# Diving and Hyperbaric Medicine

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EUBS

## The first ultra-deep rebreather dive using hydrogen

**Searching biomed databases for HBOT trials**

**Treating infants with hyperbaric oxygen**

**HBOT effect after in vivo ovarian torsion**

**Decompression procedures for saturation dives**

**Chain of events in non-fatal diving accidents**

**Outcome measures for necrotising infection studies**

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## PURPOSES OF THE SOCIETIES

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



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## DIVING AND HYPERBARIC MEDICINE

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# The Editor's offering

Welcome to the first issue of DHM for 2024! It contains a great mix of articles across both hyperbaric medicine and diving subdisciplines.

Hira Khan and colleagues have performed an interesting evaluation of the utility of various biomedical databases in identifying randomised studies involving hyperbaric oxygen treatment (HBOT). The insights into which databases provide the greatest sensitivity and precision are extremely valuable. The finding that 14% of 367 references were unique to single databases reinforces the idea that for a thorough review, multiple databases need to be searched.

Kubra Ozgok Kangal and Bengusu Mirasoglu report on their experience and strategies in treating 54 infants (< 12 months age) with HBOT. As they point out, this is a patient group who may be overlooked for HBOT even in the face of appropriate indications (most of their patients were treated for carbon monoxide [CO] poisoning) because of the challenges of providing treatment.

Eralp Bulutlar and colleagues report an experiment utilising a rat model of ovarian torsion – detorsion, effectively an ischaemia-reperfusion injury, in which HBOT after detorsion provided some protection against injury measured using certain biochemical and histologic indices. The authors suggest that a human study may now be appropriate.

JP Imbert has teamed with a group of authors with experience in saturation diving to provide a fascinating window on decompression from saturation dives. In many respects this can be seen as a review, but it is published as an original article because the authors went to the trouble of obtaining original data by surveying companies active in saturation diving to report contemporary approaches. Obtaining such information in an industry sometimes considered secretive is no small feat, and speaks to the respect these authors hold in that community.

Benjamin Turner and colleagues have adopted the 'chain-of-events' analysis typically applied to analysing diving fatalities, and used it to evaluate non-fatal accidents in a relatively young cohort of divers. It is fascinating to contemplate how the different predisposing factors, triggers, disabling agents, and disabling conditions identified in this study differ from those producing fatalities in other reported series of (frequently older) divers. It seems likely that this methodology will be applied to other cohorts of divers suffering non-fatal accidents.

Jonathan Wackett and colleagues report a comprehensive review to identify the various ways in which treatment outcomes for necrotising soft tissue infections have been reported. The ultimate goal is to establish a widely adopted core outcome set that would facilitate data pooling, or indeed, a large multicentre study of an intervention like HBOT. The fact that there were over 300 outcome measures reported across 375 studies simultaneously illustrates the difficulty and importance of this initiative.

In one of our occasional 'World as it is' articles, Bridget Devaney provides a very thoughtful evaluation of the concept of equipoise as it pertains to the ethics of joining a trial of HBOT for an indication where use of HBO is already partly accepted (at least by some). Her focus is on necrotising infections, but the principles she articulates could apply to any similar situation, and I believe this is an extremely valuable article.

There are three case reports in this issue. Ryota Tsushima and colleagues present a case that reminds us of the infrequently reported phenomenon of secondary deterioration after initial recovery following arterial gas embolism. They conclude that HBOT should be provided irrespective of any spontaneous improvement in such cases. Zebedee Wong and colleagues report a case of apparently successful treatment of severe delayed neurological sequelae after CO poisoning using HBOT. There is nothing unusual about treating CO poisoning with HBOT, but it is much less common to see reports of HBOT being used for delayed sequelae. Richard Harris and colleagues report the first use of hydrogen as a breathing gas in an ultra-deep (230 m) bounce dive using electronic closed-circuit rebreathers. In this single dive, the use of hydrogen below 200 m depth appeared to reduce symptoms of high-pressure neurological syndrome in a vulnerable diver.

Finally, after 53(4) last year, this is the second issue to which we are publishing a supplement. In this case it is a book chapter on decompression illness (DCI) written by myself for the pending Oxford Handbook of Diving and Hyperbaric Medicine. Owing to confusion over length and referencing, this work is too detailed / long and vastly over-referenced for an Oxford Handbook. Moreover, the handbook project has been delayed. There is no contemporary 'big book' chapter on DCI and rather than lose this one, the publishers have graciously given permission for it to be published in present form. While not exhaustive, it can be regarded as a comprehensive overview of pathophysiology, manifestations, prevention and treatment of decompression sickness and arterial gas embolism. It may be useful as a discrete package of educational material in diving medicine courses. It will be significantly shortened and updated at the time the handbook project moves forward.

*Professor Simon Mitchell*
*Editor*

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**Photo caption:** Dr Richard Harris about to leave surface in conducting a rebreather dive to 230 m breathing helihydrox below 200 m, Pearse Resurgence, New Zealand, February 2023.

# Original articles

## Efficacy of searching in biomedical databases beyond MEDLINE in identifying randomised controlled trials on hyperbaric oxygen treatment

Hira Khan[1], Mohammad Sindeed Islam[2], Manvinder Kaur[3], Joseph K Burns[1,3], Cole Etherington[1,3], Pierre-Marc Dion[2], Sarah Alsayadi[4], Sylvain Boet[1,3,5,6]

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**Keywords**
Biomedical databases; Research methods; Systematic review

**Abstract**
(Khan K, Islam MS, Kaur M, Burns JK, Etherington C, Dion P-M, Alsayadi S, Boet S. Efficacy of searching in biomedical databases beyond MEDLINE in identifying randomised controlled trials on hyperbaric oxygen treatment. Diving and Hyperbaric Medicine. 2024 31 March;54(1):2–8. doi: 10.28920/dhm54.1.2-8. PMID: 38507904.)
**Introduction:** Literature searches are routinely used by researchers for conducting systematic reviews as well as by healthcare providers, and sometimes patients, to quickly guide their clinical decisions. Using more than one database is generally recommended but may not always be necessary for some fields. This study aimed to determine the added value of searching additional databases beyond MEDLINE when conducting a literature search of hyperbaric oxygen treatment (HBOT) randomised controlled trials (RCTs).
**Methods:** This study consisted of two phases: a scoping review of all RCTs in the field of HBOT, followed by a a statistical analysis of sensitivity, precision, 'number needed to read' (NNR) and 'number unique' included by individual biomedical databases. MEDLINE, Embase, Cochrane Central Register of Control Trials (CENTRAL), and Cumulated Index to Nursing and Allied Health Literature (CINAHL) were searched without date or language restrictions up to December 31, 2022. Screening and data extraction were conducted in duplicate by pairs of independent reviewers. RCTs were included if they involved human subjects and HBOT was offered either on its own or in combination with other treatments.
**Results:** Out of 5,840 different citations identified, 367 were included for analysis. CENTRAL was the most sensitive (87.2%) and had the most unique references (7.1%). MEDLINE had the highest precision (23.8%) and optimal NNR (four). Among included references, 14.2% were unique to a single database.
**Conclusions:** Systematic reviews of RCTs in HBOT should always utilise multiple databases, which at minimum include MEDLINE, Embase, CENTRAL and CINAHL.

### Introduction

Hyperbaric oxygen treatment (HBOT) has been an active research field for decades, leading to the publication of numerous clinical studies investigating effectiveness and safety.[1–4] HBOT "*is the treatment of a disease or medical condition by the inhalation of near-100% (at least 95%) medical grade oxygen at pressures greater than 1 atmosphere absolute (ATA) (101.3 kilopascals [kPa]) in a pressure vessel constructed for that purpose*."[1] The resulting hyperoxia leads to a number of effects such as bactericidal properties, release of growth factors, neovascularisation, and immunomodulation.[5]

Like all medical fields, literature searches are often employed by researchers and clinicians to inform treatment decisions. It is generally recommended to search numerous databases to ensure rigorousness and avoid missing relevant studies.[6–10] Based on time and resource constraints, however, this may not always be possible – or even necessary.[11] In many cases, it may be preferable to quickly identify a number of relevant studies while reducing the number of non-relevant search results that appear. Searching multiple databases to identify relevant trials among increasing numbers of publications may delay knowledge translation of evidence or prevent swift clinical decision-making. Ideally, the search of a single well-organised and indexed database including all relevant trials would improve efficiency when identifying trials

to inform clinical practice and potentially close existing knowledge gaps. Therefore, this study aimed to determine whether searching beyond the Ovid MEDLINE (MEDLINE) database is necessary to identify the extent of the literature when performing a literature search of HBOT randomised controlled trials (RCTs).

## Methods

The study is composed of two successive steps: (1) a scoping review of all RCTs in the field of HBOT; and (2) an analysis of the 'performance' (i.e., the proportion of included RCTs retrieved) of individual biomedical databases relative to all HBOT RCTs.

### STEP 1: SCOPING REVIEW

To identify all available RCTs in the HBOT field, we first conducted a scoping review, and used the PRISMA-ScR reporting guidelines.[12] The aim of a scoping review is to *"systematically identify and map the breadth of evidence available on a particular topic"*.[13]

#### *Eligibility criteria*

Only RCTs were eligible for inclusion, and could be of any design (e.g., crossover, parallel-group, cluster, factorial). We included all studies conducted with human subjects; either patients, healthy volunteers, or healthcare providers. All contexts were included, such as clinical and simulated settings. Studies using animal populations, tissues, or cell cultures were excluded. Studies were included if they involved at least one treatment described as HBOT, offered either on its own or in combination with other treatments, for both Undersea and Hyperbaric Medical Society (UHMS) approved and non-UHMS approved indications. Diving medicine studies that did not include HBOT in a hyperbaric chamber were not included. Within each study, the comparison group was defined as a group receiving no HBOT or a different HBOT protocol than in the treatment group. Only publications in English were included for feasibility. Conference abstracts, editorials, and commentaries were excluded.

#### *Information sources and search strategy*

Based on previous systematic reviews in hyperbaric medicine, the electronic databases MEDLINE (via Ovid), Embase (via Ovid), Cochrane Central Register of Control Trials (CENTRAL), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched without language restrictions, from inception to December 31, 2022.[3,14–16] The Database of Randomized Controlled Trials in Diving and Hyperbaric Medicine was also searched.[17]

The MEDLINE search strategy was developed with an information specialist (AD), a practicing hyperbaric medicine physician (SB), and the research team. It was then reviewed by a second trained information specialist using the peer review of electronic search strategies guideline (PRESS).[18] The comprehensive MEDLINE strategy was then adapted to the unique subject headings and keywords of Embase, CENTRAL, and CINAHL (Appendix 1). To increase the sensitivity of the search strategy, a specific search filter for RCTs was incorporated within each search protocol.

#### *Study selection*

Identified references were uploaded to DistillerSR software (Evidence Partners, Ottawa, Canada) and duplicate publications were removed. The research team developed and piloted a screening tool with 20 randomly selected articles. The tool was iteratively refined until inter-rater reliability was deemed to be adequate.

Screening by title and abstract was completed in duplicate by two pairs of independent reviewers (SI, MK, PD, SA). Studies determined to meet the inclusion criteria and those marked as 'unclear' proceeded to full-text review. The independent reviewers then determined compliance with inclusion criteria for the full-text articles, again in duplicate, with disagreements resolved through consensus or a third party (CE, SB). The senior author (SB), a practising hyperbaric medicine physician, reviewed the list of included articles to determine if there were any key studies meeting our inclusion criteria that, to his knowledge, were missing from the list.

### STEP 2: STATISTICAL ANALYSIS OF DATABASES

Complete search results for each database were downloaded as separate Endnote (Clarivate, Philadelphia, USA) files, and each database was then searched for the title of every included study to determine if the study was indexed or not in each database. This information was recorded and extrapolated in a Microsoft Excel (version 16.65, Microsoft Corporation, Redmond Washington, USA) spreadsheet. Following the same methods as previous studies, we recorded the database of each reference, the number of records identified in each database, and the number remaining after duplicate removal (performed within but not across each database).[16,18,19] We descriptively summarised the number of RCTs that were unique to each database and that were unique to a combination of databases.

#### *Analysis*

For the purposes of this analysis, it was assumed that the number of RCTs identified by our search strategy was a

**Footnote:** * Appendix 1 is available on DHM Journal's website: https://www.dhmjournal.com/index.php/journals?id=331

reasonable approximation of the 'true' number of RCTs in existence, as is generally accepted in the systematic review community.[20] In addition, we are confident in our assumption, given that our literature search used wording such as 'hyperbaric medicine' and 'hyperbaric oxygen' that are both broad and specific to the area of focus. Also, the MeSH term 'hyperbaric oxygenation' was created a long time ago, in 1965 (Appendix 1) .

From the search strategy of each database, we calculated the following:

- Sensitivity: the number of RCTs retrieved from each database divided by the total number of included articles indexed across databases[11]
- Precision: the number of included RCTs identified by a source divided by the number of both included and excluded citations identified by that source[9]
- 'Number needed to read' (NNR): effectively the inverse of precision which gives a measure of how many RCTs need to be screened to find one that is included[9]
- 'Number unique' refers to the number of included RCTs that were exclusively identified by each database[7]

## Results

STEP 1: SCOPING REVIEW

Completion of the literature search identified 5,840 citations. Removal of duplicate articles resulted in 4,859 unique articles across the four databases utilised. After assessing the title and abstract of each reference against our inclusion criteria, 701 references proceeded to full-text screening. Of these, 334 articles were subsequently excluded: six were not in English, 217 were not RCTs, 11 studied animal populations or cell cultures, 39 were not original articles, 47 were not related to HBOT, and 14 were duplicates not initially detected automatically. Therefore, 367 RCTs were included in the analysis. All the details are shown in the PRISMA flow chart (Figure 1).

**Figure 1**

PRISMA flow diagram detailing the database searches, the number of abstracts screened, and the full texts retrieved as retrieved from DistillerSR

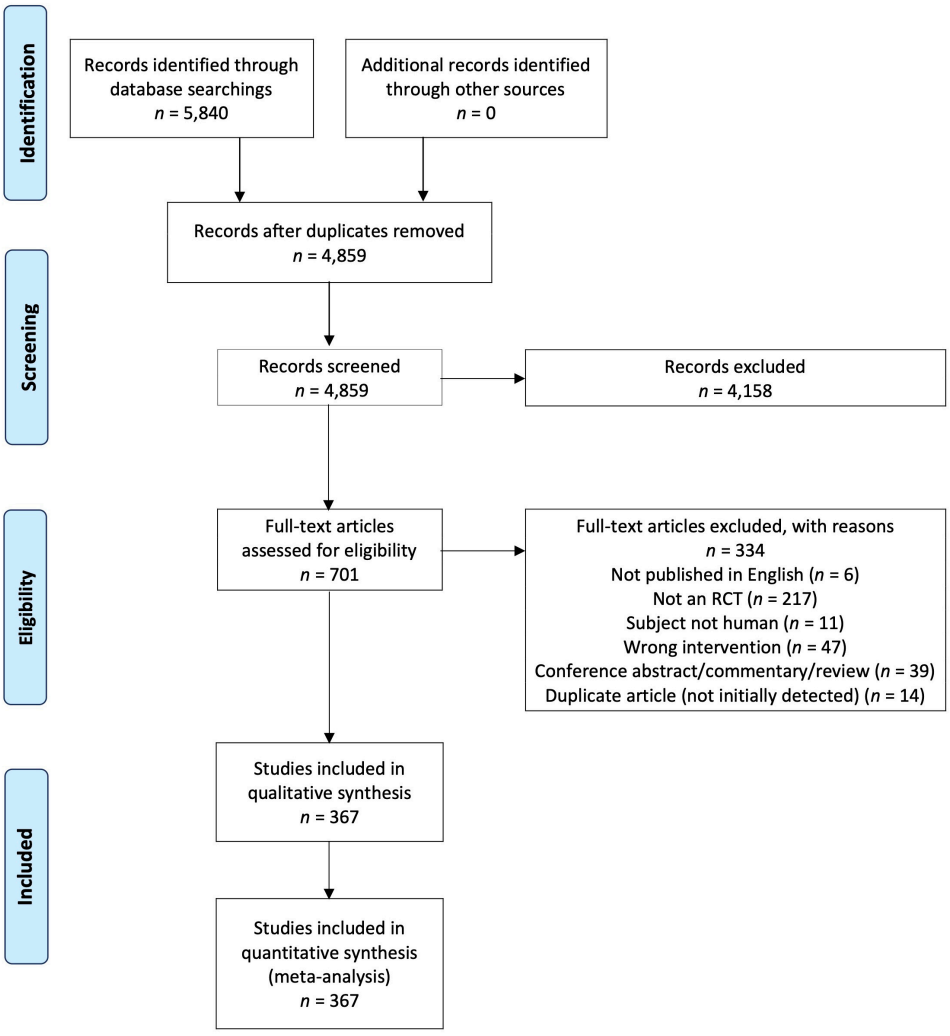

**Table 1**

Numbers of records uniquely identified by either a single database or a combination of databases. Each trial is counted only once. Overlapping articles are not included in the unique record count per database or database combination. As such, the number of records indicated for a combination of databases does not include records unique to a single database. CENTRAL – Cochrane Central Register of Control Trials; CINAHL – Cumulative Index to Nursing and Allied Health Literature

| Uniqueness status | Database(s) | Included records | |
|---|---|---|---|
| | | (*n*) | (%) |
| Unique to a single database: | MEDLINE | 8 | 2.2 |
| | Embase | 11 | 3.0 |
| | CENTRAL | 26 | 7.1 |
| | CINAHL | 7 | 1.9 |
| Unique to a combination of databases: | MEDLINE + Embase | 16 | 4.4 |
| | MEDLINE + CENTRAL | 29 | 7.9 |
| | MEDLINE + CINAHL | 2 | 0.5 |
| | CENTRAL + Embase | 31 | 8.4 |
| | CENTRAL + CINAH | 4 | 1.1 |
| | MEDLINE + CENTRAL + CINAHL | 5 | 1.4 |
| | MEDLINE + Embase + CINAHL | 3 | 0.8 |
| | MEDLINE + Embase + CENTRAL | 171 | 46.6 |
| | MEDLINE + Embase + CENTRAL + CINAHL | 54 | 14.7 |
| | Total | 367 | 100.0 |

STEP 2: STATISTICAL ANALYSIS OF DATABASES

*Included records for each database*

The number of included records from respective databases are presented in Table 1. We found that CENTRAL indexed the highest percentage of records (87.2% total: 7.1% unique to CENTRAL; 80.1% unique to combination of CENTRAL and additional database[s]) while Medline (78.5%) and Embase (77.9%) still indexed the majority of included studies. However, CINAHL indexed only 20.4% of included studies. Of note, these percentages include overlap among databases.

Meanwhile, the total overlap among multiple databases (i.e., included articles indexed by more than one database) was 85.8%, and 14.7% of included papers were indexed by all four databases. There were a total of 87 included articles indexed outside of MEDLINE, i.e., uniquely present in one of the other three databases or uniquely found across a combination of them, resulting in 23.7% of the articles (Table 2). Each database retrieved unique papers: MEDLINE (2.2%), Embase (3.0%), CENTRAL (7.1%), and CINAHL (1.9%). In total, 14.2% of all included papers were unique to a single database.

**Table 2**

Number of unique included records retrieved from outside of the MEDLINE database; note: each record is included only once. The number of records indicated for a combination of databases does not include records unique to a single database. CENTRAL – Cochrane Central Register of Control Trials; CINAHL – Cumulative Index to Nursing and Allied Health Literature

| Database(s) | Included records *n (%)* |
|---|---|
| Embase | 11 (3.0) |
| CENTRAL | 26 (7.1) |
| CINAHL | 7 (1.9) |
| Embase + CENTRAL | 31 (8.4) |
| Embase + CINAHL | 8 (1.8) |
| CENTRAL + CINAHL | 4 (1.1) |
| Embase + CENTRAL + CINAHL | 0 (0.0) |
| Total articles not found in MEDLINE | 87 (23.7) |

**Table 3**
Results of the various types of searches for HBOT RCTs; yellow cells indicate the best results among the searched databases for each category. CENTRAL – Cochrane Central Register of Control Trials; CINAHL – Cumulative Index to Nursing and Allied Health Literature

| Database | Total number of references retrieved before deduplication and screening (*n* = 5,480) | Number of included studies retrieved by database (including overlap) | Sensitivity including overlap (%) | Number unique *n* (%) | Precision (%) | Number needed to read |
|---|---|---|---|---|---|---|
| MEDLINE | 1,210 | 288 | 78.5 | 8 (2.2) | 23.8 | 4.2 |
| Embase | 1,780 | 286 | 77.9 | 11 (3.0) | 16.1 | 6.2 |
| CENTRAL | 1,585 | 320 | 87.2 | 26 (7.1) | 20.2 | 5.0 |
| CINAHL | 1,265 | 75 | 20.4 | 7 (1.9) | 5.9 | 16.9 |

*Precision, and number needed to read (NNR).*

MEDLINE hold the highest precision (23.8%) and lowest NNR (4), meaning only four papers were required to be screened to encounter one included paper. CINAHL held the lowest precision, at 5.9% and the highest NNR (17) (Table 3).

## Discussion

No single database indexed all RCTs in HBOT. While CENTRAL was the most sensitive database, the majority of HBOT RCTs were indexed by the CENTRAL, Embase and MEDLINE databases. Our findings showed that almost a quarter (23.7%) of the HBOT RCTs in the literature are not indexed in MEDLINE but can rather be found in other commonly used databases, namely Embase, CENTRAL, and CINHAL. However, MEDLINE remains the most efficient to search, as one included paper was encountered for every four papers identified.

### KEY FINDINGS AND INTERPRETATION

These findings offer practical evidence that can be utilised by a variety of stakeholders in the field of HBOT. The results suggest that multi-source comprehensive searches are necessary to identify all included RCTs in hyperbaric medicine. This result is similar to previous studies in other fields.[11,13–15] Specifically, there is no singular database that contains all available RCTs in hyperbaric medicine, indicating that there is much value to searching multiple databases for the purpose of conducting high-quality systematic reviews. Therefore, researchers conducting systematic reviews of RCTs in hyperbaric medicine should not accept the risk of missing any relevant papers. Although our results indicate that CENTRAL indexes a large number of relevant articles, at minimum, researchers should conduct literature searches from all four electronic databases (MEDLINE, Embase, CENTRAL, and CINAHL) to ensure comprehensiveness.

Second, these results may hold alternate implications to clinicians, and possibly patients, who may need to quickly identify a concentrated number of RCTs in hyperbaric medicine. That is, clinicians and patients may prefer to identify the greatest amount of evidence in the shortest amount of time to inform a treatment decision, without the need to be totally exhaustive. With this goal in mind, MEDLINE proved to be the most 'productive' database to search. With a 'number needed to read' at about four, the MEDLINE database on average requires reading only four articles to come across one relevant article, whereas the number needed to read for CINAHL reached 17. Furthermore, although it did not identify the largest number of RCTs in HBOT, MEDLINE included almost 80% of all RCTs in HBOT.

Searching multiple databases can be difficult, time consuming, and costly. A search conducted in the fewest databases that retrieves a maximum yield of relevant trials and minimum yield of non-relevant trials would be ideal in order to reduce the time and costs associated with searching. Although a large proportion of HBOT RCTs were indexed in MEDLINE (78.5%), we did not assess the quality or the clinical value of the studies retrieved, and it is important to acknowledge that other potentially valuable RCTs may be indexed elsewhere. We deliberately decided to focus purely on identifying the extent of the literature and not to score the quality/value of included RCTs because scoring the value of any RCT must account for numerous parameters. This would require a separate study to be conducted. When interested in a specific area of hyperbaric medicine such as nursing protocols in a hyperbaric environment, one might be better off looking through the CINAHL database (nursing studies) instead of the MEDLINE database. Nevertheless, MEDLINE is available free online, while the other databases

searched require institutional subscriptions, which may not be available to all clinicians depending on their institutions and likely are not accessible to most patients. Thus, for a cost-effective overview and readily accessible search capability, MEDLINE may still be preferable.

Given MEDLINE indexes publications from all areas of biomedicine, it may not be entirely surprising that it found the vast majority of RCTs in HBOT. Conversely, CINAHL includes publications related to nursing and health, along with other topics such as behavioural sciences, education and health administration, and logically found only 20% of papers included in this study. While Embase is a European-oriented database, it includes the field of biomedicine with primary areas of focus being toxicology and drug literature. CENTRAL combines multiple sources and focuses on high-quality evidence and is generally considered to be among the richest sources of trials.[10] It indeed identified the largest number of papers included in our study (87.2%), but at the expense of more 'noise' (i.e., less precision - more non-included papers) than MEDLINE.

STRENGTHS AND LIMITATIONS

The strength of this study is that it offers a methodological insight for conducting systematic reviews of RCTs in hyperbaric medicine. This work will help authors of future systematic reviews of RCTs to optimise their resources and may also help clinicians and possibly patients to optimise efficiency when evidence is needed within a limited timeframe.

The study has several limitations. First, we included a limited number of databases. Nevertheless, these databases have been carefully selected due to their wide use, particularly in healthcare, and large indexation coverage. Second, indexation of journals in databases is susceptible to change over time. We intended an exploratory decade-by-decade analysis for each database to account for this risk. We found that the number of studies was minimal for most databases and decades (often less than 10). Therefore, we decided not to conduct the decade-by-decade analysis as we believed that it would have been misleading in calculation of sensitivity, 'number needed to read' and precision for each decade and database. However, given the overall low frequency of journal indexation changes, we believe that the potential impact on our results is only marginal, at most. Third, our results are specific to the literature search algorithm we developed, and we assumed that the average clinician or patient can formulate a search in the same way as that used in this paper. Although the words used in our search were basic and intuitive (e.g., hyperbaric oxygen, randomised), we cannot know for certain what the results might be with searches conducted by other individuals. However, the terminology of hyperbaric oxygen treatment is very specific and was established decades ago (e.g., the MESH term 'Hyperbaric Oxygenation' was introduced in 1965). Therefore, there is limited risk of obtaining different results with minor variations in the literature search strategy. Fourth, while including only English-language publications may introduce some degree of bias, this is unlikely to affect the results of this study. Evidence suggests that using language restrictions in systematic reviews in medicine does not introduce systematic bias.[19] Further, trials not published in English tend to be difficult to locate and access, and published outside of the databases included here.[21]

## Conclusions

With all aspects considered, to ensure comprehensiveness and accuracy, systematic reviews of RCTs in hyperbaric medicine should always search multiple databases, which at minimum should include MEDLINE, Embase, CENTRAL, and CINAHL.

## References


1 HBO Indications – Undersea and Hyperbaric Medical Society; 2023. [cited 2023 Jan 6]. Available from: https://www.uhms.org/resources/hbo-indications.html.

2 Jain KK. Indications, contraindications, and complications of HBO therapy. In: Textbook of hyperbaric medicine. Springer; 2017. p. 79–84.

3 Kranke P, Bennett MH, Martyn-St James M, Schnabel A, Debus SE, Weibel S. Hyperbaric oxygen therapy for chronic wounds. Cochrane Database Syst Rev. 2015;(6):CD004123. doi: 10.1002/14651858.CD004123.pub4. PMID: 26106870. PMCID: PMC7055586.

4 Eskes A, Vermeulen H, Lucas C, Ubbink DT. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. Cochrane Database Syst Rev. 2013;(12):CD008059. doi: 10.1002/14651858.CD008059.pub3. PMID: 24343585.

5 Lam G, Fontaine R, Ross FL, Chiu ES. Hyperbaric oxygen therapy: exploring the clinical evidence. Adv Skin Wound Care. 2017;30:181–90. doi: 10.1097/01.ASW.0000513089.75457.22. PMID: 28301358.

6 Robinson KA, Dickersin K. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. Int J Epidemiol. 2002;31:150–3. doi: 10.1093/ije/31.1.150. PMID: 11914311.

7 Betrán AP, Say L, Gülmezoglu AM, Allen T, Hampson L. Effectiveness of different databases in identifying studies for systematic reviews: experience from the WHO systematic review of maternal morbidity and mortality. BMC Med Res Methodol. 2005;5(1):6. doi: 10.1186/1471-2288-5-6. PMID: 15679886. PMCID: PMC548692.

8 Vassar M, Yerokhin V, Sinnett PM, Weiher M, Muckelrath H, Carr B, et al. Database selection in systematic reviews: an insight through clinical neurology. Health Info Libr J. 2017;34:156–64. doi: 10.1111/hir.12176. PMID: 28383159.

9 Beyer FR, Wright K. Can we prioritise which databases to search? A case study using a systematic review of frozen shoulder management. Health Info Libr J. 2013;30:49–58. doi: 10.1111/hir.12009. PMID: 23413793.

10 Crumley ET, Wiebe N, Cramer K, Klassen TP, Hartling L. Which resources should be used to identify RCT/CCTs for systematic reviews: a systematic review. BMC Med Res Methodol. 2005;5:24. doi: 10.1186/1471-2288-5-24. PMID: 16092960. PMCID: PMC1232852.

11 Kwon Y, Powelson SE, Wong H, Ghali WA, Conly JM.

An assessment of the efficacy of searching in biomedical databases beyond MEDLINE in identifying studies for a systematic review on ward closures as an infection control intervention to control outbreaks. Syst Rev. 2014;3:135. doi: 10.1186/2046-4053-3-135. PMID: 25387523. PMCID: PMC4231196.

12 Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 2018;169:467–73. doi: 10.7326/M18-0850. PMID: 30178033.

13 Munn Z, Pollock D, Khalil H, Alexander L, Mclnerney P, Godfrey CM, et al. What are scoping reviews? Providing a formal definition of scoping reviews as a type of evidence synthesis. JBI Evid Synth. 2022;20:950–2. doi: 10.11124/JBIES-21-00483. PMID: 35249995.

14 Rhee TM, Hwang D, Lee JS, Park J, Lee JM. Addition of hyperbaric oxygen therapy vs medical therapy alone for idiopathic sudden sensorineural hearing loss: a systematic review and meta-analysis. JAMA Otolaryngol Head Neck Surg. 2018;144:1153–61. doi: 10.1001/jamaoto.2018.2133. PMID: 30267033. PMCID: PMC6583095.

15 Boet S, Cheng-Boivin O, Martin L, Hurskainen T, Etherington C. Evidence for simulation-based education in hyperbaric medicine: a systematic review. Diving Hyperb Med. 2019;49:209–15. doi: 10.28920/dhm49.3.209-215. PMID: 31523796. PMCID: PMC6884102.

16 Boet S, Martin L, Cheng-Boivin O, Etherington N, Louge P, Pignel R, et al. Can preventive hyperbaric oxygen therapy optimise surgical outcome?: a systematic review of randomised controlled trials. Eur J Anaesthesiol. 2020;37:636–48. doi: 10.1097/EJA.0000000000001219. PMID: 32355046.

17 Bennett MH. Randomized controlled trials in diving and hyperbaric medicine. Undersea Hyperb Med. 2013;40:419–38. PMID: 24224286.

18 McGowan J, Sampson M, Lefebvre C. An evidence based checklist for the peer review of electronic search strategies (PRESS EBC). Evidence based library and information practice. 2010;5:149–54. doi: 10.18438/B8SG8R.

19 Morrison A, Polisena J, Husereau D, Moulton K, Clark M, Fiander M, et al. The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. Int J Technol Assess Health Care. 2012;28:138–44. doi: 10.1017/S0266462312000086. PMID: 22559755.

20 Cochrane Information Retrieval Methods Group. Chapter 4: Searching for and selecting studies. Cochrane Handbook; c2023. [cited 2023 Jan 4]. Available from: https://training.cochrane.org/handbook/current/chapter-04.

21 Egger M, Juni P, Bartlett C, Holenstein F, Sterne J. How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study. Health Technol Assess. 2003;7:1–76. PMID: 12583822.

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# Hyperbaric oxygen treatment for infants: retrospective analysis of 54 patients treated in two tertiary care centres

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Hyperbaric medicine; Neonate; Newborn; Premature

**Abstract**
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**Introduction:** We aimed to analyse the outcomes of hyperbaric oxygen treatment (HBOT) and describe difficulties encountered in infants, a rare patient population in this therapeutic intervention, with limited scientific reports.

**Methods:** This was a retrospective analysis of patients 12 months old or younger who underwent HBOT in two different institutions. Demographic data, clinical presentation, HBOT indication, chamber type, oxygen delivery method, total number of treatments, outcome and complications were extracted from clinical records.

**Results:** There were 54 infants in our study. The patients' median age was 3.5 (range 0–12) months. The major HBOT indication was acute carbon monoxide intoxication ($n$ = 32). A total of 275 HBOT treatments were administered, mostly performed in multiplace chambers ($n$ = 196, 71%). Only one patient (2%) required mechanical ventilation. Acute signs were fully resolved in the most patients ($n$ = 40, 74%). No complications related to HBOT were reported.

**Conclusions:** This study suggests that HBOT may be a safe and effective treatment for infants. Paediatricians should consider HBOT when indicated in infants even for the preterm age group.

## Introduction

Hyperbaric oxygen treatment (HBOT) has been widely used for several conditions such as acute carbon monoxide (CO) intoxication, arterial gas emboli, impaired wound healing, and peripheral/traumatic ischaemic conditions.[1] Some of these conditions are also common in the paediatric age group and referral of these patients for HBOT has been increasing in recent decades.[2–6] A retrospective study reported favourable outcomes in 93% of the 139 children who underwent HBOT, mostly for acute CO intoxication.[5] Two consecutive Australian studies in which outcomes were not analysed, described safe administration of HBOT in paediatric patients treated mainly for acute ischaemic conditions and severe infections.[3,4] Although some paediatric series may involve patients under one year of age, data on this group are lacking.[3–5] Use of HBOT in neonates and infants remains very limited, and reports regarding its use in this patient population are scarce except for a few encouraging case reports and case series. Remarkably, HBOT is used only to treat acute indications like peripheral ischaemic conditions and acute CO intoxication in all these reports.[7–15] It is recognised that treating neonates involves difficulties such as the need for an accompanying caregiver, technical issues about administration of treatment or providing appropriate environmental conditions in the hyperbaric chambers.[16]

Scarcity of evidence about the efficacy and safety of HBOT in this age group together with challenges of managing a neonate in a hyperbaric chamber perhaps cause hesitation and reluctance in HBOT referrals. In view of the potential benefits of HBOT in this age group, the need for related studies arises. In this regard, we aimed to share our experience in treating neonates, particularly in respect of HBOT outcomes and any difficulties encountered. To our knowledge, this is the first study specifically evaluating HBOT use in patients younger than one year of age.

## Methods

This study was approved both by the Ethical Committees of University of Health Sciences – Gulhane Faculty of Medicine (approval number and date: 2020/06; April 19th, 2020) and Istanbul University Istanbul Faculty of Medicine (approval number and date: 508161; September 30th, 2021).

The present study is a retrospective analysis of neonates and infants who underwent HBOT in two university hospitals. Both institutions serve as referral HBOT centres in two different Turkish metropolises, Ankara and Istanbul.

Patients who were 12 months old or younger and treated between January 1st, 2013 and October 31st, 2019 in Gulhane Research and Training Hospital (Gulhane RTH) and between January 1990 and March 2021 at Istanbul Faculty of Medicine (Istanbul FM) were included in the study.

Demographic data, medical history, clinical presentation, HBOT indication, chamber type, oxygen delivery method, total number of HBOT sessions, HBOT outcome, complications related to HBOT and other treatment modalities during HBOT were documented from patient medical files. For acute CO intoxication cases, carboxyhaemoglobin (COHb) levels at referral and delay in HBOT initiation (from onset of intoxication signs) were also recorded.

The age groups were identified as 'neonates' (< 28 days) and 'infants' (28 days – 12 months). The patients were classified into two major groups with regard to the conditions they were treated for: 'acute CO intoxication patients' and 'patients with complicated wound-related problems'.

The acute CO intoxication patients were further grouped as 'mild', 'moderate-severe' and 'severe' based on the clinical severity at the time of referral. 'Mild' refers to discomfort, vomiting, difficulty in breastfeeding whereas patients with a minimum one end-organ injury including cardiological, neurological, respiratory or metabolic were recorded as 'moderate-severe'. The patients who required treatment with inotropic drugs, mechanical ventilation, or having multiorgan failure were defined as the 'severe' group. HBOT was continued until the resolution of all signs in a maximum of five sessions. At the end of the HBOT course, all parents were routinely informed about delayed neurological sequelae (DNS) after CO intoxication. They were also warned to present to the Department of Paediatrics or Department of Underwater and Hyperbaric Medicine as soon as possible if they had any suspicion about DNS development in their infant, and to inform their physicians about the acute CO intoxication history.

The complicated wound related problems group comprised of non-healing wounds, compromised flaps/grafts and acute peripheral ischaemia related problems.

Treatment outcomes were reported as 'full-clinical resolution', 'partial-recovery', and 'no-recovery' for all conditions treated. The definition of each treatment outcome group with regard to the condition treated is presented in Table 1. Treatment outcomes were evaluated with clinical status, related laboratory parameters and wound photos regularly recorded. No long-term follow-ups were included in this study; the patients' clinical status was evaluated at the end of the HBOT course for outcome classification.

One monoplace (Hipertech, MON-08, 2014) (Hipertech, Başakşehir/İstanbul Turkey) and one multiplace HBOT chamber (Hipertech ZYRON 12, 2008) were available in Gulhane RTH whereas in Istanbul FM the treatments were performed in two different multiplace chambers (a Patterson Kelly 1944 chamber between 1990 and 1997,

**Table 1**

The definitions of treatment outcome classifications according to medical condition groups; *amputation below the ankle joint level is defined as a 'minor amputation', while an amputation above the ankle is defined as a 'major amputation'. HBOT – hyperbaric oxygen treatment

| HBOT indication | Full clinical resolution | Partial recovery | No-recovery |
|---|---|---|---|
| Acute carbon monoxide intoxication | Resolution of all signs and symptoms in maximum five sessions | Residual symptoms after fifth HBOT session | No relief of the signs or symptoms after the fifth HBOT session, or death |
| Non-healing wounds | Complete wound closure | 50% or more reduction of wound size and relief of infection signs (redness, swelling, pus, pain) | No change in wound size or an increase in wound size, or death |
| Peripheral ischaemia related problems | Complete resolution of cyanosis/tissue ischaemia | Partial resolution of cyanosis/tissue ischemia with minimal necrosis or minor amputation* with recovered cyanotic/ischaemic tissues | Complete necrosis of the cyanotic/ischemic tissues or major amputation,* or death |
| Grafts/Flaps | Complete survival of the graft/flap | Survival of at least 50% of the graft/flap | Survival of less than 50% of the graft/flap |

**Figure 1**
The infant face mask

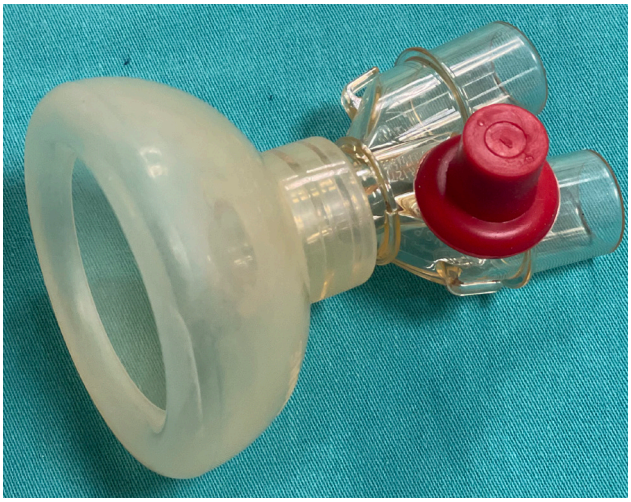


**Figure 2**
The baby incubator used for neonates inside the multiplace hyperbaric chamber

**Figure 3**
The treatment protocol for monoplace chambers which involved breathing 100% oxygen at 203 kPa (2.0 atmospheres absolute [atm abs]) for 75 minutes (10 minutes compression, 55 minutes at 2.0 atm abs, 10 minutes decompression)

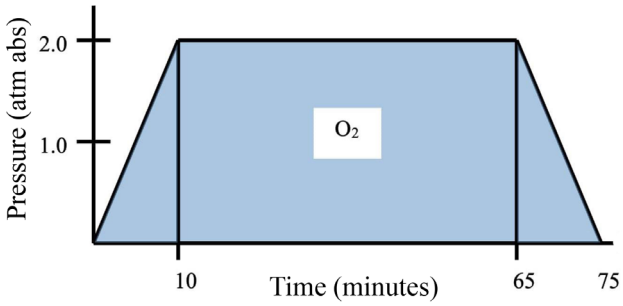
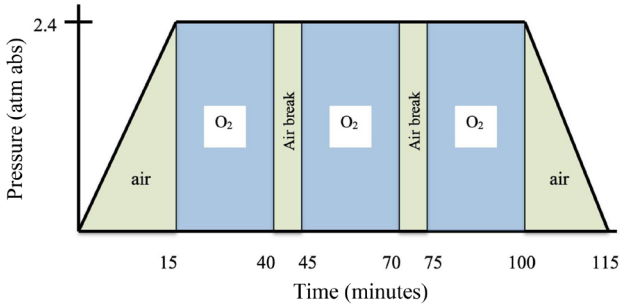



**Figure 4**
The treatment protocol for multiplace chambers in which 100% oxygen was administered at 243 kPa (2.4 atmospheres absolute [atm abs]) for 115 minutes (15 minutes compression; three 25-minute oxygen periods separated by five-minute air breaks; 15 minutes decompression)




and a Hipertech ZYRON 12 after 2008). Infants were not treated between 1997 and 2008 in Istanbul FM due to unavailability of chambers. In Gulhane RTH, patients who had emergency conditions and did not require continuous monitoring were preferably treated in the monoplace chamber with an accompanying parent. The monoplace chamber was pressurised with 100% oxygen, so patients breathed ambient oxygen. In multiplace chambers, oxygen was administered via an infant face mask (Figure 1) or hood unless the patient was intubated. A special baby incubator was used for neonates after 2019 in Istanbul FM (Figure 2). An inside attendant was present during all treatments. Treatment protocols are depicted in Figures 3 and 4.

Thermoregulation was provided by covering the baby with multilayer cotton sheets. In Istanbul FM, heated Mediflex® bags were also placed under the sheets in the special baby incubator. Special care was given to avoid direct contact between mediflex bags and the patient. Feeding was continued inside the chamber during the air breaks if necessary. Pacifier use was encouraged during compression and decompression for enabling middle ear equalisation. Patients who showed signs of discomfort during compression or decompression were examined for middle ear barotrauma by a paediatric specialist after the session.

All patients were evaluated by at least one hyperbaric medicine specialist in both centres in terms of HBOT need. The European Committee for Hyperbaric Medicine (ECHM) and the Undersea and Hyperbaric Medicine Society (UHMS) recommendations were followed.[1,17] The daily and total numbers of HBOT treatments were determined on a case by case basis. For acute CO intoxications, HBOT treatments were continued until no further clinical improvement was observed (maximum five treatments). The patients with complicated wound related problems were recommended to continue HBOT until achieving complete wound closure or complete granulation of the wound bed (ready for graft/flap). HBOT was discontinued if no change was observed for two weeks or amputation was required. For acute peripheral ischaemic tissues, HBOT was continued until

**Table 2**
Demographic data of infants, chamber type, oxygen delivery methods and treatment outcomes; *chamber is pressurised with 100% oxygen (only in monoplace chambers)

| Parameter | Overall data *n* (%) | Acute carbon monoxide intoxication *n* (%) | Complicated wound related problems *n* (%) |
|---|---|---|---|
| **Age classification (*n* = 53)** | | | |
| Neonates (< 28 days) | 15 (28.3%) | 6 (18.8%) | 9 (42.9%) |
| Infants (28 days – 12 months) | 38 (71.7%) | 26 (81.3%) | 12 (57.1%) |
| **Sex (*n* = 51)** | | | |
| Male | 30 (58.8%) | 17 (56.7%) | 13 (61.9%) |
| Female | 21 (41.2%) | 13 (43.3%) | 8 (38.1%) |
| **Chamber (*n* = 54)** | | | |
| Monoplace | 25 (46.3%) | 20 (62.5%) | 5 (22.7%) |
| Multiplace | 29 (53.7%) | 12 (37.5%) | 17 (77.3%) |
| **Oxygen delivery (*n* = 50)** | | | |
| Ambient oxygen* | 25 (50%) | 20 (62.5%) | 5 (27.8%) |
| Hood | 12 (24%) | 10 (31.3%) | 2 (11.1%) |
| Specialised baby incubator | 6 (12%) | 0 | 6 (33.3%) |
| Face mask (infant size) | 6 (12%) | 1 (3.1%) | 5(27.8%) |
| Endotracheal tube | 1 (2%) | 1 (3.1%) | 0 |
| **Outcomes (*n* = 53)** | | | |
| Full clinical resolution | 40 (75.5%) | 31 (96.9%) | 9 (42.9%) |
| Partial-recovery | 8 (15.1%) | 0 | 8 (38.1%) |
| No-recovery | 5 (9.4%) | 1 (3.1%) | 4 (19.0%) |

the demarcation line became evident if total healing was not observed.

Data analysis was performed using SPSS Statistics Version 21 (IBM Corp., Armonk NY, USA). Demographic and descriptive data were reported as *n* (%) and mean (standard deviation) where appropriate. Non-normally distributed data were reported as median (range). The Kolmogorov Smirnov test was performed to determine the normal distribution of continuous variables with data greater than 50, or the Shapiro-Wilk test was preferred for continuous variables with data less than 50.

## Results

There were 54 infants in our study. The patients' median age was 3.5 months (range 2 days to 12 months), two neonates being premature. The demographic data are presented in Table 2. Thirty-one patients (57%) were treated at Gulhane RTH and 23 (43%) were treated at Istanbul FM. The major HBOT indication was acute CO intoxication (*n* = 32). A total of 275 treatments were administered in two institutions. The majority of HBOT treatments (*n* = 196, 71%) were performed in multiplace chambers. The hyperbaric chamber type and oxygen delivery methods are presented in Table 2. The median HBOT treatment number per patient was one (range one to 48). Most patients (*n* = 40, 74%) fully recovered. No complications were reported during HBOT treatments in both institutions.

### PATIENTS WITH ACUTE CO INTOXICATION

The median age of 32 patients treated for acute CO intoxication was 5 months (range 3 days to 12 months). The median number of treatments was one (range one to five). The mean COHb level at presentation was 22.6% (SD 9.3%), and the mean delay time for HBOT was 4.6 (SD 1.9) hours. The majority (56%) of the patients had moderate-severe clinical severity at referral. Twenty-five patients (79%) had an electrocardiogram (ECG) recorded all of which were reported to be normal. Fourteen patients (44%) had elevated cardiac enzymes at the emergency department admission. Only one patient needed mechanical ventilation and was unconscious during the HBOT initiation. His condition did not change at the end of the HBOT course.

**Table 3**
The detailed classification of medical conditions grouped as 'complicated wound related problems'

| Medical conditions | *n (%)* |
|---|---|
| Post-operative non-healing wound | 3 (13.6%) |
| Compromised flaps/grafts | 2 (9.1%) |
| Epidermolysis bullosa | 1 (4.5%) |
| Acute peripheral ischaemia | 15 (68.2%) |
| Soft tissue infection | 1 (4.5%) |

PATIENTS WITH COMPLICATED WOUND RELATED PROBLEMS

Twenty-two infants were treated for complicated wound related problems (Table 3). Their median age was 1 month (range 2 days to 12 months), two neonates being premature.. The mean delay time for HBOT was 5.6 (SD 4.5) days. The median number of treatments was 11 (range two to 48).

The medical history was unremarkable only for six patients (27%). All other infants had diagnosed comorbidities including meningomyelocele, hydrocephalus, anti-phospholipid syndrome, undefined vasculitis, Wiskott-Aldrich Syndrome, Fallot tetralogy, ventricular septal defect, intrauterine sepsis and hypoxia, purpura fulminans, flexor tenosynovitis and post-coronavirus disease complications. The wound/ischaemia localisations of the infants were recorded as lower extremity ($n$ = 9), upper extremity ($n$ = 5), back ($n$ = 4), penis ($n$ = 2), sternum ($n$ = 1) and whole body ($n$ = 1).

Two patients had surgical debridement during the course of their HBOT; one patient underwent a graft operation, three patients underwent minor amputations (toe amputation in two, and finger amputation in one) and two others underwent major amputation (one below-knee amputation, and one above-knee amputation). One patient did not complete the recommended HBOT schedule. The treatment outcomes of the patients ($n$ = 21) are presented in Table 2.

## Discussion

Infant patients arguably present the most unique challenges for HBOT physicians. Referrals are few in number and consequently there is little experience reported in the literature. In this study, the characteristics and treatment outcomes of infant patients who underwent HBOT were analysed. A total of 275 HBOT treatments were administered either in monoplace ($n$ = 79) and multiplace chambers ($n$ = 196) to 54 infants in two tertiary care institutions. Most of the patients ($n$ = 40, 74.1%) completely recovered and no complications were reported during HBOT treatments.

Although many of the accepted HBOT indications are also relevant to the infant age group, common conditions for which infants receive HBOT may vary from adults. Delayed radiation injury and complicated wounds have been reported as the most common HBOT indications for adults.[18] However, emergency conditions come to forefront in paediatric series. Acute CO intoxication and acute peripheral ischaemia also involving purpura fulminans, limb ischaemia, critical ischaemia of the glans penis after circumcision are reported to be the most common indications in the paediatric population.[4,5,7–10,15] In our study, the most common HBOT indications were acute CO intoxication ($n$ = 32) and acute peripheral ischaemia ($n$ = 15) similar to other published infant case series.[7–15] There are promising clinical studies on neonatal hypoxic ischaemic encephalopathy and case reports on necrotising enterocolitis of the neonate but no patients with these conditions were referred for HBOT in this study.[14,19,20] Since these patients mostly need advanced life support and the evidence of efficacy is scarce, paediatricians may be unwilling to suggest HBOT for this critically ill patient group.[14] In contrast, our cohort included two compromised flap cases and an epidermolysis bullosa case which were not reported to be treated with HBOT in this age group before.

Although available published data on infant patients receiving HBOT is limited, their outcomes seem favorable. One study reported full clinical resolution of 13 acute CO poisoning patients among 14 infant patients treated with HBOT.[11] Similarly, two other case reports recorded complete clinical resolution with HBOT in acute CO intoxication.[12,13] In our study, the majority of the acute CO poisoning patients (96.9%) had full clinical resolution, however, the complete clinical recovery rate in the complicated wound related problem group was 40.6%. Most of the complicated wound related problem patients (68.2%) were treated for acute peripheral ischaemia which is an emergent HBOT indication. A promptly initiated frequent HBOT schedule may provide better outcomes in this group.[7] One publication reported a full term neonate with pale bluish discoloration starting at the upper thigh due to severe arterial thromboemboli in the lower extremity, who was referred for HBOT at the 7th day following onset and the outcome was below knee amputation.[15] In contrast, our own group reported complete recovery in an infant who was born with total brachial artery occlusion and severe limb ischaemia. In that case, HBOT was started much earlier (at the 48th postnatal hour) and continued with an intense schedule.[7] Similarly, another group reported different outcomes seemingly related to delay in initiating HBOT in two cases of glans penis ischaemia following circumcision.[10] Collectively, these reports suggest that delay in HBOT may significantly affect the outcome in acute ischaemic conditions. In the present study, the complicated wound-related problem group had relatively long delay times for HBOT which might have contributed to the low clinical resolution rates in this patient group. Lack of awareness, and doubts about safety and effectiveness of HBOT among paediatricians may be leading to delayed HBOT referrals of infants.

The major controversy for infants is the possibility of adverse events during HBOT. Central nervous system oxygen toxicity, pulmonary oxygen toxicity and retinopathy of the premature (ROP) are the most feared complications related to HBOT in infancy. However, no adverse events related to HBOT were reported in infants either in our study or in the available literature.[7,9,10,21] The lack of information about oxygen toxicity in infants may have hindered the application of HBOT in these patients. The literature on ROP and HBOT is scarce and limited to animal studies. Most of them do not present any evidence regarding the relationship between ROP and HBOT.[14,22–24] Only in one experimental study (using rats) was retinal vascular density significantly increased in the HBOT-exposed group. Nevertheless, their HBOT treatment table, in which rats were exposed to 506 kPa (5 atm abs) oxygen, involved a much higher oxygen dose compared to currently utilised clinical HBOT protocols.[25] Therefore, no convincing association between HBOT and ROP in human premature neonates or neonates has been proven. Likewise, a 25-day old neonate, who was born in the 32nd week of gestational age, defined as moderate preterm, underwent 16 HBOT treatments without evidence of ROP in our study. The patient was examined by an ophthalmologist before the first HBOT session, at the end of the HBOT schedule and two weeks after HBOT was ended. Still, infants with ROP risk should be examined before and after HBOT and continued to be regularly followed up by an ophthalmologist.[6]

Thermoregulation and thermoprotection may become significant challenges for infants during HBOT.[6] Newborns, particularly preterm and low-birth-weight neonates, have limited capacity for thermoregulation. Environmental temperature fluctuations can lead to considerable thermal stress in infants and both hypothermia and hyperthermia can lead to significant morbidity and mortality.[26] As temperature fluctuations may be inevitable inside an HBOT chamber, maintaining a stabilised thermoneutral environment can be challenging during HBOT treatments. Therefore, additional protective measures may need to be considered. No complications related to thermal stress were reported in either of our institutions where simple actions like covering the baby with additional sheets were utilised. Also, specialised devices like the hyperbaric chamber compatible baby incubator that was successfully used in Istanbul FM may be developed with the increased need.

Transportation related risks should also be carefully considered for patients who require long distance transfer for each HBOT session. Indeed, extubation and periods of hypotension periods have been reported during transport for HBOT in paediatric patients.[2,3] Another important drawback related to transport may be an increased risk of intraventricular haemorrhage for preterms due to immature fragile vessels.[27] We did not encounter any complication during transportation.

The major limitation was the absence of long-term follow-up, which is particularly significant for acute CO intoxication cases in which there is a recognised risk of delayed neurological sequelae. Due to the study's retrospective nature, data on long-term follow-up were not available. Thus, this study aimed to evaluate acute responses to HBOT as all infant cases with many HBOT indications have been included and evaluated together. The long-term outcomes of HBOT for acute CO intoxication in infants are beyond the aim of this study.

To our knowledge, this is the largest study presenting 54 infants treated with HBOT. We report experience from two HBOT facilities with both multiplace and monoplace chambers, thus providing a broad clinical perspective. The scientific data on HBOT use in this age group is limited. More HBOT research is required in the paediatric population. However, conducting prospective controlled studies is challenging for ethical reasons.

## Conclusions

This study suggests that HBOT is a safe and effective treatment modality for infants. Paediatricians should consider HBOT in centres with appropriate clinical experience in the delivery of HBOT to infants. Paediatricians would be correct to hesitate to refer in centres not appropriately equipped/trained for the delivery of HBOT to infants. Close collaboration between paediatric and the hyperbaric medical teams and improving technical availabilities of HBOT facilities for infant patients would result in improved outcomes. This study may guide hyperbaric physicians in their clinical care of infant patients as well as future scientific studies.

## References

1 Moon RE, editor. Hyperbaric oxygen therapy indications. 14th ed. North Palm Beach (FL): Best Publishing Company; 2019.
2 Keenan HT, Bratton SL, Norkool DM, Brogan TV, Hampson NB. Delivery of hyperbaric oxygen therapy to critically ill, mechanically ventilated children. J Crit Care. 1998;13:7–12. doi: 10.1016/s0883-9441(98)90023-5. PMID: 9556121.
3 Frawley GP, Fock A. Pediatric hyperbaric oxygen therapy in Victoria, 1998–2010. Pediatr Crit Care Med. 2012;13(4):e240–4. doi: 10.1097/PCC.0b013e318238b3f3. PMID: 22643574.
4 Frawley G, Bennett M, Thistlethwaite K, Banham N. Australian paediatric hyperbaric oxygen therapy 1998–2011. Anaesth Intensive Care. 2013;41:74–81. doi: 10.1177/0310057X1304100113. PMID: 23362893.
5 Waisman D, Shupak A, Weisz G, Melamed Y. Hyperbaric oxygen therapy in the pediatric patient: the experience of the Israel Naval Medical Institute. Pediatrics. 1998;102(5):E53. doi: 10.1542/peds.102.5.e53. PMID: 9794983.
6 Liebert EL. Hyperbaric oxygen therapy in childhood carbon monoxide poisoning. Curr Opin Pediatr. 1999;11:259–64. doi: 10.1097/00008480-199906000-00017. PMID: 10349107.
7 Mirasoglu B, Cetin H, Ozdemir Akgun S, Aktas S. Hyperbaric

oxygen treatment for intrauterine limb ischaemia: a newborn in the chamber. Diving Hyperb Med. 2021;51:220–3. doi: 10.28920/dhm51.2.220-223. PMID: 34157740. PMCID: PMC8426121.

8 Siraneci R, Hatipoğlu N, Hatipoğlu H, Dündar K, Baygın L, Yildiz C, et al. Acute arterial thrombotic purpura complicating varicella and the role of hyperbaric oxygen as an adjunctive therapy. Turk J Pediatr. 2004;46:256–8. PMID: 15503480.

9 Yılmaz A, Kaya N, Meriç R, Bayramli Z, Öroğlu B, Celkan TT, et al. Use of hyperbaric oxygen therapy of purpura fulminans in an extremely low birth weight preterm: A case report. J Neonatal Perinatal Med. 2023;16:339–42. doi: 10.3233/NPM-200428. PMID:32741781.

10 Polak N, Fishelev G, Lang E, Wang Z, Neheman A, Haim YB, et al. Hyperbaric oxygen as salvage therapy for neonates suffering from critical ischemia of the glans penis after circumcision. Urology. 2021;149:e48–e51. doi: 10.1016/j.urology.2020.09.006. PMID: 32956687.

11 Rudge FW. Carbon monoxide poisoning in infants: treatment with hyperbaric oxygen. South Med J. 1993;86:334–7. doi: 10.1097/00007611-199303000-00017. PMID: 8451675.

12 Kreshak AA, Lawrence SM, Ontiveros ST, Castellano T, VanHoesen KB. Perinatal carbon monoxide poisoning: treatment of a 2-hour-old neonate with hyperbaric oxygen. AJP Rep. 2022;12(1):e113–e116. doi: 10.1055/s-0042-1744216. PMID: 35280718. PMCID: PMC8906995.

13 Turan C, Yurtseven A, Baki Beyter M, Saz EU. A 7-day-old male infant with carbon monoxide poisoning treated with hyperbaric oxygen. Pediatr Emerg Care. 2020;36(6):e360–e361. doi: 10.1097/PEC.0000000000001612. PMID: 30335685.

14 Sánchez EC. Use of hyperbaric oxygenation in neonatal patients: a pilot study of 8 patients. Crit Care Nurs Q. 2013;36:280–9. doi: 10.1097/CNQ.0b013e318294e95b. PMID: 23736667.

15 Wiebers J, Purdy I, Lieber M, Milisavljevic V. Hyperbaric oxygen in treatment of neonatal arterial thromboembolism of lower extremities. J Perinatol. 2006;26:777–9. doi: 10.1038/sj.jp.7211606. PMID: 17122788.

16 Waisman D, Baenzinger O, Gall N. Hyperbaric oxygen therapy in newborn infants and pediatric patients. In: Neuman TS, Thom SR, editors. Physiology and medicine of hyperbaric oxygen therapy. 1st ed. Philadelphia: Saunders; 2008. p. 95–116.

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

18 Harlan NP, Ptak JA, Rees JR, Cowan DR, Fellows AM, Moses RA, et al. International multicenter registry for hyperbaric oxygen therapy: results through June 2021. Undersea Hyperb Med. 2022;49:275–87. PMID: 36001560.

19 Wei L, Wang J, Cao Y, Ren Q, Zhao L, Li X, et al. Hyperbaric oxygenation promotes neural stem cell proliferation and protects the learning and memory ability in neonatal hypoxic-ischemic brain damage. Int J Clin Exp Pathol. 2015;8(2):1752–9. PMID: 25973064. PMCID: PMC4396307.

20 Gong XB, Feng RH, Dong HM, Liu WH, Gu YH, Jiang XY, et al. Efficacy and prognosis of hyperbaric oxygen as adjuvant therapy for neonatal hypoxic-ischemic encephalopathy: a meta-analysis study. Front Pediatr. 2022;10:707136. doi: 10.3389/fped.2022.707136. PMID: 35529335. PMCID: PMC9069061.

21 Jain KK. Hyperbaric oxygenation in obstetrics and gynecology. In: Jain KK, editor. Textbook of hyperbaric medicine. Springer; 2017. p. 485–9.

22 Ricci B, Calogero G. Oxygen-induced retinopathy in newborn rats: effects of prolonged normobaric and hyperbaric oxygen supplementation. Pediatrics.1988;82:193–8. PMID: 3399291.

23 Ricci B, Calogero G, Lepore D. Variations in the severity of retinopathy seen in newborn rats supplemented with oxygen under different conditions of hyperbarism. Exp Eye Res. 1989;49:789–97. doi: 10.1016/s0014-4835(89)80039-9. PMID: 2591495.

24 Calvert JW, Zhou C, Zhang JH. Transient exposure of rat pups to hyperoxia at normobaric and hyperbaric pressures does not cause retinopathy of prematurity. Exp Neurol. 2004;189:150–61. doi: 10.1016/j.expneurol.2004.05.030. PMID: 15296845.

25 Torbati D, Peyman GA, Wafapoor H, Shaibani SB, Khoobehi B. Experimental retinopathy by hyperbaric oxygenation. Undersea Hyperb Med. 1995;22:31–9. PMID: 7742708.

26 Sherman TI, Greenspan JS, St Clair N, Touch SM, Shaffer TH. Optimizing the neonatal thermal environment. Neonatal Netw. 2006;25:251–60. doi: 10.1891/0730-0832.25.4.251. PMID: 16913236.

27 Özek E, Gülcan Kersin S. Intraventricular hemorrhage in preterm babies. Turk Pediatri Ars. 2020;55:215–21. doi: 10.14744/turkpediatriars.2020.66742. PMID: 33061747. PMCID: PMC7536465.

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# Effect of hyperbaric oxygen treatment on ischaemia-reperfusion injury in rats detorsioned after experimental ovarian torsion

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**Abstract**
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**Introduction:** This study aimed to investigate whether hyperbaric oxygen treatment (HBOT) could ameliorate ischaemia-reperfusion injury in a rat model of ovarian torsion-detorsion.
**Methods:** Twenty-seven rats were divided among four groups: surgical sham rats (S) ($n = 6$) underwent identical anaesthesia and surgical incisions to other groups ($n = 7$ per group) but with no ovary intervention; torsion rats (T) underwent laparotomy, ovarian torsion, relaparotomy and sacrifice after three hours; torsion and detorsion rats (T/DT) underwent laparotomy, ovarian torsion (three hours), relaparotomy and detorsion, and sacrifice after one week; torsion, detorsion, hyperbaric oxygen rats (T/DT/HBOT) underwent laparotomy, ovarian torsion, relaparotomy and detorsion, and sacrifice after one week during which HBOT was provided 21 times (100% oxygen at 600 kPa for 50 min). In all groups blood collection for markers of oxidative stress or related responses, and ovary collection for histology were performed after sacrifice.
**Results:** When the T/DT, and T/DT/HBOT groups were compared, 8-hydroxy-2′-deoxyguanosine (a marker of oxidative damage to DNA) and malondialdehyde (a product of lipid peroxidation) levels were lower in the T/DT/HBOT group. Anti-Mullerian hormone levels were higher in the T/DT/HBOT group compared to the T/DT group. In addition, oedema, vascular occlusion, neutrophilic infiltration and follicular cell damage were less in the T/DT/HBOT group than in the T/DT group.
**Conclusions:** When biochemical and histopathological findings were evaluated together, HBOT appeared reduce ovarian ischaemia / reperfusion injury in this rat model of ovarian torsion-detorsion.

## Introduction

Ovarian torsion may be defined as the impairment of ovarian perfusion and occurrence of ischaemic changes, as a result of rotation of the ovary around the infundibulo-pelvic and utero-ovarian ligament.[1,2] Since the majority of the cases occur in the reproductive period, the protection of ovarian function is extremely important in terms of fertility and women's health in general. Historically, the standard treatment for ovarian torsion has been salpingo-oophorectomy on the affected side, due to concerns about the risk of thromboembolism. However, in observational studies, it has been noted that ovarian function continued in cases where detorsion had been undertaken.[3]

Minimising ischaemia-reperfusion injury in detorsion cases in which ovarian tissue is preserved has become a new area of interest amongst clinicians and scientists.[3–5] We have not been able to identify reports of hyperbaric oxygen treatment (HBOT) being used in this context. The promising results of HBOT in testicular torsion,[6–9] which has similar mechanisms as cases of ovarian torsion, inspired this study. Should HBOT prove beneficial *in vivo*, this might justify a clinical study.

## Methods

The study was approved by the Ethics Committee of Animal Experiments in the Health Sciences University of Hamidiye (approval number 46418926-605.02).

### ANIMALS

Twenty-seven female Sprague-Dawley rats of about four months age, weighing 200–250 g, were used. Experimental design elements suggested by ARRIVE guidelines 2.0 were followed.[10]

### ANAESTHESIA

For surgical interventions anaesthesia was provided intraperitoneally with 80 mg·kg$^{-1}$ ketamine hydrochloride and 20 mg·kg$^{-1}$ xylazine hydrochloride. Where necessary, ketamine (25 mg·kg$^{-1}$) was repeated (based on checking reflex responses) to keep the anaesthesia depth of the rats constant.

### PROCEDURE

The rats were divided into four groups: In the surgical sham group (S), six rats' laparotomy incisions were closed after the uterus and adnexa were seen. After three hours relaparotomy was performed and bilateral ovaries were removed. In the torsion group (T) ($n$ = 7), rats underwent laparotomy, exposing the ovaries which were tied with 5/0 polydioxanone suture approximately 1 cm below the adnexal structure containing the tubal and ovarian vessels, in order to create an ovarian ischaemia model. Three hours after skin closure, both ovaries were removed by relaparotomy. Both S and T groups were sacrificed after blood and tissue samples were taken at relaparotomy. In the torsion/detorsion group (T/DT) ($n$ = 7) after performing the ischaemia intervention as above, the ovaries were reperfused by suture removal during relaparotomy at the third hour. The rats were housed in their cages for one week without any other treatment. In the torsion/detorsion/hyperbaric oxygen (T/DT/HBOT) group ($n$ = 7) rats underwent an identical procedure to the T/DT group but subsequently underwent HBOT sessions for one week (as below), in a pressure chamber designed for animals.

The HBOT protocol was designed in accordance with previous literature relevant to our study.[11] That study investigated the effect of HBOT (1,000 kPa) in testicular torsion in rats. In the present study we restricted the treatment pressure to 600 kPa (absolute). In our protocol, the pressure was increased to 600 kPa over 10 min and maintained for 50 min using oxygen. Compression began slowly to minimise discomfort. Thereafter, decompression was conducted linearly to ambient pressure at a rate of 200 kPa·min$^{-1}$. The chamber underwent continuous ventilation to avoid accumulation of carbon dioxide. In the first two days following surgery, four sessions of 50 minutes were applied. On the 3rd, 4th, and 5th days, three sessions of 50 minutes each were applied. On the 6th and 7th days, 2 sessions of 50 minutes were applied.[12] That is, 21 sessions of HBO were given over seven days, and the daily treatment sessions program can be summarised as 4/4/3/3/3/2/2.[7,12] At the end of the 7th day, both ovaries were removed by relaparotomy and blood samples taken after which the rats were sacrificed.

Blood samples underwent enzyme-linked immunosorbent assay (Bioassay Laboratory brand trade kit, China) conducted by staff unaware of group allocations. Five assays were conducted: 8-hydroxy-2′-deoxyguanosine (8-OHDG), one of the oxidative damage products when reactive oxygen species damage DNA;[13] malondialdehyde (MDA), a product of lipid peroxidation (higher levels indicate a greater degree of oxidative damage);[14] superoxide dismutase (SOD), the only enzyme in the organism that utilises the superoxide free radical as a substrate (an increase indicates antioxidant capacity as well as indirectly indicating the mitochondrial extent of oxidative damage); glutathione peroxidase (GSH-Px), found in the cell cytoplasm (an increase protects cells against oxidative damage caused by $H_2O_2$);[15] and anti-Mullerian hormone (AMH), an ovarian hormone (a decrease indicates a decrease in ovarian reserve).[16]

The ovarian tissues were fixed in 10% formaldehyde for 24 hours after which 4 μm sections were prepared from paraffin blocks and stained with hematoxylin eosin (H&E). The sections were examined with a light microscope for ischaemia-reperfusion injury and the results were evaluated semi-quantitatively as 0 – no damage, 1 – mildly damaged, 2 – moderately damaged, 3 – severely damaged, in respect of oedema, follicular cell damage, vascular congestion, haemorrhage, neutrophil infiltration and cohesion failure. The examining pathologist was blinded to group allocation.

### STATISTICAL ANALYSIS

The 'E value' method was used to determine the number of animals to be used in our study. According to this analysis, the E value should be between 10 and 20.[17] The E value (effectively the degrees of freedom for analysis of variance) was calculated from total number of animals – total number of groups. Assuming use of six rats per group in four groups, one of which is the control group, the total number of animals needed was 24 and the E value was 24-4 = 20.[17]

Statistical analyses were undertaken with the Statistical Package for Social Sciences, version 22.0 (SPSS Inc, Chiago, III, USA). Individual group biochemical parameters were assessed with the 1-sample Kolmogorov-Smirnov Z test and found normally distributed. The data were therefore expressed as means and standard deviations (SD). Analysis of variance was performed on the biochemical data to examine differences among groups. If a significant group effect was found, a Tukey honestly significant difference (HSD) test was used to identify the location of

differences between groups. Statistical significance was defined as $P < 0.05$. Tissue damage scores were compared by nonparametric analysis, and statistical significance was assessed by Kruskal-Wallis followed by a Bonferroni-corrected Mann-Whitney U test.

## Results

### 8-OHDG VALUES

The one-way ANOVA test showed a statistically significant difference between the mean 8-OHDG levels of the groups ($P < 0.05$). The values in the T/DT/HBOT group were significantly decreased compared to the T/DT group (2.42 [SD 0.54] vs 2.79 [0.43] ng.ml$^{-1}$), $P < 0.05$. Group T had the lowest data compared to the other three groups 1.28 (0.17) ng.ml$^{-1}$ (Figure 1).

### MDA VALUES

The one-way ANOVA test showed a statistically significant difference between the mean MDA levels of the groups ($P < 0.05$). The values in the T/DT/HBOT group were significantly decreased compared to the T/DT group (1.20 [0.19] vs 2.03 [0.59] nmol.ml$^{-1}$), $P < 0.05$. In addition, the significantly lower value in Group T compared to Group T/DT (0.76 [0.24] vs 2.03 [0.59] nmol.ml$^{-1}$), $P < 0.05$ showed that reperfusion injury was more prominent than ischaemic injury (Figure 2).

### GSH-PX VALUES

The one-way ANOVA test showed a statistically significant difference between the mean GSH-Px levels of the groups ($P < 0.05$). The values in the T/DT group were higher compared to the T/DT/HBOT group (142.74 [28.22] vs 98.37 [42.99] U.ml$^{-1}$) but the difference was statistically insignificant ($P = 0.085$). While the differences between the other three groups were statistically insignificant, the significant decrease in the torsion-only group (T) was considered an interesting result. (Figure 3).

### SOD VALUES

The one-way ANOVA test showed a statistically significant difference between the mean SOD levels of the groups ($P < 0.05$). Similar to the GSH-Px result, the only result significantly different from the other groups was the low value in the torsion-only group (T) (0.94 [0.11] ng.ml$^{-1}$). The differences between the other three groups were statistically insignificant ($P = 0.833$) (Figure 4).

### AMH VALUES

The one-way ANOVA test showed a statistically significant difference between the means of the AMH levels of the groups ($P < 0.05$). The highest AMH value was found in Group S, and the lowest AMH value was found in Group T (Figure 5). One potentially exciting finding was that the AMH value in Group T/DT/HBOT was higher than Group T/DT (2.95 [0.56] ng·ml$^{-1}$ vs 2.10 [0.97] ng.ml$^{-1}$) although this difference was not statistically significant.

### PATHOLOGICAL ANALYSIS OF OVARIAN TISSUE

The histopathological damage grades are summarised in Table 1.

#### *Oedema*

No oedema was found in Group S. Severe oedema was observed in Group T/DT, while moderate oedema was observed in Group T/DT/HBOT and Group T. The increased oedema in Group T/DT was significantly greater than in Group T/DT/HBOT and Group T ($P < 0.05$).

#### *Vascular congestion*

Relatively mild vascular congestion was seen in Group S, with the most severe congestion seen in Group T/DT. Severe vascular congestion was also observed in Group T. Vascular congestion in Group T/DT/HBOT was significantly less than both Group T/DT and Group T ($P < 0.05$).

#### *Neutrophil infiltration*

No neutrophilic infiltration was observed in Group S. While severe infiltration was observed in Group T/DT and Group T, mild infiltration was observed in Group T/DT/HBOT and these differences with other groups were statistically significant ($P < 0.05$) (Figure 6).

#### *Follicular cell damage*

Follicular damage was not seen in Group S and Group T. Moderate damage was observed in Group T/DT, while mild damage was observed in Group T/DT/HBOT.

#### *Haemorrhage*

No haemorrhage was observed in Group S. Moderate haemorrhage was observed in the right ovary of only one rat in Group T. This has been interpreted as a surgical complication. Although the haemorrhage seen in Group T/DT was higher than seen in Group T/DT/HBOT, this difference was statistically insignificant ($P = 0.71$) (Figure 7).

#### *Cohesion failure*

Cohesion failure was not seen in Group S. Mild loss of cohesion was observed in Group T, Group T/DT and Group T/DT/HBOT, and there were no significant differences between groups.

**Figure 1**
Comparison of 8-OHDG values between groups; data are mean and standard deviation; S – surgical control group; T – surgery plus ovarian torsion group; T/DT – surgery plus torsion plus detorsion (reperfusion) group; T/DT/HBOT – surgery plus torsion plus detorsion (reperfusion) plus hyperbaric oxygen treatment group

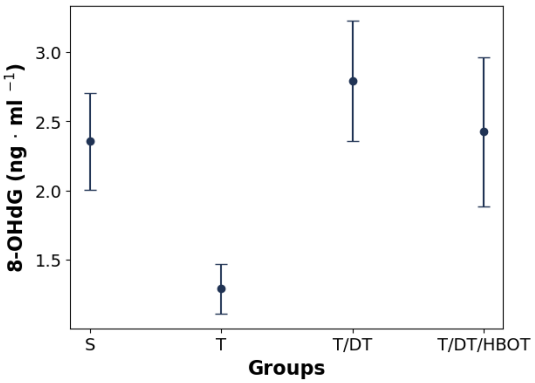



**Figure 2**
Comparison of MDA values between groups; data are mean and standard deviation; S – surgical control group; T – surgery plus ovarian torsion group; T/DT – surgery plus torsion plus detorsion (reperfusion) group; T/DT/HBOT – surgery plus torsion plus detorsion (reperfusion) plus hyperbaric oxygen treatment group

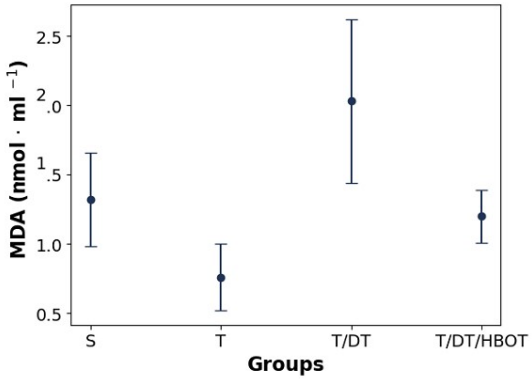



**Figure 3**
Comparison of GSH-Px values between groups; data are mean and standard deviation; S – surgical control group; T – surgery plus ovarian torsion group; T/DT – surgery plus torsion plus detorsion (reperfusion) group; T/DT/HBOT – surgery plus torsion plus detorsion (reperfusion) plus hyperbaric oxygen treatment group

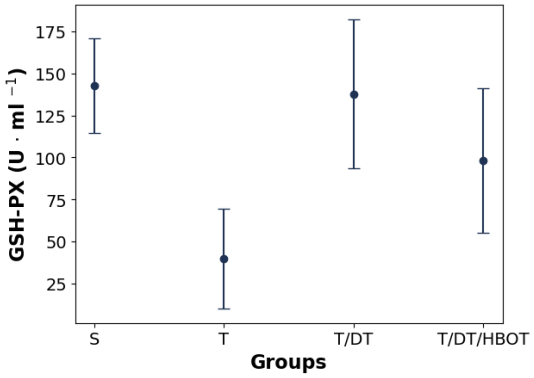



**Figure 4**
Comparison of SOD values between groups; data are mean and standard deviation; S – surgical control group; T – surgery plus ovarian torsion group; T/DT – surgery plus torsion plus detorsion (reperfusion) group; T/DT/HBOT – surgery plus torsion plus detorsion (reperfusion) plus hyperbaric oxygen treatment group

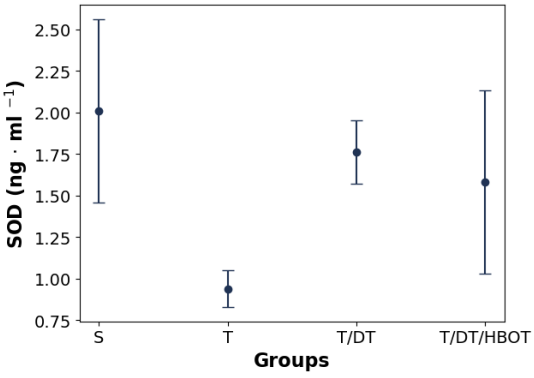
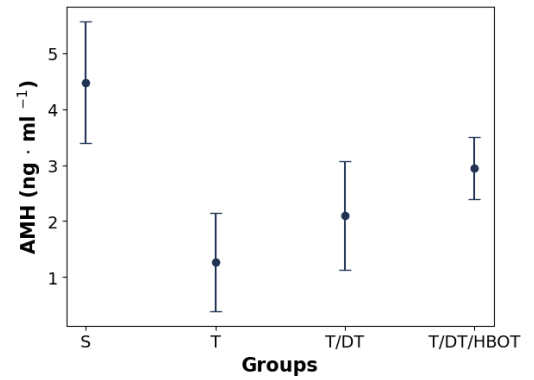



**Figure 5**
Comparison of AMH values between groups; data are mean and standard deviation; S – surgical control group; T – surgery plus ovarian torsion group; T/DT – surgery plus torsion plus detorsion (reperfusion) group; T/DT/HBOT – surgery plus torsion plus detorsion (reperfusion) plus hyperbaric oxygen treatment group




## Discussion

The significant decrease in 8-OHDG values in Group T/DT/HBOT compared to Group T/DT ($P < 0.05$) indicated that HBOT reduced DNA damage resulting from reperfusion-induced oxidative stress. The highest MDA value was found in Group T/DT, while the values in Group S and Group T/DT/HBOT were similar and statistically significantly lower compared to Group T/DT ($P < 0.05$). This result is further evidence that HBOT may have suppressed reperfusion-induced oxidative stress. There is no obvious basis for the lower MDA values in Group T compared with Group S, and specifically targeted studies would be required to understand this clearly. Nevertheless, the fact that MDA in Group T/DT is significantly higher than Group S suggests that the secondary oxidative damage that follows ovarian ischemia-reperfusion is greater than after a simple laparotomy and anaesthetic.

**Table 1**

Comparison of discrete scores for histopathological variables between groups; data are numbers of ovaries in each category; score key: 0 – no damage, 1 – mildly damaged, 2 – moderately damaged, 3 – severely damaged; L – left; R – right; S – surgical control group; T – surgery plus ovarian torsion group; T/DT – surgery plus torsion plus detorsion (reperfusion) group; T/DT/HBOT – surgery plus torsion plus detorsion (reperfusion) plus hyperbaric oxygen treatment group

| Histologic parameter | Score | Group S | | Group T | | Group T/DT | | Group T/DT/HBOT | |
|---|---|---|---|---|---|---|---|---|---|
| | | R | L | R | L | R | L | R | L |
| Oedema | 0 | 6 | 6 | 2 | 3 | 0 | 0 | 1 | 0 |
| | 1 | 0 | 0 | 5 | 4 | 4 | 3 | 6 | 7 |
| | 2 | 0 | 0 | 0 | 0 | 3 | 4 | 0 | 0 |
| | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vascular congestion | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 1 | 3 | 3 | 2 | 1 | 1 | 1 | 7 | 6 |
| | 2 | 1 | 1 | 4 | 5 | 6 | 3 | 0 | 0 |
| | 3 | 0 | 0 | 1 | 1 | 0 | 3 | 0 | 0 |
| Neutrophilic infiltration | 0 | 6 | 6 | 1 | 0 | 0 | 0 | 6 | 5 |
| | 1 | 0 | 0 | 5 | 4 | 0 | 4 | 1 | 2 |
| | 2 | 0 | 0 | 1 | 3 | 7 | 3 | 0 | 0 |
| | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Follicular cell damage | 0 | 6 | 6 | 7 | 7 | 4 | 5 | 7 | 5 |
| | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| | 2 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 |
| | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cohesion failure | 0 | 6 | 6 | 2 | 0 | 0 | 0 | 1 | 1 |
| | 1 | 0 | 0 | 5 | 5 | 7 | 7 | 6 | 6 |
| | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 |
| | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Haemorrhage | 0 | 6 | 6 | 7 | 6 | 4 | 4 | 3 | 3 |
| | 1 | 0 | 0 | 0 | 0 | 3 | 3 | 4 | 4 |
| | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Group T had lower GSH-Px and SOD values compared to the other three groups. The likely reason for this result is the reperfusion damage suffered by Groups T/DT and T/DT/HBOT, whereas Group T's rats were sacrificed prior to reperfusion damage. The reperfusion damage might have caused a secondary anti-oxidant capacity increase in the rat system. It is acknowledged that this explanation is somewhat inconsistent with the high GSH-Px and SOD values measured in Group S. Further studies are necessary to determine the cause of these results.

The significantly lower AMH level of Group T compared to Group S ($P < 0.05$) can be explained by isolation of the ovaries such that the AMH levels in the plasma fell during

**Figure 6**

Post-reperfusion neutrophilic infiltration; A – mild infiltration in Group T/DT/HBOT (surgery plus torsion plus detorsion [reperfusion] plus hyperbaric oxygen treatment); B – severe infiltration in Group T/DT (surgery plus torsion plus detorsion [reperfusion])

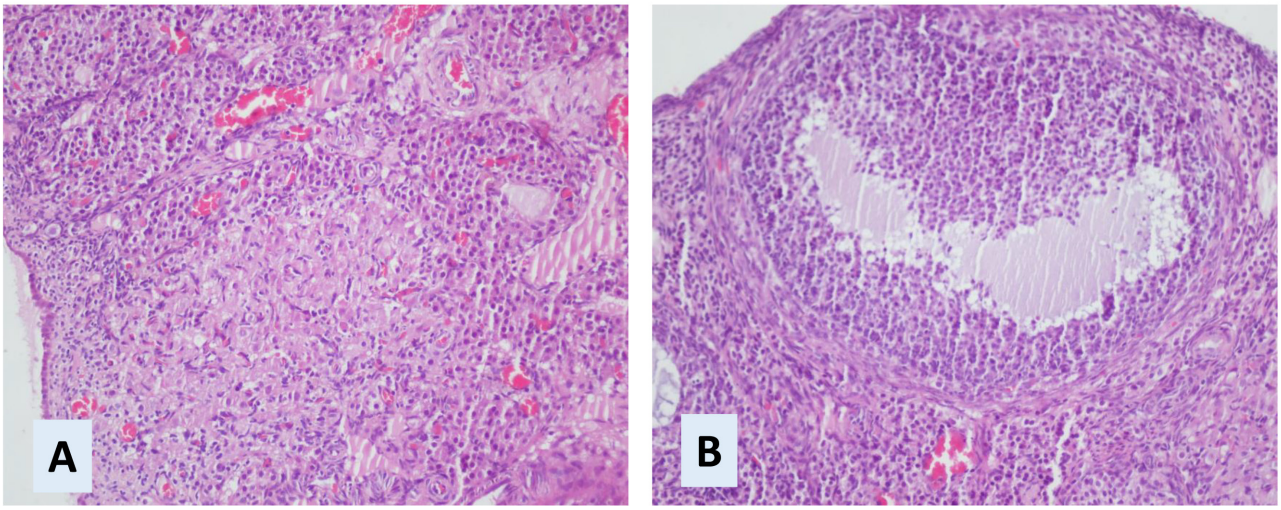
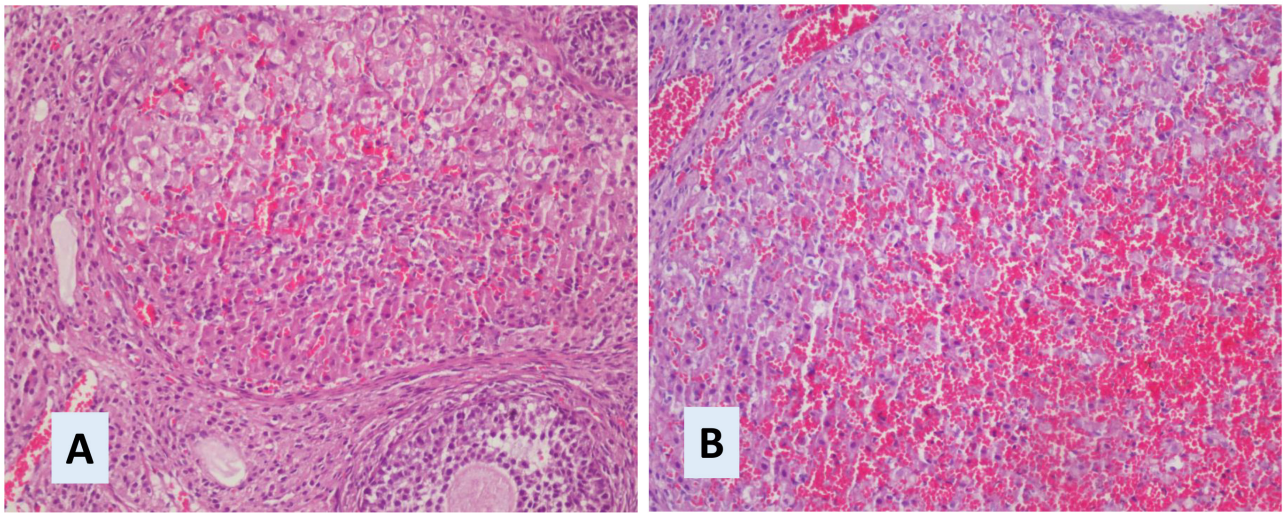



**Figure 7**

Post-reperfusion haemorrhage; A – moderate haemorrhage in Group T/DT/HBOT (surgery plus torsion plus detorsion [reperfusion] plus hyperbaric oxygen treatment); B – severe haemorrhage in Group T/DT (surgery plus torsion plus detorsion [reperfusion])




the period of ischaemia. The fact that Group T/DT was lower than Group S ($P < 0.05$) but higher than Group T ($P < 0.05$) is perhaps explained by backwashing of AMH into plasma from a previously isolated (but dysfunctional) ovary after ischaemia and reperfusion. There was a trend toward increased AMH levels in the T/DT/HBOT group compared to the T/DT group, perhaps suggesting some degree of protection of ovarian reserve by HBOT, but this difference was statistically insignificant.

The most severe histologic oedema was seen in Group T/DT, with significantly less oedema in Group T/DT/HBOT suggesting an anti-inflammatory effect of HBOT in this context. Perhaps not surprisingly, HBOT exposure was also associated with reduced vascular congestion and reduced neutrophilic infiltration. The latter finding was consistent with previously reported oxygen-dose-dependent reduction in expression of adhesion molecules on cultured neutrophils activated in an *in vitro* ischaemia-reperfusion simulation.[18] When follicular cell damage and haemorrhage were examined, No follicular cell damage or haemorrhage was observed in Groups S and T (bleeding in one Group T ovary was thought to be surgical artefact). There was a decrease in the follicular cell damage in Group T/DT/HBOT compared to Group T/DT supporting a protective effect of HBOT during ovarian ischaemia-reperfusion.

These results, collectively indicate a potential role in for HBOT in protecting the ovaries from reperfusion injury after detorsioning. However, there are some obvious limitations

in extrapolating beyond our small study in rats, not least being the possibility that results in an animal model may not translate into humans. We also acknowledge that the HBOT regimen was highly atypical of human treatment paradigms with oxygen being administered at 600 kPa and the treatment frequency being much higher than in typical clinical practice. We selected the study parameters to be consistent with previous successful work in a rat model of testicular torsion-detorsion, but further dose-finding studies, perhaps with a narrower outcome focus (concentrating on those outcome measures that appeared to benefit here), would be required to explore whether clinically relevant treatment regimens also seem effective.

## Conclusions

Our study has demonstrated that HBOT appears to reduce ovarian damage both biochemically and histopathologically in this ovarian ischaemia-reperfusion model. As a 'first of type' study with small sample sizes, it is clear that more comprehensive studies will be needed to further clarify effects and to optimise HBOT schedules and timing. We see potential for clinical testing following more comprehensive *in vivo* studies.

## References


1 McWilliams GDE, Hill MJ, Dietrich CS 3rd. Gynecologic emergencies. Surg Clin North Am. 2008;88:265–83. doi: 10.1016/j.suc.2007.12.007. PMID:18381113.

2 Tielli A, Scala A, Alison M, Vo Chieu VD, Farkas N, Titomanlio L, et al. Ovarian torsion: diagnosis, surgery, and fertility preservation in the pediatric population. Eur J Pediatr. 2022;181:1405–11. PMID: 35094159.

3 Bristow RE, Nugent AC, Zahurak ML, Khouzhami V, Fox HE. Impact of surgeon specialty on ovarian-conserving surgery in young females with an adnexal mass. J Adolesc Health. 2006;39:411–6. doi: 10.1016/j.jadohealth.2005.12.022. PMID: 16919804.

4 Anders JF, Powell EC. Urgency of evaluation and outcome of acute ovarian torsion in pediatric patients. Arch Pediatr Adolesc Med. 2005;159:532–5. doi: 10.1001/archpedi.159.6.532. PMID: 15939851.

5 Tamura H, Takasaki A, Miwa I, Taniguchi K, Maekawa R, Asada H, et al. Oxidative stress impairs oocyte quality and melatonin protects oocytes from free radical damage and improves fertilization rate. J Pineal Res. 2008;44:280–7. doi: 10.1111/j.1600-079X.2007.00524.x. PMID: 18339123.

6 Alp BF, Cebi G, Özdemir A, Irkilata HC, Uzun G. Hyperbaric oxygen treatment for unilateral testicular torsion in a child. Diving Hyperb Med. 2014;44:161–2. PMID: 25311324.

7 Karlı G. Erginel B, Yanar F, Üstyol EA, Ozluk Y, Karadeniz MS, et al. Comparison of hyperbaric oxygen and ozone treatment for ischemia/re-perfusion injury in an experimental testicular torsion model. Ulus Travma Acil Cerrahi Derg. 2023;29:259–65. doi: 10.14744/tjtes.2023.98861. PMID: 36880629. PMCID: PMC10225826.

8 Kolski JM, Mazolewski PJ, Stephenson LL, Texter J, Grigoriev VE, Zamboni WA. Effect of hyperbaric oxygen therapy on testicular ischemia-reperfusion injury. J Urol. 1998;160:601–4. PMID: 9679936.

9 Zhang Y, Lv Y, Liu YJ, Yang C, Hu HJ, Meng XE, et al. Hyperbaric oxygen therapy in rats attenuates ischemia-reperfusion testicular injury through blockade of oxidative stress, suppression of inflammation, and reduction of nitric oxide formation. Urology. 2013;82:489.e9–489.e15. doi: 10.1016/j.urology.2013.04.016. PMID: 23769121.

10 Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. Br J Pharmacol. 2020;177:3617–24. doi: 10.1111/bph.15193. PMID: 32662519. PMCID: PMC7393194.

11 Alici B, Kalkan M, Tunç B, Çetïnkaya M, Aktaş Ş, Uzun H. Testiküler torsiyonda hiperbarik oksijen tedavisinin etkinliği. Türk Üroloji Dergisi/Turkish Journal of Urology. 2004;30(3):273–8.

12 Konak M, Cincik H, Erkul E, Kucukodaci Z, Gungor A, Ozdemir S, Cekin E, et al. The protective effects of different treatments on rat salivary glands after radiotherapy. Eur Arch Otorhinolaryngol. 2016;273:4501–6. doi: 10.1007/s00405-016-4159-2. PMID: 27324888.

13 Graille M, Wild P, Sauvain JJ, Hemmendinger M, Guseva Canu I, Hopf NB. Urinary 8-OHdG as a biomarker for oxidative stress: a systematic literature review and meta-analysis. Int J Mol Sci. 2020;21(11):3743. doi: 10.3390/ijms21113743. PMID: 32466448. PMCID: PMC7313038.

14 Ayala A, Muñoz MF, Argüelles S. Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. Oxid Med Cell Longev. 2014;2014:360438. doi: 10.1155/2014/360438. PMID: 24999379. PMCID: PMC4066722.

15 Evans MD, Dizdaroglu M, Cooke MS. Oxidative DNA damage and disease: induction, repair and significance. Mutat Res. 2004;567:1–61. doi: 10.1016/j.mrrev.2003.11.001. PMID: 15341901.

16 Di Clemente N, Racine C, Pierre A, Taieb J. Anti-müllerian hormone in female reproduction. Endocr Rev. 2021;42:753–82. doi: 10.1210/endrev/bnab012. PMID: 33851994.

17 Charan J, Kantharia ND. How to calculate sample size in animal studies? J Pharmacol Pharmacother. 2013;4:303–6. doi: 10.4103/0976-500X.119726. PMID: 24250214. PMCID: PMC3826013.

18 Buras JA, Stahl GL, Svoboda KK, Reenstra WR. Hyperbaric oxygen downregulates ICAM-1 expression induced by hypoxia and hypoglycemia: the role of NOS. Am J Physiol Cell Physiol. 2000;278(2):C292–302. doi: 10.1152/ajpcell.2000.278.2.C292. PMID: 10666024.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# Review of saturation decompression procedures used in commercial diving

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**Abstract**
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**Introduction:** This is a review of commercial heliox saturation decompression procedures. The scope does not include compression, storage depth or bell excursion dive procedures. The objectives are to: identify the sources of the procedures; trace their evolution; describe the current practice; and detect relevant trends.
**Methods:** Eleven international commercial diving companies provided their diving manuals for review under a confidentiality agreement.
**Results:** Modern commercial diving saturation procedures are derived from a small number of original procedures (United States Navy, Comex, and NORSOK). In the absence of relevant scientific studies since the late 80's, the companies have empirically adapted these procedures according to their needs and experience. Such adaptation has caused differences in decompression rates shallower than 60 msw, decompression rest stops and the decision to decompress linearly or stepwise. Nevertheless, the decompression procedures present a remarkable homogeneity in chamber $PO_2$ and daily decompression rates when deeper than 60 msw. The companies have also developed common rules of good practice; no final decompression should start with an initial ascending excursion; a minimum hold is required before starting a final decompression after an excursion dive. Recommendation is made for the divers to exercise during decompression.
**Conclusions:** We observed a trend towards harmonisation within the companies that enforce international procedures, and, between companies through cooperation inside the committees of the industry associations.

## Introduction

Dr Albert Benkhe is credited with formulating the concept of saturation diving following the salvage of the crew of the USS Squalus submarine in 1942. The first human heliox saturation to 30 metres of seawater (msw) was performed at the Navy Experimental Diving Unit in 1963 following the Genesis Project of Dr George Bond.

Preliminary developments of saturation operations were undertaken in underwater habitats (Conshelf, Sealab, Tektite, Pre-Continent, etc.). Then, the technology evolved to saturation chambers installed on deck rather than on the seabed: logistics were easier; energy was directly supplied from the vessel. It became possible to abandon the site in bad weather.

The first commercial diving helium-oxygen saturation operations began in the late sixties. In 1965, the Undersea Division of Westinghouse Electric Corporation, under the direction of Jerry O'Neill and Alan Krasberg, carried out the first commercial saturation project for clearing the trash rack of the Smith Mountain dam at 61 m in Virginia. The system, called Cachalot, consisted of a large decompression chamber and a personnel transfer capsule, which could be mated to the chamber under pressure. In 1969, Comex carried out a saturation operation to 100 msw in the Gulf of Biscayne onboard the Astragale vessel.

In 1971, the Brent field was discovered at a depth of 140 msw exceeding the possibilities of surface-oriented diving. The installation of the North Sea platforms drove the development of heliox saturation diving and triggered the demand for qualified personnel. The first divers came from the navies, the only institutions at the time with a formal training scheme, and set the discipline that still prevails during dive supervision. American divers arrived from the Gulf of Mexico and brought along the fiberglass helmets, the hot water suits and the silver duct tape. This diversity of culture is the foundation on which saturation diving developed. The diving companies established associations such as the Association of Diving Contractors (AODC) and later the International Marine Contractors Association (IMCA), which turned saturation diving into a mature and

efficient technology in less than ten years. By the 1980's, more than 6,000 divers were working in the North Sea and the 'North Sea Standards' ruled the offshore world.

However, the standardisation effort did not include heliox saturation procedures. In the 70s, safe and efficient saturation provided a commercial advantage over competition. Diving manuals were stamped 'Secret'. Even though companies are now developing numerous industrial guidelines, they continue to use different diving procedures.

A heliox saturation dive includes the following phases (Figure 1):

- The initial pressurisation or 'blowdown' of divers to target pressure corresponding to the storage depth. The pressurisation may include stops. Its duration is around 2 hours (h) for compression to 120 msw storage depth. It is significantly slower for saturations deeper than 180 msw to control high-pressure nervous syndrome (HPNS) and compression arthralgia.
- A minimal hold period after the divers arrive at storage depth and before they may start their first bell dive. This allows the divers to adapt to depth. The hold duration varies with storage depth: it is around 2 h at 120 msw storage depth.
- The 'bottom phase' during which the divers live in a chamber, at storage depth.
- The bell dives. Divers are transferred daily from the storage chamber to the dive site in the diving bell. The allowed excursion vertical distance depends on depth. It is around 20 msw at 120 msw storage depth.
- The final decompression to surface pressure. The initial phase is carried out with a constant chamber $PO_2$. The last phase proceeds from 15 msw to the surface with a constant chamber oxygen fraction. A typical decompression from 120 msw storage depth lasts five days.
- The saturation time is limited to 28 days by Diving Medical Advisory Committee (DMAC) guidance note 21.[1] This limitation may differ with local regulations, for instance in Norway.

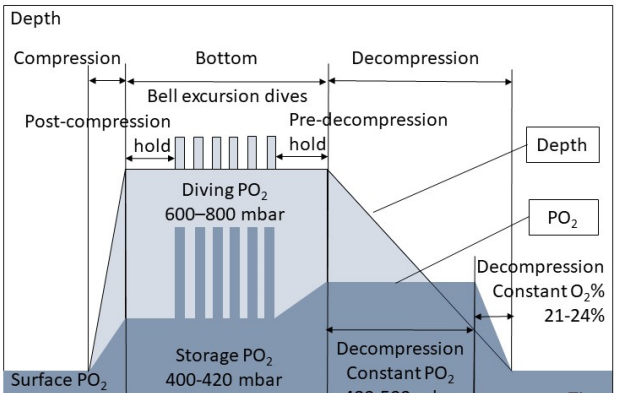
The purpose of this review is to document the current international saturation decompression procedures used in the offshore industry. The objectives are to 1) identify the source of the procedures, 2) trace their evolution, 3) describe the current practice and 4) detect any relevant trends.

## Methods

### SOURCES

The documentation related to the development of commercial diving in general, and saturation diving in particular, is dispersed, mainly located in company internal and restricted documents. The authors have been involved in commercial diving operations during their career. Non-referenced information in this review should be considered as sharing of personal experience. In particular, two authors worked for Comex and Stolt Comex Seaway and provided information on their historical diving manuals.

**Figure 1**
A typical commercial diving saturation showing depth profile and divers inhaled partial pressure of oxygen ($PO_2$); mbar – millibar




### UNITS

The documents reviewed are operational procedures where depth is used instead of ambient pressure and where expressions such as 'shallower', 'deeper', 'ascending' or 'surface' are common terms. With editorial consent we deliberately kept this technical jargon for consistency. For the same reason:

- Gas partial pressures are expressed in mbar (1 mbar = 0.1 kPa). Gas fractions are expressed in percentages.
- Pressures are expressed in msw (1 msw = 10.0381 kPa according to EN 13319).
- Imperial units have been converted using 1 foot of seawater (fsw) = 0.30643 msw as specified in the US Navy diving manual. When procedures used both imperial and metric systems, only the provided metric values were considered.

### DIVING COMPANIES

The IMCA website lists 50 companies that hold a certificate for 'unrestricted diving' which covers saturation diving. This number must be reduced to around 30 considering that some companies have multiple registrations. We selected 11 leading international companies for which we had connections through our professional activities. The conditions for participation were defined in a memorandum of understanding, signed by the authors and each diving company, stating that:

- The procedures could be used scientifically with the name of the company being unidentifiable.
- The company could review the final paper and retain the right to withdraw from the publication.

The eleven companies are:
- Boskalis, Papendrecht, The Netherlands
- DOF Subsea, Perth, WA
- Fugro, Singapore
- Helix Well Ops, Aberdeen, UK
- K Subsea, Singapore
- McDermott, Houston, Texas, USA
- Mermaid Subsea Services, Bangkok, Thailand
- Rever Offshore, Aberdeen, UK
- Shelf Subsea, Perth, WA
- Subsea7, Aberdeen, UK
- TechnipFMC, Aberdeen, UK

They are later de-identified as company A, company B, etc in an order unrelated to the above list. For each of these diving manuals received we associated a saturation procedure called procedure A, procedure B, etc. Note that we compared procedures in the range of 200 msw to surface, independently of the deepest storage depth specified in the manual. We excluded from the study any specific procedures used for deeper diving. We considered procedures in use in 2020 and disregarded any subsequent versions.

It should be noted that changes have occurred in the industry since 2022. Rever Offshore was taken over by the company Boskalis Subsea Services, but their procedures were reviewed by the former Rever Offshore diving manager. Fugro have ceased manned diving operations and no longer maintain their diving manuals. Simon Binsted, the former Fugro Diving Manager received authorisation from Fugro management to review this paper on their behalf.

### HELIOX SATURATION DECOMPRESSION PROCEDURES

We focused on the final decompression of saturation dives for which we identified several operational characteristics:
- The minimal hold period at storage depth that is generally required after the divers have returned from their last excursion dive, before final decompression.
- An initial 'pull-up'. This corresponds to a rapid pressure drop equivalent to an upward excursion that was historically used to initiate decompression.
- The decompression protocol. The decompression generally takes place as a continuous pressure reduction ('continuous bleed'), or alternatively through incremental steps of typically 0.2–0.3 msw.
- The daily decompression period. Decompression can be continuous (24 h/24 h) or include interruptions for divers' comfort.
- These interruptions are called 'rest stops' by the US Navy. The rest stop can be set at a fixed time (at night for instance) or after a given daily decompression time. In that case, the time of the rest stop depends on the final decompression start time ('sliding rest stop').
- The chamber oxygen. The decompression starts with a constant chamber $PO_2$. However, the chamber oxygen fraction increases as the pressure decreases and must be limited to less than 23% because of the fire risk. A common chamber $PO_2$ of 500 mbar will exceed 20% at 15 msw. From 15 msw to surface, the decompression proceeds with a constant oxygen fraction.
- The decompression rates, which vary depending on depth ranges. The term 'decompression profile' characterises the distribution of decompression rates over depth.
- The daily decompression rate which is the pressure reduction achieved in 24 h, including rest hold periods.

### ANALYSIS

We first studied the operational features of the decompression such as initial pull-up, decompression hold, daily rate of ascent, etc. We have compared decompression procedures from these companies as well as reference procedures such as:
- The procedures published in the regulations of Norway, Brazil and France.
- The procedures of the US Navy Diving Manual.
- The procedures from historical diving companies, Comex and Stolt Comex Seaway, for which two authors worked.

We then attempted to discuss the safety performances by using four endpoints:
- The decompression sickness (DCS) incidence recorded during operations.
- The venous gas emboli (VGE) grade measured during or after the decompression.
- The oxygen exposure and its level of pulmonary toxicity.

### DIVER POPULATION

To characterise the diving population, at least in the frame of the North Sea operations, one of the participating companies provided the age distribution of 131 divers who rotated onboard one of their vessels in 1979.

It is the authors' view that saturation divers have significant experience; They traditionally start as air divers at 30 years old, move to saturation diving 10 years later and stay in the career. At the time of the study, the mean age of the saturation divers was 47 (range 30–61) (Figure 2).

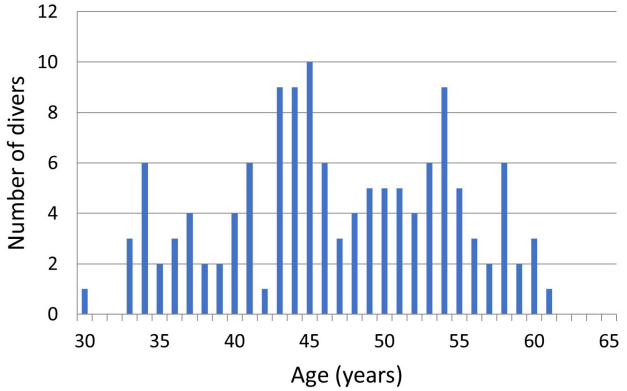
## Results

### HISTORICAL REFERENCE PROCEDURES

*US Navy procedures*

The US Navy saturation procedures were first published in the 1979 revision 2 of the US Navy Diving Manual.[2] They were characterised by:
- The possibility to initiate decompression by an ascending excursion.

**Figure 2**
Age distribution of 131 saturation divers working on a large North Sea diving support vessel




- A constant rate of decompression deeper than 60 msw and, varying rates from 60 msw to surface.
- Slow decompression rates and a low chamber $PO_2$ (350 to 400 mbar) until the fire risk zone is reached.
- A typical rest stop pattern during the decompression with a night stop from 00:00 to 06:00 and an afternoon stop from 14:00 to 16:00, leaving a total decompression time of 16 h per day.
- A chamber oxygen fraction controlled between 19% and 23% in the last metres of the decompression due to the fire risk.

The 2016 rev 7 US Navy Diving Manual brought few changes: the rates of decompression remained unchanged; the chamber decompression $PO_2$ was increased to 440–480 mbar; the timing of rest stop could be shifted depending on operational requirements.[3]

*Comex procedures*

Comex was a leading diving company during the 70's and 80's. This French company invested heavily in research and conducted a series of developments on deep diving in its Marseille hyperbaric center. Comex designed original diving procedures that have significantly influenced the industry.

The first Comex saturation manual was published by Dr Xavier Fructus in 1974 after the deep dives of the Sagittaire and Physalie experimental series. A system was set up to collect the dive logs into a database.[4] This database supported and monitored all the Comex procedure developments until 1994.

In their early versions, Comex saturation decompression procedures were characterised by:

- An oxygen protocol based on a 600 mbar chamber $PO_2$.
- A constant rate of decompression for a constant chamber $PO_2$ until the fire risk zone was reached.
- A continuous decompression with no rest stops.

In 1986, Comex conducted intensive research on decompression that initiated a large-scale revision of their diving manuals. The chamber $PO_2$ was reduced to 500 mbar for decompressions deeper than 155 msw. Later, in 1994, with the experience of the Norwegian contracts (Statoil, 3DP and Norsk Hydro Oseberg) and after the development of deep diving in Brazil, the 500 mbar $PO_2$ was standardised throughout the full depth range.

*Seaway procedures*

Seaway was a Norwegian company operating four diving vessels in the North Sea during the 80's. The Seaway 1984 saturation manual included procedures designed after the experimental dives DeepX I and II conducted at the Norwegian Underwater Technology Center (NUTEC) in Bergen. They were characterised by a constant rate of decompression with a constant chamber $PO_2$, similar to the Comex procedures. They had a rest stop set at a fixed time (00:00 to 06:00) and for the first time, a minimum 8 h hold before starting final or intermediate decompression. The Seaway procedures were representative of the Norwegian experience and later influenced the NORSOK standards (Norwegian acronym for "*the Norwegian shelf's competitive position*").

## INTERNATIONAL REFERENCE PROCEDURES

Three countries, France, Norway and Brazil, have regulated diving to the level where ascent rates, rest stops, chamber $PO_2$, etc. are specified for saturation. These regulations cannot be used directly for operations but build a strict frame for editing saturation procedures. We mention hereafter the French, Norwegian and Brazilian procedures in this context.

*French saturation procedures*

The 1992 revision of the French diving regulations was associated with the publication of official air tables and saturation procedures referred to as 'MT92'.[5] These procedures corresponded to the Comex 1986 diving manual and proposed two options for decompression: one with 600 mbar chamber $PO_2$ from storages depths not exceeding 155 msw and one with 500 mbar chamber $PO_2$ for deeper operations. These procedures have been used in France and in West Africa. The French diving regulations were revised in 2016 but no changes were made to the saturation procedures.

*Norwegian saturation procedures*

During the 80's, divers' unions in Norway raised the issue of commercial competition that could push companies to shorten decompression. In 1984, the Norwegian Petroleum Directorate (NPD) took a stand and contracted Dr Val Hempleman, from the British Royal Navy, to evaluate the saturation procedures in use and organise an international conference on the subject.[6] The NPD then initiated an action to standardise saturation procedures in the Norwegian sector.

Representatives from the Norwegian oil and gas industry, divers' unions and the AODC participated in:

- Assessing the practice of five diving contractors operating in the Norwegian sector.
- Proposing a common framework designed by a working group of experts putting together the most conservative features of existing commercial tables for diving down to 180 msw.

The frame conditions in the NPD report were included in 1999 in the first edition of the NORSOK U-100 standards for manned underwater intervention. Up to now, the NPD frame conditions have remained unchanged and the following revisions of the NORSOK U-100 have not affected the saturation specifications.[7]

The NORSOK procedures are a blend of the US Navy for the decompression, Comex for the excursions and Seaway for the decompression hold. The overall results are conservative procedures with reduced excursion distances, slow rates of decompression and restricted saturation times. Although they lack operational flexibility, they benefit from a good reputation among the divers' community as documented in a recent questionnaire survey of Petroleum Safety Authority (PSA).[8]

The NORSOK procedures specify a $PO_2$ for chamber decompression widely defined between 400 to 500 mbar. However, company A, which operates in the Norwegian sector, provided a copy of their Norwegian saturation procedures that use the higher end of this range. Because of the wide range of chamber $PO_2$ specified, the safety of these procedures depends on how they are being implemented.

*Brazilian saturation procedures*

In the 80's, the diving companies operating in Brazil were using their own rules in the absence of comprehensive Brazilian legislation. When deep operations started in the Campos field, Comex, which had been involved in two of the Norwegian deep development contracts, brought along its expertise and became highly influential.[9]

The first national diving legislation was published in 1988, closely aligned with the North Sea standards. It included saturation procedures based on the Comex manual. The Brazilian Navy then built a hyperbaric centre and validated the procedures through a series of onshore dives. Brazilian diving regulations NORMAM-15/DPC are now available as Rev. 2, 2016 and are characterised by:

- A continuous decompression without any rest stop.
- A constant decompression rate with a constant chamber 500 mbar $PO_2$ till 20 msw.

The NORMAM-15 procedures are freely accessible from the Brazilian regulations website.[10] Grounded in three decades of Brazilian deep diving experience, they have become an international reference.[11,12]

REVIEW OF COMPANY PROCEDURES

These procedures are summarised in Tables 1 to 4, along with the ones from the references already mentioned.

**Discussion**

SOURCES OF C URRENT SATURATION PROCEDURES

The US Navy procedures have played a major role in the development of commercial diving because they were readily and freely available at the time it all started. The diving managers liked to claim they were complying with the US Navy because it was an unchallenged reference. Companies have since gained experience and introduced their own modifications such as increasing the $PO_2$ during the decompression and restricting excursion distances during the bell dives. Yet procedures C, F, G, H, I and K (six out of 11 companies) still reference the 2016 Rev 7 edition of the US Navy Diving Manual as the source of their saturation procedures.

The Comex manual largely inspired the Brazilian NORMAM-15 procedures. It also influenced procedures A, B, D and E that include a constant rate of decompression from bottom to 15 msw (four out of 11 companies).

The source of company J procedures are unknown.

These reference procedures have been empirically modified by the companies in consultation with their respective diving experts (medical advisors, consultants, etc.). The authors have participated in several of these diving manual revisions. However, the rationale behind these changes has often been lost. Only companies A, B, C, D and K (five out of 11 companies) have formally compiled documents called 'Justifications' or 'Provenance' that trace and explain the evolution of their diving procedures.

STORAGE DEPTH $PO_2$

The procedures all specify a chamber $PO_2$ at storage depth set around 400 mbar (Table 1).

The $PO_2$ at storage depth is raised to avoid complications in the event of hypoxia due to improper mixing of oxygen and inert gases. However, two other reasons are identified.

The first reason is historical. In the early 70's, Comex mobilised a saturation system on the deck of the Choctaw I barge with an external regeneration system. The barge was experiencing bad weather, the system at 120 msw and the chamber $PO_2$ at 400 mbar, when a large wave swept the regeneration plant away. The 2-inch hoses burst and the pressure rapidly dropped inside the chambers. Divers started closing all the valves in panic, including the pressurisation valve, and the surface team had to use the bell pressurisation valve to re-establish the pressure. By that time, the chamber

**Table 1**

Pre-decompression procedures; *decompression can start with an upward excursion if the time spent at storage depth exceeds the equivalent decompression time; **for storage depths shallower than 61 msw, a 2 hour (h) hold is required after an upward excursion; ***after an extended excursion, the chamber must be recompressed to divers' deepest depth and divers have to hold for 8 h; Max – maximum; mbar – millibar; min – minutes; Min – minimum; msw – metres of seawater; N/A – not applicable; Opt – optimal

| Group | Deepest storage depth available (msw) | Chamber storage $PO_2$ (mbar) | | | Initial saturation decompression with an upward excursion | Hold time (h) before decompression after a: | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Min | Opt | Max | | Downward normal excursion | Downward extended excursion | Upward normal excursion | Upward extended excursion |
| US Navy 1979 | 487 | 350 | | 400 | Permitted | 0 | N/A | 0 | N/A |
| Seaway 1984 | 304 | 380 | 400 | 420 | Forbidden | 8 | N/A | 8 | N/A |
| Comex 1986 std | 155 | 400 | 425 | 500 | 1 msw in 10 min | 12 | N/A | 12 | N/A |
| Comex 1986 deep | 200 | 400 | 425 | 500 | 1 msw in 10 min | 0 | N/A | 0 | N/A |
| Comex 1994 | 300 | 300 | 400 | 500 | 1 msw in 10 min | 0 | 12 | 0 | 12 |
| France MT 1992 | 180 | | | | 1 msw in 10 min | 0 | 12 | 0 | 12 |
| Brazil 2021 | 350 | | | | Forbidden* | 0 | 12 | 0 | 12 |
| US Navy 2016 | 350 | 440 | | 480 | Permitted** | 0 | N/A | 0 | N/A |
| NORSOK 2016 | 180 | 400 | | 500 | Forbidden | 8 | N/A | 8 | N/A |
| Company A | 180 | 380 | 400 | 420 | Forbidden | 8 | 12 | 8 | 12 |
| Company B | 180 | 380 | 400 | 420 | Forbidden | 8 | 12 | 8 | 12 |
| Company C | 300 | 370 | 400 | 430 | Forbidden | 8 | 8*** | 8 | 8*** |
| Company D | 180 | 380 | 400 | 420 | Forbidden | 8 | 12 | 8 | 12 |
| Company E | 305 | 370 | 400 | 430 | Forbidden | 6 | N/A | 6 | N/A |
| Company F | 300 | 440 | 450 | 480 | Forbidden | 6 | N/A | 6 | N/A |
| Company G | 487 | 350 | 400 | 450 | Forbidden | 8 | N/A | 0 | N/A |
| Company H | 306 | 370 | 400 | 430 | Forbidden | 2 | N/A | 2 | N/A |
| Company I | 201 | 380 | 400 | 450 | Forbidden | 8 | N/A | 8 | N/A |
| Company J | 487 | 380 | 400 | 450 | Forbidden | 6 | 24 | 6 | 24 |
| Company K | 310 | 380 | 400 | 450 | Forbidden | 8 | N/A | 8 | N/A |

had dropped half of the initial pressure. Since then, the industry policy has been to set the storage $PO_2$ around 400 mbar so that the atmosphere could remain breathable if the pressure were to accidentally drop to half of its initial value.

The second reason is related to excursion dives. In case of an ascending excursion, the storage depth becomes the deepest depth. The storage depth $PO_2$ therefore influences the permitted excursion distance. If storage $PO_2$ and dive mix $PO_2$ are too different, ascending and descending excursions become asymmetrical. With modern procedures that use a sliding excursion window, a higher storage $PO_2$ provides a higher flexibility.

INITIAL 'PULL-UP'

The US Navy Diving Manual paragraph 13.23 allows starting a saturation decompression with an ascending excursion (initial pull-up), based on the concept of the diver's deepest depth, which directs the selection of saturation excursion distance. The excursion amplitude can be significant, as for instance, a 30 msw excursion from 120 msw to 90 msw. It is, however, specified that this initial pull-up remains within the discretion of the person in charge.

Even if the initial pull-up is limited, the problem is to measure the influence of this sudden pressure change on potential bubbles remaining from the last excursion dive and

**Table 2**
Rest stops during decompression; h – hours; msw – metres of seawater; N/A – not applicable

| Group | Rest stop | Daily stop duration (h) | Daily decompression duration (h) | Shallow rest stops |
|---|---|---|---|---|
| US Navy 1979 | Fixed | 2 + 6 | 16 | |
| Seaway 1984 | Fixed | 6 | 18 | |
| Comex 1986 std | None | N/A | 24 | |
| Comex 1986 deep | None | N/A | 24 | |
| Comex 1994 | None | N/A | 24 | |
| France MT 1992 | None | N/A | 24 | |
| Brazil 2021 | None | N/A | 24 | |
| US Navy 2016 | Sliding | 2 + 6 | 16 | |
| NORSOK 2016 | Fixed | 6 | 18 | Stop < 3 msw performed at 3 msw |
| Company A | Sliding | 5 | 19 | No stop between 15 msw and surface |
| Company B | Sliding | 5 | 1 | No stop between 15 msw and surface |
| Company C | None | N/A | 24 | |
| Company D | Sliding | 5 | 19 | No stop between 15 msw and surface |
| Company E | Sliding | 4 | 20 | No stop between 15 msw and surface |
| Company F | Sliding | 8 (2 stops) | 16 | |
| Company G | Fixed | 2 + 6 | 16 | |
| Company H | Fixed | 8 | 16 | Stop < 3 msw ignored |
| Company I | Fixed | 2 + 6 | 16 | Option left for continuous decompression |
| Company J | None | N/A | 24 | |
| Company K | Sliding | 2 + 6 | 16 | Stop < 3msw performed at 3–4 msw |

the impact of these bubbles on the following decompression. Flook used a bubble growth algorithm developed by Van Liew and Burkard to estimate this impact.[13] Flook modeled the bubble population after excursions and during saturation decompression and concluded that neither the excursion nor the decompression alone was likely to cause DCS. However, she pointed out that if a decompression was to follow an excursion with a too short interval, the residual bubble population from the excursion could interfere with the final decompression process and carried a risk.[14]

All the procedures reviewed have removed the possibility of starting a decompression with an ascending excursion.

## DECOMPRESSION HOLD

Companies now specify a minimal time interval, called decompression hold, after an excursion dive, before starting a final decompression (Table 1).

This decompression hold is only required after a descending excursion dive for procedures C and G. All the other procedures request a pre-decompression hold regardless of the type of excursion dive (nine out of 11 companies).

The hold duration varies from 2 h (procedure H), to 6 h (procedures E, F, J) and 8 h (procedures A, B, C, D, G, I and K, i.e., seven out of 11 companies). In practice, a few hours are needed to raise $PO_2$ inside the chamber before decompression and this hold has a minimal impact on the operations.

Note that Comex authorised a 1 msw ascent performed in 10 minutes at the start of the decompression but this was only intended to create a small pressure drop to seal the door of adjacent chambers. A similar procedure is proposed by company K.

**Table 3**

Decompression with constant chamber $PO_2$; the decompression rate is defined for the ascent between rest stops. The daily decompression includes the ascent phase and the rest stops. DDR – daily decompression rate; Deco – decompression; h – hours; Max – maximum; mbar – millibar; min – minutes; Min – minimum; msw – metres of seawater; Opt – optimal

| Group | Chamber $PO_2$ (mbar) | | | Deco time (h) | Bottom–60 msw | | 60 msw–30 msw | | 30 msw–15 msw | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Min | Opt | Max | | Deco rate min·msw$^{-1}$ | DDR msw·day$^{-1}$ | Deco rate min·msw$^{-1}$ | DDR msw·day$^{-1}$ | Deco rate min·msw$^{-1}$ | DDR msw·day$^{-1}$ |
| US Navy 1979 | 350 | | 400 | 16 | 32.6 | 29.4 | 39.2 | 24.5 | 49.0 | 19.6 |
| Seaway 1984 | 500 | | 530 | 18 | 36.0 | 30.0 | 36.0 | 30.0 | 36.0 | 30.0 |
| Comex 1986 std | 575 | | 600 | 24 | 45.0 | 32.0 | 45.0 | 32.0 | 45.0 | 32.0 |
| Comex 1986 deep | 500 | | 525 | 24 | 50.0 | 28.8 | 50.0 | 28.8 | 50.0 | 28.8 |
| Comex 1994 | 480 | 500 | 500 | 24 | 50.0 | 28.8 | 50.0 | 28.8 | 50.0 | 28.8 |
| France MT 1992 | 500 | | 525 | 24 | 50.0 | 28.8 | 50.0 | 28.8 | 50.0 | 28.8 |
| Brazil 2021 | 440 | | 480 | 24 | 50.0 | 28.8 | 50.0 | 28.8 | 50.0 | 28.8 |
| US Navy 2016 | 440 | | 480 | 16 | 32.6 | 29.4 | 39.2 | 24.5 | 49.0 | 19.6 |
| Norsok 2016 | 400 | | 500 | 18 | 40.0 | 27.0 | 50.0 | 21.6 | 60.0 | 18.0 |
| Company A | 480 | 500 | 520 | 19 | 40.0 | 28.5 | 40.0 | 28.5 | 40.0 | 28.5 |
| Company B | 480 | 500 | 520 | 19 | 40.0 | 28.5 | 40.0 | 28.5 | 40.0 | 28.5 |
| Company C | 480 | 490 | 500 | 24 | 50.0 | 28.8 | 60.0 | 24.0 | 70.0 | 20.6 |
| Company D | 480 | 500 | 520 | 19 | 40.0 | 28.5 | 40.0 | 28.5 | 40.0 | 28.5 |
| Company E | 500 | 530 | 560 | 20 | 40.0 | 30.0 | 40.0 | 30.0 | 40.0 | 30.0 |
| Company F | | 500 | | 16 | 30.0 | 32.0 | 40.0 | 24.0 | 50.0 | 19.2 |
| Company G | 470 | 500 | 530 | 16 | 33.3 | 28.8 | 40.0 | 24.0 | 50.0 | 19.2 |
| Company H | | 500 | 530 | 16 | 32.8 | 29.3 | 39.5 | 24.3 | 49.2 | 19.5 |
| Company I | | 500 | | 16 | 33.3 | 28.8 | 40.0 | 24.0 | 50.0 | 19.2 |
| Company J | 480 | 500 | 520 | 24 | 49.0 | 29.4 | 78.3 | 18.4 | 78.3 | 18.4 |
| Company K | | 500 | | 16 | 32.0 | 30.0 | 39.0 | 24.6 | 49.0 | 19.6 |

## CHAMBER BLEED VERSUS STAGED DECOMPRESSION

Saturation decompressions are slow, e.g., a 90 min·msw$^{-1}$ rate of decompression corresponds to 11 millimetres depth change every minute. They require continuous attention from the chamber operators. Operationally, two methods are available for decompressing the chamber:

- Continuous decompression ('continuous bleed') typically controlled by computers onboard modern diving support vessels.
- Staged decompression with repeated small decrements of depth.

Several procedures have been identified for staged decompression:

- Comex 1979 used an optional 1 msw step decrement with 10 min ascent time to the next stop when deeper than 50 msw.
- Procedure D proposes an optional 0.33 msw decrement as in US Navy Rev 7 procedures.
- Procedure F proposes an optional 5 msw step with 5 min ascent time to the next stop.
- Procedure K proposes an optional 0.2 msw step resulting in an ascent rate equivalent to continuous decompression using the last minute of the stop time to travel to the next stop depth.

A problem of staged decompression is what Comex divers used to call 'passage de bulles' during the step changes near the surface (literally translated as feeling bubbles passing by, or, alternatively, feeling 'niggles'). Because the effect of Boyle's law becomes more important close to the surface, it can be speculated these small but sudden pressure variations increase bubble volume, resulting in a greater likelihood to produce symptoms in whatever tissue in which they are present (such as periarticular connective tissue). The staged

**Table 4**

Decompression with constant chamber O2%; the decompression rate is defined for the ascent between rest stops. The daily decompression includes the ascent phase and the rest stops. DDR – daily decompression rate; h – hours; Max – maximum; min – minutes; Min – minimum; msw – metres of seawater; Opt – optimal

| Group | Chamber $O_2$ % | | | 15 msw to surface | | |
|---|---|---|---|---|---|---|
| | Min | Opt | Max | Decompression rate min·msw$^{-1}$ | Decompression time (h) | DDR msw·day$^{-1}$ |
| US Navy 1979 | 21 | | 23 | 65.3 | 16 | 14.7 |
| Seaway 1984 | 21 | | 22 | 80.0 | 18 | 13.5 |
| Comex 1986 std | 21 | | 24 | 60.0 | 24 | 24.0 |
| Comex 1986 deep | 21 | | 24 | 60.0 | 24 | 24.0 |
| Comex 1994 | 21 | | 24 | 80.0 | 24 | 18.0 |
| France MT 1992 | 21 | | 24 | 60.0 | 24 | 24.0 |
| Brazil 2021 | | 21 | | 90.0 | 24 | 16.0 |
| US Navy 2016 | 19 | | 23 | 65.3 | 16 | 14.7 |
| Norsok 2016 | 19 | | 23 | 80.0 | 18 | 13.5 |
| Company A | 21 | 22 | 23 | 100.0 | 19 | 11.4 |
| Company B | 21 | 22 | 23 | 100.0 | 19 | 11.4 |
| Company C | 21 | 22 | 23 | 90.0 | 24 | 16.0 |
| Company D | 21 | 22 | 23 | 100.0 | 19 | 11.4 |
| Company E | 21 | 22 | 23 | 100.0 | 24 | 14.4 |
| Company F | | 21 | 23 | 60.0 | 16 | 16.0 |
| Company G | | 21 | 23 | 66.7 | 16 | 14.4 |
| Company H | | 21 | 23 | 66.7 | 16 | 14.4 |
| Company I | 21 | 21 | 24 | 66.7 | 16 | 14.4 |
| Company J | 20 | 21 | 22 | 97.9 | 24 | 14.7 |
| Company K | 21 | | 24 | 66.0 | 16 | 14.5 |

decompression option was removed in the later versions of the Comex manuals and the symptoms disappeared. The other companies only propose continuous chamber bleed (eight out of 11 companies).

## REST STOPS VERSUS CONTINUOUS DECOMPRESSION

Rest stops were first defined in the US Navy Diving Manual as a daily interruption in the decompression process (or 'night stops' when stops take place during sleeping time). The justification presented at the time was to avoid divers sleeping in a cramped position that could reduce perfusion during decompression. Another story told was that in the early times, the US Navy doctors were annoyed by awakening every night and decided to stop decompression to get some sleep (personal communication with Dr Spaur).

We identified several rest stop patterns in our review (Table 2):

- Rest-stops set at fixed times identical to the US Navy pattern (00:00 to 06:00 and 14:00 to16:00) or the NORSOK pattern (00:00 to 06:00) as in procedures F, G, H and I (four out of 11 companies).
- A rest stop set after a given decompression duration that slides around the clock depending on the start decompression time (procedures A, B, D, E and K, i.e., five out of 11 companies)
- Continuous decompression without any rest stop (procedures C and J)

The stop durations vary from 4 h (procedure E) to 5 h (procedures A, B, D) and the classic US Navy 8 h split over two stops (procedures F, G, H, I, K, i.e., five out of 11 companies).

From our experience, when divers are asked their comments on rest stops, they typically provide the following answers:

- Stops prevent the 'popping' of my ears when I sleep in the last part of the decompression.
- Fixed stops permit synchronising back to normal day rhythm (for divers on night shift).
- I do not care, I sleep a lot anyway during decompression, at any time.

Operationally, rest stops set at a fixed time raise the problem of calculating the end decompression time because the number of rest stops depends on the start decompression time. Rest stops may also happen a few metres from the surface, causing technical problems (toilet no longer in operation, risk of sudden surfacing) and frustration. One way around this is to forbid rest stops shallower than 3 msw (procedures H and K) or to carry them out at 3 msw (procedure A). Another way is to remove any rest stop in the last 24 hours of the decompression and adapt the ascent rate accordingly, which corresponds to a slow and conservative end of decompression (procedures B, D, E and I).

Theoretically, rest stops reduce the daily time available for decompression. For a given daily decompression rate, rest stops require a faster rate during the active decompression phase. The question remains whether the recovery during the rest stop exactly balances the increase of the decompression rate during the ascent phase. No theoretical work could be found on the subject. In 1984, an attempt was made during the DeepX II experiment at NUTEC to compare the performances of the two methods of decompression. Three divers were decompressed continuously while another group of three divers were decompressed with rest stops, both groups with the same 24 h decompression rate. No difference could be documented.[15] A similar conclusion was derived from the Comex database (Imbert JP, presentation at the NPD conference, 1988).

The presence of rest stops therefore remains more a matter of company culture than a strategy for improving the decompression safety.

## DECOMPRESSION RATES AND DURATIONS

Decompression rates are linked to the chamber $PO_2$ and govern the decompression duration. They have a critical operational and commercial importance (Table 3 and 4). Decompression rate patterns determine two characteristics of the decompression: duration and profile.

We calculated the decompression durations and the instructions specified in the procedures. We compared these decompression durations for several typical storage depths. Note that the final decompression duration may vary depending on the starting time (we used 06:00 in the program) and the conversion factor used for fsw and msw. We added the NORSOK procedures for comparison.

Table 5 and Figure 3 display the difference between the slowest and the fastest decompression durations. This difference reaches 25.7 h at 150 msw. However, Table 5 also indicates that for procedures A, B, C, D, E, F and H, this difference is less than 5 h over the 60–150 msw range. This means that seven out of 11 companies have very similar decompression durations.

We then plotted the daily decompression rate versus depth to compare the decompression profiles between procedures. Figure 4 shows that procedures have a similar decompression rate to 60 msw while there are greater differences in the shallower depths.

Deeper than 60 msw, all the procedures reviewed are characterised by a constant decompression rate. This has been a characteristic of the Comex saturation decompression since 1984 (and derived procedures like the NORMAM-15).[16] It is a consequence of the Comex method of calculation that used a safe ascent criterion based on Hennessy's critical volume assumption.[17] The same result can be obtained using Vann's model that predicts a linear relation between the rate of decompression and the $PO_2$.[18] This is also a consequence of the concept of extended oxygen windows.[19] According to these algorithms, the rate of decompression is a linear function of the $PO_2$ and should remain constant as long as the chamber $PO_2$ remains constant, regardless of depth.

The shallower part from 60 to 15 msw is also conducted with a constant $PO_2$ but reveals two practices, one with a constant decompression rate (as per the Comex algorithm), and the other with varying decompression rates (as per the US Navy tradition). The US Navy has never published the way their saturation decompressions were computed. It is likely that in the early 70's, they used trial and error and involved a combination of various models. This profile consisting of deep constant decompression rates and shallow varying decompression rates is typical of procedures that use the US Navy as parent procedures. It is also found in the NORSOK procedures that adopted this profile as a best practice at the time they were written.

## INTERMEDIATE DECOMPRESSION

Projects often require intervention at various working depths. When depth variations exceed the possibilities of bell excursion dives, the storage depths can be adjusted by intermediate compressions and/or decompressions.

In the early time of North Sea installation, some clients insisted in decompressing divers during bad weather, based on the idea that they would be safer closer to the surface if the situation was to deteriorate. Divers could be subjected to a significant series of intermediate decompressions just because of bad weather. Following three intermediate decompressions in a row imposed on Comex divers by the November weather conditions in the Shetlands, the practice was eventually banned.

**Table 5**
Final decompression durations in decimal hours for several typical storage depths for the companies. The pre-decompression hold is excluded from the decompression time. h – hours; msw – metres of seawater

| Company | Decompression duration (h) by storage depth | | | |
|---|---|---|---|---|
| | 60 msw | 90 msw | 120 msw | 150 msw |
| A | 60.0 | 85.0 | 110.0 | 135.0 |
| B | 60.0 | 85.0 | 110.0 | 135.0 |
| C | 59.0 | 83.0 | 107.0 | 131.0 |
| D | 60.0 | 85.0 | 110.0 | 135.0 |
| E | 59.0 | 83.0 | 107.0 | 131.0 |
| F | 65.5 | 88.5 | 111.5 | 134. |
| G | 73.2 | 97.8 | 122.5 | 147.1 |
| H | 64.7 | 89.1 | 113.5 | 137.9 |
| I | 73.2 | 97.8 | 122.5 | 147.1 |
| J | 85.0 | 110.0 | 135.0 | 160.0 |
| K | 74.2 | 107.7 | 129.0 | 153.3 |
| Range | 59.0–85.0 | 83.0–110.7 | 107.0–135.0 | 131–160.0 |
| Median | 64.7 | 88.5 | 111.5 | 135.0 |
| NORSOK | 78.0 | 104.0 | 130.0 | 156.0 |

**Figure 3**
Decompression times in decimal hours for several typical storage depths, for the company procedures reviewed; the pre-decompression hold is excluded from the decompression time. std – standard

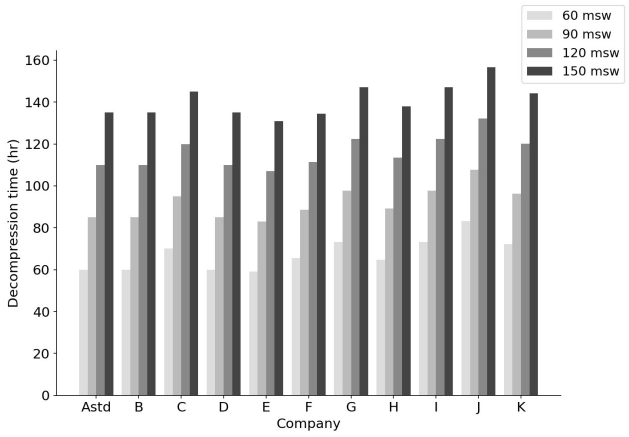
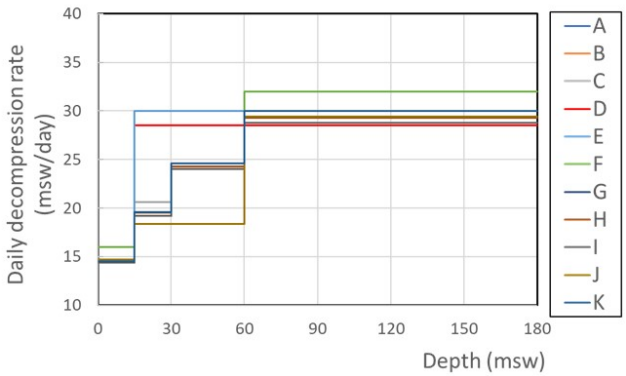



**Figure 4**
Daily decompression rate (msw·day$^{-1}$) versus depth (msw), for the 11 different procedures analysed




In 1986, Comex introduced a limitation to intermediate decompression based on the understanding that decompression was stressful and limitations should be based on a 'maximal acceptable dose'. The maximum dose was defined as a decompression distance of 200 msw, which corresponded to the deepest available storage depth in their manual. The principle was that this distance could be split into a series of intermediate decompressions. Intermediate decompressions could be cumulated as long as their total distance would not exceed 200 msw. The system could be 'pushed' beyond reasonable limits if multiple small intermediate compressions/decompressions were used (saw tooth-shaped profile).

Around the same time, another company, Rockwater, introduced a limitation based on the number of intermediate decompressions followed by a compression to a new storage depth, known as the 'W' profile (Figure 5). The W-profile

was restricted to one intermediate decompression and one intermediate compression before final decompression. The system could also be 'pushed' by using an intermediate decompression/compression of high amplitude but many companies adopted it because of its simplicity.

Finally, in Norway, NPD referred to a publication from the Hades database to justify the notion that the dive planning should be based on minimum change of storage depths and excursion exposures. The NORSOK standards thus included the more restrictive rule of the 'V' profile where divers can work at intermediate storage depths during decompression but cannot be recompressed to any deeper storage depth.[20] This position was later judged as a misinterpretation by JE Jacobsen, one of the main authors of the Hades paper, during a presentation at a DMAC meeting in 2017.[21]

The review shows that current practice for limiting intermediate decompression is a mixture of the V, W profiles and Comex cumulative decompression distance.

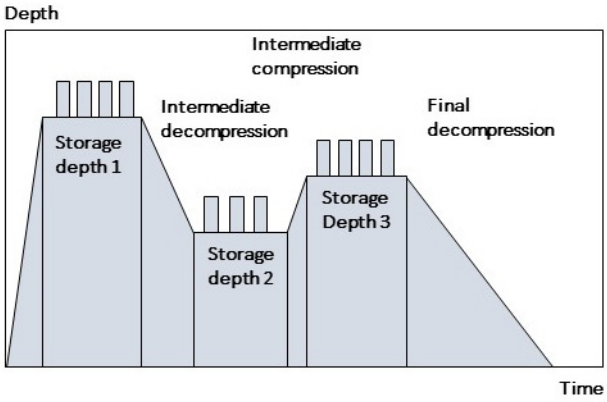
## EXERCISE DURING DECOMPRESSION

Exercise can be associated with muscle stretch, impacts on joints and vibrations. Preconditioning studies on divers have shown that exercise reduces VGE levels after the dive.[22,23] It has been postulated that vibrations and vasodilatation affect a pre-existing population of bubble precursors and therefore could reduce the source of bubble formation [24, 25]. On the other hand, Madden et al. showed that exercise after diving increases the incidence of bubbles appearing in the arterial circulation, possibly because of the increase in the pulmonary artery pressure.[26] It is therefore assumed that a light and measured exercise could be beneficial during decompression.

Such potential benefit was subjectively evaluated via a questionnaire survey performed in 2017 onboard a North Sea diving support vessel by one of the authors but not published in the associated paper.[27] Answers evoked a matter of lifestyle. Old divers are reluctant to exercise because, during their long careers, they have been consistently told that exercising is harmful. Younger and fitter divers exercise during decompression and claim that they feel and sleep better during this long boring period.

Our review has shown that eight out of 11 companies encourage divers to lightly exercise during the decompression. This takes the form of a small paragraph named good or healthy practice during decompression stating: "*Move around regularly. Do not maintain a cramped position that restricts blood circulation*" (procedures G,E and J). The more detailed form (procedure A for instance) specifies that the exercise must remain moderate such as steppers, bungees and static bicycles. In the absence of definitive scientific evidence, light exercise during saturation decompression remains a matter of diver's personal choice.

**Figure 5**
The 'W' rule used for storage depth adjustments during one saturation




## PUBLISHED DECOMPRESSION SICKNESS INCIDENCE

The evaluation of the DCS risk in modern saturation operations is difficult. Companies do not share information. We did not request this information from the 11 companies participating in the study.

Among the historical procedures, Comex documented their safety performances with an exposure database and published their saturation diving track records. The average DCS incidence was 1.02% (59 DCS cases in 5,744 exposures) for dives performed using procedures described in the 1979 Comex manual.[28] It decreased to 0.54% (12 DCS in 2,200 exposures) for dives performed with Comex procedures later implemented in the French 1992 diving regulations (unreferenced report). All symptoms were exclusively articular pain, reported during the last metres of the ascent and never at surface.

Seaway also developed a database (Hades) for the monitoring of their diving operations.[20] In 1978, the results published for their saturation decompressions indicated an overall DCS incidence of 0.83% (22 DCS cases in 2,662 exposures,). As in the Comex database, all cases were articular pain occurring in the last part of the decompression.

The only modern source is PSA in Norway that has been collecting and publishing saturation safety records since 1990.[29] The cases are all recorded in the Norwegian sector and therefore associated with use of the NORSOK procedures. The site accessed on 21/09/2023 indicates one DCS case recorded since 2000. The corresponding incidence cannot to be evaluated because the exposures are expressed as men x hours in saturation and not saturation dives.

Finally, the diving manager of one of the participating companies indicated to the authors that DCS has become a rare event and stated "*we have not had a bend in the last 10 years*". This is in line with the authors' experience with

other companies. Nowadays, across the industry, DCS is not observed in saturation diving.

## MEASURED VGE GRADES

Venous gas emboli are commonly observed after asymptomatic dives using acoustic doppler or ultrasound imaging. Although the presence of VGE is by itself not predictive of DCS for a given diver, a statistical link is observed in surface-oriented diving between the amount of observed VGE in a group of divers and the incidence of DCS.[30,31]

Significant VGE grades were detected during deep saturation decompression in the experimental dives and operational dives conducted in Norway.[32,33] These high levels of VGE contrast with recent measurements performed during operations in the North Sea. In 2017, we monitored 49 saturation divers after decompression from 120 and 140 msw using echocardiography and detected no bubbles.[34] In 2022, we monitored 15 divers using ultrasound subclavian Doppler detection during and after saturation decompression from 40–50 msw storage depths, and found no bubbles.

Our experience with bubble monitoring is that high grades of VGE are no longer a concern in the saturation decompression we monitored, at least to 140 msw.

## PULMONARY OXYGEN TOXICITY

Oxygen plays a major role during decompression. It increases the inert gas gradient between tissue and blood as well as the oxygen window and permits accelerating the decompression.[19] However, high levels of oxygen generate reactive oxygen species that interfere with normal cell functions. While central nervous system toxicity is not a concern in saturation diving, pulmonary toxicity can be a limiting factor.

The $PO_2$ should not be too low. An experimental saturation dive to 240 msw was conducted in Norway with slow decompression rates and reduced $PO_2$ during decompression (500 mbar during the day, 300 mbar during the 8 h night stop). No change in pulmonary function was observed. However, one case of DCS was recorded among the eight divers.[35] This suggests the difficulty of safely decompressing from saturation with a low oxygen level. Prof. Lambertsen had a definite position on the subject that he summarised as "*better cope with the effects of oxygen than with the ones of DCS*".[36]

On the other hand, a high $PO_2$ cannot be sustained for too long. Early saturation decompressions used a 600 mbar chamber $PO_2$ (Comex 1979) but when diving moved to deeper depths in Norway and in Brazil, longer decompressions raised the problem of pulmonary toxicity. The $PO_2$ was reduced to 500 mbar and the use of a 600 mbar $PO_2$ was restricted to less than 155 msw (Comex 1986 manual). Ultimately, a 500 mbar chamber $PO_2$ became the company standard for all depths.

Our survey has shown that while one company uses a chamber $PO_2$ of 530 mbar (procedure E), most companies use 500 mbar as an optimal value (procedures A, B, F, G, H, I, J and K, i.e., eight out of 11 companies) or 490 mbar (procedures C and D).

The divers' tolerance of pulmonary oxygen toxicity is difficult to measure and predict.[37] The industry approach was based on 'units of pulmonary toxicity dose' (UPTD) because of their simplicity.[38] However, it has been shown that the UPTD dose is not an appropriate tool for measuring oxygen toxicity, in surface oriented diving.[39]

Arieli developed a dose index accounting for recovery and validated it against a sample of saturation exposures.[40] However, given the paucity of exposure data at the lower end of the hyperoxic spectrum, the model remains to be validated for operational use in saturation diving. It is therefore currently not possible to reliably estimate a pulmonary toxic threshold dose for the company procedures.

It must be noted that the higher $PO_2$ to which the divers are exposed is the one used during the bell dives, for six continuous hours, daily. Therefore, most of the hyperoxic exposure takes place during the bottom phase.

It appears that the $PO_2$ used in current saturation procedures is the result of successive empirical adjustments and a better understanding of both the excursion and decompression design. Hence, the oxygen toxicity dose calculations could help optimising the diver's hyperbaric oxygen exposure.

## EVOLUTION OF SATURATION PROCEDURES

In the 70's, navies, universities and governments conducted research and provided diving procedures to the industry. The last large research led by the industry was the Norwegian deep diving program of the 80's. Today, companies rely on themselves to improve their diving procedures.

The drive for such changes is no longer DCS occurrence but instead, the need for more flexible procedures. Managing operations of large and expensive diving vessels requires options and alternatives.

The ethical principles and the practical procedures for the development of decompression tables, were published by the Undersea Medical and Hyperbaric Society in the conclusions of a workshop on validation of decompression tables, in 1987.[41] These conclusions have been since considered as the reference for developing and improving decompression procedures. The principles developed in these conclusions are based on small step changes and careful evaluation. They include the following activities:

1. Evaluation of the latest scientific and medical information.

2. Definition of the models. Publication of the new procedures.
3. Monitoring operations to identify areas of improvement of the provisional procedures.
4. Validating the changes on selected worksites under controlled conditions before acceptance.
5. Review and analysis of data collected.
6. Approval of the new procedures or reiteration.

These principles are in line with the industry procedures of management of change that also stress the importance of validation and monitoring. They provide referenced standards permitting the companies to monitor and improve their diving procedures.

TRENDS

We have seen discrepancies between procedures. Table 5 shows a difference of 25.7 hours between the slowest and the fastest decompression time from 150 msw storage depth. However, as discussed during the DMAC 2014 meeting in Aberdeen, we do not have any information that would enable us to evaluate the consequence of these differences on the divers' health.[42]

We have also observed a convergence within procedures (moving towards similar $PO_2$, similar daily decompression rates, similar pre-decompression holds, etc.). Table 5 also shows that for seven companies, there is less than 5 h difference in the decompression time from 60 to 150 msw storage depth.

Because no large-scale research project has been conducted since the Norwegian deep diving contracts, we identified three ways the company procedures have evolved through:
- Internal evolution based on empirical adjustments. This is facilitated by freelance personnel freely moving between companies and carrying along their knowledge and experience.
- Forced evolution after takeovers and mergers between companies.
- Guided evolution by regulations, industry standards and client's requirements.

These evolutions have been made possible by the sharing of the company experiences within the industry associations such DMAC, IMCA and the International Association of Oil and Gas Producers (IOGP).
From this analysis, we foresee two possible paths for this evolution: standardisation and harmonisation:
- Standardisation assumes a stakeholder's association, i.e., contractors or clients, that defines, endorses and publishes policies. As opposed to government authorities, such associations have the capacity to rapidly adapt and change their policies.
- Harmonisation results from free adhesion to a practice. It supposes a consensual objective and sharing of scientific evidence, experiences and policies. Harmonisation is likely to continue with the internationalisation of the offshore industry.

KNOWLEDGE GAP

We believe that saturation procedures will continue to evolve and that this evolution must be supported by scientific research. Our experience is that divers' monitoring, which part of the Undersea and Hyperbaric Medical Society recommendations, brings valuable support to this evolution.

Commercial diving faces, at least two physiological challenges:
- The ageing of the population of divers and their capacity to cope with the various diving stresses.
- The oxygen partial pressures during saturation dive. We said that accurate models are required to evaluate pulmonary oxygen toxicity dose over a saturation. This dose must be managed considering that the bell excursion dives expose the divers to high $PO_2$'s and this impacts the use of oxygen in decompression.

Companies seek flexibility to manage the modern and expensive diving support vessels that keep moving from one contract to the other. They need instructions on how to deal with these multi project campaigns that periodically change the working depths. They seek clear guidance for using all the possibilities of intermediate decompressions and ascending/descending/extended excursions.

Companies also need guidance in managing divers' rotation onboard these vessels. It is known that saturation diving is associated with endothelial dysfunction and inflammatory stress, followed by a recovery.[34,43,44] Hence, the way the divers manage their careers, alternating saturations and rest periods, is important. The DMAC note 21 seems to provide adequate guidance in managing saturation duration and between dive intervals since we noted in the sample diver's population that a 61-year-old diver can still obtain his saturation diving certificate. However, it is believed that more information is required to combine saturation diving and air diving, standard diving and deep diving, etc.

**Conclusions**

Eleven leading diving companies have provided their saturation procedures under a confidentiality agreement.
The comparison of procedures shows that:
- Current saturation procedures are derived essentially from the US Navy, Comex and NORSOK procedures.
- Diving companies have since empirically modified these procedures according to their needs and experience. This explains discrepancies like rest stops versus continuous decompression, intermediate decompression limitations and decompression holds.
- Chamber $PO_2$ settings and decompression rates

exhibit a surprising homogeneity, probably due to the convergence of independent efforts for improvement, clients' requests and requirements from regulations.

The review reveals trends:

- An ongoing harmonisation of procedures, based on the company systems for management of change and influenced by the internationalisation of the offshore industry.
- DCS has become a rare event for the companies participating in this review.
- Companies seek a higher flexibility for the management of modern diving support vessels. They need guidance pertaining to intermediate decompressions.

Finally, we believe that the companies need to seek scientific expertise to address pending physiological problems:

- Evaluation of the impact of an ageing population of divers.
- Optimisation of inspired oxygen pressure during saturation.
- Guidance on how to manage intervals between saturation and air diving, standard saturation and deep diving.

## References


1 DMAC. Guidance note 21, rev 2. The duration of saturation exposures and surface intervals following saturations. 2006 June. [cited 2023 Dec 5]. Available from: https://www.dmac-diving.org/guidance/DMAC21.pdf.

2 US Navy Diving Manual Change 2. Mixed gas diving. NAVSEA 0994-LP-001-9010. Washington (DC): US Department of the Navy; 1977. [cited 2023 Dec 5]. Available from: https://apps.dtic.mil/sti/tr/pdf/ADA112710.pdf.

3 US Navy Diving Manual, Revision 7. NAVSEA 0910-LP-115-1921. Washington (DC): US Department of the Navy; 2016. [cited 2023 Dec 5]. Available from: https://diving-rov-specialists.com/index_htm_files/docs-14-usn-manual-rev7.pdf.

4 Imbert JP, Montbarbon S. Use of the comex diving data base. In: Sterk W, Hamilton, RW, editors. Proceedings of the European Underwater and Biomedical Society workshop on operational dives and decompression data: collection and analysis; 11-18th August 1990. Amsterdam, The Netherlands: EUBS; 1990. p. 122–32.

5 Mesures particulières de protection applicables aux scaphandriers. Imprimerie du Journal Officiel, 26 rue Desaix, 75732 Paris cedex 15: Bulletin Officiel du Ministère du Travail; 1992. [cited 2023 Dec 5]. Available from: https://diving-rov-specialists.com/index_htm_files/history-27-french-decree-30-october-2012.pdf.

6 Hempleman V. The safety evaluation of saturation decompression tables. Norwegian Petroleum Directorate; 1986. Report No.: I82-7527-203.6. [cited 2023 Dec 5]. Available from: https://www.ptil.no/contentassets/350fcc45128449329b7b92c78f6100a4/hempelman---safety-evaluation-of-saturation-decompression-tables-1986.pdf.

7 NORSOK. U-100 Manned underwater operations. Fifth ed, corrected version 2016-05-09. 2015. [cited 2023 Dec 5]. Available from: https://standard.no/en/sectors/petroleum/norsok-standards/u-underwater-op/u-100manned-underwater-operationsedition-5-december-2015-corrected-version-2016-05-09/.

8 Trend in risk level (RNNP). Report 2023. Norway. [cited 2023 Dec 5]. Available from: https://www.ptil.no/en/technical-competence/rnnp/

9 Imbert JP. Deep diving: the Comex experience. In: Hope A, Risberg J, editors. Long-term health effects of diving. The Godøysund 1993 consensus conference revisited; 15-17th September. Bergen: Norway; 2005. [cited 2023 Dec 15]. Available from: https://www.nui.no/open-nui-reports/.

10 Normam-15 DPC, Atividades Subaquáticas, Capitulo 11 Tabelas de mergulho, rev 2. 2016. [cited 2023 Dec 5]. Available from: https://www.marinha.mil.br/dpc/normas.

11 Vivacqua R. Practical experience of the use of deep heliox tables with specific focus on medical, physical and psychological aspects – Fugro Brasil. Proceedings of the annual IMCA diving seminar and DMAC Workshop; 25-26th September 2017. London: UK; 2017.

12 Cadieux C. Diving management study no 5: Implement Normam 15/DPC saturation diving procedures. [cited 2023 Dec 5]. Available from: https://diving-rov-specialists.com/docs-diving-rov-specialists.htm.

13 Van Liew HD, Burkard ME. Density of decompression bubbles and competition for gas among bubbles, tissue, and blood. J Appl Physiol (1985). 1993;75:2293–301. doi:10.1152/jappl.1993.75.5.2293. PMID: 8307888.

14 Flook V. Excursion tables in saturation diving - decompression implications of current UK practice. Unimed Scientific Limited, 2004. Report No.: 244. [cited 2023 Dec 5]. Available from: https://www.hse.gov.uk/Research/rrpdf/rr244.pdf.

15 Peterson RE, Segadal K. Deep Ex 80: Project IX. Compression / decompression. NUTEC, December 1980. Report No.: 52/80. [cited 2023 Dec 15]. Available from: https://www.nui.no/open-nui-reports/.

16 Imbert JP. Commercial diving. In: Balestra C, Germonpré P, editors. The science of diving: things your instructor never told you. London, UK: Lambert Academic Publishing; 2014. p. 118–36.

17 Hennessy TR, Hempleman HV. An examination of the critical released gas volume concept in decompression sickness. Proc R Soc Lond B Biol Sci. 1977;197(1128):299–313. doi:10.1098/rspb.1977.0072. PMID: 19749.

18 Vann RD. Decompression from saturation dives. In: Cox F, editor. Proceedings of the 3rd annual Canadian ocean technology congress, 1984. Toronto, Canada: 1984. [cited 2023 Dec 5]. Available from: https://apps.dtic.mil/sti/pdfs/ADA151743.pdf.

19 Kot J, Sicko Z, Doboszynski T. The extended oxygen window concept for programming saturation decompressions using air and nitrox. PLoS One. 2015;10(6):e0130835. doi:10.1371/journal.pone.0130835. PMID: 26111113. PMCID: PMC4482426.

20 Jacobsen G, Jacobsen JE, Peterson RE, McLellan JH, Brooke ST, Nome T, et al. Decompression sickness from saturation diving: a case control study of some diving exposure characteristics. Undersea Hyperb Med. 1997;24:73–80. PMID: 9171466.

21 DMAC. Minutes of the 14th November 2017 Meeting. [cited 05/12/2023]. Available via request from: Info@dmac-diving.org.

22 Germonpré P, Pontier JM, Gempp E, Blatteau JE, Deneweth S, Lafère P, et al. Pre-dive vibration effect on bubble formation

after a 30-m dive requiring a decompression stop. Aviat Space Environ Med. 2009;80:1044–8. doi: 10.3357/asem.2588.2010. PMID: 20027852.
23 Balestra C, Theunissen S, Papadopoulou V, Le Mener C, Germonpré P, Guerrero F, et al. Pre-dive whole-body vibration better reduces decompression-induced vascular gas emboli than oxygenation or a combination of both. Front Physiol. 2016;7:586. doi: 10.3389/fphys.2016.00586. PMID: 27965591. PMCID: PMC5127795.
24 Gempp E, Blatteau JE. Preconditioning methods and mechanisms for preventing the risk of decompression sickness in scuba divers: a review. Res Sports Med. 2010;18:205–18. doi: 10.1080/15438627.2010.490189. PMID: 20623437.
25 Imbert J, Egi S, Germonpré P, Balestra C. Static metabolic bubbles as precursors of vascular gas emboli during divers' decompression: a hypothesis explaining bubbling variability. Front Physiol. 2019;10:807. doi: 10.3389/fphys.2019.00807. PMID: 31354506. PMCID: PMC6638188.
26 Madden D, Lozo M, Dujic Z, Ljubkovic M. Exercise after SCUBA diving increases the incidence of arterial gas embolism. J Appl Physiol (1985). 2013;115:716–22. doi: 10.1152/japplphysiol.00029.2013. PMID: 23766500.
27 Imbert JP, Balestra C, Kiboub FZ, Loennechen Ø, Eftedal I. Commercial divers' subjective evaluation of saturation. Front Psychol. 2018;9:2774. doi: 10.3389/fpsyg.2018.02774. PMID: 30692957. PMCID: PMC6340096.
28 Imbert J, Bontoux M. Diving data bank: a unique tool for diving procedures development. Proceedings of the 20th Annual Offshore Technology Conference; 2-5th May, 1988. Houston, Texas, USA: Offshore Technology Conference; 1988. [cited 2023 Dec 5]. Available from: https://diving-rov-specialists.com/index_htm_files/scient-b_17-diving-data-bank-a-tool-for-diving-procedrues-development.pdf.
29 Rapport fra ptil's dykkedataabse dsy. [cited 2023 Dec 5]. Available from: https://www.ptil.no/contentassets/7284426234ae40cdaa62e2037ed2bf35/dsys_2022-rapport.pdf.
30 Doolette DJ. Venous gas emboli detected by two-dimensional echocardiography are an imperfect surrogate endpoint for decompression sickness. Diving Hyperb Med. 2016;46:4–10. PMID: 27044455. [cited 2023 Dec 5]. Available from: https://dhmjournal.com/images/IndividArticles/46March/Doolette_dhm.46.1.4-10.pdf.
31 Nishi RY, Brubakk AO, Eftedhal OS. Bubble detection. In: Brubakk AO, Neumann TS, editors. Physiology and medicine of diving. 5th ed. London, UK: Saunders; 2003. p. 501–29.
32 Thorsen E, Hjelle J, Segadal K, Gulsvik A. Exercise tolerance and pulmonary gas exchange after deep saturation dives. J Appl Physiol (1985). 1990;68:1809–14. doi: 10.1152/jappl.1990.68.5.1809. PMID: 2361882.
33 Risberg J, Brubbak OA, Vangsnes T, Ferguson S, Eftedal O, Kambestad B, et al. Project P11324. Doppler monitoring under decomprejon fra operasjonelle metningsdykk. NUTEC 1994. Report No.: 44-93, Rev 2. [cited 2023 Dec 15]. Available from: https://www.nui.no/open-nui-reports/.
34 Imbert JP, Egi SM, Balestra C. Vascular function recovery following saturation diving. Medicina (Kaunas). 2022;58(10):1476. doi: 10.3390/medicina58101476. PMID: 36295636. PMCID: PMC9610043.
35 Thorsen E, Segadal K, Stuhr LE, Troland K, Grønning M, Marstein S, et al. No changes in lung function after a saturation dive to 2.5 MPa with intermittent reduction in $PO_2$ during decompression. Eur J Appl Physiol. 2006;98:270–5. doi: 10.1007/s00421-006-0276-8. PMID: 16969641.
36 NPD Conference on the health examination of divers – fitness to dive – decompression – use of oxygen. Stavanger, Norway; 1988.
37 Shykoff BE, Lee RL. Risks from breathing elevated oxygen. Aerosp Med Hum Perform. 2019;90:1041–9. doi: 10.3357/amhp.5393.2019. PMID: 31748001.
38 Bardin H, Lambertsen CJ. A quantitative method for calculating pulmonary oxygen toxicity. use of the unit pulmonary toxicity dose (UPTD). Pennsylvania, USA: Institute for Environmental Medicine, University of Pennsylvania; 1971.
39 Risberg J, van Ooij PJ, Matity L. From UPTD to ESOT: monitoring hyperoxic exposure in surface-oriented diving. Undersea Hyperb Med. 2023;50:301–6. PMID: 37708063.
40 Arieli R. Pulmonary oxygen toxicity in saturation dives with $PO_2$ close to the lower end of the toxic range - A quantitative approach. Respir Physiol Neurobiol. 2019;268:103243. doi: 10.1016/j.resp.2019.05.017. PMID: 31158523.
41 Schreiner HR, Hamilton RW, editors. 37th Workshop of the UHMS. Validation of decompression tables; 1987 Feb 13-14. Bethesda (MD): UHMS; 1987. [cited 2023 Dec 5]. Available from: https://diving-rov-specialists.com/index_htm_files/scient-b_71-validation-decompression-tables.pdf.
42 DMAC. Improving diver safety – current medical issues. Report of a workshop held in October 2014. Aberdeen, UK: DMAC; 2014. [cited 2023 Dec 5]. Available from: https://www.dmac-diving.org/guidance/DMAC-Workshop-20141008.pdf.
43 Brubakk AO, Ross JA, Thom SR. Saturation diving; physiology and pathophysiology. Compr Physiol. 2014;4(3):1229–72. doi: 10.1002/cphy.c130048. PMID: 24944036.
44 Mrakic-Sposta S, Vezzoli A, D'Alessandro F, Paganini M, Dellanoce C, Cialoni D, et al. Change in oxidative stress biomarkers during 30 days in saturation dive: a pilot study. Int J Environ Res Public Health. 2020;17(19):7118. doi: 10.3390/ijerph17197118. PMID: 32998440. PMCID: PMC7579105.

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# Chain of events analysis in diving accidents treated by the Royal Netherlands Navy 1966–2023

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**Keywords**
Arterial gas embolism; Decompression sickness; Incidents; Risk factors; Safety; Underwater hazards

**Abstract**
(Turner BL, van Ooij P-JAM, Wingelaar TT, van Hulst RA, Endert EL, Clarijs P, Hoencamp R. Chain of events analysis in diving accidents treated by the Royal Netherlands Navy 1966-2023. Diving and Hyperbaric Medicine. 2024 31 March;54(1):39–46. doi: 10.28920/dhm54.1.39-46. PMID: 38507908.)
**Introduction:** Diving injuries are influenced by a multitude of factors. Literature analysing the full chain of events in diving accidents influencing the occurrence of diving injuries is limited. A previously published 'chain of events analysis' (CEA) framework consists of five steps that may sequentially lead to a diving fatality. This study applied four of these steps to predominately non-lethal diving injuries and aims to determine the causes of diving injuries sustained by divers treated by the Diving Medical Centre of the Royal Netherlands Navy.
**Methods:** This retrospective cohort study was performed on diving injuries treated by the Diving Medical Centre between 1966 and 2023. Baseline characteristics and information pertinent to all four steps of the reduced CEA model were extracted and recorded in a database.
**Results:** A total of 288 cases met the inclusion criteria. In 111 cases, all four steps of the CEA model could be applied. Predisposing factors were identified in 261 (90%) cases, triggers in 142 (49%), disabling agents in 195 (68%), and 228 (79%) contained a (possible-) disabling condition. The sustained diving injury led to a fatality in seven cases (2%). The most frequent predisposing factor was health conditions (58%). Exertion (19%), primary diver errors (18%), and faulty equipment (17%) were the most frequently identified triggers. The ascent was the most frequent disabling agent (52%).
**Conclusions:** The CEA framework was found to be a valuable tool in this analysis. Health factors present before diving were identified as the most frequent predisposing factors. Arterial gas emboli were the most lethal injury mechanism.

## Introduction

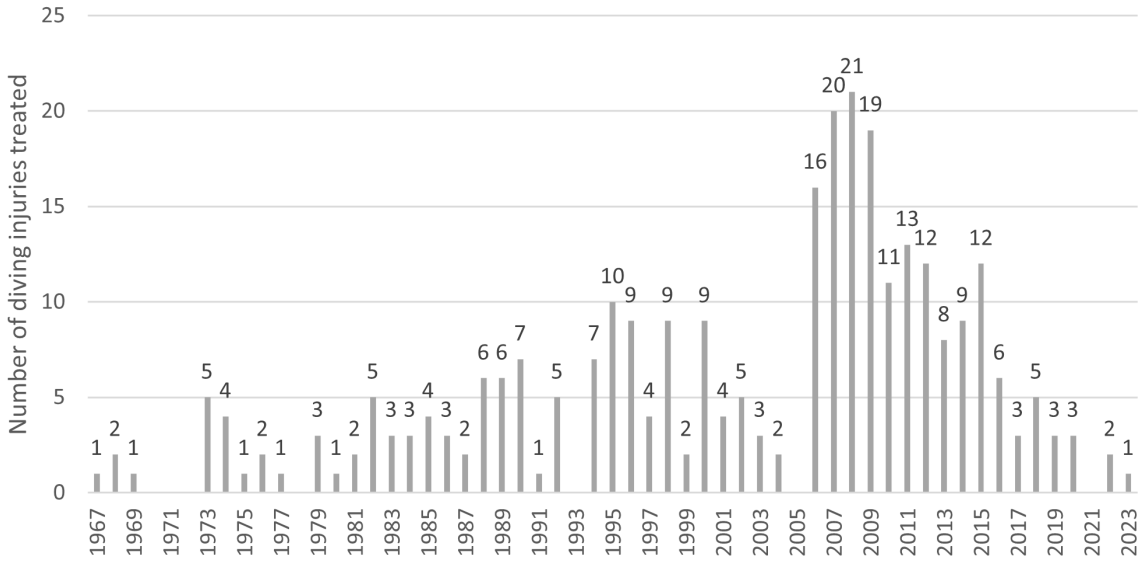
Scuba diving is a popular, growing sport practiced by more than six million divers worldwide.[1] Due to the physiological changes induced by water immersion and submersion, exercise, and the usage of specialised equipment, every dive contains inherent risks, albeit small, for the diver's health and safety.[2] Other factors influencing the safety of a dive are, for example, human factors (e.g., mistakes made due to a lack of training), a diver's medical history and environmental factors (e.g., water conditions including temperature). In addition, injuries sustained while diving can occur due to various mechanisms, such as sudden pressure changes and insufficient decompression.

Due to the complex interplay between the aforementioned factors influencing the risk of incidents, determining a single causal factor for a diving injury is rarely possible. There are several studies available presenting data on diving injuries.[3–7] However, literature often focusses on specific aspects or outcomes of diving accidents.[3–6,8–10] Data on the full spectrum of factors influencing the occurrence of a diving injury are limited.

**Table 1**
Definitions of the phases contained within the chain of events analysis, adapted from Lippmann[9]

| Step | Definition | Example |
|---|---|---|
| Predisposing factor | A relevant factor that was present prior to the dive, and/or prior to the trigger occurring, and which is believed to have predisposed to the incident and/or to key components in the accident chain (e.g., the trigger or disabling agent) | A diver with acute rhinitis and limited training |
| Trigger | The earliest identifiable event that appeared to transform an unremarkable dive into an emergency | A malfunctioning communication system |
| Disabling agent | An action or circumstance (associated with the trigger) that caused injury or illness. It may be an action of the diver or other persons, reaction of the equipment, effect of a medical condition or a force of nature | A rapid ascent |
| Disabling condition | An injury caused by the diving accident | Decompression sickness |

**Figure 1**
The distribution of included cases per year




The 'chain of events analysis' (CEA) was first introduced by Denoble and further developed by Lippmann.[6,9] It allows for consideration of the entire accident sequence of a diving fatality. The CEA framework consists of five steps: (1) predisposing factors, (2) triggers, (3) disabling agents, (4) disabling conditions and (5) cause of death. In non-fatal incidents the final phase is not applicable, so the CEA is reduced to the initial four steps (Table 1). Older studies using CEA contain data discrepancies due to the use of varying categorisation and terminology.[6,7] The root cause analysis method used by other studies does not allow for including predisposing factors.[7,11] Human factors, which have been shown to be a significant factor in the occurrence of diving accidents, can also be taken into account in the CEA framework.[9,12]

Applying the CEA framework on a large dataset could generate meaningful insights for the diving medical community due to its structured approach and inclusion of human factors. For example, frequently identified predisposing factors could help dive medical physicians to screen more effectively, and frequently identified triggers could show diving instructors important focus points for training.

The primary aim of this study was to analyse the frequency and causes of diving injuries sustained by divers seen or treated by the Diving Medical Centre of the Royal Netherlands Navy (DMC) using the standardised CEA method. The secondary aim was to assess the value of the CEA method in determining mechanisms of diving injuries for future research and documentation.

## Methods

This retrospective cohort study was performed by applying CEA on pseudonymised medical records and related documents at the DMC. The study was conducted in accordance with the recommendations of the surgeon general of the Ministry of Defence (reference: DGO20230511). The data collected during this study was stored and analysed in compliance with national privacy legislation and European Data Protection Regulations (GDPR).

### INCLUSION AND EXCLUSION CRITERIA

Injury reports and medical files of potentially eligible diving injuries between 1966 (the year of inception of the DMC) up to August 2023 were screened. The population consisted of civilian and military divers treated or examined by a dive medical physician. A record was included if both the description of the diving incident and the medical files of the diver were available and the dive medical physician at the time of the incident deemed the injury to be related to a diving accident. Records were excluded if the description of the diving incident was not available or the injury was not sustained through diving.

### DATA EXTRACTION AND OUTCOMES OF INTEREST

Aside from baseline characteristics, such as age, sex, and weight, data on dive profiles, treatment, and recovery of the divers were collected as well. Furthermore, the categories for each step in the CEA, as defined by Lippmann, were compared to the information described in the record. Except for sex, all baseline characteristics were assessed for normality using a Jarque-Bera test.

### ANALYSIS

The records were analysed and encoded by author BT. Additionally, cases were cross-checked by two senior dive medical physicians (RH and PJvO), and, if necessary, discussed until a consensus was reached.

The definition provided for each step of the CEA is described in Table 1. Because most cases seen by the DMC are non-fatal, it was decided to extend Lippmann's framework by utilising the 'Disabling condition' category for non-fatal diving injuries as well as fatal diving injuries. The symptoms and diagnoses were encoded using ICD-10 Version 2019 codes.[13]

Descriptive statistics were obtained from the assembled dataset using SPSS Statistics for Windows software (2020, version 27.0; IBM Corp; Armonk, NY).

## Results

In total, 288 cases met the inclusion criteria for the period 1966–2023. The distribution of the cases per year is shown in Figure 1.

Height was normally distributed, while body mass index BMI, weight, and age showed a non-normal distribution. The median age of the casualties was 34 (IQR 28.0–43.3), and 76.7% were male. Males had a slightly higher median BMI than females, respectively 24.5 (IQR 24.5–25.3) and 23.8 (IQR 21.6–26.7). Baseline characteristics are presented in Table 2. In total, 81.3% of cases concerned civilians and 17.0% military divers. Of these military divers, 18.4% were part of the Royal Netherlands Army, 79.6% were part of the Royal Netherlands Navy, and one diver's military branch was not specified. Furthermore, in three cases (1.0%) the divers were part of the fire brigade.

In 38.5% of cases (111/288) one or more risk categories in each of the four steps within the CEA model could be identified. All 288 cases were included in the final analysis, including the 61.5% (177/288) of cases in which not all steps were identified. In some cases, multiple relevant categories were identified per step, especially the predisposing factors. Table 3 presents the distribution of the identified categories within each step.

### PREDISPOSING FACTORS

Predisposing factors were identified in 90.6% (261/288) of cases. The most frequently identified categories were *'Health'* ($n = 308$, divided over 159 unique cases), '*Activity'* ($n = 90$), *'Planning'* ($n = 47$) and '*Training'* ($n = 31$). The category *'Health'* was comprised of multiple subcategories, including the most frequently identified subcategories

**Table 2**

Baseline characteristics; data depict median (interquartile range, and number of observations); BMI – body mass index

| Parameter | Total ($n = 288$) | Male ($n = 221$) | Female ($n = 67$) |
|---|---|---|---|
| Age (years) | 34.0 (28–43.3, $n = 261$) | 34.0 (27–44, $n = 197$) | 34.0 (28–40, $n = 64$) |
| Height (cm) | 179.0 (171–186, $n = 131$) | 183.0 (179–188, $n = 89$) | 169.0 (167–174, $n = 42$) |
| Weight (kg) | 78.0 (69–89, $n = 131$) | 84.0 (76–91.5, $n = 89$) | 65.0 (61–70.5, $n = 42$) |
| BMI ($kg \cdot m^{-2}$) | 24.4 (22.4–27.1, $n = 131$) | 24.5 (24.5–25.3, $n = 88$) | 23.8 (21.6–26.7, $n = 42$) |

**Table 3**

Distribution of the identified categories; *this subcategory contains decompression sickness type 1 ($n$ = 41 for Diagnosis, $n$ = 4 for Possible diagnosis), decompression sickness type 2 ($n$ = 90 for Diagnosis, $n$ = 15 for Possible diagnosis) and air embolism ($n$ = 22 for Diagnosis, $n$ = 8 for Possible diagnosis)

| Step | Row Labels | Occurrence (% of total) | |
|---|---|---|---|
| Predisposing factors | Activity | 90 (17.1%) | |
| | Communication | 1 (0.2%) | |
| | Equipment | 39 (7.4%) | |
| | Health | 308 (58.6%) | |
| | Organization | 9 (1.7%) | |
| | Other | 1 (0.2%) | |
| | Planning | 47 (8.9%) | |
| | Training | 31 (5.9%) | |
| | **Category total** | **526** | |
| Triggers | Anxiety | 14 (9.6%) | |
| | Buddy diver error | 11 (7.5%) | |
| | Buoyancy | 12 (8.2%) | |
| | Communication | 4 (2.7%) | |
| | Environment | 8 (5.5%) | |
| | Equipment | 25 (17.1%) | |
| | Exertion | 28 (19.2%) | |
| | Gas supply | 17 (11.6%) | |
| | Health | 1 (0.7%) | |
| | Primary diver error | 26 (17.8%) | |
| | **Category total** | **146** | |
| Disabling agents | Anxiety | 7 (3.4%) | |
| | Ascent | 107 (51.9%) | |
| | Buoyancy | 2 (1.0%) | |
| | Descent | 1 (0.5%) | |
| | Environment | 5 (2.4%) | |
| | Equipment | 6 (2.9%) | |
| | Gas supply | 4 (1.9%) | |
| | Medical | 34 (16.5%) | |
| | Other | 13 (6.3%) | |
| | Post-dive | 27 (13.1%) | |
| | **Category total** | **206** | |
| Disabling conditions | | Diagnosis (% of total) | Possible diagnosis (% of total) |
| | Congenital and chromosomal abnormalities | 2 (0.7%) | 2 (0.7%) |
| | Diseases of the circulatory system | 2 (0.7%) | 0 |
| | Diseases of the digestive system | 2 (0.7%) | 0 |
| | Diseases of the ear and mastoid process | 6 (2.2%) | 1 (0.4%) |
| | Diseases of the musculoskeletal system and connective tissue | 5 (1.8%) | 3 (1.1%) |
| | Diseases of the nervous system | 0 | 5 (1.8%) |
| | Diseases of the respiratory system | 14 (5.0%) | 2 (0.7%) |
| | Endocrine, nutritional and metabolic diseases | 4 (1.4%) | 1 (0.4%) |
| | External causes of morbidity and mortality | 9 (3.2%) | 2 (0.7%) |
| | Injury, poisoning and certain other external causes* | 168 (60.2%) | 31 (11,1%) |
| | Mental and behavioural disorders | 2 (0.7%) | 1 (0.4%) |
| | Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | 14 (5.0%) | 2 (0.7%) |
| | Diseases of the skin and subcutaneous tissue | 1 (0.4%) | 0 |
| | **Category total** | **229** | **50** |

'*diagnosis in medical history*' (*n* = 144), *'health problems present before dive*' (*n* = 60) and '*history of smoking*' (*n* = 39). Further analysing the '*diagnosis in medical history*' category for medically relevant diagnoses resulted in 83 remaining identifications.

TRIGGERS

Triggers were identified in 49.3% (142/288) of cases. '*Exertion'* (*n* = 28), '*Primary diver error'* (*n* = 26), and '*Equipment'* (*n* = 25) were the most frequently identified triggers.

Each overarching trigger category contains multiple subcategories. The most frequently identified subcategories were '*out of air*' (*n* = 9, belonging to *Gas supply),* '*mask filled with water*' (*n* = 8, belonging to *Equipment*), '*accidental ascent*' (*n* = 7, belonging to *Buoyancy*) and '*ignoring diving computer*', '*ascending too fast*' (*n* = 7, belonging to *Primary diver error*).

DISABLING AGENTS

Disabling Agents were identified in 67.7% (195/288) of cases. '*Ascent'* (*n* = 107), '*Medical'* (*n* = 34), and '*Post-dive'* (*n* = 27) were most frequently identified as disabling agents. Within the '*Other*' category, two frequently occurring subcategories, '*Ascent to altitude after diving'* (*n* = 11) and '*Exertion after dive'* (*n* = 10), were grouped under the new category '*Post-dive'*.

Two of the most frequently occurring subcategories are contained within '*Ascent*: *Ascending too fast'* (*n* = 63) and '*Staying at depth too long'* (*n* = 15). Another frequently occurring subcategory is contained within '*Medical': 'Volume depletion'* (*n* = 17), which represents cases where dehydration was considered a disabling agent.

DISABLING CONDITIONS

The disabling conditions were divided into '*Diagnosis'* (229/288 cases) and *Possible diagnosis* (50/288 cases) based on the information present in the case reports and medical charts. A disabling condition was only scored as a '*Diagnosis*' if the report specified it as such, otherwise, it was categorised as a '*Possible diagnosis*'. In the remaining cases, no (possible-) diagnosis was provided by the diving medicine physician.

The most frequently identified category was '*Injury, poisoning, and certain other consequences of external causes'* (*n* = 168 for *Diagnosis*, *n* = 31 for *Possible diagnosis).* This category contained the three most frequently occurring diagnoses and possible diagnoses: '*Decompression sickness type 1'* (*n* = 41 for *Diagnosis*, *n* = 4 for *Possible diagnosis*), '*Decompression sickness type 2'* (*n* = 90 for *Diagnosis*, *n* = 15 for *Possible diagnosis*) and '*Air embolism'* (*n* = 21 for *Diagnosis*, *n* = 8 for *Possible diagnosis*).

The second most frequently occurring category contained in *Diagnosis* was '*Diseases of the respiratory system'* (*n* = 14), containing, among other subcategories, '*Pneumothorax'* (*n* = 5) and '*Pulmonary oedema'* (*n* = 4). The third category, '*External causes of morbidity and mortality'* (*n* = 9), contained, among other things, the diagnosis '*Exposure to high and low air pressure and changes in air pressure'* (*n* = 6).

FATALITIES

In 2.4% (7/288) of cases, the diver died due to the sustained diving injury. Arterial gas emboli were the most frequent cause (*n* = 3), one resulted from a complication of immersion pulmonary oedema. Unspecified, either venous or arterial, gas emboli, drowning, and an allergic asthma attack were each the cause of one fatality. No data on the autopsies of the fatal injuries were available.

## Discussion

This retrospective cohort study performed on the medical records of the Diving Medical Center of the Royal Netherlands Navy utilised the CEA method to analyse diving injuries. In our opinion, the CEA framework is valuable for diving medicine, due to the inclusion of predisposing factors that can directly translate to dive medical screenings performed by diving physicians, as well as the insights gained about the importance of training and planning.

Assessing the occurrence of categories identified in our application of the framework provides us with insights regarding risk factors influencing diving injuries. We identified a category for each step within the CEA model in 40% of cases. The '*health*' category represented over half of all identified predisposing factors. Both formally diagnosed medical conditions and health problems present before the dive started, as reported by the diver, were included in this category. However, the distinction must be made between relevant health factors and health factors of unknown clinical significance. Making this distinction in our analysis resulted in a reduction of 42.4% (from 144 to 83 diagnoses). The health category still remained the most frequently identified category, which seems to be in agreement with the literature, since underlying co-existing medical conditions have been shown to be a risk factor for diving fatalities and injuries.[11,14–16]

Interestingly, we have not identified cardiac events as disabling agents, which previous studies analysing diving fatalities have labelled as the most frequent disabling agent, albeit in cohorts of older recreational divers.[7,17,18] We did, however, observe cardiac conditions as predisposing factors. This difference could, therefore, be due to the use of our classification system and our data, which mainly consisted of diving injuries instead of diving fatalities.[7,17] The relatively young age, 34 years on average, of our cohort could further contribute to our lack of observed cardiac issues.

An important note is that not all health factors identified as predisposing factors may have had the same amount of causal influence on the diving injury. For example, a shoulder contusion may have had less influence on the occurrence of the diving injury than the dehydrated status of the diver, while both have been identified as predisposing factors.

Undertaking exertional activities while diving, such as moving heavy objects underwater and swimming for long distances, appeared to contribute to the triggering of a diving injury, which is in accordance with risk factors for diving injuries identified by other studies.[8,19] A possible causal relation could exist between the 'activity' and 'exertion' categories used as *predisposing factors* and *triggers* respectively. Underlying medical conditions and a lack of training can affect the level of exertion that a diver experiences. This illustrates the value of chain of events analysis, which enables us to take the influence of predisposing factors on factors occurring during the dive into account.

Triggers regarding equipment and gas supply were also frequently identified, which other studies have shown as well, underlining the importance of pre-dive checks and showing the influence of human factors when these checks are lacking.[6,17,20]

We identified a rapid ascent, a well-known risk factor for developing decompression sickness, as a frequent disabling agent, which is in agreement with other studies.[6,8,17,21,22]

In our application of the framework, we chose to include each case that contained at least one identifiable step in the CEA model in our dataset. Cases in which not all steps are identified, for example due to a lack of documentation, can still provide interesting information when analysing individual steps. For example, a case containing only predisposing factors and a disabling condition can be of value when researching risk factors. However, in our opinion the value of the CEA is in the connections made between each step. Therefore, we suggest future studies aiming to analyse the entire chain of events to only include cases without missing steps.

Further research utilising this framework should consider our findings of utilising a filter for relevant medical diagnoses as well as utilising ICD-10 coding for predisposing factors and disabling injuries. A limitation of ICD-10 coding is that the most frequent diagnoses and fatal injuries are all part of one overarching category. Therefore, we suggest explicitly distinguishing between arterial gas embolism and decompression sickness types 1 and 2 when using ICD-10 coding for other parts of CEA. A category within the '*Disabling agents*' step concerning '*Ascent to altitude after diving*' should be added, especially as this is a (risk) factor for developing decompression sickness. Further application of the framework will no doubt give rise to even more novel categories.

Furthermore, a way to analyse casual relations between categories, such as triggers causing diving injuries when specific predisposing factors are present, should be developed. This could result in valuable insights for diving injury prevention and treatment. These inter-categorical trends could be analysed by performing a multinomial regression analysis, keeping the risk of overfitting in mind and focusing on the relations between categories one step at a time.

A limitation of the CEA model is that the exact causal relationship between the predisposing factors and the diving injury sustained is not fully retraceable by only analysing the overview of identified categories but requires looking at each case in more detail. Furthermore, human factors, which have been shown to play a major role in the occurrence of diving injuries, are not fully incorporable in the analysed CEA model, especially detailed contextual factors such as psychological aspects.[23]

The strength of each CEA relies on the documentation of the diving injuries. Because of the potentially invaluable insights that could be gained by performing large-scale CEA, we suggest the application of a standardised format to document diving injuries that ensures the recording of essential information for future CEA applications. This format could be digitalised and should consist of a field for each step in the CEA model. Special attention should be paid to human factors that influenced the diving injury and medical factors. Of course, to ensure the usage of this format, it should not take the physicians a substantial amount of extra time to use this new documentation system.

## STRENGTHS AND LIMITATIONS

This study's main strength is that it is, to our knowledge, the first application of CEA on a dataset of this size and in predominantly non-fatal incidents. Furthermore, it could serve as a proof of concept of the proposed model, albeit with the addition of the ICD-10 classification.

There are also some limitations. The collection and analysis of data in a retrospective cohort using chart review is subject to certain limitations by default. The data quality is dependent on the information contained within the medical records and eyewitness accounts, which may be incomplete, speculative, and biased. This could have influenced the quality of our CEA. While from an academic perspective, this is a limitation, we feel it represents reality - not all information may be accessible in accident investigations.

We have utilised the medical records and additional material available in our archives, which did not contain all documentation of follow-ups. Therefore, some cases contained less information than others, which could have led to an underrepresentation of some categories. However, as the model has proven useful even with this limitation, we feel having all data would only increase its validity.

Moreover, not all (fatal) diving injuries in The Netherlands are treated at the DMC, which means our dataset contains a level of selection bias. Generalisation of our results to other populations should be done carefully.

Lastly, classifying cases into categories of the CEA, which is a simplified representation of reality, contains subjectivity. Therefore, misclassification could have occurred. This is, however, an inherent limitation of models utilising categories. We have tried to mitigate this bias by involving multiple researchers when doubt arose. Furthermore, we feel that simplification could perhaps contribute to grasping the complexity of reality and identifying valuable lessons, in contrast to trying to understand known and unknown factors and their multifactorial interactions and failing to reach a conclusion.[24]

## Conclusions

We have found the CEA framework to be a valuable tool in analysing diving injuries and have made suggestions to improve the framework, including the application of filtering for relevant health factors and using standardised ICD coding.

In the cohort of diving accidents from 1966–2023, '*health problems*' was the most commonly identified predisposing factor for diving injuries (~58%). Furthermore, the '*activity*' undertaken by the diver seems to contribute to a diving injury occurring as well (~18%). '*Exertion*' (~19%), '*primary diver errors*' (~18%) and '*faulty equipment*' (~17%) were the most common diving injury triggers. The '*ascent of the diver*' was the most often occurring disabling agent (~52%).

The most frequently occurring diving injuries were decompression sickness type 1 (~15%) and type 2 (~32%) and arterial gas embolism (~8%). Arterial gas embolism was the most lethal injury (~43% of fatalities).

## References


1 2023 Diving Fast Facts. [Internet]: Diving Equipment and Marketing Association; 2023. [cited 2023 Oct 4]. Available from: https://www.dema.org/store/download.aspx?id=7811B097-8882-4707-A160-F999B49614B6.

2 Bosco G, Rizzato A, Moon RE, Camporesi EM. Environmental physiology and diving medicine. Front Psychol. 2018;9:72. doi: 10.3389/fpsyg.2018.00072. PMID: 29456518. PMCID: PMC5801574.

3 Buzzacott P, Hornsby A, Shreeves K. Mortality rate during professionally guided scuba diving experiences for uncertified divers, 1992-2019. Diving Hyperb Med. 2021;51:147–51. doi: 10.28920/dhm51.2.147-151. PMID: 34157729. PMCID: PMC8426127.

4 Monnot D, Michot T, Dugrenot E, Guerrero F, Lafère P. A survey of scuba diving-related injuries and outcomes among French recreational divers. Diving Hyperb Med. 2019;49:96–106. doi: 10.28920/dhm49.2.96-106. PMID: 31177515. PMCID: PMC6704004.

5 Kojima Y, Kojima A, Niizeki Y, Yagishita K. Recreational diving-related injury insurance claims among Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014. Diving Hyperb Med. 2020;50:92–7. doi: 10.28920/dhm50.2.92-97. PMID: 32557409. PMCID: PMC7481107.

6 Denoble PJ, Caruso JL, Dear Gde L, Pieper CF, Vann RD. Common causes of open-circuit recreational diving fatalities. Undersea Hyperb Med. 2008;35:393–406. PMID: 19175195.

7 Vinkel J, Bak P, Hyldegaard O. Danish diving-related fatalities 1999-2012. Diving Hyperb Med. 2016;46:142–9. PMID: 27723014. [cited 2023 Oct 4]. Available from: https://dhmjournal.com/images/IndividArticles/46Sept/Vinkel_dhm.46.3.142-149.pdf.

8 Casadesús JM, Aguirre F, Carrera A, Boadas-Vaello P, Serrando MT, Reina F. Diving-related fatalities: multidisciplinary, experience-based investigation. Forensic Sci Med Pathol. 2019;15:224–32. doi: 10.1007/s12024-019-00109-2. PMID: 30915609.

9 Lippmann J, Stevenson C, Taylor DMcD, Williams J, Mohebbi M. Chain of events analysis for a scuba diving fatality. Diving Hyperb Med. 2017;47:144–54. doi: 10.28920/dhm47.3.144-154. PMID: 28868594. PMCID: PMC6159623.

10 Svendsen Juhl C, Hedetoft M, Bidstrup D, Jansen EC, Hyldegaard O. Decompression illness treated in Denmark 1999-2013. Diving Hyperb Med. 2016;46:87–91. PMID: 27334996. [cited 2023 Oct 4]. Available from: https://dhmjournal.com/images/IndividArticles/46June/Juhl_dhm46.2.87-91.pdf.

11 Potts L, Buzzacott P, Denoble P. Thirty years of American cave diving fatalities. Diving Hyperb Med. 2016;46:150–4. PMID: 27723015. [cited 2023 Oct 4]. Available from: https://dhmjournal.com/images/IndividArticles/46Sept/Potts_dhm.46.3.150-154.pdf.

12 Febriyanto K, Rachman A, Rahman FF. The contribution of human error related to occupational accident among traditional divers. Gac Sanit. 2021;35(Supp 1):S27–9. doi: 10.1016/j.gaceta.2020.12.008. PMID: 33832619.

13 ICD-10 Version: 2019. [Internet]: World Health Organization; 2019. [cited 2023 Oct 4]. Available from: https://icd.who.int/browse10/2019/en#/.

14 Lippmann J, Tayor DMcD. Scuba diving fatalities in Australia 2001 to 2013: Chain of events. Diving Hyperb Med. 2020;50:220–9. doi: 10.28920/dhm50.3.220-229. PMID: 32957123. PMCID: PMC7819731.

15 Lippmann J, Stevenson C, Taylor DM. Scuba diving fatalities in Australia, 2001 to 2013: Diver demographics and characteristics. Diving Hyperb Med. 2020;50:105–14. doi: 10.28920/dhm50.2.105-114. PMID: 32557411. PMCID: PMC7481108.

16 Komdeur P, Wingelaar TT, van Hulst RA. A survey on the health status of Dutch scuba diving instructors. Diving Hyperb Med. 2021;51:18–24. doi: 10.28920/dhm51.1.18-24. PMID: 33761537. PMCID: PMC8313785.

17 Tillmans F, editor. DAN Annual Diving Report 2020 Edition: A report on 2018 diving fatalities, injuries, and incidents. Durham (NC): Divers Alert Network; 2021.

18 Lippmann J. A review of snorkelling and scuba diving fatalities in Queensland, Australia, 2000 to 2019. Diving Hyperb Med. 2022;52:108–18. doi: 10.28920/dhm52.2.108-118. PMID: 35732283. PMCID: PMC9522589.

19 Cialoni D, Pieri M, Balestra C, Marroni A. Dive risk factors, gas bubble formation, and decompression illness

in recreational SCUBA diving: Analysis of DAN Europe DSL data base. Front Psychol. 2017;8:1587. doi: 10.3389/fpsyg.2017.01587. PMID: 28974936. PMCID: PMC5610843.
20 Lippmann J, Lawrence C, Davis M. Scuba diving-related fatalities in New Zealand, 2007 to 2016. Diving Hyperb Med. 2021;51:345–54. doi: 10.28920/dhm51.4.345-354. PMID: 34897599. PMCID: PMC8920894.
21 Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. Lancet. 2011;377(9760):153–64. doi: 10.1016/S0140-6736(10)61085-9. PMID: 21215883.
22 Jain KK. Textbook of hyperbaric medicine. 6th ed. Cham, Switzerland: Springer; 2017.
23 Lock G. Under Pressure: Diving Deeper with Human Factors. Great Britain: Vision Maker Press; 2019.
24 Kahneman D, Sibony O, Sunstein CR. Noise: A flaw in human judgment. London: Little, Brown Spark; 2022.

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# Review article

## Reported outcome measures in necrotising soft tissue infections: a systematic review

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Fournier's gangrene; Gas gangrene; Hyperbaric oxygen treatment; Intensive care medicine; Systematic review

**Abstract**
(Wackett J, Devaney B, Chau R, Ho J, King N, Grewal J, Armstrong J, Mitra B. Reported outcome measures in necrotising soft tissue infections: a systematic review. Diving and Hyperbaric Medicine. 2024 31 March;54(1):47–56. doi: 10.28920/dhm54.1.47-56. PMID: 38507909.)
**Introduction:** There are inconsistencies in outcome reporting for patients with necrotising soft tissue infections (NSTI). The aim of this study was to evaluate reported outcome measures in NSTI literature that could inform a core outcome set (COS) such as could be used in a study of hyperbaric oxygen in this indication.
**Methods:** A systematic review of all NSTI literature identified from Cochrane, Ovid MEDLINE and Scopus databases as well as grey literature sources OpenGrey and the New York Academy of Medicine databases which met inclusion criteria and were published between 2010 and 2020 was performed. Studies were included if they reported on > 5 cases and presented clinical endpoints, patient related outcomes, or resource utilisation in NSTI patients. Studies did not have to include intervention. Two independent researchers then extracted reported outcome measures. Similar outcomes were grouped and classified into domains to produce a structured inventory. An attempt was made to identify trends in outcome measures over time and by study design.
**Results:** Three hundred and seventy-five studies were identified and included a total of 311 outcome measures. Forty eight percent (150/311) of outcome measures were reported by two or more studies. The four most frequently reported outcome measures were mortality without time specified, length of hospital stay, amputation performed, and number of debridements, reported in 298 (79.5%), 260 (69.3%), 156 (41.6%) and 151 (40.3%) studies respectively. Mortality outcomes were reported in 23 different ways. Randomised controlled trials (RCTs) were more likely to report 28-day mortality or 90-day mortality. The second most frequent amputation related outcome was level of amputation, reported in 7.5% (28/375) of studies. The most commonly reported patient-centred outcome was the SF-36 which was reported in 1.6% (6/375) of all studies and in 2/10 RCTs.
**Conclusions:** There was wide variance in outcome measures in NSTI studies, further highlighting the need for a COS.

### Introduction

Necrotising soft tissue infections (NSTI) are a collection of rare but serious infections that can lead to widespread tissue destruction and threaten considerable morbidity and mortality. NSTI encompasses conditions such as necrotising fasciitis, Fournier's gangrene, necrotising cellulitis and necrotising myonecrosis.[1] A large Danish registry-based study demonstrated all-cause mortality rates of 19% at 30 days, 25% at 90-days, and 30% at one-year.[2] Treatment modalities include early surgical debridement, broad spectrum antibiotics and often organ support in an intensive care unit, however there is ongoing discourse as to the effectiveness of adjuvant therapies such as hyperbaric oxygen treatment (HBOT) and intravenous immunoglobulin (IVIG) administration.[1]

Treatment with hyperbaric oxygen involves breathing 100% oxygen at greater than atmospheric pressures, substantially increasing serum partial pressures of oxygen. There are a number of proposed phyiological mechanisms by which repeated increased partial pressures of oxygen may improve outcomes in NSTI. Multiple retrospective observational studies and a recent meta-analysis demonstrate reduced in-hospital mortality in NSTI patients treated with HBOT, however Level 1 evidence is currently lacking and the use of HBOT varies between centres.[3] Heterogeneity in outcome reporting limits the quality of data available for meta-analysis.

Thus, it follows that the selection of outcome measures for prospective trials is critical.[4] A core outcome set (COS) is an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care.[4] High quality prospective trials use outcomes that are predetermined, but in the absence of a COS, findings are variably reported, and reporting bias may be introduced.[5] Currently, there is no consensus amongst clinicians, researchers and patients regarding the outcome measures that should be collected and reported in studies assessing potential interventions for NSTI.[6] A Cochrane Review of interventions for NSTIs in adults demonstrated that only one third of included studies reported all the predetermined outcomes.[7] Such inconsistencies preclude the synthesis of data in meta-analyses and reduce the quality of evidence available to form clinically relevant conclusions that ultimately benefit patient care.

The aim of this systematic review was to develop an inventory of outcome measures used in NSTI studies. We evaluated associations between methodological design and outcome reporting. It was expected that the findings will inform the development of a COS for NSTI, which will lead to enhanced ability to evaluate the efficacy of adjuvant therapies such as HBOT.

## Methods

This systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[8] The review protocol was developed *a priori* and registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42022330268. The inventory of reported outcome measures generated by this review will inform Delphi surveys and consensus meetings as part of a broader initiative to develop a COS in NSTI.

After the initial search, all steps were undertaken in duplicate by independent reviewers.

### SEARCH STRATEGY

A comprehensive literature search was undertaken using Cochrane, Ovid MEDLINE and Scopus databases as well as grey literature sources OpenGrey and the New York Academy of Medicine databases. Searches were performed for a 10-year period (January 2010 – August 2020) to record an extensive list of outcomes being reported for this relatively rare group of conditions, as well as to identify how research in NSTI may have changed over time. Medical subject headings and keywords such as "*Necrotising soft tissue infections*", "*Fournier gangrene*", and "*Gas gangrene*" were combined using the "*OR*" operator to ensure a breadth of results were returned. An example of the full search strategy as was used for Ovid MEDLINE is provided in * Appendix 1.

### STUDY ELIGIBILITY

Studies were included if they related to NSTI and reported one or more patient outcomes provided they also met the following criteria:

*Types of studies:* All study designs were included except for case reports, case series of < 5 cases, case series that only express their outcomes individually or qualitatively (e.g., a case series of eight cases described in detail but with no pooling or tabulation of patient outcomes). These study designs were excluded to avoid outcome measures that are less relevant or achievable for larger studies.

*Types of participants*: We included studies that reported outcomes of NSTI patients of all ages, geographic locations, and disease phenotypes (necrotising fasciitis, Fournier's gangrene etc) that were at any stage in the course of their disease (inpatient or outpatient).

*Types of interventions:* Studies of any/all interventions for NSTI were included. Studies not assessing an intervention were also included, provided they reported on patient outcomes.

*Types of outcomes:* Studies were included if they reported any patient related outcome or clinical endpoint, including outcomes related to mortality, morbidity, recovery, quality of life, and adverse events. Outcomes reported in the body of text, tables and/or figures were included. Patient and observer reported outcomes were included. Studies that did not include any patient centred outcomes or resource utilisation outcomes were excluded (e.g., laboratory-based studies reporting specific biomarkers only).

### STUDY SELECTION PROCESS

All reviewers involved in the study selection process underwent training to ensure they understood the context of

**Footnote:** * Appendix 1 is available on DHM Journal's website: https://www.dhmjournal.com/index.php/journals?id=330

the review, the inclusion/exclusion criteria and how to use the Covidence software prior to study screening.

The title and abstract of each study were screened independently and in duplicate by two reviewers (BD, JA, JW). The primary reason for exclusion at this stage was study design (e.g., case study or case series with < 5 cases). The full text of studies found to meet the inclusion criteria were then retrieved. Again, two reviewers (JA, JG, JH, JW, RC) reviewed each study independently and in duplicate. Disputes at either stage were reviewed and resolved by the senior reviewer (JW).

## QUALITY ASSESSMENT

Examination and synthesis of data related to patients or treatment effects was not performed. To produce an exhaustive list of outcomes and to compare potential differences in reporting between different study designs, all relevant studies were included, regardless of methodology. Thus, no risk of bias or quality assessment of studies was performed, as we only sought to extract the relevant outcome measures that were reported in each study.

## DATA EXTRACTION

Online software from Research Electronic Data Capture (REDCap) was used to extract and securely store data.[9] Alongside the outcome measures reported by each study, we recorded each study's author, year of publication, country it was primarily conducted in, study design and number of NSTI patients included. We noted whether studies declared sources of funding or potential sources of bias, although this data is not presented here.

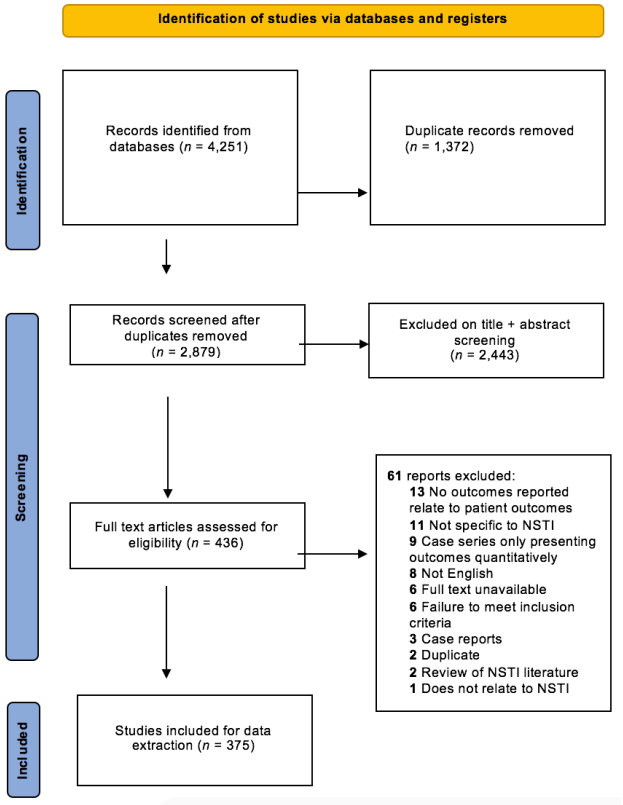
Data were extracted from each study independently and in duplicate by two reviewers (JG, JH, JW, NK, RC). Both primary and secondary outcomes were recorded.

## DATA ANALYSIS

Following extraction in duplicate, the two sets of data were exported into Microsoft® Excel. Any discrepancies were flagged and reviewed by the senior reviewer (JW).

Outcomes that were similar but spelt or worded differently were reviewed by the senior reviewer to ensure the meaning was the same and subsequently merged, for example; "*days in hospital*" and "*length of hospital stay (days)*". Many studies reported the same outcome measure but at different time points, such as; "*mortality at 7 days*", "*mortality at 3 months*", "*in-hospital mortality*". In these cases, they were included as separate outcomes, as it is the intent of this study to identify the individual outcomes and time points that were considered important to researchers of NSTI. Ultimately, an individual list of outcomes that were reported by each study was generated. This list was used to create a comprehensive outcome inventory.

**Figure 1**
Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram; outcome reporting of patients with NSTI




One group has developed a taxonomy for outcome measures to increase the efficiency of searching resources and databases by facilitating uniformity of outcome classification.[10] This taxonomy has been adopted by the Core Outcome Measures in Effectiveness Trials (COMET) initiative as well as the Cochrane Linked Data Project.[10] With this work in mind, the outcome measures identified in this systematic review were organised into eleven different outcome domains and then classified under five core areas based on their subject matter; mortality, physiological/clinical, resource use, life impact and adverse outcomes.

## Results

The online search retrieved 4,256 titles and they were exported to the reference management tool EndNote X8 where 1,069 duplicates were removed.[11] Remaining studies were input into the online systematic review software Covidence where a further 303 duplicates were identified and removed.[12] After abstracts had been screened, 436 studies were selected for full text review. Figure 1 outlines this process.

**Table 1**
Mortality/survival outcomes; ICU – intensive care unit; RCTs – randomised controlled trials

| Outcome | % of total studies | *n* patients | Reported in % of prospective studies | Reported in % of RCTs | Reported in % of studies 2010–2015 | Reported in % of studies 2016–2020 |
|---|---|---|---|---|---|---|
| Mortality without time specified | 79.5% (298/375) | 267,990 | 45.1% (23/51) | 20% (2/10) | 85.5% (171/200) | 72.6% (127/175) |
| In hospital mortality / 'survival to discharge' | 25.1% (94/375) | 11,3154 | 23.5% (12/51) | 20% (2/10) | 24.5% (49/200) | 25.7% (45/175) |
| Survival time | 6.7% (25/375) | 48,607 | 11.7% (6/51) | 0% (0/10) | 8.5% (17/200) | 4.6% (8/175) |
| 30-day mortality | 5.6% (21/375) | 10,184 | 21.6% (11/51) | 0% (0/10) | 4.5% (9/200) | 6.9% (12/175) |
| 28-day mortality | 5.3% (20/375) | 5,465 | 21.6% (11/51) | 40% (4/10) | 4.5% (9/200) | 6.3% (11/175) |
| 90-day mortality | 5.1% (19/375) | 1,900 | 29.4% (15/51) | 30% (3/10) | 3.0% (6/200) | 7.4% (13/175) |
| ICU mortality | 3.5% (13/375) | 1,273 | 3.9% (2/51) | 0% (0/10) | 3.0% (6/200) | 4.0% (7/175) |

Three hundred and seventy-five studies were included; references are provided in *Appendix 2. Of these, 86% (324/375) of studies were retrospective which included a total of 276,119 patients and 2.7% (10/375) were randomised controlled trials including 904 patients. In total, 7,062 patients were included in prospective studies.

A total of 311 distinct outcomes were reported 2,629 times by the included studies. Of these, 48% (150/311) of outcome measures were reported by two or more studies. Outcome measures were classified into 11 outcome domains and are presented under the five core areas consistent with the taxonomy developed elsewhere; mortality, physiological/clinical, life impact, resource use and adverse events.[10] These are detailed below. A full inventory of the outcomes reported, their relative frequency and their stratified domains can be found in *Appendix 3.

Tables 1–5 show the most reported outcomes in each domain. Each table outlines the total number of studies that reported an outcome and the number of patients in those studies. The total pool of studies is also further subdivided into study design, either prospective or randomised controlled trials (RCT) and by year of publication, either 2010–2015 or 2016–2020, to give an indication on how outcome reporting may be changing over time.

CORE AREA: MORTALITY/SURVIVAL (TABLE 1)

Mortality without time specified was the most frequently reported mortality related outcome, appearing in 79.5% (298/375) of studies. Sixty percent (6/10) of RCTs reported a mortality outcome, of which four specified a time point. *28-day mortality* was the most commonly reported time point, appearing in 40% (4/10) of RCTs. *Ninety-day mortality* was more frequently reported in the second five-year period of extraction (2016-2020), being reported in 13/175 (7.4%) of included manuscripts. *Survival time* was less frequently reported among studies in the second five-year period at 9.7% (17/175), compared to 8.5% (17/200) in the earlier period of this study. A further 16 mortality related outcomes can be found in *Appendix 3.

CORE AREA: PHYSIOLOGICAL/CLINICAL (TABLE 2)

*Amputation performed* was an outcome reported in 41.6% (156/375) of studies and 50% (5/10) of RCTs. The next most reported amputation related outcome, *level of amputation*, was reported in 7.5% (28/375) of studies but was not recorded in any RCTs. There were 13 other amputation related outcomes identified and can be found in *Appendix 3, but none were reported by more than three studies.

**Footnote:** * Appendices 2 and 3 are available on DHM Journal's website: https://www.dhmjournal.com/index.php/journals?id=330

**Table 2**

Physiological/clinical outcomes; NICCE – necrotizing infection clinical composite endpoint; RCTs – randomised controlled trials; SOFA – sequential organ failure assessment

| Outcome | % of total studies | *n* patients | Reported in % of prospective studies | Reported in % of RCTs | Reported in % of studies 2010–15 | Reported in % of studies 2016–20 |
|---|---|---|---|---|---|---|
| **Amputation outcomes** | | | | | | |
| Amputation performed | 41.6% (156/375) | 141,271 | 41.0% (25/51) | 50% (5/10) | 45% (90/200) | 37.7% (66/175) |
| Level of amputation | 7.5% (28/375) | 8,133 | 7.8% (4/51) | 0% (0/10) | 9.5% (19/200) | 5.1% (9/175) |
| **Debridement outcomes** | | | | | | |
| Number of debridements required | 40.3% (151/375) | 110,122 | 33.3% (17/51) | 40% (4/10) | 37% (74/200) | 45.1% (79/175) |
| Required debridement AND fasciotomy | 1.3% (5/375) | 362 | 0% (0/51) | 0% (0/10) | 1.5% (3/200) | 1.1% (2/175) |
| Extent of debridement ($cm^2$) | 1.1% (4/375) | 1,258 | 0% (0/51) | 0% (0/10) | 0.5% (1/200) | 1.7% (3/175) |
| **Closure/reconstruction outcomes** | | | | | | |
| Skin graft requirement | 23.5% (88/375) | 8,129 | 15.7% (8/51) | 10% (1/10) | 25% (50/200) | 21.7% (38/175) |
| Surgical flap requirement | 11.7% (44/375) | 2,628 | 2.0% (1/51) | 0% (0/10) | 11% (22/200) | 12.6% (22/175) |
| Surgical reconstruction requirement | 10% (38/375) | 4,012 | 5.9% (3/51) | 10% (1/10) | 10% (20/200) | 10.3% (18/175) |
| Primary wound closure | 5.9% (22/375) | 3,063 | 2.0% (1/51) | 0% (0/10) | 4% (8/200) | 8.0% (14/175) |
| Split thickness skin graft requirement | 4.3% (16/375) | 808 | 2.0% (1/51) | 10% (1/10) | 5.5% (11/200) | 2.9% (5/175) |
| Area healed by secondary intention | 2.7% (10/375) | 671 | 0% (0/51) | 0% (0/10) | 3.5% (7/200) | 1.7% (3/175) |

**Table 2 continued.**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Healing outcomes** | | | | | | |
| Wound healing time (cicatrisation time) | 2.7% (10/375) | 316 | 5.9% (3/51) | 10% (1/10) | 2.5% (5/200) | 2.9% (5/175) |
| Time to cure | 1.0% (3/375) | 315 | 0% (0/51) | 0% (0/10) | 1% (2/200) | 0.6% (1/175) |
| **Other surgical outcomes** | | | | | | |
| Number of operations required | 22.9% (86/375) | 7,1081 | 9.8% (5/51) | 0% (0/10) | 22.5% (45/200) | 23.4% (41/175) |
| Colostomy | 20.0% (75/375) | 17,348 | 11.8% (6/51) | 10% (1/10) | 18.5% (37/200) | 21.7% (38/175) |
| Orchidectomy | 12.3% (46/375) | 13,838 | 3.9% (2/51) | 10% (1/10) | 10.5% (21/200) | 14.3% (25/175) |
| Cystostomy | 9.1% (34/375) | 2,288 | 7.8% (4/51) | 10% (1/10) | 9.5% (19/200) | 8.6% (15/175) |
| Suprapubic tube placement | 5.6% (21/375) | 12,190 | 2.0% (1/51) | 0% (0/10) | 3.5% (7/200) | 8.0% (14/175) |
| Penectomy | 4.0% (15/375) | 12,501 | 2.0% (1/51) | 0% (0/10) | 3.5% (7/200) | 4.6% (8/175) |
| Faecal diversion | 3.2% (12/375) | 9,832 | 2.0% (1/51) | 0% (0/10) | 3.0% (6/200) | 3.4% (6/175) |
| **Composite outcomes** | | | | | | |
| SOFA score (Day 14) | 1.1% (4/375) | 821 | 5.9% (3/51) | 30% (3/10) | 1.5% (3/200) | 0.6% (1/175) |
| NICCE endpoint | 0.8% (3/375) | 778 | 3.9% (2/51) | 20% (2/10) | 0.5% (1/200) | 1.1% (2/175) |
| SOFA score (Day 28) | 0.5% (2/375) | 821 | 2.0% (1/51) | 10% (1/10) | 0.5% (1/200) | 0.6% (1/175) |
| m-SOFA (Day 14) | 0.5% (2/375) | 488 | 2.0% (1/51) | 10% (1/10) | 0.5% (1/200) | 0.6% (1/175) |

*Number of debridements* required was the most reported debridement related outcome, being reported in 40.3% (151/375) of total studies, including 33.3% (17/51) of prospective studies and 40% (4/10) of RCTs. No other debridement related outcomes were reported in more than five studies. A further 10 debridement related outcomes can be found in *Appendix 3.

*Skin graft requirement* was reported in 23.5% (88/375) of studies including 15.7% (8/51) of prospective studies. Surgical flap requirement (without regard to the specific type, e.g. rotational, free etc) was reported in 11.7% (44/375) of papers but only 2.0% (1/51) of prospective studies. There were 26 other closure/reconstruction outcomes *Appendix 3.

*Healing related outcomes.* A total of 18 healing related outcomes were identified and can be found in *Appendix 3. Only two, however, were reported by more than two studies. The most frequently recorded outcome was wound healing time (cicatrisation time) which could be found in 2.7% (10/375) of studies, including 316 patients.

*Other Surgical outcomes*. Number of procedures/surgeries required was recorded in 22.9% (86/375) of studies. Of those, 33.7% (29/86) also reported number of debridements required. There were 26 other surgical outcomes reported in *Appendix 3.

*Composite scores/endpoints.* Numerous studies recorded sequential organ failure assessment (SOFA) scores at different stages of admission (e.g., score at Day 1, Day 2, Day 7 etc). In an attempt to distinguish between patient characteristics and outcomes, the authors decided to include SOFA scores at time points longer than 14 days as outcomes. This juncture was chosen as the day-14 modified 'mSOFA' has been validated for NSTI patients as a part of the Necrotising Infection Clinical Composite Endpoint (NICCE).[13] A total of seven composite score outcomes are listed in *Appendix 3, five of which were included in RCTs. The SOFA score (Day 14) was reported by 30% (3/10) of RCTs.

CORE AREA: LIFE IMPACT (TABLE 3)

*Patient perspective related outcomes.* Outcomes relating to the patient's perspective were recorded infrequently, with only four outcomes being reported by more than one study. The Medical Outcomes Short Form-36 questionnaire result (SF36) was the most reported patient perspective related outcome and was found in 1.6% (6/375) of all studies and was measured in 20% (2/10) of RCTs. Twenty more outcomes can be found in *Appendix 3, all of which were only reported in one study each.

CORE AREA: RESOURCE USE (TABLE 4)

*Length of hospital stay* was reported in 69.3% (260/375) of studies, making it the second most commonly reported outcome overall after mortality without time specified. It was also reported in 47.1% (24/51) of prospective studies and 80% (8/10) of RCTs. Ventilation (days) was more frequently reported than ventilation (hours) appearing in 8.8% (33/375) of studies compared to 1.3% (5/375). There are 17 more resource use related outcomes listed in *Appendix 3.

*Discharge related outcomes.* The most frequently reported discharge related outcome, discharge home, was reported in 4.8% (18/375) of studies, representing 40,466 patients. Discharge to skilled nursing facility was reported in 2.4% (9/375) of studies representing 113,368 patients. Nine further discharge related outcomes can be found in *Appendix 3.

CORE AREA: ADVERSE EVENTS (TABLE 5)

A total of 102 adverse event/complication outcomes are listed and further classified into subcategories in *Appendix 3. Eighty-four of these were recorded in five or less studies.

## Discussion

The major strength of this review is its comprehensive nature. A systematic and predetermined approach was utilised, and by using broad search terms, the studies identified are likely a thorough representation of the NSTI literature. All stages of the review were conducted in duplicate to reduce recording bias. To the best of the authors' knowledge, this is the only study reporting systematically on outcome measures in contemporary NSTI literature. This review demonstrated variability in outcome reporting for NSTI. No single outcome was consistently found in every study and only four outcomes (mortality without time specified, length of hospital stay, amputation performed, number of debridements required) appeared in more than one third of studies. This heterogeneity of reporting limits evidence synthesis and the ability to compare data sets.[14] Varied and inconsistent use of outcomes measures leaves meta-analyses unable to include data from all relevant studies or forces them to make assumptions about unclear reporting.[7,15]

Studies representing less than five patients were excluded from this review, as were those that made no attempt to summarise or pool their results. Therefore, it is probable that certain novel or unique NSTI outcomes were missed in these smaller studies. This potential limitation was accepted given the broader intent of this study was to inform the development of a COS for future prospective trials. The frequently reported outcomes may also not be relevant to key stakeholders, as demonstrated by a profound lack of patient-centred outcome measures.

**Table 3**
Life impact outcomes; RCTs – randomised controlled trials

| Outcome | % of total studies | *n* patients | Reported in % of prospective studies | Reported in % of RCTs | Reported in % of studies 2010–15 | Reported in % of studies 2016–20 |
|---|---|---|---|---|---|---|
| Short Form-36 (SF36) | 1.6% (6/375) | 324 | 3.9% (2/51) | 20% (2/10) | 1% (2/200) | 2.3% (4/175) |
| Pain score (visual analogue scale) | 0.5% (2/375) | 92 | 2.0% (1/51) | 20% (1/10) | 0% (0/200) | 1.1% (2/175) |
| Derriford appearance scale | 0.5% (2/375) | 92 | 0% (0/51) | 0% (0/10) | 0.5% (1/200) | 0.6% (1/175) |
| Disability | 0.5% (2/375) | 597 | 0% (0/51) | 0% (0/10) | 0% (0/200) | 1.1% (2/175) |

**Table 4**
Resource use outcomes; ICU – intensive care unit; RCTs – randomised controlled trials

| Outcome | % of total studies | *n* patients | Reported in % of prospective studies | Reported in % of RCTs | Reported in % of studies 2010–5 | Reported in % of studies 2016–20 |
|---|---|---|---|---|---|---|
| **Resource outcomes** | | | | | | |
| Length of hospital stay | 69.3% (260/375) | 61,784 | 47.1% (24/51) | 80% (8/10) | 67.5% (135/200) | 71.4% (125/175) |
| Length of ICU stay (days) | 27.5% (103/375) | 60,749 | 23.5% (12/51) | 40% (4/10) | 26% (52/200) | 29.1% (51/175) |
| Ventilation (days) | 8.8% (33/375) | 4,127 | 13.7% (7/51) | 30% (3/10) | 9.5% (19/200) | 8.0% (14/175) |
| Cost per patient | 2.9% (11/375) | 49,987 | 0% (0/51) | 0% (0/10) | 3.5% (7/200) | 2.3% (4/175) |
| Ventilator-free days | 2.4% (9/375) | 11,730 | 7.8% (4/51) | 3% (3/10) | 2.5% (5/200) | 2.3% (4/175) |
| **Discharge outcomes** | | | | | | |
| Discharged home | 4.8% (18/375) | 40,466 | 5.9% (3/51) | 10% (1/10) | 4.5% (9/200) | 5.1% (9/175) |
| Discharged to skilled nursing facility | 2.4% (9/375) | 113,368 | 2.0% (1/51) | 0% (0/10) | 1.5% (3/200) | 3.4% (6/175) |
| Discharged to rehabilitation | 1.6% (6/375) | 1,576 | 2.0% (1/51) | 0% (0/10) | 2.5% (5/200) | 1.7% (3/175) |
| Discharged to other hospital | 1.6% (6/375) | 10,237 | 0% (0/51) | 0% (0/10) | 1% (2/200) | 2.3% (4/175) |
| Routine discharge | 1.6% (6/375) | 5,6151 | 2.0% (1/51) | 0% (0/10) | 2% (2/200) | 1.1% (2/175) |

**Table 5**
Adverse events outcomes; CVS – cardiovascular system; RCTs – randomised controlled trials

| Outcome | % of total studies | *n* patients | Reported in % of prospective studies | Reported in % of RCTs | Reported in % of studies 2010–15 | Reported in % of studies 2016–20 |
|---|---|---|---|---|---|---|
| Septic shock | 16.3% (61/375) | 60,019 | 15.7% (8/51) | 0% (0/10) | 13% (26/200) | 20% (35/175) |
| Sepsis | 12.3% (46/375) | 13,215 | 7.8% (4/51) | 0% (0/10) | 13.5% (27/200) | 10.9% (19/175) |
| Organ failure/ dysfunction | 11.2% (42/375) | 59,832 | 7.8% (4/51) | 20% (2/10) | 16% (32/200) | 5.7% (10/175) |
| Acute kidney injury | 8.8% (33/375) | 10,037 | 7.8% (4/51) | 0% (0/10) | 8.5% (17/200) | 9.1% (16/175) |
| Pneumonia | 6.1% (23/375) | 53,992 | 5.9% (3/51) | 10% (1/10) | 6.5% (13/200) | 5.7% (10/175) |
| CVS complications (not otherwise spec) | 5.6% (21/375) | 116,920 | 3.9% (2/51) | 0% (0/10) | 5.5% (11/200) | 5.7% (10/175) |
| Acute respiratory failure | 5.6% (21/375) | 63,160 | 2.0% (1/51) | 10% (1/10) | 6.5% (13/200) | 4.6% (8/175) |

One-hundred-and-two discreet adverse event outcomes were reported, many of them only appearing in a small number of studies. This is likely a representation of papers investigating NSTIs affecting specific anatomical regions (e.g., craniofacial NSTI) and reporting anatomically specific outcomes (e.g., proptosis) that would not be generalisable or relevant to all studies of NSTI.

When comparing outcome measures reported by studies published between 2010–2015 to those published between 2016–2020 a possible trend towards reporting more specific outcomes is noted. Vague outcome measures such as 'organ failure/dysfunction' and 'mortality without time specified' became less frequent, whilst more specific outcomes such as 28-day mortality, 30-day mortality, 90-day mortality appear more frequently. This is consistent with an increased emphasis on reporting transparency through preregistration of study protocols, which aims to decrease the risk of data being manipulated to support a hypothesis.[16] Also of note is that patient reported outcomes such as Medical Outcomes Short Form-36 (SF-36) and pain score (visual analogue scale) were reported more frequently in the latter period, however the total number of studies utilising these outcomes remains very low.

Although a trend towards more specific outcome reporting is promising, in the absence of a COS the ability to generalise data is still limited. As has been previously noted in the literature, the limited number of studies that have investigated HBOT and other adjuvant therapies for NSTI have not reported consistent outcome sets,[7,17–19] posing significant challenges in performing meta-analyses.[3] This is a particularly important issue in NSTI given the rarity of the condition as well as the paucity of high-quality prospective trials. Thus, there remains ongoing discourse regarding the role of HBOT and other measures in NSTI management. The inconsistency in reporting is evidenced in this review by mortality being reported in 23 different ways with varying time points or qualifiers.

Quality assessments of the included studies were not performed, as examination and synthesis of data was beyond the scope of this review. In developing a COS, it may be useful to further investigate the outcome measures utilised specifically in high quality studies. Potential weaknesses of this review include that the search was limited to English language results (although most studies identified and included were produced in countries where English is not the official language) and the exclusion of studies which reported solely laboratory-based outcome measures. Exclusion of qualitative outcomes that were neither pooled nor tabulated is another potential, although likely minor, limitation.

This study is the first in a series that aims to develop a COS for NSTI. It offers an inventory of outcomes reported in NSTI research which can now be proposed to an expert panel through a Delphi study, for determination of the most important outcomes to be included in future trials.

## Conclusion

This systematic review provides a comprehensive inventory of the outcome measures currently being utilised for NSTI research and demonstrates a marked heterogeneity in outcome reporting. This inventory is a critical first step in the development of a COS, a process which is now underway in a separate Delphi study.

## References


1 Stevens D, Bryant A. Necrotising soft-tissue infections. N Engl J Med. 2017;377:2253–65. doi: 10.1056/NEJMra1600673. PMID: 29211672.

2 Hedetoft M, Madsen M, Madsen L, Hyldegaard O. Incidence, comorbidity and mortality in patients with necrotising soft-tissue infections, 2005–2018: a Danish nationwide register-based cohort study. BMJ Open. 2020;10:e041302. doi: 10.1136/bmjopen-2020-041302. PMID: 33067303. PMCID: PMC7569942.

3 Hedetoft M, Bennett M, Hyldegaard O. Adjunctive hyperbaric oxygen treatment for necrotising soft-tissue infections: A systematic review and meta-analysis. Diving Hyperb Med. 2021;51:34–43. doi: 10.28920/dhm51.1.34-43. PMID: 33761539. PMCID: PMC8081587.

4 Williamson P, Altman D, Bagley H, Barnes K, Blazeby, J, Brookes S, et al. The COMET handbook: version 1.0. Trials. 2017;18:280. doi: 10.1186/s13063-017-1978-4. PMID: 28681707. PMCID: PM5499094.

5 Boers M, Kirwan J, Wells G, Beaton D, Gossec L, d'Agostino M, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. J Clin Epidemiol. 2014;67:745–53. doi: 10.1016/j.jclinepi.2013.11.013. PMID: 24582946.

6 COMET-Initiative. COMET Database. Liverpool, United Kingdom. [cited 2023 Apr 25]. Available from: https://www.comet-initiative.org/Studies.

7 Hua C, Bosc R, Sbidian E, De Prost N, Hughes C, Jabre P, et al. Interventions for necrotizing soft tissue infections in adults. Cochrane Database Syst Rev. 2018;5:CD011680. doi: 10.1002/14651858.CD011680.pub2. PMID: 29851032. PMCID: PMC6494525.

8 Page M, McKenzie J, Bossuyt P, Boutron I, Hoffman T, Mulrow C, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71. PMID: 33782057. PMCID: PMC8005924.

9 Harris P, Taylor R, Thielke R, Payne J, Gonzalez N, Conde J. Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–81. doi: 10.1016/j.jbi.2008.08.010. PMID: 18929686. PMCID: PMC2700030.

10 Dodd S, Clarke M, Becker L, Mavergames C, Fish R, Williamson PR. A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. J Clin Epidemiol. 2018;96:84–92. doi: 10.1016/j.jclinepi.2017.12.020. PMID: 29288712. PMCID: PMC5854263.

11 Clarivate Analytics. EndNote X8. Philadelphia, United States of America. [cited 2023 Apr 25]. Available from: https://endnote.com/downloads.

12 Vertias Health Innovation. Covidence systematic review software. Melbourne, Australia. [cited 2023 Apr 25]. Available from: https://www.covidence.org/.

13 Bulger E, May A, Dankner W, Maislin G, Robinson B, Shivran A. Validation of a clinical trial composite endpoint for patients with necrotizing soft tissue infections. J Trauma Acute Care Surg. 2017;83:622–7. doi: 10.1097/TA.0000000000001564. PMID: 28538644.

14 Williamson P, Altman D, Blazeby J, Clarke M, Gargon E. Driving up the quality and relevance of research through the use of agreed core outcomes. J Health Serv Res Policy. 2012;17:1–2. doi: 10.1258/jhsrp.2011.011131. PMID: 22294719.

15 Nawin F, Smeeing D, Houwert R, Leenen L, Hietbrink F. Time is of the essence when treating necrotizing soft tissue infections: a systematic review and meta-analysis. World J Emerg Surg. 2020;15:4. doi: 10.1186/s13017-019-0289-6. PMID: 31921330. PMCID: PMC6950871.

16 Mitra-Majumdar M, Kesselheim A. reporting bias in clinical trials: progress toward transparency and next steps. PLoS Med. 2022;19:e1003894. doi: 10.1371/journal.pmed.1003894. PMID: 35045078. PMCID: PMC8769309.

17 Devaney B, Frawley G, Frawley L, Pilcher DV. Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality. Anaesth Intensive Care. 2015;43:685–92. doi: 10.1177/0310057X1504300604. PMID: 26603791.

18 Soh CR, Pietrobon R, Freiberger JJ, Chew ST, Rajgor D, Gandhi M, et al. Hyperbaric oxygen therapy in necrotising soft tissue infections: a study of patients in the United States Nationwide Inpatient Sample. Intensive Care Med. 2012;38:1143–51. doi: 10.1007/s00134-012-2558-4. PMID: 22527074.

19 Creta M, Longo N, Arcaniolo D, Giannella R, Cai T, Cicalese A, et al. Hyperbaric oxygen therapy reduces mortality in patients with Fournier's Gangrene. Results from a multi-institutional observational study. Minerva Urol Nefrol. 2020;72:223–8. doi: 10.23736/S0393-2249.20.03696-6. PMID: 32083420.



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# World as it is

## Equipoise: an important ethical consideration when contemplating participation in a randomised controlled trial of hyperbaric oxygen treatment in necrotising soft tissue infections

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**Abstract**

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A proposal for a large, multi-centre, randomised controlled trial investigating the role of hyperbaric oxygen treatment (HBOT) in necrotising soft tissue infections (NSTI) has led to much discussion locally and internationally about whether participation is ethical for a centre where stakeholders already consider HBOT standard practice. This article systematically addresses the concept of clinical equipoise specific to the role of HBOT in NSTI, and presents a series of considerations to be taken into account by key stakeholders at potential participating sites.

### Introduction

Highly regarded and widely published Danish colleagues are in the advanced phases of planning a multinational randomised controlled trial (RCT) investigating the use of hyperbaric oxygen treatment (HBOT) for necrotising soft tissue infections (NSTI). The trial involves patients with NSTI being randomised to receive either standard care (surgical debridement, antibiotics, intensive care support) or standard care plus HBOT.

Some Australian hospitals have used HBOT as part of the treatment for NSTI for many years, based on early work in clostridial infections, clinical experience and several retrospective and prospective studies that indicate HBOT may provide a mortality benefit.[1–3]

There has not previously been an RCT addressing this. Challenges in planning an RCT are imposed by the rarity of NSTI (requiring a multicentre, international study to achieve adequate power), the practical issues and considerations for the management of severely ill patients, as well as uncertainty amongst stakeholders regarding the presence or absence of equipoise for the role of HBOT in the treatment of NSTI.

Equipoise is a state of genuine uncertainty regarding the role of a treatment modality or the superiority of one treatment over another. It is a fundamental requirement of ethical clinical research, seeking to first do no harm. Equipoise may exist in an individual clinician who is indifferent to the treatment modalities ('individual equipoise') or amongst the expert medical community where 'honest professional disagreement' exists regarding the role of a treatment, or regarding which treatment modality is best ('clinical equipoise').[4,5] A reliance on individual equipoise of all clinician investigators in a trial, presents potentially insurmountable obstacles to the commencement or completion of a controlled trial, and the impact of such a scenario on an RCT for HBOT in NSTI will be discussed below. In contrast, clinical equipoise considers the entire range of expert medical opinion as *a priori* equally valuable; essentially constituting a 'fair bet' procedure – and as such RCTs in areas of clinical equipoise are considered to not present a risk of harm to trial participants.[6]

In this article I will endeavour to systematically address the concept of clinical equipoise specific to the role of HBOT in NSTI.

**Commentary**

The critical question is 'is it ethical for centres which already utilise HBOT as an adjunct to standard treatment for NSTI, to be involved in a study where fifty percent of patients will be randomised to not receive HBOT? The answer involves another question (a few, actually):

IS HBOT STANDARD TREATMENT FOR NSTI?

My health service treats more cases of NSTI with HBOT per year than all other Australian and New Zealand centres combined, so this question requires particular consideration.[7] To adequately answer the question, we need to review whether the provision of HBOT for NSTI is considered standard practice at the individual clinician level, Health Service level, State level, national level, and also at an international level.

IS TREATMENT OF NSTI WITH HBOT CONSISTENTLY OFFERED BY ALL CLINICIANS AT YOUR HEALTH SERVICE?

Or does the provision of HBOT depend on specific clinicians being present, rostered on, and aware of an NSTI case in your centre (e.g., an anaesthetist who is also a hyperbaric physician being made aware of the case in theatre, hyperbaric doctors 'finding' cases, or a 'believer' specialty doctor making a referral to the Hyperbaric Service)?

In centres where there is variability between clinicians, patients with NSTI are essentially already receiving 'random' care (e.g., receiving HBOT or not, based on factors independent of any evidence). In this case, it is roster allocations or plain chance that determine the treatment pathway the patient is allocated to, without the advantages of an RCT to advance the level of evidence for (or against) this practice. Participating in an RCT simply changes the mode of allocation of treatment that is already occurring in many centres (amongst numerous other advantages).

IS THERE A CONSENSUS AMONGST CLINICIANS AT YOUR HEALTH SERVICE ABOUT THE ROLE OF HBOT FOR NSTI?

In Melbourne, we treat more cases of NSTI with HBOT than any other centre in Australia or New Zealand.[7] Despite this, there is still a lack of consensus about the role of HBOT for NSTI.

Indeed, we evaluated this specific question and published our findings in ANZ Journal of Surgery in 2021.[8] We surveyed experts at our centre on their beliefs about the role of HBOT in the treatment of NSTI. Whilst some clinicians felt strongly ($n$ = 4, 6% strongly disagreed that HBOT has a role in the treatment of NSTI and $n$ = 8, 12% strongly agreed), the most common response ($n$ = 31, 45%) was not being sure if HBOT has a role in the treatment of NSTI. We concluded that there is clinical equipoise at our centre regarding the role of HBOT in the treatment of NSTI, that an RCT should be considered ethical, and that further work towards increasing the level of evidence is highly necessary.

ARE PATIENTS WITH NSTI ROUTINELY OFFERED HBOT IN YOUR STATE?

In Victoria, Australia, they are not. Results from a (currently unpublished) project in which data from the Victorian admitted episodes dataset (VAED) and the Australia and New Zealand Intensive Care Society (ANZICS) adult patient database (APD) were linked by the Centre of Victorian Data Linkage (CVDL), indicate that less than one third of NSTI patients admitted to intensive care units in Victoria receive HBOT. That means that over two-thirds of Victorians who develop NSTI are not currently being referred for or receiving HBOT. Of interest, no statistically significant difference was found in APACHE III score or predicted risk of death in the groups who went on to receive, or not receive, HBOT.

WHAT ABOUT ON A REGIONAL LEVEL? IS HBOT FOR NSTI CONSIDERED STANDARD ACROSS AUSTRALIA AND NEW ZEALAND?

It is not. Table 1 contains the number of cases of NSTI who received HBOT as reported by each Hyperbaric facility around Australasia in the 2022–2023 financial year; if the Alfred's case numbers reflect less than one third of the Victorian NSTI case load, these statistics indicate that only a very small fraction of patients from around Australasia are currently receiving HBOT for NSTI. Assuming that disease incidence is similar across Australia and New Zealand, these data indicate a greater than ten-fold variation in the use of HBOT between regions.[9,10]

WHAT ABOUT ON AN INTERNATIONAL LEVEL? IS HBOT STANDARD PRACTICE FOR NSTI INTERNATIONALLY?

It is not. The use of HBOT for NSTI varies markedly between countries.

In July 2018 the NHS England published their *Clinical Commissioning Policy: Hyperbaric Oxygen Therapy for necrotising soft tissue infections (all ages).*[11] They concluded that there is not enough evidence to make the treatment available at this time, and funding was removed for the use of HBOT for NSTI from 1 April 2019. Likewise in the USA, only ~1% of NSTI cases are treated with HBOT.[12]

In contrast, more than one third of patients with NSTI in Denmark receive HBOT.[3]

**Table 1**

Cases of necrotising soft tissue infections treated with hyperbaric oxygen in Australia and New Zealand (NZ) (data are from 2022-23 financial year); ACT – Australian Capital Territory; NSW – New South Wales; NT – Northern Territory; pop – population; QLD – Queensland; SA – South Australia; TAS – Tasmania; VIC – Victoria; WA – Western Australia

| Institution | The Alfred Hospital (VIC) | Fiona Stanley Hospital (WA) | Royal Hobart Hospital (TAS) | Royal Adelaide Hospital (SA) | Prince of Wales Hospital (NSW, ACT) | Royal Brisbane & Women's Hospital (QLD) | Wesley Hospital (QLD) | Townsville University Hospital (QLD) | Royal Darwin Hospital (NT) | North Shore Hospital Auckland (NZ) | Christchurch Hospital (NZ) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cases treated[4] | 27 | 5 | 3 | 1 | 6 | 1 | 0 | 1 | 0 | 2 | 0 |
| Population[6,7] | 6,766,600 | 2,855,600 | 572,700 | 1,844,600 | 8,758,600 | 5,418,500 | | | 251,700 | 5,223,100 | |
| Cases treated per $10^6$ pop | 3.99 | 1.75 | 5.24 | 0.54 | 0.69 | 0.37 | | | 0.00 | 0.38 | |

## DO INTERNATIONAL SCIENTIFIC SOCIETIES UNIVERSALLY RECOMMEND HBOT FOR NSTI?

The recommendations from international societies vary; some *do not* recommend HBOT (e.g., The American Infectious Disease Society),[13] some *do* recommend HBOT (e.g., The European and American Societies for diving and hyperbaric medicine),[14,15] and some suggest consideration of HBOT if available and not interfering with standard treatment (e.g., World Society of Emergency Surgery and the Surgical Infection Society Europe).[16]

## WHAT DOES COCHRANE SAY?

The authors of a Cochrane review published in 2015 concluded: "*This systematic review failed to locate relevant clinical evidence to support or refute the effectiveness of HBOT in the management of necrotizing fasciitis. Good quality clinical trials are needed to define the role, if any, of HBOT in the treatment of individuals with necrotising fasciitis*".[17]

## SO DOES CLINICAL EQUIPOISE EXIST?

Irrefutably, at every level.

Nevertheless, one could argue that with all this uncertainty, maybe it will be simpler to just stay sitting on the fence? Definitely. This trial won't be quick, or easy. However, without a unified effort, the likelihood of completion of this RCT falls. The status quo will remain; ongoing uncertainty amongst experts, ongoing inequity for patients, and ongoing inconsistency in the delivery of care for people with NSTI at hospital, state, national and international levels.

It is critical that such an RCT is planned by experts. If a poorly planned or inadequately powered trial were to be conducted, the outcome would likely be negative and may result in reduced use of HBOT for NSTI at centres which currently utilise HBOT, regardless of the actual impact HBOT has on NSTI. Clinical opinion may also shift away from a state of equipoise, which would reduce the possibility of a future, well conducted trial.

## ARE THERE ANY OTHER ETHICAL CONSIDERATIONS WE SHOULD BE THINKING ABOUT?

I think it's important to think about the ethics of not participating in a large, well-designed, multi-national, randomised controlled trial.

Our centre could take the position that HBOT is standard practice that would be unethical to withhold from 14 of the 28 Victorian patients with NSTI we treat on average per year.

However approximately 60 other Victorians are admitted to intensive care units with NSTI each year and are not referred for HBOT, no doubt in part because the current level

of evidence isn't considered adequately robust. There are hundreds of people around Australia who develop NSTI each year who do not receive HBOT, and there will be countless other people, around the world, who will develop NSTI into the future. When deciding whether or not to participate in an RCT, we must consider the large number of people into the future who this choice will impact.

## Conclusion

A carefully designed, multi-centre, international randomised controlled trial investigating whether HBOT has a mortality benefit in patients with NSTI, has the potential for profound and lasting impact regardless of the outcome. A negative study may result in reduced workload of hyperbaric units around the world, millions of healthcare dollars saved and the substantial logistics involved with transferring patients with NSTI to hyperbaric services reduced. A positive study may impact the lives of thousands of NSTI sufferers into the future by resulting in increased use of HBOT and increased survival for these patients.

Without clearer answers, health services are unlikely to invest healthcare dollars into improving capacity for hyperbaric treatment of intensive care patients (which may already contribute to the low treatment numbers currently reported in many hyperbaric centres), and many NSTI patients will not be offered HBOT as a result.

If we do nothing, and maintain the status quo, only a small fraction of NSTI cases will receive HBOT at a state, national and international level. If there is a survival benefit from HBOT – which observational data suggest may be the case – remaining at status quo will do more harm than good. Perhaps the real question should be: is it ethical not to participate?

What's your position?

## References


1 Devaney B, Frawley G, Frawley L, Pilcher DV. Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality. Anaesth Intensive Care. 2015;43:685–92. doi: 10.1177/0310057X1504300604. PMID: 26603791.

2 Hedetoft M, Bennett MH, Hyldegaard O. Adjunctive hyperbaric oxygen treatment for necrotising soft-tissue infections: A systematic review and meta-analysis. Diving Hyperb Med. 2021;51:34–43. doi: 10.28920/dhm51.1.34-43. PMID: 33761539. PMCID: PMC8081587.

3 Hedetoft M, Madsen MB, Madsen LB, Hyldegaard O. Incidence, comorbidity and mortality in patients with necrotising soft-tissue infections 2005–2018: a Danish nationwide register-based cohort study. BMJ Open. 2020;10(10)e041302. doi: 10.1136/bmjopen-2020-041302. PMID: 33067303. PMCID: PMC7569942.

4 Nardini C. The ethics of clinical trials. Ecancermedicalscience. 2014;8:387. doi: 10.3332/ecancer.2014.387. PMID: 24482672. PMCID: PMC3894239.

5 Freedman B. Equipoise and the ethics of clinical research. N Engl J Med. 1987;317(3):141–5. doi: 10.1056/NEJM198707163170304. PMID: 3600702.

6 Edwards SJ, Lilford RJ, Braunholtz DA, Jackson JC, Hewison J, Thornton J. Ethical issues in the design and conduct of randomised controlled trials. Health Technol Assess. 1998;2(15):i–vi, 1–132. PMID: 10194615.

7 Hyperbaric Technicians and Nurses Association. Australian and New Zealand Hyperbaric Treatment Data, 1 July 2022 – 30 June 2023. HTNA 2023.

8 Devaney B, Pilcher D, Mitra B, Watterson J. Does equipoise exist amongst experts regarding the role of hyperbaric oxygen treatment for necrotising soft tissue infection? ANZ J Surg. 2021;91:485–7. doi: 10.1111/ans.16337. PMID: 33847053.

9 Australian Bureau of Statistics. *National, state and territory population. Reference period: March 2023*. [cited 2023 Oct 3]. Available from: https://www.abs.gov.au.

10 Statistics New Zealand. Tatauranga Aotearoa. *National population estimates: At 30 June 2023.* [cited 2023 Oct 3]. Available from: https://www.stats.govt.nz.

11 NHS England. *Clinical Commissioning Policy: Hyperbaric Oxygen Therapy for necrotising soft tissue infections (all ages).* July 2018. [cited 2023 Oct 3]. Available from: https://www.england.nhs.uk/wp-content/uploads/2018/07/hbot-for-necrotising-soft-tissue-infections-v2.pdf.

12 Soh CR, Pietrobon R, Freiberger JJ, Chew ST, Rajgor D, Gandhi M, et al. Hyperbaric oxygen therapy in necrotising soft tissue infections: a study of patients in the United States Nationwide Inpatient Sample. Intensive Care Med. 2012;38:1143–51. doi: 10.1007/s00134-012-2558-4. PMID: 22527074.

13 Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis. 2014;59:147–59. doi: 10.1093/cid/ciu296. PMID: 24947530.

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

15 Moon RE, editor. Undersea and Hyperbaric Medical Society. Hyperbaric oxygen therapy indications. 14th ed. North Palm Beach (FL): Best Publishing Company; 2019.

16 Sartelli M, Coccolini F, Kluger Y, Agastra E, Abu-Zidan FM, Abbas AES, et al. WSES/GAIS/WSIS/SIS-E/AAST global clinical pathways for patients with skin and soft tissue infections. World J Emerg Surg. 2022;17:1–23. doi: 10.1186/s13017-022-00406-2. PMID: 35033131. PMCID: PMC8761341.

17 Levett D, Bennett MH, Millar I. Adjunctive hyperbaric oxygen for necrotizing fasciitis. Cochrane Database Syst Rev. 2015;1(1):CD007937. doi: 10.1002/14651858.CD007937.pub2. PMID: 25879088. PMCID: PMC6516968.


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# Case reports

## Secondary deterioration in a patient with cerebral and coronary arterial gas embolism after brief symptom resolution: a case report

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**Keywords**
Air embolism; Case reports; Hyperbaric oxygen treatment

**Abstract**
(Tsushima R, Mori K, Imaki S. Secondary deterioration in a patient with cerebral and coronary arterial gas embolism after brief symptom resolution: a case report. Diving and Hyperbaric Medicine. 2024 31 March;54(1):61–64. doi: 10.28920/dhm54.1.61-64. PMID: 38507911.)
**Introduction:** Hyperbaric oxygen treatment (HBOT) is recommended for arterial gas embolism (AGE) with severe symptoms. However, once symptoms subside, there may be a dilemma to treat or not.
**Case presentation:** A 71-year-old man was noted to have a mass shadow in his left lung, and a transbronchial biopsy was performed with sedation. Flumazenil was intravenously administered at the end of the procedure. However, the patient remained comatose and developed bradycardia, hypotension, and ST-segment elevation in lead II. Although the ST changes spontaneously resolved, the patient had prolonged disorientation. Whole- body computed tomography revealed several black rounded lucencies in the left ventricle and brain, confirming AGE. The patient received oxygen and remained supine. His neurological symptoms gradually improved but worsened again, necessitating HBOT. HBOT was performed seven times, after which neurological symptoms resolved almost completely.
**Conclusions**: AGE can secondarily deteriorate after symptoms have subsided. We recommend that HBOT be performed promptly once severe symptoms appear, even if they resolve spontaneously.

### Introduction

Arterial gas embolism (AGE) is an arterial occlusion caused by bubbles that results in organ ischaemia. Most cases occur in compressed gas diving or medical procedures, including arterial catheterisation, cardiovascular surgery, positive pressure ventilation, and bronchoscopy. The incidence rate of AGE during bronchoscopy is 0.00096% for all bronchoscopic procedures.[1]

Hyperbaric oxygen treatment (HBOT) and normobaric oxygen (NBO)[2] are recommended as treatments. Among the types of AGE, HBOT is recommended for treating coronary and cerebral artery embolisms.[3] Most experts recommend HBOT even if initial symptoms are mild or improving because of the possibility of secondary deterioration. However, reports of secondary deterioration in humans are very limited.[4] Herein, we report a case of cerebral and coronary AGE with deterioration after brief symptom resolution.

### Case presentation

This patient was lost to follow-up, but consent for publication of his anonymised case details were obtained from an immediate family member.

A 71-year-old man with a history of chronic obstructive pulmonary disease and pulmonary fibrosis presented with a mass shadow in the S6 lower lobe of the left lung detected on a chest radiograph. The patient was referred to our respiratory medicine department for bronchoscopy.

Endobronchial ultrasound-guided sheath transbronchial biopsy was performed with mild sedation using intravenous midazolam (3 mg), and oxygen was administered via a nasal cannula at a rate of 2 L·min$^{-1}$. Flumazenil (0.5 mg) was intravenously administered 27 min after the beginning of the procedure; nevertheless, the patient remained comatose, with a Glasgow coma scale (GCS) score of 3 (E1 V1 M1). A few minutes later, the patient developed bradycardia,

hypotension, and ST-segment elevation in lead II, with a heart rate of 46 beats·min$^{-1}$ and blood pressure of 90/70 mmHg. Atropine (0.5 mg) was intravenously administered for symptomatic bradycardia. Subsequently, haemodynamics and consciousness improved slightly. The heart rate was 106 beats·min$^{-1}$, blood pressure was 142/98 mmHg, and the GCS score was 7 (E2 V1 M4). A 12-lead electrocardiogram (ECG) was obtained, which showed ST-segment elevation at II, III, and ST depression at I and aVL (Figure 1A). Therefore, myocardial infarction was diagnosed. However, the ST changes spontaneously resolved approximately 8 min later (Figure 1B). Although the ECG changes disappeared, the patient had prolonged disorientation with a GCS score of 9 (E4 V1 M4), complete left hemiplegia (manual muscle testing [MMT] scale score of 1), and total aphasia. Thus, we performed whole-body computed tomography (CT), which revealed several black rounded lucencies in the left ventricle and left cerebral hemispheres, confirming AGE (Figure 2A). While the patient received NBO and remained in the supine position the neurological symptoms gradually improved, evidenced by a GCS score of 14 (E4 V4 M6), improvement in left hemiparesis (MMT scale score of 3), and improvement in aphasia. A CT scan performed again after 90 min showed oedematous changes in the right cerebral hemisphere, although the gas had disappeared (Figure 2B). The patient was then admitted to the intensive care unit for conservative treatment. However, shortly after admission, the patient became restless and neurological symptoms deteriorated again (GCS score 11 [E4 V2 M5]) along with worsened left hemiparesis (MMT scale score: 2), and HBOT was deemed necessary. The patient was transferred to a medical institution equipped with a multiplace HBOT chamber.

The first round of HBOT was initiated seven hours and 15 minutes after the onset of symptoms and was performed according to the US Navy Treatment Table 6. During treatment, tonic-clonic convulsions were observed three times. At each instance, diazepam (5 mg) was intravenously administered, and the convulsions were successfully controlled. On a once daily basis, the second and third round of HBOT were performed according to the US Navy Treatment Table 5, and an additional four treatments were administered at 152 kPa (1.5 atmospheres absolute) for 90 minutes.

The neurological findings improved over time, with a GCS score of 14 (E4 V4 M6), MMT scale score of 4 in the left upper limb, and MMT scale score of 5 in the left lower limb at the end of the seventh round of HBOT. Brain magnetic resonance imaging fluid-attenuated inversion recovery showed an enlarged high-signal intensity area in the right cerebral hemisphere (Figure 3). Eight days later, the patient was referred to our hospital for rehabilitation.

Neurological findings improved almost completely, except for a mild decrease in writing ability and mild paralysis of the left finger.

**Figure 1**

(A) A 12-lead electrocardiogram showing ST-segment elevation at II, III, and ST depression at I and aVL; (B) spontaneous ST change improvement noted approximately 8 min later

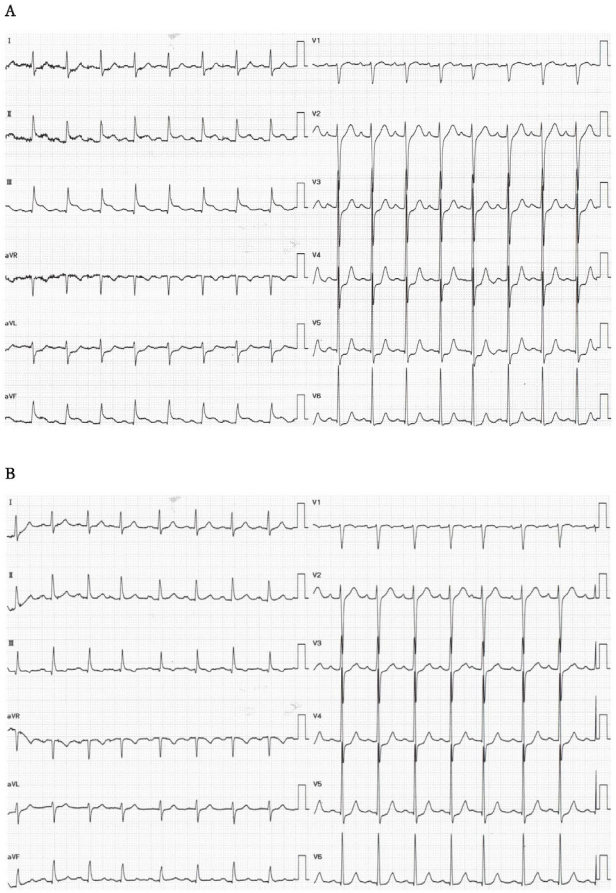



**Figure 2**

(A) Computed tomography (CT) scan showing rounded lucencies in the left ventricle and left cerebral hemisphere; (B) Repeat CT 90 min later showing bubble disappearance and new edematous changes in the right cerebral hemisphere

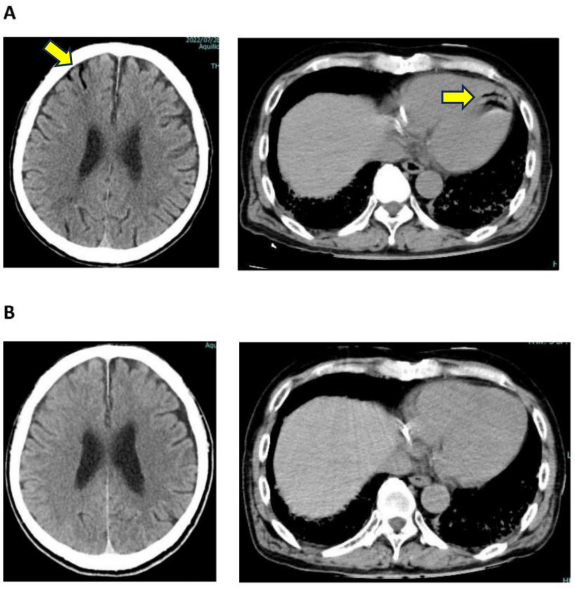
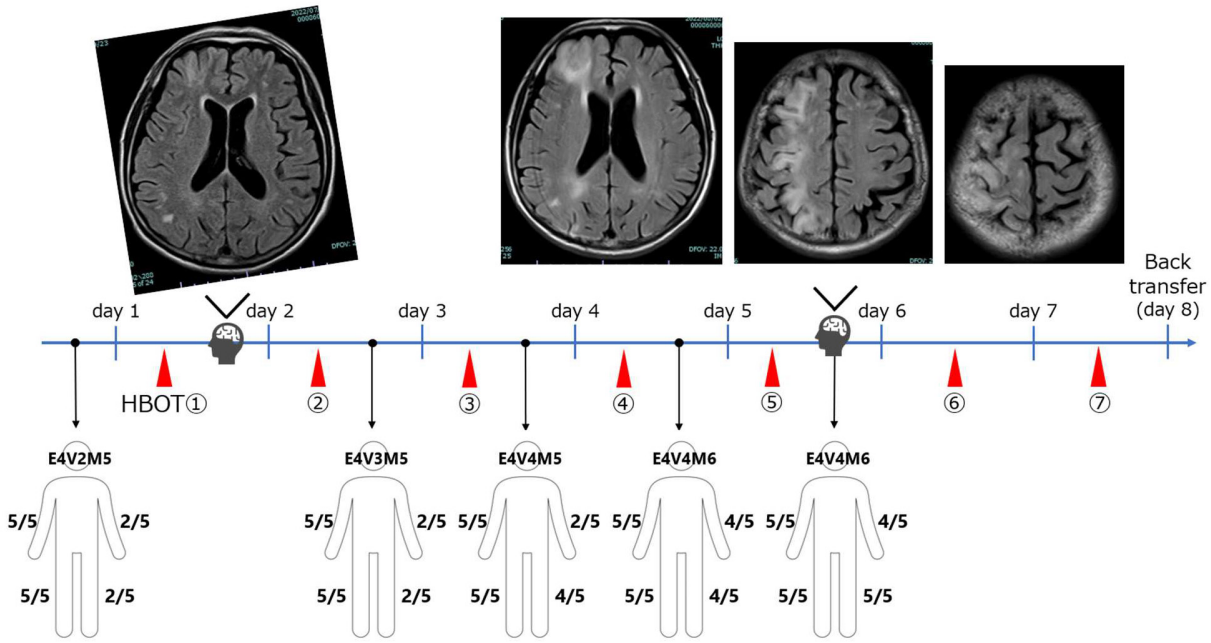


**Figure 3**
Magnetic resonance imaging signal-change transitions and changes in the manual muscle testing (MMT) score over the course of the patient's treatment with hyperbaric oxygen (HBOT)




The patient was discharged on day 30, with subsequent planned outpatient rehabilitation.

## Discussion

We encountered a case of cerebral and coronary AGE during bronchoscopy. After secondary deterioration, the patient was treated with HBOT, resulting in a good outcome. To the best of our knowledge, reports of secondary deterioration in AGE are limited.[4]

There are four possible mechanisms involved in secondary deterioration: first, there may be re-embolisation by gas trapped in one of the heart chambers or pulmonary veins that has not yet passed into the systemic circulation;[5] second, minute gas bubbles undetectable on CT may cause progression of organ ischaemia; third, inflammatory changes in the cerebral blood vessels incited by the passage of bubbles may cause a progressive reduction of cerebral blood flow;[6,7] and fourth, reperfusion may induce inflammation. In cases of AGE, it is recommended that the patient is kept in a supine position,[8] and NBO (as first aid) and HBOT are recommended. There are four potential mechanisms by which HBOT helps in AGE: first, it encourages bubble redistribution and reduces vascular occlusion by decreasing bubble volume;[9] second, it markedly increases the partial pressure of dissolved oxygen in plasma, increases oxygen delivery to ischaemic tissues, and inhibits cellular damage;[10] third, it counters vasodilation of the capillaries within hypoxic tissues, thereby minimising collection of extravascular fluids, reducing brain vasogenic oedema and potentially reducing intracranial pressure;[11] and fourth, it suppresses leukocyte β2 integrin function, inhibiting inflammatory cell adhesion to vascular endothelial cells after reperfusion, and suppresses consequent inflammatory damage in adjacent tissue.[12]

Early administration of HBOT, especially within 6–8 h, is associated with improved neurological prognosis. A systematic review and meta-analysis published in 2023 showed that increased time-to-HBOT is associated with decreased probability of favorable outcome in iatrogenic gas embolism.[13] Although adverse events such as lung injury, pneumothorax, and tympanic trauma have been reported, all are rare and manageable,[14] and HBOT should be performed promptly after the onset of serious symptoms. In this case, when the symptoms initially resolved the patient was treated with supine positioning and NBO, but later experienced secondary deterioration and was treated with HBOT. With the benefit of hindsight, HBOT should have been performed at the time the symptoms first appeared, with the possibility of secondary deterioration in mind.[15]

## Conclusions

This case is a contemporary reminder that AGE can secondarily deteriorate after apparent spontaneous recovery. We acknowledge that close observation without HBOT has been successfully employed after spontaneous recovery from AGE where compression was considered risky (because of concomitant pneumothoraces).[16] However, unless (as in that case) there are other complicating factors, we recommend that HBOT be provided promptly after diagnosis of AGE, irrespective of any spontaneous recovery.

## References


1 Maemura K, Kage H, Isago H, Takeshima H, Makita K, Amano Y, et al. Cerebral arterial air embolism after diagnostic flexible fiberoptic bronchoscopy: A case report and review of the literature. Case Rep Pulmonol. 2018;2018:7108215. doi: 10.1155/2018/7108215. PMID: 29854532.

2 Brull SJ, Prielipp RC. Vascular air embolism: A silent hazard to patient safety. J Crit Care. 2017;42:255–63. doi: 10.1016/j.jcrc.2017.08.010. PMID: 28802790.

3 Closon M, Vivier E, Breynaert C, Duperret S, Branche P, Coulon A, et al. Air embolism during an aircraft flight in a passenger with a pulmonary cyst: A favorable outcome with hyperbaric therapy. Anesthesiology. 2004;101:539–42. doi: 10.1097/00000542-200408000-00037. PMID: 15277939.

4 Leitch DR, Green RD. Pulmonary barotrauma in divers and the treatment of cerebral arterial gas embolism. Aviat Space Environ Med. 1986;57:931–8. PMID 3778391.

5 J Tingleff, F S Joyce, G Pettersson. Intraoperative echocardiographic study of air embolism during cardiac operations. Ann Thorac Surg. 1995;60:673–7. doi: 10.1016/0003-4975(95)00577-8. PMID: 7677498.

6 Helps SC, Parsons DW, Reilly PL, Gorman DF. The effect of gas emboli on rabbit cerebral blood flow. Stroke. 1990;21:94–9. doi: 10.1161/01.str.21.1.94. PMID: 2300997.

7 Helps SC, Gorman DF. Air embolism of the brain in rabbits pretreated with mechlorethamine. Stroke. 1991;22:351–4. doi: 10.1161/01.str.22.3.351. PMID: 2003304.

8 Banham NDG, Saw J, Hankey GJ, Ghia D. Cerebral arterial gas embolism proven by computed tomography following transthoracic echocardiography using bubble contrast. Diving Hyperb Med. 2020;50:300–2. doi: 10.28920/dhm50.3.300-302. PMID: 32957135. PMCID: PMC7819724.

9 Kindwall EP, Whelan HT, editors. Hyperbaric medicine practice. 2nd ed. Flagstaff (AZ): Best Publishing Company; 2002.

10 Sunami K, Takeda Y, Hashimoto M, Hirakawa M. Hyperbaric oxygen reduces infarct volume in rats by increasing oxygen supply to the ischemic periphery. Crit Care Med. 2000;28:2831–6. doi: 10.1097/00003246-200008000-00025. PMID: 10966258.

11 Lei Huang, Andre Obenaus. Hyperbaric oxygen therapy for traumatic brain injury. Med Gas Res. 2011;1:21. doi: 10.1186/2045-9912-1-21. PMID: 22146562. PMCID: PMC3231802.

12 Thom SR, Mendiguren I, Hardy K, Bolotin T, Fisher D, Nebolon M, et al. Inhibition of human neutrophil β2-integrin-dependent adherence by hyperbaric $O_2$. Am J Physiol. 1997;272:C770–7. doi: 10.1152/ajpcell.1997.272.3.C770. PMID: 9124510.

13 Fakkert RA, Karlas N, Schober P, Weber NC, Preckel B, van Hulst RA, Weenink RP. Early hyperbaric oxygen therapy is associated with favorable outcome in patients with iatrogenic cerebral arterial gas embolism: systematic review and individual patient data meta-analysis of observational studies. Crit Care. 2023;27(1):282. doi: 10.1186/s13054-023-04563-x. PMID: 37434172. PMCID: PMC10337083.

14 Hadanny A, Meir O, Bechor Y, Fishlev G, Bergan J, Efrati S. The safety of hyperbaric oxygen treatment – retrospective analysis in 2,334 patients. Undersea Hyperb Med. 2016;43:113–22. PMID: 27265988.

15 Mitchell SJ, Bennett MH, Moon RE. Decompression sickness and arterial gas embolism. N Engl J Med. 2022;386:1254–64. doi: 10.1056/NEJMra2116554. PMID: 35353963.

16 Banham N, da Silva E, Lippmann J. Cerebral arterial gas embolism (CAGE) during open water scuba certification training whilst practising a controlled emergency swimming ascent. Diving Hyperb Med. 2023;53:345–50. doi: 10.28920/dhm53.4.345-350. PMID: 38091595.



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# Hyperbaric oxygen for the treatment of carbon monoxide-induced delayed neurological sequelae: a case report and review of the literature

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**Keywords**
Hyperbaric medicine; Morbidity; Pain; Neurology; Psychology; Radiological imaging; Toxicity

**Abstract**
(Wong ZKR, Teo CKA, Kwek JWM, Kim SJ, See HG. Hyperbaric oxygen for the treatment of carbon monoxide-induced delayed neurological sequelae: a case report and review of the literature. Diving and Hyperbaric Medicine. 2024 31 March;54(1):65–68. doi: 10.28920/dhm54.1.65-68. PMID: 38507912.)
**Introduction:** Hyperbaric oxygen treatment (HBOT) remains a recognised treatment for acute carbon monoxide (CO) poisoning, but the utility of HBOT in treating CO-induced delayed neurological sequelae (DNS) is not yet established.
**Case description**: A 26-year old woman presented with reduced consciousness secondary to CO exposure from burning charcoal. She underwent a single session of HBOT with US Navy Treatment Table 5 within six hours of presentation, with full neurological recovery. Eight weeks later, she represented with progressive, debilitating neurological symptoms mimicking Parkinsonism. Magnetic resonance imaging of her brain demonstrated changes consistent with hypoxic ischaemic encephalopathy. The patient underwent 20 sessions of HBOT at 203 kPa (2 atmospheres absolute) for 115 minutes, and received intravenous methylprednisolone 1 g per day for three days. The patient's neurological symptoms completely resolved, and she returned to full-time professional work with no further recurrence.
**Discussion:** Delayed neurological sequelae is a well-described complication of CO poisoning. In this case, the patient's debilitating neurocognitive symptoms resolved following HBOT. Existing literature on treatment of CO-induced DNS with HBOT consists mainly of small-scale studies and case reports, many of which similarly suggest that HBOT is effective in treating this complication. However, a large, randomised trial is required to adequately determine the effectiveness of HBOT in the treatment of CO-induced DNS, and an optimal treatment protocol.

## Introduction

Carbon monoxide (CO) poisoning affects an estimated 50,000 people and causes more than 1,000 deaths annually in the US.[1] In Singapore, the incidence of CO poisoning is low.[2] Most cases are caused by faulty vehicles and house fires, with a small proportion due to workplace accidents.[3,4] Besides acute signs and symptoms, up to 46% of patients with CO poisoning may also manifest delayed neurological sequelae (DNS) weeks to months after acute poisoning, including changes in personality, cognitive disturbances, disordered motor movement and focal neurological deficits.[5,6]

Aside from potentially reducing mortality in patients with acute CO poisoning,[7] hyperbaric oxygen treatment (HBOT) has been associated with a reduced incidence of DNS.[8] HBOT has also been reported as a potential treatment modality for DNS.[9] We report a case of CO-induced DNS successfully treated with HBOT, and assess the utility of HBOT for the prevention and treatment of CO-induced DNS.

## Case report

A 26-year-old professional working woman with a background history of depression was brought to the emergency department after being found unconscious in an enclosed space next to a tank of burning charcoal. On arrival, she was haemodynamically stable but was drowsy and confused, with a Glasgow Coma Scale of 11 (Eye 3 Verbal 3 Motor 5) and a carboxyhaemoglobin level of 24%. Within six hours of discovery, she was treated with US Navy Treatment Table 5 (USN TT5) as per the HBOT protocol at our centre. Post-procedure, she regained her full mental faculty which allowed her to verbalise her left lower leg weakness and gluteal pain. Magnetic resonance imaging demonstrated bilateral gluteal myositis with left compressive sciatic neuropraxia, which was attributed to prolonged immobility in the supine position on the hard floor. This was complicated by severe rhabdomyolysis requiring medical management. On day seven of admission, she was transferred to a private healthcare institution for continuation of psychiatric care.

**Table 1**

Detailed neuropsychological assessment; neuropsychological assessment demonstrated significant impairment in multiple tested domains of general intelligence, executive function, attention and working memory, language, verbal memory, visuospatial, construction, and processing speed. RAVLT – Rey auditory verbal learning test; sec – seconds; WAIS – Wechsler adult intelligence scale

| Domain | Test | Score/Percentile | Range |
|---|---|---|---|
| General intelligence | Advanced progressive matrices | 2 out of 12 | – |
| Executive function | Trail making test – B | 215 sec (discontinued) | – |
| | Stroop: dots | < 1.00% | Extremely low |
| | Stroop: neutral words | 9.2% | Low average |
| | Stroop: colour words | 4.7% | Very low |
| | Stroop: colour words / dots | 50.0% | Average |
| Attention and working memory | Digit Span | 62.9% | Average |
| | Spatial Span | 2.3% | Very low |
| Language | Controlled oral word association test | 30% | Average |
| | Verbal fluency: Animals | 75% | High average |
| | Modified Boston naming test 30 items | 28 out of 30 | Average |
| Verbal memory (RAVLT) | Trial A1 | 69.1% | Average |
| | Trial A5 | 14.8% | Low average |
| | Learning trial A1-A5 | 72.2% | Average |
| | Immediate recall (A6) | 18.9% | Low average |
| | Delayed recall (A7) | 75.9% | High average |
| | Delayed recognition | 37.7% | Average |
| Visuospatial (WAIS) | WAIS-III block design test | 4.7% | Very low |
| Construction | Clock drawing test | 5% | Very low |
| Processing speed | Trail making test – A | < 10.0% | Low average |
| | Symbol search | 0.1% | Extremely low |

Eight weeks after her initial presentation, she presented again with progressive decline in her motor and cognitive function. On assessment, she exhibited new onset neurological disturbances with disorientation, inattention, and Parkinsons-like features including gait unsteadiness, hand tremors, bradykinesia, and apraxia. Coupled with her severe left chronic sciatic pain which evolved from her left sciatic neuropraxia, she was wheelchair-bound and unable to perform basic functional tasks and activities of daily living (ADLs). Her detailed neuropsychological assessment is presented in Table 1.

Magnetic resonance imaging (MRI) of her brain demonstrated diffuse white matter signal abnormalities within both cerebral hemispheres consistent with hypoxic ischaemic encephalopathy.

The attending neurologist started her on intravenous methylprednisolone 1 g per day for three days without improvement. Her psychiatric medications were also stopped, although those were not known to be associated with extrapyramidal side effects. Hyperbaric medicine input was sought after a week of failed inpatient management. With a working diagnosis of CO-induced DNS, and with no other cause identified and no alternative treatment options, the patient was offered a trial of HBOT at 203 kPa (2 atmospheres absolute) for 115 min, which is the treatment protocol routinely conducted for wound care in our centre. She underwent a total of 20 HBOT sessions, demonstrating progressive improvement in her symptoms. At completion, she had regained independence in her activities of daily living, full resolution of her neurocognitive deficits, marked improvement in her chronic sciatic pain, and was able to mobilise independently and return to full-time professional work with no further recurrence.

## Discussion

### RADIOLOGICAL FINDINGS IN CO POISONING AND DNS

Radiological abnormalities of the globus pallidus and deep white matter are known to be associated with acute CO poisoning and similarly have been reported in patients with

CO-induced DNS.[10,11] A prospective observational study reported the presence of acute brain lesions on diffusion-weighted imaging to be an independent predictor of DNS.[12]

While our patient declined further interval and follow-up neuroimaging given the clinical improvement and subsequent full resolution of her neurological symptoms, similar studies have documented interval reduction in radiological abnormalities on serial MRI scans, in tandem with clinical improvements following prolonged treatment with HBOT.[13,14] This suggests that MRI may present a quantitative method to monitor and assess treatment response in patients with CO-induced DNS.

## HBOT FOR PREVENTION OF DNS

The effects of HBOT on the prevention of DNS remain uncertain in the literature. Some studies showed a reduced risk,[5] while others conversely reported a higher risk of developing DNS with HBOT compared to normobaric oxygen therapy (NBOT).[15] A Cochrane review in 2011[16] presented a pooled analysis of six randomised controlled trials (RCTs) suggesting no statistically significant difference in DNS incidence between patients treated with HBOT versus NBOT. Notably, the only HBOT RCT meeting CONSORT criteria demonstrated a significant reduction in the incidence of DNS in CO poisoned patients treated with HBOT.[5] For our patient, due to more pressing medical management, she was only able to undergo one session of HBOT within a 24-hour period as compared to the three HBOT sessions as advocated by Weaver.[5] The patient's severe rhabdomyolysis was also suggestive of a prolonged duration of non-fatal CO exposure, which may have translated to increased cerebral insult. These two factors may have further contributed to her marked DNS manifestation despite full neurological recovery following HBOT in her initial presentation.

## HBOT FOR TREATMENT OF DNS

From a review of the literature, no large-scale studies have investigated therapeutic outcomes of DNS patients treated with HBOT. In the available reports, Parkinsons-like symptoms are frequently described as part of the DNS spectrum with resolution post-HBOT. One series of nine patients reported that HBOT decreased the severity of impairment in patients with DNS.[9] While this finding is similarly supported in our case report, as well as other small series,[14,17] a large, randomised trial is required to adequately determine the effectiveness of HBOT in the treatment of DNS, as well as to recommend an optimal treatment protocol.

## Conclusion

Delayed neurological sequelae is an established and potentially debilitating complication of CO poisoning. While HBOT remains a recommended treatment for acute CO poisoning, there are few reports of its efficacy in the treatment of CO-induced DNS.

This case report suggests that despite the lack of robust evidence for the use of HBOT in CO-induced DNS, it may still be very worthy of consideration, as our patient who was completely debilitated by her neurocognitive symptoms and severe chronic pain was able to regain full independence and function as an active member of her profession. Our experience in this case suggests that the possible benefits outweigh the relatively low risks of HBOT. However, more work needs to be done to quantify the effectiveness of HBOT in the treatment of CO-induced DNS, and define an optimal HBOT protocol.

## References


1 Rose JJ, Wang L, Xu Q, McTiernan CF, Shiva S, Tejero J, et al. Carbon monoxide poisoning: pathogenesis, management, and future directions of therapy. Am J Respir Crit Care Med. 2017;195:596–606. doi: 10.1164/rccm.201606-1275CI. PMID: 27753502. PMCID: PMC5363978.

2 Handa PK, Tai DYH. Carbon monoxide poisoning: a five year review at Tan Tock Seng Hospital, Singapore. Ann Acad Med Singap. 2005;34:611–4. PMID: 16382246.

3 Chua IS, Tan KB, Ponampalam R. Carbon monoxide poisoning in a group of restaurant workers: lessons learnt and how to prevent future occurrences. Singapore Med J. 2021 Nov 26 (Online ahead of print). doi: 10.11622/smedj.2021217. PMID: 34823325.

4 Cheow SH, Cheng CT. Carbon monoxide poisoning in Singapore. Singapore Med J. 1975;16(3):174–6. PMID: 1209280.

5 Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG, Clemmer TP, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med. 2002;347:1057–67. doi: 10.1056/NEJMoa013121. PMID: 12362006.

6 Choi IS. Delayed neurologic sequelae in carbon monoxide intoxication. Arch Neurol. 1983;40:433–5. doi: 10.1001/archneur.1983.04050070063016. PMID: 6860181.

7 Rose JJ, Nouraie M, Gauthier MC, Pizon AF, Saul MI, Donahoe MP, et al. Clinical outcomes and mortality impact of hyperbaric oxygen therapy in patients with carbon monoxide poisoning. Crit Care Med. 2018;46:e649–55. doi: 10.1097/CCM.0000000000003135. PMID: 29629990. PMCID: PMC6005724.

8 Thom SR, Taber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. Ann Emerg Med. 1995;25:474–80. doi: 10.1016/s0196-0644(95)70261-x. PMID: 7710151.

9 Chang DC, Lee JT, Lo CP, Fan YM, Huang KL, Kang BH, et al. Hyperbaric oxygen ameliorates delayed neuropsychiatric syndrome of carbon monoxide poisoning. Undersea Hyperb Med. 2010;37:23–33. PMID: 20369650.

10 Finelli PF, DiMario FJ. Hemorrhagic infarction in white matter following acute carbon monoxide poisoning. Neurology. 2004;63:1102–4. doi: 10.1212/01.wnl.0000138495.61717.86. PMID: 15452310.

11 Moon JM, Chun BJ, Baek BH, Hong YJ. Initial diffusion-weighted MRI and long-term neurologic outcomes in charcoal-burning carbon monoxide poisoning. Clin Toxicol (Phila).

2018;56:161–9. doi: 10.1080/15563650.2017.1352098. PMID: 28753048.
12 Sert ET, Kokulu K, Mutlu H. Clinical predictors of delayed neurological sequelae in charcoal-burning carbon monoxide poisoning. Am J Emerg Med. 2021;48:12–7. doi: 10.1016/j.ajem.2021.04.001. PMID: 33838469.
13 Martani L, Giovanniello A, Bosco G, Cantadori L, Calissi F, Furfaro D, et al. Delayed neurological sequelae successfully treated with adjuvant, prolonged hyperbaric oxygen therapy: review and case report. Int J Environ Res Public Health. 2022;19(9):5300. doi: 10.3390/ijerph19095300. PMID: 35564694. PMCID: PMC9104642.
14 Lo CP, Chen SY, Chou MC, Wang CY, Lee KW, Hsueh CJ, et al. Diffusion-tensor MR imaging for evaluation of the efficacy of hyperbaric oxygen therapy in patients with delayed neuropsychiatric syndrome caused by carbon monoxide inhalation. Eur J Neurol. 2007;14:777–82. doi: 10.1111/j.1468-1331.2007.01854.x. PMID: 17594334.
15 Yang CC, Chuang YF, Chen PE, Tao P, Tung TH, Chien CW. The occurrence of delayed neuropsychologic sequelae in acute carbon monoxide poisoning patients after treatment with hyperbaric or normobaric oxygen therapy. Medicine (Baltimore). 2021;100(2):e24183. doi: 10.1097/MD.0000000000024183. PMID: 33466193. PMCID: PMC7808522.
16 Buckley NA, Juurlink DN, Isbister G, Bennett MH, Lavonas EJ. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database Syst Rev. 2011;2011(4):CD002041. doi: 10.1002/14651858.CD002041.pub3. PMID: 21491385. PMCID: PMC7066484.
17 Myers RA, Snyder SK, Emhoff TA. Subacute sequelae of carbon monoxide poisoning. Ann Emerg Med. 1985;14:1163–7. doi: 10.1016/s0196-0644(85)81022-2. PMID: 4061987.

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# The first deep rebreather dive using hydrogen: case report

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**Keywords**
Helihydrox; High pressure neurological syndrome; HPNS; Hydreliox; Hydrox; Technical diving; Trimix

**Abstract**

(Harris RJ, Challen CJ, Mitchell SJ. The first deep rebreather dive using hydrogen: case report. Diving and Hyperbaric Medicine. 2024 31 March;54(1):69–72. doi: 10.28920/dhm54.1.69-72. PMID: 38507913.) Bounce diving with rapid descents to very deep depths may provoke the high-pressure neurological syndrome (HPNS). The strategy of including small fractions of nitrogen in the respired gas to produce an anti-HPNS narcotic effect increases the gas density which may exceed recommended guidelines. In 2020 the 'Wetmules' dive team explored the Pearse Resurgence cave (New Zealand) to 245 m breathing trimix (approximately 4% oxygen, 91% helium and 5% nitrogen). Despite the presence of nitrogen, one diver experienced HPNS tremors beyond 200 m. The use of hydrogen (a light yet slightly narcotic gas) has been suggested as a solution to this problem but there are concerns, including the potential for ignition and explosion of hydrogen-containing gases, and accelerated heat loss. In February 2023 a single dive to 230 m was conducted in the Pearse Resurgence to experience hydrogen as a breathing gas in a deep bounce dive. Using an electronic closed-circuit rebreather, helihydrox (approximately 3% oxygen, 59% helium and 38% hydrogen) was breathed between 200 and 230 m. This was associated with amelioration of HPNS symptoms in the vulnerable diver and no obvious adverse effects. The use of hydrogen is a potential means of progressing deeper with effective HPNS amelioration while maintaining respired gas density within advised guidelines.

## Introduction

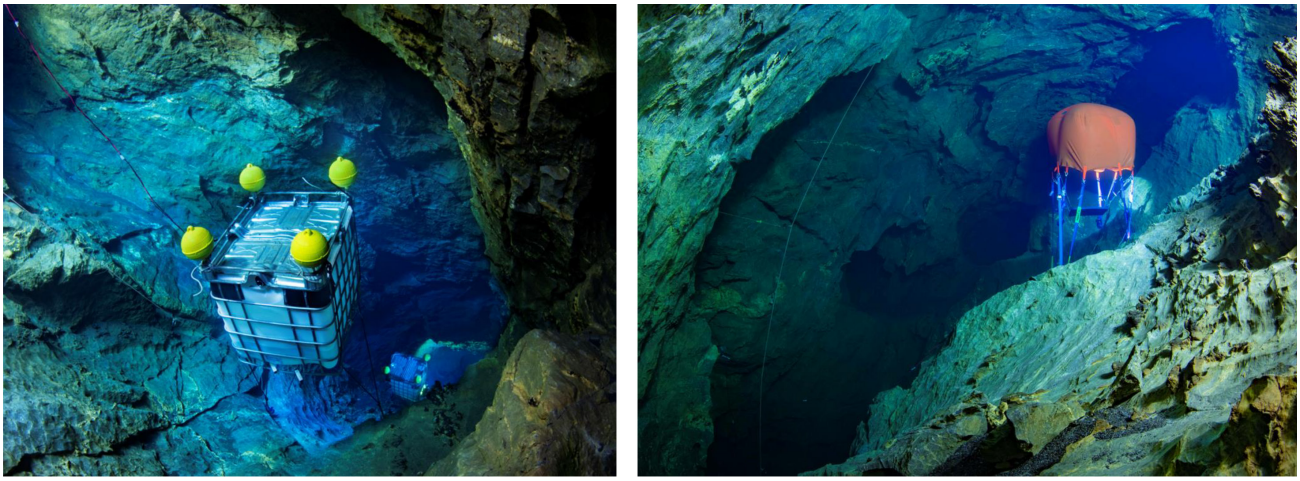
In 2020 the Australian 'Wetmules' technical diving team explored the Pearse Resurgence cave in New Zealand to a depth of 245 metres of fresh water (mfw). The dive was achieved using electronic closed-circuit rebreathers with the 'diluent gas' for the deep phase of the dive being trimix 4% oxygen, 91% helium and 5% nitrogen (Trimix 4/91); a composition very similar to what the divers would actually be breathing at the deepest point. The purpose of the small fraction of nitrogen was that its narcotic effect is known to help ameliorate symptoms of the high-pressure neurological syndrome (HPNS),[1] including troublesome tremors, that may arise during the fast ~35 minute descent to 245 mfw. One diver (author RJH) was more affected than the other (author CJC) consistent with previous observations of inter-subject variability,[2,3] with tremors appearing around 200m depth. Four dry habitats at 40, 27, 16, and 7 mfw (Figure 1) and active drysuit heating were utilised to facilitate the 16-hour dive in cold (6°C) water. At the deepest point reached, the cave continued descending meaning any further exploration would require visiting depths beyond 250 mfw.

The desire to descend beyond 250 mfw in future dives introduced two problems whose solutions are somewhat mutually exclusive.

First, the density of the mix utilised at 245 mfw was approximately 7.2 g·L$^{-1}$. The risk of carbon dioxide ($CO_2$) retention during rebreather diving appears to increase at respired gas densities greater than 6 g·L$^{-1}$,[4] albeit almost always when denser gas is breathed during diving-relevant levels of exercise (e.g., peaking at 125 Watts).[5] In turn, $CO_2$ retention may produce unpleasant / dangerous symptoms, although some divers do not appear to develop or notice early progressive symptoms and may be at risk of sudden cognitive impairment.[6] Moreover, whether symptomatic or not, $CO_2$ retention almost certainly increases a diver's risk of cerebral oxygen toxicity.[7] Progressing deeper using the same trimix diluent would result in potentially hazardous gas densities.

Second, HPNS symptoms (primarily tremors) experienced by RJH from 200 m on the previous 2020 dive would progressively increase with descent to 250 m and beyond.

**Figure 1**
The 40 and 27 mfw habitats (left) and the 16 mfw habitat (right); the 7 mfw habitat was identical to the 16 mfw habitat. The 40 mfw habitat was not used on the hydrogen dive



Any attempt to ameliorate this by increasing the fraction of nitrogen in the diluent mix would significantly worsen the gas density problem. Conversely, removing the small amount of nitrogen in the mix would improve gas density but may exacerbate the likelihood of experiencing HPNS.

The solution would be a gas that is both light and slightly narcotic, thus allowing elimination of nitrogen from the mix and thereby reducing gas density whilst reproducing nitrogen's anti-HPNS effect. It was largely for these reasons that commercial and military groups had previously undertaken experimentation with hydrogen for deep diving. During World War II the Swedish Navy conducted six hydrox (hydrogen and oxygen) dives as deep as 160 metres of seawater (msw).[8] The 'hydra' program conducted by the French company COMEX over three decades from 1968 had seen hydrogen used in dry and wet compressions (primarily in saturation diving conditions) as deep as a dry dive to 701 m equivalent.[8] These trials demonstrated that hydrogen could be safely breathed by humans with no obvious toxicity although its use accelerated heat loss. Hydrogen did exert a narcotic effect which helped ameliorate the HPNS, but it was too narcotic as an oxygen-hydrogen mix ('hydrox') beyond about 160 msw, necessitating blending hydrogen with helium and oxygen ('helihydrox' or 'hydreliox') to avoid excessive narcosis. An overarching concern throughout these trials was the potential for hydrogen to burn or explode if combined with oxygen in suitable stoichiometric blends. Previous work has shown that the minimum oxygen concentration for burning in hydrogen – helium mixtures is within the range 4.2 to 6 volume % with the tolerated fraction slightly increasing as ambient pressure increases.[9]

## Case report

With the goal of deep diving while controlling the anticipated problem with HPNS and keeping gas density within safe limits, the Wetmules undertook the first deep rebreather dive using hydrogen at the Pearse Resurgence in February 2023. Initial plans included the dual aims of using hydrogen and pushing beyond the 245 mfw mark set in 2020, but as the expedition evolved the goal was distilled down to evaluating hydrogen on a dive to 230 mfw which, based on past experience, was likely to provoke HPNS in RJH.

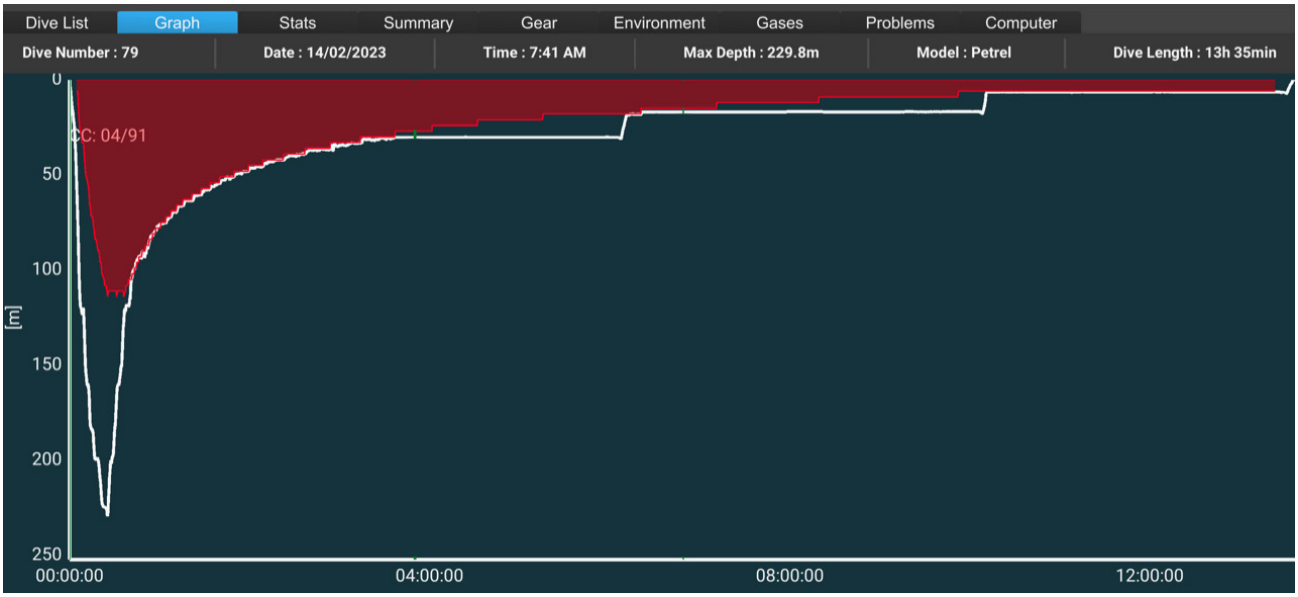
A G-size cylinder (50 L water capacity) of hydrogen was transported to the dive site with other expedition equipment. Hydrogen was decanted from this cylinder into a small 2 L carbon composite cylinder for use during the dive. The source hydrogen cylinder was only pressurised to 13.7 MPa thus necessitating careful use of a Haskell pneumatically driven booster pump to achieve adequate pressure (≥ 15 MPa) in the target cylinder.

The dive was undertaken by two divers (RJH and CJC) each using twin Megalodon™ rebreathers (Innerspace Systems, Centralia, USA) to provide gas supply redundancy without the need to carry large numbers of open circuit 'bailout' cylinders. These twin systems comprise two independent rebreathers joined by a common mouthpiece that allows easy switching between rebreathers. Only one diver (RJH), selected for his previous susceptibility to HPNS, used hydrogen and only in his primary rebreather.

The divers descended to 200 mfw over approximately 18 minutes using trimix 4:91 (4% oxygen, 91% helium, 5% nitrogen) as the diluent and (for RJH) with the $PO_2$ 'setpoint' at 70 kPa (0.7 atmospheres absolute [atm abs]) which, at 200 mfw resulted in 3.3% oxygen in the rebreather loop. At this point RJH introduced hydrogen by exhaling gas into the water (initially one small tidal volume), and replacing the volume from the hydrogen cylinder, now being the source of diluent gas. After establishing there were no obvious adverse effects, several more tidal volumes were exhaled into the water and replaced with hydrogen; a procedure based loosely on RJH's perception of what it would take to replace

**Figure 2**

The dive profile with depth (mfw) on the Y axis and time (hours) on the X axis; the red shaded area represents the decompression ceiling. Note the three long periods at constant depth which correspond to occupation of the habitats during segmented staged decompression




approximately 30% of the loop volume with hydrogen. The divers then continued the descent to the target depth of 230 mfw with hydrogen feeding into the loop via the automatic diluent addition valve on RJH's rebreather. Subsequent back calculation from the hydrogen cylinder pressure and the rebreather loop volume suggested RJH was breathing approximately 38% hydrogen at 230 mfw.

There were no apparent adverse effects and the most significant observation was that having experienced onset of HPNS tremors on this occasion at 180 mfw, RJH noticed they had disappeared at 230 mfw; a very atypical event for him. The gas felt easy to breathe, no change in temperature perception was noted, and there was no subjective sensation of narcosis. The accompanying diver (CJC), who based on past experience was less vulnerable to HPNS, had minor HPNS tremors using trimix 4:91 at the same depth.

At approximately 25 minutes run time the divers began ascending and at 27 minutes reached 200 mfw where the hydrogen cylinder was isolated. With the aim of eliminating most of the hydrogen from the loop, a large breath was exhaled and replaced with trimix 4:91 at 200 mfw and every 10 mfw thereafter up to 150 mfw where a complete loop flush was undertaken. The $PO_2$ setpoint was then increased to 130 kPa (1.3 atm abs) for the remainder of the decompression.

Other logistics included the use of three dry habitats at 27, 16 and 7 mfw during decompression (Figure 1). Thermal protection included O'Three crushed neoprene drysuits (O'Three, Portland, UK) and heated undergarments (Santi, Gdynia, Poland) with unlimited 12-volt power supplied from 40 mfw upward via a cable from the surface. Seacraft diver propulsion vehicles (Seacraft, Krosno, Poland) were used to minimise exertion at depth. The dives were controlled by Shearwater NERD 2 and Petrel 3 computers (Shearwater, Vancouver, Canada) programmed with 80/85 gradient factors. For decompression the use of hydrogen was effectively ignored because hydrogen could not be programmed into the computers, there was no previously researched basis for adjusting decompression from a bounce dive of this nature using hydrogen, and the exposure to hydrogen was very short; approximately 11 minutes below 200 mfw and another 8 minutes of progressive rebreather loop flushing between 200 and 150 mfw in the context of a 13.5 hour dive. The decompression was controlled based on the use of Trimix 4:91 in the deep phase.

After reaching the 27 mfw habitat, decompression differed from a typical dive in that the divers cleared decompression to the depth of the next habitat before leaving the one currently occupied (Figure 2). Harris has coined the termed 'segmented staged decompression' for this approach. Small Triton rebreathers (M3S, Toulon, France) were used inside the 27 mfw habitat which was air-filled, while the habitat atmosphere (nitrox 50 and 80 at 16 and 7 mfw respectively) was breathed in the shallower habitats which were equipped with carbon dioxide scrubbers. Multiple support dives were undertaken to facilitate habitat entry, egress, and transfers.

The divers emerged after a 13-hour 35-minute run time with no adverse effects other than mild pulmonary oxygen toxicity symptoms.

## Discussion

This dive represents the first use of hydrogen as a breathing gas in an ultra-deep rebreather bounce dive. With the

obvious and important caveat that the dive represents a single datapoint, there are some related observations that can be made.

First, there was no problem with ignition, fire or explosion in any of the processes where hydrogen was handled in relation to this dive. These included: a preliminary unmanned pool test conducted by RJH, where the rebreather's electronic oxygen addition solenoid valve was operated, and the counter lungs vigorously manipulated when the loop contained hydrogen and more than 4% oxygen; boosting hydrogen using a Haskell pump; and the dive itself where the loop oxygen fraction was kept ≤ 4% when hydrogen was present. There was (and remains) anxiety that despite the latter, there could be transient 'micro-regions' of much greater oxygen concentration where the solenoid injects oxygen to the loop.

Second, the use of hydrogen did appear to ameliorate HPNS symptoms in a susceptible diver more effectively than nitrogen. It is acknowledged that nitrogen was not completely eliminated from the loop by the hydrogen addition procedure, but the initially greater fraction of nitrogen did not prevent the onset of symptoms which subsided after hydrogen was introduced.

Third, there were no obvious adverse physiological effects such as thermal stress or decompression issues. There was also no narcotic effect noted at the $PH_2$ respired (approximately 922 kPa or 9.1 atmospheres absolute). This is perhaps not surprising because hydrogen has previously been breathed at an inspired pressure of 1,287 kPa or 12.7 atmospheres absolute during a 120 m hydrox hyperbaric chamber dive with only 'very slight' narcosis reported.[10] It is acknowledged that on our dive the duration of exposure to hydrogen breathing was relatively short. We cannot exclude the possibility that problems related to factors like decompression stress and heat loss might become more challenging with longer exposures.

## Conclusions

With the $n = 1$ caveat in mind, this dive suggests that the use of hydrogen is a potential means of progressing beyond 250 mfw with effective HPNS amelioration while maintaining respired gas density within advised guidelines. However, the potential hazards of hydrogen are not disproved. Progress should be cautious and incremental.

## References


1 Bennett PB, Rostain JC. The high pressure nervous syndrome. In Brubakk AO, Neuman TS, editors. Bennett and Elliot's physiology and medicine of diving. 5th ed. Edinburgh: Saunders; p. 323–57.

2 Kot J. Extremely deep recreational dives: the risk for carbon dioxide (CO(2)) retention and high pressure neurological syndrome (HPNS). Int Marit Health. 2012;63(1):49–55. PMID: 22669812.

3 Rostain JC, Lemaire C, Gardette-Chauffour MC, Doucet J, Naquet R. Estimation of human susceptibility to the high-pressure nervous syndrome. J Appl Physiol Respir Environ Exerc Physiol. 1983;54:1063–70. doi: 10.1152/jappl.1983.54.4.1063. PMID: 6853282.

4 Anthony G, Mitchell SJ. Respiratory physiology of rebreather diving. In: Pollock NW, Sellers SH, Godfrey JM, editors. Rebreathers and Scientific Diving. Proceedings of NPS/NOAA/DAN/AAUS June 16-19, 2015 Workshop. Durham (NC): 2016. [cited 2024 Feb 6]. Available from: https://www.omao.noaa.gov/sites/default/files/documents/Rebreathers%20and%20Scientific%20Diving%20Proceedings%202016.pdf.

5 Anthony G. Diving rebreathing apparatus testing and standards UK/EU perspective. In: Vann RD, Mitchell SJ, Denoble PJ, Anthony TG, editors. Technical Diving Conference Proceedings. Durham (NC): Divers Alert Network; 2009; p. 218–36. [cited 2024 Feb 6]. Available from: http://www.swiss-cave-diving.ch/PDF-dateien/2008TechDiverReport.pdf.

6 Warkander DE, Norfleet WT, Nagasawa GK, Lundgren CE. $CO_2$ retention with minimal symptoms but severe dysfunction during wet simulated dives to 6.8 atm abs. Undersea Biomed Res. 1990;17:515–23. PMID: 2288042.

7 Lambertsen CJ, Ewing JH, Kough RH, Gould R, Stroud MW 3rd. Oxygen toxicity; arterial and internal jugular blood gas composition in man during inhalation of air, 100% $O_2$ and 2% $CO_2$ in $O_2$ at 3.5 atmospheres ambient pressure. J Appl Physiol. 1955;8:255–63. doi: 10.1152/jappl.1955.8.3.255. PMID: 13271251.

8 Gardette B, Comet M, Gortan C, Imbert JP, Fructus X, Delauze HG. Life in a hyperbaric environment. A new $O_2$-$H_2$ breathing mixture for industrial diving. In: Proceedings of a colloquium on 'Space & Sea'. Marseille, France. p. 24–27 November 1987.

9 Brauer RW, editor. Hydrogen as a diving gas. Proceedings of the thirty-third Undersea and Hyperbaric Medical Society workshop. Wilmington (NC): UHMS Publication 69 (WS-HYD); 1987.

10 Edel P. Evaluation of the use of hydrogen-oxygen as a breathing gas in deep-sea diving. Harvey (LA): Sea-Space Research Company; 1986. [cited 2024 Feb 6]. Available from: https://apps.dtic.mil/sti/tr/pdf/ADA165797.pdf.



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# Letters to the Editor

## Time to shock people

Andrew Taber et al. provide valuable insight into the significant challenges of resuscitation in the confines of a diving bell.[1,2] We understand that their main objective is to compare effectiveness of manual CPR vs NUI compact chest compression device (NCCD) in prolonged resuscitation in a diving bell.[1] However, they miss a significant educational opportunity. In resuscitating a casualty from an out-of-hospital cardiac arrest (OHCA), there is no mention of the potential importance of early defibrillation. The authors advise readers that it may take 40 minutes to recover a diving bell. They advocate the use of the NUI compact chest compression device (NCCD), without warning of its limitations in this scenario, specifically that it may slow the progression to possible early defibrillation in the diving bell. Out-of-hospital cardiac arrest is arguably the most time critical, medical emergency. Cardiac arrest can generally be divided into shockable and non-shockable rhythms. The potential for survival from an OHCA non-shockable rhythm would be nigh on impossible to influence in a diving bell. Survival is much more likely from a shockable rhythm.[3] Good quality, uninterrupted, chest compression is critical, however defibrillation is arguably the vital step to achieving the return to viable circulation in a shockable rhythm arrest. Defibrillation within 3–5 minutes of collapse can produce survival rates of up to 50%, potential survival decreases very rapidly, every one minute of delay to defibrillation reduces survival by ten percent.[4]

A review of 17,238 cases of OHCA indicated that the probability of one month survival with favourable neurological outcome falls to 0.4% with a CPR duration of 30 minutes; and declines even further after this period.[5] Time constraints exist, for example, the diver's hot water suit needs removing, with safety harness left in place; of the thirteen saturation diving vessels that regularly operate in the UK sector of the North Sea, nine (70%) only have a bell 'bottom door' (no side door) meaning CPR must be interrupted, the casualty moved off the 'bottom door', to allow opening and to access the ships diving complex. Diving vessels that operate in the UK and Norwegian sector have defibrillators, either as customised static units, machine outside the chamber, paddles inside, or customised defibrillators in large pressure housings. Static defibrillators introduce further time constraints being located several interconnecting chambers away from the bell's point of connection, requiring the unconscious casualty to be transferred, whilst still being resuscitated. With slow compression, defibrillators tolerate the pressure changes seen in saturation diving bells. The need for safe defibrillation in a wet environment has long been recognised.[6] Medical device regulatory authorities have standards such as ISO 13485 which outlines specified requirements for medical devices including automated external defibrillator batteries. We contend that in an OHCA in a 'diving bell' without access to a defibrillator (within 10 but certainly 30 minutes) the chances of meaningful survival are the same 'with or without' NCCD. Resuscitation of an OHCA for greater than 30 minutes with repeated cessation to chest compression is questionably futile. If industry accepts divers are a population at risk, providing a defibrillator and safe protocols for its use in a diving bell are the key issue.

### References


1 Tabner A, Bryson P, Tilbury N, McGregor B, Wesson A, Hughes GD, et al. An evaluation of the NUI Compact Chest Compression Device (NCCD), a mechanical CPR device suitable for use in the saturation diving environment. Diving Hyperb Med. 2023;53:181–8. doi: 10.28920/dhm53.3.181-188. PMID: 37718291. PMCID: PMC10597600.

2 Johnson G, Bryson P, Tilbury N, McGregor B, Wesson A, Hughes GD, et al. Delivering manual cardiopulmonary resuscitation (CPR) in a diving bell: an analysis of head-to-chest and knee-to-chest compression techniques. Diving Hyperb Med. 2023;53:172–80. doi: 10.28920/dhm53.3.172-180. PMID: 37718290. PMCID: PMC10597601.

3 Rajan S, Folke F, Møller Hansen S, Malta Hansen C, Kragholm K, Gerds TA, et al. Incidence and survival outcome according to heart rhythm during resuscitation attempt in out-of-hospital cardiac arrest patients with presumed cardiac aetiology. Resuscitation. 2017;114:157–63. doi: 10.1016/j.resuscitation.2016.12.021. PMID: 28087286.

4 Holmberg M, Holmberg S, Herlitz J. Incidence, duration and survival of ventricular fibrillation in out-of-hospital cardiac arrest patients in Sweden. Resuscitation. 2000;44:7–17. doi: 10.1016/s0300-9572(99)00155-0. PMID: 10699695.

5 Goto Y, Funada A, Goto Y. Relationship between the duration of cardiopulmonary resuscitation and favourable neurological outcome after out-of-hospital cardiac arrest: A prospective nationwide population-based cohort study. J Am Heart Assoc. 2016; 5(3):e002819. doi: 10.1161/JAHA.115.002819. PMID: 26994129. PMCID: PMC4943259.

6 DAN Divers Alert Network. Are AEDs safe in wet environments. 1 August 2014. [cited 2023 Oct 1]. Available from: https://dan.org/alert-diver/article/are-aeds-safe-in-wet-environments/.


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Cardiac; CPR, Defibrillation; First aid; Resuscitation



## Response to Laden et al.

We are grateful to Laden et al. for their response[1] to our article,[2] which is part of a work package with the overall objective of developing an evidence-based approach to the management of cardiac arrest in a diving bell.[2,3] Currently taught techniques lacked any supporting data.

The first article[3] in this work package evaluates commonly taught approaches to manual chest compression delivery. The article referenced by Laden et al. presents the first efficacy evaluation of the only mechanical cardiopulmonary resuscitation (mCPR) device suitable for this environment.[2] Ongoing work addresses the overall approach to cardiac arrest management, including a discussion of the optimal order of events when resuscitating a casualty.

Laden et al. are concerned regarding the lack of discussion of defibrillation; defibrillation in a diving bell is neither the focus of this article nor currently possible. We therefore disagree with the suggestion that a "*significant educational opportunity*" has been missed.

It is irrefutable that defibrillation of shockable rhythms is a vital, well-evidenced component in the effective management of cardiac arrests, and increasing time to defibrillation is associated with progressively poor outcomes. Equally, a focus on defibrillation to the exclusion of effective chest compression delivery in this scenario is unlikely to be effective; every minute without CPR, even for casualties in a shockable rhythm, reduces survival by 7–10%.[4] Even when a defibrillator is available, chest compressions between shocks are essential; the potential lack of a flat surface on which to deliver chest compressions may render CPR without an mCPR device impossible in a diving bell. We have presented an evaluation of alternative approaches,[3] but suffice to say none are as effective as either conventional or mCPR, and head-to-chest CPR should no longer be taught or practiced.

Delays in the recognition and management of cardiac arrest in this setting are likely. Delays in the provision of effective CPR reduce the amplitude of ventricular fibrillation (VF);[5] good quality chest compressions are thought to increase the amplitude of VF and improve the likelihood of conversion to a perfusing rhythm[6] and it has been hypothesised that CPR prior to defibrillation may improve outcomes.

There are currently no defibrillators that can be deployed in a diving bell. Whilst a device may survive a slow compression process, there are no data suggesting that repeated pressurisation/depressurisation cycles, coupled with the corrosive effects of the environment, are tenable for existing devices. There are also logistical challenges to safe defibrillation in a wet, confined, metal environment. This is not to say that overcoming the technical and logistical challenges to safe provision of defibrillation in a diving bell should not be a target for future work; we endorse this goal wholeheartedly, and it would undoubtedly be the 'best next step' in improving the effectiveness of resuscitation in this challenging environment.

Laden et al. have questioned whether the provision of chest compressions without defibrillation would be futile. We agree that the outcome of a cardiac arrest in a saturation diver is unfortunately likely to be poor irrespective of their management. Cardiac arrest in the general population has a poor prognosis, and the saturation diving setting presents myriad additional challenges. Nevertheless, an evidence-based approach to management is vital, both to ensure the best possible chance of survival for the casualty in case of an immediately reversible pathology (e.g., hypoxia[7]) and to minimise the long-term psychological trauma (i.e., 'second victim syndrome') caused to fellow divers (and often friends) who are forced to act in the role of rescuer. The alternative, that they sit next to their deceased colleague throughout their ascent to the surface without providing aid of any sort, is unthinkable.

### References

1 Laden G, Mathew B, Ananthasayanam A. Time to shock people. Diving Hyperb Med. 2024;54:73–4. doi: 10.28920/dhm54.1.73-74. PMID: 38507914.
2 Tabner A, Bryson P, Tilbury N, McGregor B, Wesson A, Hughes GD, et al. An evaluation of the NUI Compact Chest Compression Device (NCCD), a mechanical CPR device suitable for use in the saturation diving environment. Diving Hyperb Med. 2023;53:181–8. doi: 10.28920/dhm53.3.181-188. PMID: 37718291. PMCID: PMC10597600.
3 Johnson G, Bryson P, Tilbury N, McGregor B, Wesson A, Hughes GD, et al. Delivering manual cardiopulmonary resuscitation (CPR) in a diving bell: an analysis of head-to-chest and knee-to-chest compression techniques. Diving Hyperb Med. 2023;53:172–80. doi: 10.28920/dhm53.3.172-180. PMID: 37718290. PMCID: PMC10597601.

4 Ibrahim WH. Recent advances and controversies in adult cardiopulmonary resuscitation. Postgrad Med J. 2007;83:649–54. doi: 10.1136/pgmj.2007.057133. PMID: 17916874. PMCID: PMC2600120.
5 Waalewijn RA, Nijpels MA, Tijssen JG, Koster RW. Prevention of deterioration of ventricular fibrillation by basic life support during out-of-hospital cardiac arrest. Resuscitation. 2002;54:31–6. doi: 10.1016/s0300-9572(02)00047-3. PMID: 12104106.
6 Resuscitation Council UK. Advanced life support algorithm. Resuscitation Council UK LMS. [cited 2023 Nov 26]. Available from: https://lms.resus.org.uk/modules/m25-v2-als-algorithm/11118/resources/chapter_6.pdf.
7 Jackson D. Diver cheated death in North Sea miracle. BBC Scotland. [cited 2023 Nov 26]. Available from: https://www.bbc.co.uk/news/uk-scotland-north-east-orkney-shetland-47826802.

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Resuscitation; Defibrillation; Mechanical CPR; Cardiovascular; Letters (to the Editor)

SPUMS
South Pacific Underwater Medicine Society

# Notices and news

SPUMS notices and news and all other society information can be found on:
https://spums.org.au/

## President's report

Neil Banham

It is now 2024 – I hope that all members and their family and friends had a safe and happy festive season and that you had some time off to recharge and re-enthuse, as I did. The 52nd SPUMS Annual Scientific Meeting (ASM) being held at the Pearl Resort, Pacific Harbour, Fiji from Sunday 12 – Friday 17 May 2024 is fast approaching.

Registrations numbers are good, with over 100 registered already.

**Conference theme:** *A plunge into recreational diving and diver health*

**Convenors:** David Smart and Neil Banham (Scientific Convenor)

The Pearl Resort offers direct access to Beqa Lagoon with its famous soft corals and shark feeding dives.

Our Keynote Speaker is Dr Peter Wilmshurst, a British cardiologist who some will remember from our highly successful 2014 Bali ASM, which culminated in the publication of the SPUMS and the United Kingdom Sports Diving Medical Committee (UKSDMC) Joint Position Statement (JPS) on persistent foramen ovale (PFO) and diving in 2015.[1] Peter is a world authority on PFO and diving as well as immersion pulmonary oedema (IPO), reporting the first case.

Workshops will be held with a view to update the JPS on PFO and diving and to develop one for return for diving (or not) following an episode of IPO, as well as diver information for both.

Supporting speakers include Dr John Lippmann (Snorkelling deaths / Shark attacks on divers in Australia) and Professor Simon Mitchell (Update on Decompression Illness), both very knowledgeable and engaging speakers.

Registration, the preliminary programme and further information can be found at: https://spums.au/index.php/asm-registration. Registrations close 12 April 2024.

A form for submitting an abstract is linked to the registration page. Only a few slots in the programme currently remain unfilled.

The venue for our 53rd ASM in 2025 has been decided. The options considered were Bali, Palau and the Philippines, with Bali being chosen as the preferred destination by a majority of SPUMS ExCom members. Those who wish to assist with convening our Bali ASM are welcome to contact me.

SPUMS has decided to withdraw its key guidance documents which related to COVID-19, with effect from 1 January 2024.

These documents were:

- SPUMS return to diving post COVID Flowchart
- Diver post COVID review Questionnaire
- Diving medical fitness post COVID Certification

The reasons for withdrawing the documents were as follows: High vaccination rates in Australian and New Zealand populations coupled with lower virulence of current SARS-CoV-2 variants has meant that the health threats from the disease are now reduced.

Mild COVID infections in vaccinated divers have not been demonstrated to affect fitness to dive. Divers have successfully returned to diving once asymptomatic.

Current expert medical opinion is that COVID-19 infections can be managed in the same way as for other seasonal virus infections.

Further information can be found at: South Pacific Underwater Medicine Society – COVID-19 updates (spums.au).

The ANZHMG Introductory Course in Diving and Hyperbaric Medicine will be next held 17–28 February 2025, again in Fremantle. The 2024 course was fully subscribed, and a great success. Many thanks to Ian Gawthrope the course coordinator and to all faculty who gave up precious time to contribute. Link here: https://spums.au/index.php/education/spums-approved-courses-for-doctors.

The recipient of the Unsworth-Bennett prize for the dux of the course was Simon Johnson from Townsville. Congratulations Simon!

Scholarships for trainees to attend this course are available thanks to the generosity of the Australasian Diving Safety Foundation (ADSF). Please contact John Lippmann at johnl@adsf.org.au for more information. ADSF has also kindly sponsored SPUMS membership for a year for Course participants.

*Dr Neil Banham*
*SPUMS President*

**Reference**

1 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 Hyperb Med. 2015;45:129–31. PMID: 26165538.

## HBOEvidence

HBO Evidence is seeking an interested person/group to continue the HBOEvidence site. The database of randomised controlled trials in diving and hyperbaric medicine: hboevidence_wikis.unsw.edu.au. The HBOEvidence site is planned to be integrated into the SPUMS website in the near future.

Those interested in participating in this project can contact Neil Banham president@spums.org.au

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## Royal Australian Navy Medical Officers' Underwater Medicine Course

**Date:** 2025 dates to be confirmed
**Venue:** HMAS Penguin, Sydney

**Cost:** TBC

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.

***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)2-9647-511*
***Email:*** *rajeev.karekar@defence.gov.au*

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## SPUMS Facebook page

Like us at:
SPUMS on Facebook

## The Australian and New Zealand Hyperbaric Medicine Group

**Introductory course in diving and hyperbaric medicine**

**Dates:** 2025 dates to be confirmed.
**Venue:** Hougoumont Hotel, Fremantle, Western Australia
**Cost:** TBC
Successful completion of this course will allow the doctor to perform Recreational and Occupational (as per AS/ NZS 2299.1) fitness for diving medicals and be listed for such on the SPUMS Diving Doctors list (provided that they continue to be a financial SPUMS member).

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
- Visit to RFDS base for flying and diving workshop
- Accepted indications for hyperbaric oxygen treatment
- Hyperbaric oxygen evidence based medicine
- Wound management and transcutaneous oximetry
- In water rescue and management of a seriously ill diver
- Visit to HMAS Stirling
- Practical workshops
- Marine Envenomation

***Contact for information:***

*Sam Swale, Course Administrator*
*Phone:+61-(0)8-6152-5222*
***Fax:****+61-(0)8-6152-4943*
***Email:*** *fsh.hyperbaric@health.wa.gov.au*
*Accommodation information can be provided on request.*

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The SPUMS South Pacific Underwater Medicine Society

website is at
https://spums.org.au/

Members are encouraged to login and check it out! Keep your personal details up-to-date.

The latest issues of *Diving and Hyperbaric Medicine* are via your society website login.

# SPUMS Diploma in Diving and Hyperbaric Medicine

## Requirements for candidates (May 2014)

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

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

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

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

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

**Additional information – prospective approval of projects is required**

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

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

It is expected that all research will be conducted in accordance with the joint NHMRC/AVCC statement and guidelines on research practice, available at: https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018, or the equivalent requirement of the country in which the research is conducted. All research involving humans, including case series, or animals must be accompanied by documentary evidence of approval by an appropriate research ethics committee. Human studies must comply with the Declaration of Helsinki (1975, revised 2013). Clinical trials commenced after 2011 must have been registered at a recognised trial registry site such as the Australia and New Zealand Clinical Trials Registry http://www.anzctr.org.au/ and details of the registration provided in the accompanying letter. Studies using animals must comply with National Health and Medical Research Council Guidelines or their equivalent in the country in which the work was conducted.

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

Projects will be deemed to have lapsed if:

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

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

The Academic Board reserves the right to modify any of these requirements from time to time. As of October 2020, the SPUMS Academic Board consists of:

Associate Professor David Cooper, Education Officer, Hobart
Professor Simon Mitchell, Auckland

***All enquiries and applications should be addressed to:***
*Associate Professor David Cooper*
*education@spums.org.au*

**Keywords**
Qualifications; Underwater medicine; Hyperbaric oxygen; Research; Medical society

SPUMS

South Pacific Underwater Medicine Society

# 52nd Annual Scientific Meeting

## REGISTRATIONS CLOSE 12 APRIL 2024

**Sunday May 12th to Friday May 17th 2024**

## The Pearl Resort, Pacific Harbour Fiji

## THEME:

***A plunge into recreational diving and diver health***

## KEYNOTE SPEAKER:

***Dr Peter Wilmshurst***

***UK Cardiologist and world authority on patent foramen ovale and diving and immersion pulmonary oedema***

## SUPPORTING SPEAKERS

**Dr John Lippmann and Professor Simon Mitchell**

**Register at:**

**https://spums.au/index.php/asm-registration**

Diveplanit Travel

Your personal dive travel agency

# Notices and news

EUBS notices and news and all other society information can be found on:
http://www.eubs.org/

**Annual Scientific Meeting 2024**


After the great success of its 47th edition in Porto, the EUBS Annual Scientific Meeting will move to Brest (France) for our 48th meeting which will take place from 16–20 September 2024.

At the heart of a beautiful harbour, Brest is a city oriented towards the ocean. As a military, commercial and yachting port with one of Europe's largest centres dedicated to the sea, the city has a centuries old maritime tradition. The region has managed to preserve its beauty and authenticity, and its coastline, dotted with magnificent beaches and lighthouses, is well worth a visit.

EUBS will be delighted to welcome you to join us for this meeting and contribute to its success.

If you have been monitoring the conference website https://eubs2024.sciencesconf.org/ you will have noticed that the 'Registration' and 'Abstract submissions' are now open.

**Important deadlines are**: 21 May 2024 – end of Early Bird Registration period; and 16 April 2024 Abstract submission deadline.

*We invite you to gear up, write your abstract, register – bring your partner and kids – and we'll see you soon.*

You will need to create a conference profile first, by registering on the conference website – note : this registration is separate from your EUBS membership.

If you would like to apply for a student Travel Grant for this meeting, please read the rules and procedure here: https://www.eubs.org/?page_id=914. There are several other grants and prizes to be awarded, see https://eubs2024.sciencesconf.org/resource/page/id/21.

**EUBS Executive Committee**

Every year, a new Executive Committee member needs to be elected – elections start well before our next General Assembly (during the EUBS Annual Scientific Meeting).

This year we will need a new Member-at-Large, who will be nominated for **a period of four years**.

Candidates will be presented by the Executive Committee by 15 June 2024, and the voting will be, as usual, by internet ballot, starting on 30 June. If you want to contribute and help our Society, please come forward and send your short CV to our secretary (secretary@eubs.org) before June 1st.

If you do not wish to present yourself, you can nominate someone else? Suggestions are welcome at the same email address above.

**EUBS Affiliate Society agreements**

For 2024, the agreement has been renewed with the following Scientific Societies in order to promote membership and contact among the hyperbaric and diving scientists and practitioners in Europe and worldwide. Members of these Societies benefit from a 10% reduction of EUBS membership fees, when providing proof of their membership of the 'other' society. Simply indicate the Affiliate Society from the drop-down list on the EUBS Membership Application or Renewal Form.

Belgian Society for Diving and Hyperbaric Medicine (https://www.sbmhs-bvoog.be)
Scott Haldane Foundation, The Netherlands (https://www.scotthaldane.org)
Italian Society for Diving and Hyperbaric Medicine (https://www.simsi.it/)
German Society for Diving and Underwater Medicine (https://www.gtuem.org/)
French Society for Diving and Hyperbaric Medicine (https://www.medsubhyp.fr/)
Swiss Society for Underwater and Hyperbaric Medicine (https://suhms.org/)
Undersea and Hyperbaric Medical Society (https://www.uhms.org/)

Spanish Society for Diving and Hyperbaric Medicine (https://www.asemhs.org/)
Austrian Society for Underwater and Hyperbaric Medicine (https://www.oeguhm.at/)
Dutch Society for Diving Medicine (https://duikgeneeskunde.nl/)

**New for 2024**

Finnish Society for Diving and Hyperbaric Medicine (https://sukelluslaakarit.yhdistysavain.fi/)

We are pleased to announce that in exchange, EUBS members benefit from a substantial reduction in their UHMS membership fee – simply mention your EUBS membership when enrolling/renewing your UHMS membership.

**EUBS website**

Please visit the EUBS Website for the latest news and updates. The 'EUBS History' section (under the Menu item 'The Society') is still missing some information missing in the list of EUBS Meetings, Presidents and Members-at-Large – please dig into your memories and help us complete this list!

By popular demand, EUBS members can also download the complete abstract book of previous EUBS meetings from the member's area.

While on the EUBS website, make sure you take a look at our Corporate Members' webpage (http://www.eubs.org/?page_id=91). On this page, logos and links are placed of those organisations, societies and companies that support EUBS financially. EUBS is grateful for their continuing support and would suggest that if you contact any of them, please do so by clicking on the link at that page, so they will know that you did so through the EUBS website.

**OXYNET Database**

Since 2004, a public online database of European Hyperbaric Chambers and Centers has been available, started and initially maintained by the OXYNET Working Group of the COST B14 project of the European Commission, later by the European Committee for Hyperbaric Medicine (ECHM). The original website http://www.oxynet.org/ will soon no longer be accessible, and the full OXYNET database of hyperbaric centers has been placed on the EUBS website (http://www.eubs.org/?page_id=1366).

If you have updated information or any other request or remark, please send an email to oxynet@eubs.org. If you can collect information for more than one centre in your area or country, please do.

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The EUBS website is at
**http://www.eubs.org/**
Members are encouraged to log in and keep their personal details up to date.

The latest issues of *Diving and Hyperbaric Medicine* are via your society website login.

# Courses and meetings

## Scott Haldane Foundation

As an institute dedicated to education in diving medicine, the Scott Haldane Foundation has organized more than 300 courses all over the world, over the past 32 years. SHF is targeting on an international audience with courses world wide.

Below the schedule of upcoming SHF-courses in the first half of 2024.

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

**2024**

| | |
|---|---|
| 5–6 April | Medical Examiner of Divers part 1 (level 1) Zeist, The Netherlands |
| 11–13 April | Medical Examiner of Divers part 2 (level 1) Amersfoort, The Netherlands |
| 13 April | Refresher course Diving Medical in Practice, Amersfoort, The Netherlands |
| 11–18 May | Medical Examiner of Divers part 2 (level 1) Bonaire, Dutch Caribbean |
| 31 May–1 June | In-depth course Brain under pressure (level 2d) Putten, The Netherlands |
| On request | Internship HBOt (level 2d) NL/Belgium |

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

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Historical Diving Society Australia - Pacific

P O Box 347, Dingley Village Victoria, 3172, Australia
**Email:** info@historicaldivingsociety.com.au
**Website:** https://www.historicaldivingsociety.com.au/

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# BIS_on_DHM_2024

The third edition of the Baltic International Symposium on Diving and Hyperbaric Medicine (BIS_on_DHM) is taking place in Gdynia, Poland, from 6–8 June 2024.

This conference aims to exchange knowledge between scientists and clinical practitioners on diving and hyperbaric medicine. Lectures in this symposium will be by invitation only, and speakers are cherry-picked to verify that they bring the latest scientific and medical perspectives to the forum. There will also be vivid sessions on emergency scenarios to discuss the real cases in diving and hyperbaric practice.

**Visit the Symposium website at:**
http://www.BISDHM.events

Register now for an early registration discount.

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

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

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## The Science of Diving

Support EUBS by buying the PHYPODE book '*The science of diving*'. Written for anyone with an interest in the latest research in diving physiology and pathology. The royalties from this book are being donated to the EUBS.

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

# Diving and Hyperbaric Medicine: Instructions for Authors

(updated February 2023)

*Diving and Hyperbaric Medicine* (DHM) is the combined journal of the South Pacific Underwater Medicine Society (SPUMS) and the European Underwater and Baromedical Society (EUBS). It seeks to publish papers of high quality on all aspects of diving and hyperbaric medicine of interest to diving medical professionals, physicians of all specialties, scientists, members of the diving and hyperbaric industries, and divers. Manuscripts must be offered exclusively to *Diving and Hyperbaric Medicine* unless clearly authenticated copyright exemption accompanies the manuscript. All manuscripts will be subject to peer review. Accepted contributions will also be subject to editing.

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Contributions should be submitted electronically by following the link:
http://www.manuscriptmanager.net/dhm

There is on-screen help on the platform to assist authors as they assemble their submission. In order to submit, the corresponding author needs to create an 'account' with a username and password (keep a record of these for subsequent use). The process of uploading the files related to the submission is simple and well described in the on-screen help provided the instructions are followed carefully. The submitting author must remain the same throughout the peer review process.

## Types of articles

DHM welcomes contributions of the following types:

**Original articles, Technical reports and Case series**: up to 3,000 words is preferred, and no more than 30 references (excluded from word count). Longer articles will be considered. These articles should be subdivided into the following sections: an **Abstract** (subdivided into Introduction, Methods, Results and Conclusions) of no more than 250 words (excluded from word count), **Introduction, Methods, Results, Discussion, Conclusions, References, Acknowledgements**, **Funding** sources and any **Conflicts of interest**. **Legends/captions** for illustrations, figures and tables should be placed at the end of the text file.

**Review articles**: up to 5,000 words is preferred and a maximum of 50 references (excluded from the word count); include an informative **Abstract** of no more than 300 words (excluded from the total word count); structure of the article and abstract is at the author(s)' discretion.

**Case reports, Short communications** and **Work in progress** reports: maximum 1,500 words, and 20 references (excluded from the word count); include an informative **Abstract** (structure at author's discretion) of no more than 200 words (excluded from the word count).

**Educational articles, Commentaries** and **Consensus reports** for occasional sections may vary in format and length but should generally be a maximum of 2,000 words and 15 references (excluded from word count); include an informative **Abstract** of no more than 200 words (excluded from word count).

**Letters to the Editor**: maximum 600 words, plus one figure or table and five references.

The journal occasionally runs **'World as it is'** articles; a category into which articles of general interest, perhaps to divers rather than (or in addition to) physicians or scientists, may fall. This is particularly so if the article reports an investigation that is semi-scientific; that is, based on methodology that would not necessarily justify publication as an original study. Such articles should follow the length and reference count recommendations for an original article. The structure of such articles is flexible. The submission of an abstract is encouraged.

## Formatting of manuscripts

All submissions must comply with the following requirements. **Manuscripts not complying with these instructions will be suspended** and returned to the author for correction before consideration. Guidance on structure for the different types of articles is given above.

**Documents on DHM website** https://www.dhmjournal.com/index.php/author-instructions

The following pdf files are available on the DHM website to assist authors in preparing their submission:

Instructions for Authors 2023 (this document)
DHM Keywords 2021
DHM Mandatory Submission Form 2020
Trial design analysis and presentation
English as a second language
Guideline to authorship in DHM 2015
Helsinki Declaration revised 2013
Is ethics approval needed?

# DIVER EMERGENCY SERVICES PHONE NUMBERS

**AUSTRALIA – DAN**
**1800-088200 (in Australia toll free)**
**+61-8-8212-9242 User pays**
**(outside Australia)**

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

**ASIA, PACIFIC ISLANDS – DAN World**
**+618-8212-9242**

**EUROPE – DAN**
**+39-06-4211-8685 (24-hour hotline)**

**SOUTHERN AFRICA – DAN**
**+27-10-209-8112 (International call collect)**

**USA – DAN**
**+1-919-684-9111**

**JAPAN – DAN**
**+81-3-3812-4999 (Japan)**

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ADSF
AUSTRALASIAN DIVING SAFETY FOUNDATION

## Scholarships for Diving Medical Training for Doctors

The Australasian Diving Safety Foundation is proud to offer a series of annual Diving Medical Training scholarships. We are offering these scholarships to qualified medical doctors to increase their knowledge of diving medicine by participating in an approved diving medicine training programme. These scholarships are mainly available to doctors who reside in Australia. However, exceptions may be considered for regional overseas residents, especially in places frequented by Australian divers. The awarding of such a scholarship will be at the sole discretion of the ADSF. It will be based on a variety of criteria such as the location of the applicant, their working environment, financial need and the perception of where and how the training would likely be utilised to reduce diving morbidity and mortality. Each scholarship is to the value of AUD5,000.00.

There are two categories of scholarships:

1. ADSF scholarships for any approved diving medical training program such as the annual ANZHMG course at Fiona Stanley Hospital in Perth, Western Australia.
2. The Carl Edmonds Memorial Diving Medicine Scholarship specifically for training at the Royal Australian Navy Medical Officers' Underwater Medicine Course, HMAS Penguin, Sydney, Australia.

Interested persons should first enrol in the chosen course, then complete the relevant ADSF Scholarship application form available at: https://www.adsf.org.au/r/diving-medical-training-scholarships and send it by email to John Lippmann at johnl@adsf.org.au.

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