009–2010 may be considered.[4] With the outliers removed using ROUT's test,[5] the significant difference in the delay time to surgery remains (LA median 1, IQR 2, range 0–5 days; GA median 7.5, IQR 6, range 0–24 days; $P < 0.0001$; Figure 2).

The data values of 98 days and 86 days from the GA group published in our paper are corrected to six days and 12 days respectively. On review, the first individual was found to have had two HBOT courses, and it was only in the second round of HBOT that an ENT referral for grommets was made. The second individual was found to have been offered two ENT referrals after experiencing MEBT, the first

Figure 1
Number of patients per year identified in the databases

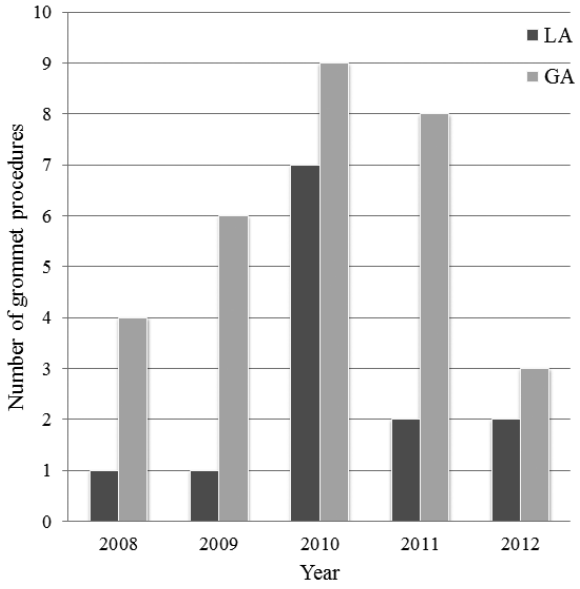
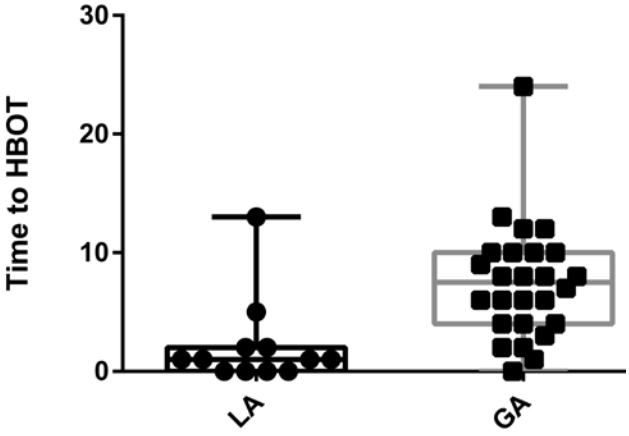


Figure 2
Box and whisker plot of the delay time to surgery remains (LA – local anaesthesia; GA – general anaesthesia



was followed by the patient declining further HBOT until representing to TTH HMU four months later and receiving prophylactic grommets before recommencing HBOT; this second ENT referral date has been used in the amended data. These corrections have not been found to change the primary outcome of statistical significance between the LA and GA groups.

A delay of seven days may not be considered clinically relevant in the most common cases requiring HBOT, aside from affecting patient convenience and logistics as well as hospital efficiency and resources. In emergency cases, knowledge of factors able to reduce the delay for grommet insertion is clinically relevant. In centres where a long wait for GA is the norm, LA may convey a clinically important lesser waiting time.

As a retrospective study, only data documented in the patient records could be studied, and patient discomfort was not consistently recorded in the charts. We would liken this to undertaking other surgical procedures, where clinicians often do not routinely document pain scores for the benefit of retrospective research. Several studies have examined patients' tolerance of grommets under LA, finding the technique tolerable.[6,7]

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Key words
Corrections; ear barotrauma; middle ear; ENT; hyperbaric oxygen therapy

Continuing professional development

Persistent (patent) foramen ovale and diving

Peter Germonpré

Accreditation statement

INTENDED AUDIENCE
The intended audience consists of all physicians subscribing to *Diving and Hyperbaric Medicine* (DHM), including anaesthetists and other specialists who are members of the Australia and New Zealand College of Anaesthetists (ANZCA) Diving and Hyperbaric Medicine Special Interest Group (DHM SIG). However, all subscribers to DHM may apply to their respective CPD programme coordinator or specialty college for approval of participation.

This activity, published in association with DHM, is accredited by the ANZCA Continuing Professional Development Programme for members of the ANZCA DHM SIG under Learning Projects: Category 2 / Level 2: 2 credits per hour.

OBJECTIVES
The questions are designed to affirm the takers' knowledge of the topics covered, and participants should be able to evaluate the appropriateness of the clinical information as it applies to the provision of patient care.

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

DO I HAVE TO PAY?
All activities are free to subscribers.

Key words
Patent Foramen Ovale (PFO); persistent foramen ovale; decompression illness; risk factors

Recommended background reading

Practitioners are referred to the following background references as well as the papers in this issue.

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How to answer the questions

Please answer all responses (A to E) as True or False. Answers should be posted by email to the nominated CPD coordinator.
EUBS members should send their answers to Lesley Blogg
E-mail: <lesley.blogg@eubs.org>
ANZCA DHM SIG and other SPUMS members should send their answers to Neil Banham
E-mail: <Neil.Banham@health.wa.gov.au>
If you would like to discuss any aspects with the author, contact him at**:** <peter.germonpre@eubs.org>

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

Question 1. Patent foramen ovale contributes to the risk of decompression sickness by

A. increasing pulmonary artery pressure beyond left atrial pressure;
B. being a preferred place for thrombus formation;
C. increasing the cardiac output and thus nitrogen saturation;
D. allowing paradoxical embolization of venous gas bubbles;
E. generating post-decompression bubbles by cavitation.

Question 2. The prevalence of patent foramen ovale in divers

A. is approximately 2.5 times higher than in the normal population;
B. is lower than in the non-diving population;
C. is higher in female divers than in male divers;
D. is higher in divers with a history of neurological decompression sickness only when occurring early after surfacing;
E. is higher in smokers than in non-smokers.

Question 3. The degree of shunting through a PFO

A. does not depend on the anatomical size of the PFO;
B. correlates with the risk for DCI in retrospective studies;
C. can be estimated using correctly executed contrast imaging studies, or by injecting contrast medium in the femoral vein;
D. is only one of many factors that determine the risk of DCI;
E. is increased by performing sustained Valsalva-like straining manoeuvres.

Question 4. Screening for / diagnosing PFO in divers

A. is warranted because the absolute risk for neurological DCI is high when PFO is present;
B. is not indicated in divers who have not suffered from DCI;
C. should be done before starting high-risk diving because preventive PFO closure is possible;
D. must be considered if the diver has had pain-only DCI;
E. is warranted in smokers.

Question 5. Scientifically sound advice for divers who worry about the possibility of having a PFO, should

A. include a detailed explanation on the significance of PFO in diving;
B. encourage them to dive conservatively, using proven 'low bubble' diving techniques, such as no-stop diving, using nitrox on air profiles, avoiding the limits of the dive computer;
C. advise them not to perform strenuous exercise shortly after the dive, as right-to-left shunting through a PFO or pulmonary arteriovenous anastomoses may be increased;
D. encourage them to have a PFO test with a cardiologist knowledgeable in diving medicine;
E. encourage them to undergo brain MRI to detect cerebral lesions.

Notices and news

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

SPUMS Annual Scientific Meeting 2016
Preliminary notice
Diver resuscitation: in and out of the water

Dates: 15–21 May
Venue: Intercontinental Fiji Golf Resort and Spa, Natadola Coast
Probable speakers include: Chris Lawrence, Simon Mitchell, John Lippmann, Mike Bennett; the 2015 revised BLS/ALS guidelines reviewed.
Full information to come soon on the SPUMS website

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

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

ANZ Hyperbaric Medicine Group Introductory Course in Diving and Hyperbaric Medicine

Dates: 22 February–04 March 2016
Venue: The Prince of Wales Hospital, Randwick, Sydney
Cost: AUD2,400.00 (inclusive of GST)
Course Conveners: Associate Professor David Smart (Hobart), Dr John Orton (Townsville)

The Course content includes:
- History of diving medicine and hyperbaric oxygen treatment
- Physics and physiology of diving and compressed gases
- Presentation, diagnosis and management of diving injuries
- Assessment of fitness to dive
- Accepted indications for hyperbaric oxygen treatment
- Wound management and transcutaneous oximetry
- In water rescue and simulated management of a seriously ill diver
- Visit to HMAS Penguin
- Practical workshops
- Marine Envenomation

Approved as a CPD learning project by ANZCA: (knowledge and skills category)
56 hours for attendance at lectures and presentations for one credit per hour
24 hours for workshops/PBLDs/small group discussions for two credits per hour

Contact for information:
Ms Gabrielle Janik, Course Administrator
Phone: +61-(0)2-9382-3880
Fax: +61-(0)2-9382-3882
E-mail: <Gabrielle.Janik@sesiahs.health.nsw.gov.au>

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

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

All details are available on the ANZCA website at:
<http://anzca.edu.au/edutraining/DHM/index.htm>
or:
Suzy Szekely, FANZCA, Chair, ANZCA/ASA Special Interest Group in Diving and Hyperbaric Medicine.
E-mail: <Suzy.Szekely@health.sa.gov.au>

Advertising in *Diving and Hyperbaric Medicine*

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

Details of advertising rates and formatting requirements are available on request from:
E-mail: <editorialassist@dhmjournal.com>

Erratum

In the paper Blake DF, Young DA, Brown LH. Transcutaneous oximetry: normal values for the lower limb. *Diving Hyperb Med*. 2014;44:146-53, the first reference was incorrectly cited. This should have read: Huch R, Huch A. Fetal and maternal $P_{tc}O_2$ monitoring. *Crit Care Med*. 1981;9:694-7.

SPUMS Diploma in Diving and Hyperbaric Medicine

Requirements for candidates (May 2014)

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

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

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

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

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

Additional information – prospective approval of projects is required

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

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

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

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

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

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

With respect to 1 above, for unforeseen delays where the project will exceed three years, candidates must advise the Education Officer in writing if they wish their diploma project to remain active, and an additional three-year extension will be granted.
With respect to 2 above, if there are extenuating circumstances that a candidate is unable to maintain financial membership, then these must be advised in writing to the Education Officer for consideration by the SPUMS Executive.

If a project has lapsed, and the candidate wishes to continue with their DipDHM, then they must submit a new application as per these guidelines.

The Academic Board reserves the right to modify any of these requirements from time to time.
As of June 2014, the SPUMS Academic Board consists of:
Dr David Wilkinson, Education Officer;
Associate Professor Simon Mitchell;
Associate Professor (retired) Mike Davis;
Dr Denise Blake.

All enquiries and applications should be addressed to:
David Wilkinson
Fax: +61-(0)8-8232-4207
E-mail: <education@spums.org.au>

Key words
Qualifications; underwater medicine; hyperbaric oxygen; research; medical society

Notices and news

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

41st EUBS Annual Scientific Meeting 2015

Dates: 19–22 August
Venue: The Academic Medical Center (AMC), Amsterdam

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

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

Albert van den Brink, General Secretary
For more information and to register: <www.eubs2015.org>

EUBS President's message

Dear Friends,

After three years as your President, I am about to let the floor to the next President, Jacek Kot. At the start of a new presidency many open questions remain to be resolved. For EUBS, these include: an electronic version of *Diving and Hyperbaric Medicine*; downloading of individual articles; the opening of journal subscriptions to non-members; increasing the journal's impact; fostering young scientists and doctors to join EUBS; sponsoring educational courses; organizing the next tricontinental meeting with SPUMS and SAUHMA; ensuring that *The Science of Diving* is not the only book to benefit EUBS, etc…

Certainly the close collaboration that now exists between SPUMS and EUBS and our shared aims will help to achieve sensible decisions on many of these issues. Complimentary to this, we should also acknowledge the increasingly close collaboration with the UHMS, evident, for instance, through their offer to EUBS and SPUMS members of a 50% discount on the registration fee for their fortieth anniversary meeting in Puerto Rico in 2017.

Returning to Jacek, I am very happy that he is taking over at the August ASM. With his long experience in international organisations, and as an academic member of a Polish University and Medical Director of the National Center for Hyperbaric Medicine in Gdynia, Poland, he will provide a perfect bridge between UHMS and EUBS, as much on the diving as on the hyperbaric medicine side. As you can see, he is very gifted and dedicated; I am more than assured that he will do a great job for our society. Last but not least, he is the happy father of twins, as am I!

All the best!

Costantino Balestra, President EUBS
E-mail: *<costantino.balestra@eubs.org>*

EUBS Elections

Elections will be held for the EUBS Member-at-Large 2015 and Vice-President positions. All members will receive an internet ballot sheet in the course of the month of June and should vote electronically. If no ballot sheet is received by the end of June, please contact Peter Germonpré at:
E-mail: <secretary@eubs.org>

Important message: Do not renew your EUBS membership until January

During our last Meeting in Wiesbaden 2014, the EUBS General Assembly decided to change the Membership year timings. Instead of running from 01 July to 30 June, it will, as from now, run from 01 January to 31 December. Although you might have received an e-mail reminder, please disregard this and wait until January.

International Meeting on Ultrasound for Diving Research – Ultrasound 2015

Dates: 25–26 August
Venue: The Swedish Armed Forces Diving and Naval Medical Centre (DNC), Karlskrona, Sweden

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

Convenors: Lesley Blogg (SLB Consulting) and Andreas Møllerløkken (NTNU Norway)

To register, please visit:
<ultrasound2015.wix.com/ultrasound2015>
Facebook: <www.facebook.com/Ultrasound2015>
E-mail: <ultrasound2015@yahoo.co.uk>

Advanced Professional Diving Medicine 1st course according to EDTC Training Standards

Dates: 03–10 October
Venue: Institut National de la Plongée Professionnelle (INPP), Marseille (France)

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

Speakers/Faculty: Alf Brubakk, Alain Barthélemy, Marc Borgnetta (Course director), Michel Hugon, Pasquale Longobardi, Jack Meintjes, Roland van den Eede, Jürg Wendling.

For further information and applications:
<www.edtcmed.ch >

British Hyperbaric Association ASM 2015

Dates: 22–24 October
Venue: National Exhibition Centre, Birmingham

Jointly with the UK Sport Diving Medical Committee (UKSDMC) and chosen to coincide with DIVE 2015.
The content of 22–23 October will be aligned to the requirements of refresher training for Health and Safety Executive-approved Medical Examiners of Divers.

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

Scott Haldane Foundation

The Scott Haldane Foundation is dedicated to education in diving medicine, organizing more than 180 courses over the past 20 years. In 2015 SHF will organize more courses then ever, targeting an international audience.

The courses Medical Examiner of Diver (parts I and II) and the modules of the Diving Medicine Physician course comply fully with the ECHM/EDTC curriculum for Level 1 and 2d respectively and are accredited by the European College of Baromedicine.

SHF courses for 2015
25–26 August: International Meeting on Ultrasound for Diving Research; Karlskrona, Sweden
3 October: ENT and diving refresher course; Rotterdam, Netherlands
7–14 November: Basic course diving medicine (level 1 part 1); Kubu, Bali
14–21 November: 23rd SHF In-depth course "*A life long diving*" (full); Kubu, Bali
21–28 November: 23rd SHF In-depth course "*A life long diving*"; Kubu, Bali

For further information: <www.scotthaldane.org>

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

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

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

Hyperbaric Oxygen, Karolinska

Welcome to: <http://www.hyperbaricoxygen.se/>.
This site, supported by the Karolinska University Hospital, Stockholm, Sweden, offers publications and free, high-quality video lectures from leading authorities and principal investigators in the field of hyperbaric medicine.

You need to register to obtain a password via e-mail. Once registered, watch the lectures online, or download them to your iPhone, iPad or computer for later viewing.

For further information contact:
Folke Lind, MD PhD
E-mail: <folke.lind@karolinska.se>
Website: <www.hyperbaricoxygen.se>

Royal Australian Navy Medical Officers' Underwater Medicine Course 2015

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

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

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

For information and application forms contact:
Rajeev Karekar, for Officer in Charge,
Submarine and Underwater Medicine Unit
HMAS PENGUIN
Middle Head Rd, Mosman
NSW 2088, Australia
Phone: +61-(0)2-9647-5572
Fax: +61-(0)2-9647-5117
E-mail: <Rajeev.Karekar@defence.gov.au>

German Society for Diving and Hyperbaric Medicine

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

Royal Adelaide Hospital Hyperbaric Medicine Unit Courses 2015

Medical Officers' Courses
30 November – 04 December: Basic
07–11 December: Advanced

DMT Refresher Courses
14–18 September
21–25 September

All enquiries to:
Lorna Mirabelli, Course Administrator
Phone: +61-(0)8-8222-5116
Fax: +61-(0)8-8232-4207
E-mail: <Lorna.Mirabelli@health.sa.gov.au>

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/>

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

DIVER EMERGENCY SERVICES PHONE NUMBERS

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

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

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

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

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

UNITED KINGDOM
+44-7740-251-635

USA
+1-919-684-9111

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

DAN ASIA-PACIFIC DIVE ACCIDENT REPORTING PROJECT

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

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

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

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

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

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