REVIEW ARTICLE

Acclimatization to diving: a systematic review

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ABSTRACT

Multiday hyperbaric exposure has been shown to reduce the incidence of decompression sickness (DCS) of compressed-air workers. This effect, termed acclimatization, has been addressed in a number of studies, but no comprehensive review has been published. This systematic review reports the findings of a literature search. PubMed, Ovid Embase, The Cochrane Library and Rubicon Research Repository were searched for studies reporting DCS incidence, venous gas embolism (VGE) or subjective health reports after multiday hyperbaric exposure in man and experimental animals. Twenty-nine studies fulfilled inclusion criteria. Three epidemiological studies reported statistically significant acclimatization to DCS in compressed-air workers after multiday hyperbaric exposure. One experimental study observed less itching after standardized simulated dives. Two human experimental studies reported lower DCS incidence after multiday immersed diving.

Acclimatization to DCS has been observed in six animal species. Multiday diving had less consistent effect on VGE after hyperbaric exposure in man. Four studies observed acclimatization while no statistically significant acclimatization was reported in the remaining eight studies. A questionnaire study did not report any change in self-perceived health after multiday diving. This systematic review has not identified any study suggesting a sensitizing effect of multiday diving, and there is a lack of data supporting benefit of a day off diving after a certain number of consecutive diving days.

The results suggest that multiday hyperbaric exposure probably will have an acclimatizing effect and protects from DCS. The mechanisms causing acclimatization, extent of protection and optimal procedure for acclimatization has been insufficiently investigated. ∎

INTRODUCTION

Norwegian regulations for surface-oriented diving [1, 2] stipulate a day off diving after three consecutive days of diving (multiday break). The background for this requirement is dated back to the 1970s when a disturbing high incidence of decompression sickness (DCS) was experienced in offshore diving [3].

U.S. Navy (USN) decompression tables were used at this time, and dive supervisors commonly modified the tables to improve safety. Norwegian national decompression tables were initially issued 1980 [3] based on modified Royal Navy and USN procedures. Some further modifications were motivated by recommendations from North Sea diving supervisors at that time. Of particular interest for the present study was the statement in the NUI report [3] claiming that diving every day in a week frequently resulted in bends by the end of the week. This perception motivated a recommendation for the multiday break. The multiday break has later been formalized as a requirement in the Norwegian Diving- and Treatment Tables (NDTT) [1] and the Norwegian Petroleum related standard for inshore occupational diving [2], though there are minor phrasing disparities between the two documents.

Diving for many consecutive days (multiday diving) could be expected to increase DCS risk (sensitization) – e.g., due to accumulation of inert gas, decrease risk (acclimatization) due to physiological conditioning or alternatively have no significant effect of DCS risk at all. Though acclimatization has been investigated in a number of studies, the topic has not yet been addressed in a comprehensive and systematic literature review.

The leading textbook in diving physiology and medicine limits the discussion to a brief introductory text to compressed-air work [4]. The objective of this study was to review the literature for studies investigating health

KEYWORDS: acclimatization; decompression sickness; diving; health; review article; systematic review; venous gas embolism

effects of multiday diving. Diving may cause health effects secondary to a number of mechanisms such as breathing of dense breathing gas, hyperoxia, immersion or thermal stress. Though it may be difficult to iso-late the mechanism causing a specific health effect, it was our intention to focus on health effects secondary to those caused by decompression. Decompression sickness, venous gas embolism (VGE) and self-reported health were considered relevant outcome measures.

METHODS

This work was completed in two phases. The first part was a structured literature completed December 2019. After manuscript revision the review was restructured to conform with the PRISMA statement [5] for systematic reviews. The systematic review sought human and animal studies investigating the relationship between multiday hyperbaric exposure and the outcomes DCS, VGE and subjective health assessment. PubMed and Ovid Embase were searched with (((Compressed air) OR (compressed gas)) AND ((decompression sickness) OR (decompression illness))) OR (Diving AND ((repeated) OR (repetitive) OR (multiday) OR (multiday) OR (multi day) OR acclimatization) AND ((dcs) OR (decompression sickness) OR (decompression illness) OR (vge) OR (venous gas embolism) OR (venous gas emboli) OR (health))).

Qualifiers (e.g., MeSH terms or title words) were intentionally omitted to reduce the likelihood of excluding relevant titles. The Cochrane library was searched for "hyperbaric." These three database searches were performed up to 15 December 2020. Rubicon Research Repository ("Rubicon", *http://archive.rubicon-foundation.org/*) was searched December 2019 for "Acclimatization" (17), "Multiday" (10), "Multiday diving" (3) and "multiday diving" (1) (number of results listed in parentheses). Regrettably, Rubicon was inaccessible when this manuscript was restructured December 2020. The literature search was supported by a senior librarian (see Acknowledgment), but the search structure remains the responsibility of the manuscript author.

Human and animal studies on health effects of multiday hyperbaric exposure were included. Studies published in other languages than English were considered eligible if an abstract in English language was available. Full-text manuscripts in languages other than English were not translated. When a relevant study was identified it was entered in PubMed to learn whether it had been cited by a more recent manuscript in PubMed Central. The reason for this was to ensure that relevant studies not identified by the search terms listed above would be reviewed. In addition, studies referenced in the full-text manuscripts were reviewed and included if they met the inclusion criteria.

To be considered for inclusion the studies should report DCS, VGE or self-reported health effects as the outcome measure(s) after two or more days of hyperbaric exposure. Most studies included consecutive days of hyperbaric exposure, but a few have either omitted details of the exact interval between dives or have day(s) without hyperbaric exposure in the dive series. We have detailed this in the description of the studies. Reviews were excluded as were studies reporting diving-related acclimatization to heat, cold, Eustachian tube function or barotrauma.

Studies were rated on the level of evidence provided according to the criteria of the Centre for Evidence-Based Medicine in Oxford [6].

For the purpose of simplification, this review utilizes the term "acclimatization" whenever a study has suggested that multiday diving decreased the risk for the investigated outcome measures (DCS, health complaints or VGE). The term "sensitization" will be used for statements suggesting increased incidence of these outcome measures.

Pressure and depth data are cited by the units presented in the original reports, but additionally presented in parentheses after conversion to the SI-units of meters and kPa. Factors for conversion of pressure units to kPa are those published in the U.S. Navy Diving Manual Rev. 7 [7]. Some of the studies have not compared DCS incidence rates between groups by means of statistical tests. When sufficient data has been published in the original report, we have applied Barnard's exact test for such comparison. P-values <0.05 have been considered statistically significant. Statistical tests not published in the original reports but completed by the author of this review are indicated by †.

RESULTS

The results of the search strategy are presented in Figure 1. A total of 682 studies were identified after duplicate exclusion. A total of 54 full-text manuscripts were reviewed as a result of the literature search. These manuscripts referenced another 13 studies relevant for review and five of these were included. A total of 21 human

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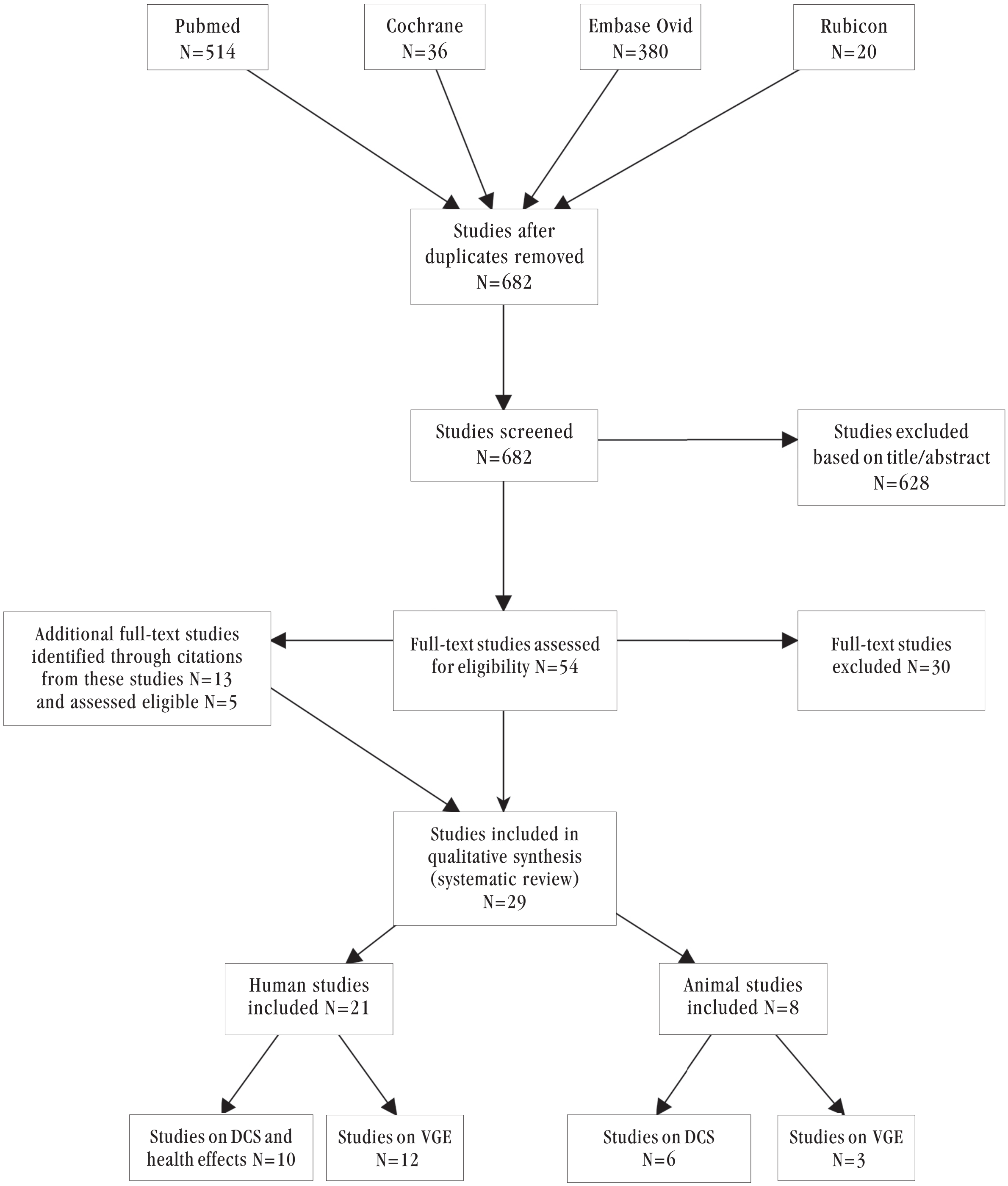

FIGURE 1

Literature search flowchart according to the PRISMA statement.

One study on humans and one study on animals included both DCS and VGE outcome.

Ref.	Pub	Specie	Design	Exposure	N	P_{max} kPa	Days of exposure	Outcome	Comment	LoE
Dunford et al. [14]	J	Man	§Co	NS, AN	10358	966		--/0/++	Compared number of multiday dives between recreational divers-reporting DCS to those not reporting. Results suggesting sensitization in one group of divers, acclimatization in another and no effect in the third.	2b
Eckenhoff & Hughes [15]	P	Man	§E	Si,St	15	555	12	++ (It)	Self-reported grade of itching reduced Day 9-11 compared to Day 1	2b
Elliott [16]	J	Man	§E	St	12	1021	14	++	Significantly less DCS and "niggles" in six divers "worked up" during two weeks before two test dives compared to another group of six divers not "worked up" to the same dive profiles. (P<0.05)	
Golding et al. [10]	J	Man	Co	Ca,NS	22	294	28	++	DCS incidence halved after 7±4d	2b
Paton and Walder [8]	J	Man	Co	Ca,NS	376	391	2-300	++	DCS reduced from 7.3%>3.6% comparing compression 1-5 with compression 6-10.	2b
Thalmann [18]	J	Man	§E	S,He,St	36	469	3	++	41% DCS after initial test dive without work up dives. 10% DCS after test dive preceded by three work up dives (P<0.05).	2b
Rose [11]	J	Man	Co	Ca,NS	155	439	?	+	No statistical analysis of data, more than fourfold increase in DCS incidence after an 11-day strike	3b
Lam & Yau [13]	J	Man	Co	Ca,NS	?	432	?	++	RR of DCS in "new starters" (see text) 3.69 compared to "non-new starters)	3b
Doolette [23]	J	Man	§Q	NS		321	2-29	0 (DHS)	No trend of change in self-reported health during multiday diving in occupational divers.	4
El-Ghawabi et al. [12]	J	Man	Co	Ca,NS	55	376	?	+	Neither detailed results nor statistical analysis is presented, but the authors claim that DCS incidence declined once maximum pressure	4-

Table 1: Studies on DCS and health effects of multiday hyperbaric pressure exposure on man sorted by level of evidence.

Exposure was standardized exposure, breathing gas was compressed air and outcome measure is DCS unless otherwise specified.

Legend: Ca Caisson exposure with linear decompression; Co Cohort; DHS Self assessed health by means of Diver Health Score [23]; E Experimental; It Itching; J Journal; NS Not standardized exposure; P Proceeding; Pub Type of publication; Q Questionnaire; Si Simulated dive (pressure chamber); St Staged decompression. -- Statistically significant ($p<00.5$) trend of sensitization; 0 No trend of either acclimatization or sensitization; + Results suggest acclimatization, but either not statistically significant or no statistical analysis performed; ++ Results demonstrate a statistically significant ($p<0.05$) reduction in DCS or itching after multiday exposure; § Study designed (primary or secondary objective) to assess the effect of multiday diving on outcome variable.

Ref.	Pub	Specie	Design	Exposure	N	P_{max} kPa	Days of exposure	Outcome	Comment	LoE
Montcalm-Smith et al. [42]	J	Rat	§E	Si,St	435	638	5 and 10	++	Significantly ($P<0.05$) less DCS in rats after dive to 435 kPa if acclimatized with daily dives to 316 kPa for 5 or 9 days, but not if acclimatized to 224 kPa.	1b
Ward et al. [43]	A	Rabbit	E	Si,St,O2	20	101	4	++	Rabbits decompressed from surface to 21 kPa (subatmospheric) pressure. DCS significantly less (23% vs 100%, $P<0.01$) in rabbits exposed to simulated dives the four days preceding the test dive. Detailed data are missing.	1b-
Aver'yanov [47]	B	Dog	E	Si	5	426	10-24	+	Minimum pressure to exert DCS after 4h exposure increased during a multiday exposure if exposure pressure was increased ~20 kPa/day. Threshold reached 385-426 kPa. However if first exposure was too high (385 kPa) DCS was developed and pressure during successive dives was reduced by ~20 kPa/day until a lower threshold of 304-345 kPa was reached. No statistical analysis provided	2b
Lehner et al. [44]	A	Sheep	E	Si,St	8	466	5+8	++	Five work up dives claimed to decrease DCS significantly, but detailed data are missing	4
Nazarkin [45]	A	Cat	E	Si	?	811	?	+	Cats exposed to multiday hyperbaric exposure with gradual increased bottom time. DCS incidence did not increase. Detailed data are missing.	4
Hills [48]	J	Goat	E	Si,St	4	362	?	+	The author suggests that the high threshold for DCS in one goat was due to acclimatization, but does not provide further data to support the theory.	5

Table 2: Studies on DCS after multiday hyperbaric pressure exposure on experimental animals sorted by level of evidence.

Breathing gas was compressed air unless otherwise specified.

Legend: A Abstract; B Book (chapter); E Experimental; J Journal; Pub Type of publication; Si Simulated dive (pressure chamber); St; Staged decompression; + Results suggest acclimatization, but either not statistically significant or no statistical analysis performed; ++ Results demonstrate a statistically significant ($p<0.05$) reduction in DCS after multiday exposure; § Study designed (primary or secondary objective) to assess the effect of multiday diving on DCS incidence.

Ref.	Pub	Specie	Design	Exposure	N	P_{max} kPa	Days of exposure	Outcome	Comment	LoE
Bilopavlovic et al. [27]	J	Man	E		16	278	4	0	No difference in VGE Day 1 vs Day 4	2b
Breedijk et al. [35]	J	Man	Co	Ca	4	214	2	0	Subgroup analysis in 4 out of 15 workers exposed two successive days. No difference in VGE Day 1 vs Day 2.	2b
Eckenhoff & Hughes [15]	P	Man	§E	Si,St	15	555	12	0	No difference in VGE during multiday simulated dives	2b
Marinovic et al. [28]	P	Man	E	AN	10	278	3	0	No difference in VGE during three days of diving	2b
Zanchi et al. [26]	J	Man	§E		16	278	4	++	Lower OR for a higher VGE grade Day 4 compared to Day 1 (0.50, 95% CI 0.34-0.73)	2b
Thom et al. [40]	J	Man	E		16	278	4	0	Pattern of VGE reduction two hours following the dive was similar after each dive (Days 1-4). No detailed results of VGE scores for Days 2-4.	2b-
Dunford et al. [33]	J	Man	Co	NS,AN	67	441	6-8	++	Relative odds of high bubble grade decreased by 0.68 per dive day (95% CI 0.56-0.84, P<0.01)	4
Fife et al. [34]	A	Man	Co	NS,O2	5	653	24	0	A trend to decreasing VGE from Week 1 to 4 was suggested but ns	4
Ljubkovic et al. [37]	J	Man	Co	NS,AN,Tri	7	~740	3	0	Less VGE Day 3 compared to Day 1, but ns. Different dive profile each day.	4-
Marinovic et al. [36]	J	Man	E	AN,Tri	9	640	4	++	Less VGE Day 1 and 4 compared to Day 2 and 3, but dive profiles Day 1-2 were different from Day 3-4.	4-
Marinovic et al. [38]	J	Man	E	Tri	7	885	6	++	Significantly less VGE Day 4-6 compared to Day 1-3, but different dive profile for each day.	4-
Souday et al. [29]	J	Man	E	Si,AN	12	376	3	+	Less VGE after the second air dive compared to the first, but intervals between the dives not standardized and no statistical analysis detailed.	4-
Havnes et al. [50]	J	Rat	E	Si	14	700	2	+	Lower VGE score Day 2 compared to Day 1, but difference ns.	2b
Lehner et al. [44]	A	Sheep	E	Si,St	?	466	5+8	0	No trend for change in VGE score as a function of dive days.	4
Bassett [49]	T	Dog	E	Si	2	408	32	0	Authors state that no acclimatization occurred, insufficient data provided for independent analysis.	4-

Table 3: Studies on VGE after multiday hyperbaric pressure exposure sorted by level of evidence and specie.

Exposure was standardized sea dives and breathing gas compressed air unless otherwise specified. Legend: A Abstract AN; Air and/or oxygen enriched air (nitrox) as breathing gas; Ca Caisson exposure; Co Cohort; E Experimental; J Journal; LoE Level of evidence [6]; NS Not standardized exposure; ns Not statistically significant; O_2 Oxygen breathing during decompression; P Proceeding; Pub Type of publication; Si Simulated dive (pressure chamber); St Staged decompression; T PhD Thesis; Tri Helium, oxygen and nitrogen gas mixture (trimix) as breathing gases in bottom phase; 0 No trend of either acclimatization or sensitization; + Results suggest acclimatization, but either not statistically significant or no statistical analysis performed; ++ Results demonstrate a statistically significant ($p<0.05$) reduction in DCS or itching after multiday exposure;
§ Study designed (primary or secondary objective) to assess the effect of multiday diving on VGE.

Continued from page 128

and eight animal studies met the inclusion criteria; these are summarized in Tables 1-3. Some studies reporting DCS and VGE after multiday exposure were not eligible for inclusion due to methodological concerns or lack of details. These are not included in the tables but are presented in the text.

Studies on humans

Decompression sickness

Acclimatization has been studied in detail in compressed-air workers. Paton and Walder [8] reported the incidence of DCS during construction of the Tyne cyclist and pedestrian tunnel during 1948-1950. A total of 40,000 compressions to a maximum pressure of 42 psig (391 kPa) were completed on 376 men. Out of these 177 worked eight-hour shifts while 199 entered and left the tunnel for shorter work periods. Working pressure varied during the construction period due to water depth and tide, but typically ranged 300-360 kPa except for a few weeks in the beginning and end of the project when pressure was lower. The report does not detail the number of successive working days or days off (weekends, holidays, etc.) The work caused 350 incidences of DCS in 150 of these men. The diagnosis of DCS was made by a "medical orderly" but not routinely reviewed by a physician. The report states that each individual experienced between nil and nine occurrences of DCS, while "the vast majority of those liable to bends incurred an attack only one to three times." The incidence of DCS was analyzed for cohorts of workers enduring 10, 50, 100 and 300 compressions. The cohort of workers participating in 300 compressions was included in the 100 compressions cohort, the 100 compressions cohort was included in the 50 compressions cohort, and so on. The cohort of 90 men exposed to 60 compression observed a reduction of DCS incidence from 7.3% during the first five compression to 3.6% during the sixth to tenth compression (Figure 2). The best fit power regression curve fits data with $R^2=0.58$ ($p=0.01$). Further reduction in DCS incidence occurred during the next compressions and ranged 0.4-1.8% during the next 50 compressions. The report by Paton and Walder [8] as well as a later report by Walder [9] discuss in detail whether the observed reduction in DCS incidence could be due to inclusion bias caused by exclusion of workers experiencing DCS ("healthy worker effect"). However, the authors estimate the inclusion bias to explain approximately a 1% reduction in DCS incidence over 150 compressions. In contrast the effect size of acclimatization was in an order higher. (DCS incidence was observed to decrease from 12% after the first decompression compared to 2% after the tenth compression.)

In a later work Golding et al. [10] reported the DCS incidence in a cohort of 22 steel erectors working in on the Dartford tunnel who had never previously entered compressed air. They were followed for one month "during which the pressure was relatively constant" to a maximum of 28 psi (294 kPa). The DCS incidence declined as a function of number of compressions and was halved after seven compressions ($r=0.97$, $p=0.05$, Figure 2). The same study reported that initial exposures to a low pressure would not provide acclimatization for a succeeding higher pressure. The study reported a gradual loss of acclimatization for workers leave period of two to six days and an apparent loss of acclimatization after 10 days (Figure 3).

Rose [11] published a survey of DCS in compressed-air workers during construction of Auckland Harbour Bridge from 1956 to 1958. Six piers were placed on the sea bottom. Working pressure ranged 3-49 psi (122-439 kPa); a total of 10,026 compressions caused 262 cases of DCS (2.6%). The effect of acclimatization is recognized and discussed in detail, but the author acknowledges the challenge of analyzing the data since pressure and length of shift periods varied between the different piers. However, work on Pier 2 was interrupted by a strike, which allowed some assessment of acclimatization. The work on this pier was completed by 69 caisson workers pressurized to 37-47 psi (256-325 kPa) for a total of 1,823 compressions. Fifty cases of DCS occurred, giving a crude DCS rate of 2.7%. DCS incidence on Pier 2 would be in the order of 1.8% during the initial 34 days, but was raised to 8.0% during the last five days after an 11-day break caused by the strike. This happened in spite of approximately equal pressure exposure during the period preceding and following the strike. DCS incidence is reported for workers experienced with caisson work immediately before the work on Piers 2 and 3 (Termed "old sinkers" in the original work) as well as those without such immediately preceding experience ("new sinkers"). Though data are not statistically analyzed, the numbers suggest a decreasing DCS incidence as a function of number of compressions (Figure 4). A decreasing incidence could be explained by extraction of injured workers (healthy worker effect), but the similar trend in "new sinkers" and "old sinkers" makes this explanation

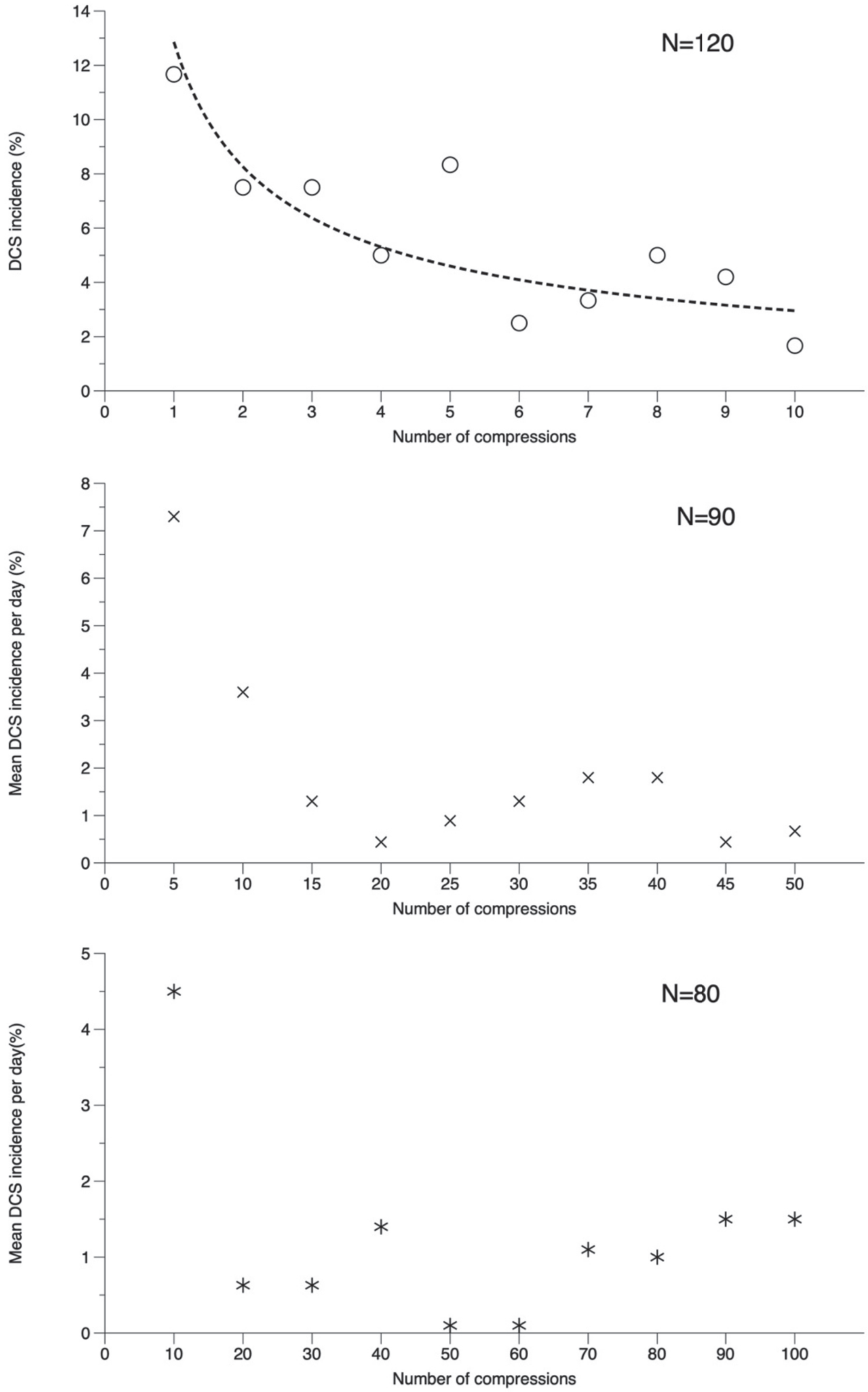

FIGURE 2: Mean daily DCS incidence in cohorts of compressed-air workers observed for 10, 50 and 100 days (upper, mid and lower panel).

Number of each cohort indicated in upper right part. Best fit power regression line in upper panel (dotted line) with R^2=0.58, p=0.01. Data from Paton and Walder [8].

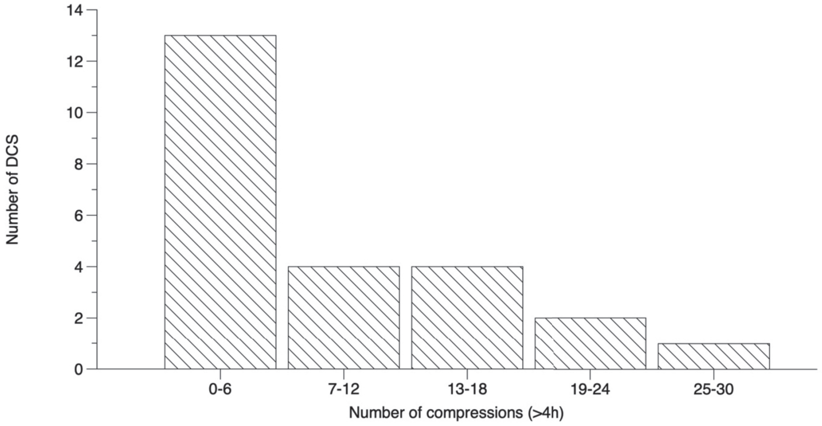

FIGURE 3: Number of DCS incidences in a group of 22 compressed-air workers during construction of the Dartford tunnel.

Occurrence of DCS grouped according to the sequence of compression (first six compressions, following six compression and so on). Data from Golding et al. [10].

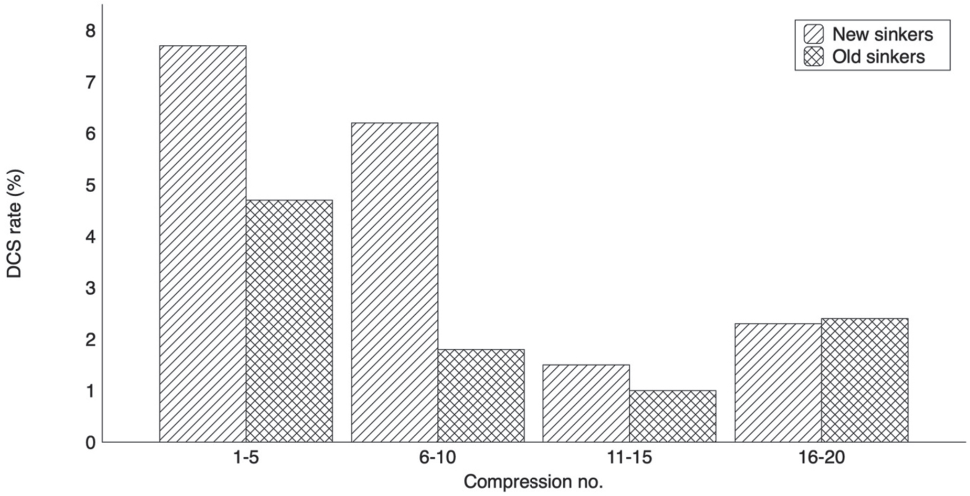

FIGURE 4: DCS rate in compressed-air workers during work on Pier 2 and 3 on the Auckland Harbour Bridge.

DCS rate is averaged for five-day intervals.

"New sinker": A worker not being exposed to hyperbaric work immediately before work on these piers.

"Old sinker": A worker exposed to hyperbaric work before start of work on these piers. Data from Rose [11].

less plausible. During the full period of construction of this bridge, the highest DCS incidence was reported after compressions on Tuesday (4.6%), followed by Thursday, Wednesday and Friday (3.2%). The colloquial expression of "Friday bends" was thus not supported in this survey.

El-Ghawabi et al. [12] reported incidence of DCS and dysbaric osteonecrosis in 55 caisson workers at the Egyptian Giza and Ramses bridges. Maximum pressure was 2.8 kg/cm^2 (376 kPa). During this work 330 cases of DCS were observed in 34,164 compressions giving an overall DCS rate of 0.97%. The authors do not provide data allowing an analysis of acclimatization or sensitization but state that "We found that the bends rate began to rise when the pressure exceeded 1.2 kg/cm^2 (210 kPa), then rose to a high level for a brief period and tended to fall away thereafter even though the pressure was maintained."

Lam and Yau [13] reported findings from a compressed- air tunneling contract in Hong Kong with 142,140 exposures to 1.97 ATA (200 kPa) or above. Shift length was gradually increased from four to eight hours during the first five days of exposure for new starters as well as absentees. A total of 792 cases of DCS (0.6%) occurred. The authors clearly state that "There was also a lack of accurate and specific data on the number of man-decompressions among new starters, absentees, and others for the calculation of DCS rate in these groups so as to study the effect of acclimatization." The authors compared DCS incidence in workers during the first five shifts after pre-employment medical examination ("new starters") to DCS incidence in the other workers. The authors suggest that acclimatization did reduce DCS risk; the assumption seems valid since relative risk for DCS in the new starters was 3.69 (95% CI 3.1-4.4†) compared to workers acclimatized to hyperbaric work. This increased relative risk occurred in spite of shorter shift lengths in the first hyperbaric exposures in the new starters.

A recent study by Dunford et al. [14] expanded the data of DCS in recreational diving. During 1995-2008 a total of 122,129 recreational dives were completed by 10,358 divers. The divers were monitored with dive computers, and they provided information related to the dives. The divers were grouped according to the diving platform: Scapa Flow (typically deep, strenuous dives in cold water with staged decompression stops); dive guides (repetitive dives for many days); shore/day boat (half or one day of diving); and liveaboard (five to seven days of repetitive diving). The shore/day boat and liveaboard dives were collated in one group termed "basic" dives. In addition to the collection of information from the divers and the dive computers the dive profile was analyzed with a probabilistic model for the expected risk of DCS (P_{DCS}). Repetitive dives were defined as dives with less than a 12-hour surface interval; multiday diving would be dives interspaced by less than 48 hours. A multiday dive series would consist of two or more dives with at least one surface interval ranging 12-48 hours and the last surface interval exceeding 48 hours. Thirty-four cases of DCS (0.03%) were reported, and the small number challenges detailed statistical analysis. The number of dives in the multiday dive series causing DCS ("DCS dive series") was compared to the number of dives in multiday dive series without DCS ("No-DCS dive series").

Scapa Flow: The number of dives in the DCS dive series was significantly less than the No-DCS dive series (5.3 vs. 9.6, respectively, $p<0.001$). P_{DCS} was significantly higher in the DCS dive series.

Basic: The number of dives in the DCS dive series was not different from the No-DCS dive series, in addition the P_{DCS} was equal in the two groups. However, for dive guides, the number of dives in the DCS dive series was significantly higher than the No-DCS dive series (21.2 and 8.1 dives, respectively, $p=0.0018$), though P_{DCS} was equal.

The results are difficult to interpret. If the DCS dive series had consistently more or less dives than the No-DCS dive series – across all groups and with equal P_{DCS} – the data would have suggested that multiday diving would tend to provide sensitization or acclimatization respectively for DCS. The results of this study suggested that multiday diving could provide acclimatization for Scapa Flow divers, not influence "basic" divers and sensitize dive guides for DCS. It should be noted that the study compared the number of multiday dives rather than days of diving. Further, the selection bias and lack of standardization of dive profiles in this study makes it difficult to assess the effect of multiday diving on DCS risk.

Eckenhoff and Hughes [15] exposed 15 subjects breathing compressed air to a simulated (dry) dive to 148 fsw (555 kPa) for 28 minutes. This exposure was repeated daily for 12 consecutive days. The subjects were monitored for VGE (results will be referred in detail later), and each completed a questionnaire. The questionnaire included a scoring of itching on a 0-10 scale. One subject experienced DCS on the very first day and was excluded from further participation. Among the remaining 14 subjects there was a significant ($p<0.001$) reduction in skin itching during the period.

Elliott [16] reported incidence of DCS during testing of decompression procedures for deep diving. Of particular interest was the open-sea dives to 270 feet/20 minutes and 300 feet/15 minutes (82 and 91 meters, respectively) with the divers breathing 10% oxygen in balance helium. In a group of six divers who had "recently completed a predetermined series of air dives" none experienced DCS; one subject experienced "niggles." These "work up" dives consisted of four dives interspaced evenly during a 14 day period. The first work up dive was 80 feet breathing oxygen-helium, followed by two dives to 180 and 250 feet breathing compressed air. The final work up dive was to 300 feet breathing oxygen-helium. In another group of six divers without such "work up" dives, two experienced DCS and four cases of "niggles" were observed. The difference in incidence of symptoms – DCS and "niggles" – was statistically different between these two groups (Barnard's exact test, p<0.01†) and suggested an effect of acclimatization after such work-up dives.

The effect of acclimatization on DCS incidence was repeatedly emphasized by Thalmann in the UHMS workshop on Validation of Decompression Tables [17]. One of the data sets supporting acclimatization was the testing of USN 0.7 ATA (71 kPa) constant pO_2 in helium decompression tables [18]. The testing consisted of five phases.

Phase III started with a 120-fsw (469-kPa) dive for 40 minutes with 35 minutes of decompression time: It caused DCS in 4/30 test dives (13%). The next two days the same profile was repeated with 40 minutes of decompression time, and no further incidences of DCS were observed in 40 dives. The intention of Phase IV was to verify that air could be used as an emergency (bailout) gas during decompression.

Phase IV testing was initiated in the autumn without work-up dives. Since the 120-fsw/40-minute profile had been shown to be safe in the Phase III testing, this profile was selected for retesting with air as the decompression gas. During the initial test, seven of 17 divers (41%) suffered DCS. None of these divers had made a dive in the immediate preceding days. It was speculated that lack of acclimatization might have caused the high incidence of DCS in Phase IV compared to Phase III, and a decision was made to precede further testing of the 120-fsw/40-minute profile with two work up dives. The work-up dives were completed on the two days preceding the 120-fsw/40-minute test dive. The first work-up dive was to 80 fsw/50 minutes, the second to 100 fsw/30 minutes (346 and 407 kPa)). When the 120-fsw/40-minute profile was retested after these work-up dives, significantly fewer – only three out of 29 test dives (10%) – caused DCS (Barnard's exact test, p<0.05†).

Two studies were insufficiently designed to be considered eligible for inclusion, but are briefly mentioned for completion.

Andersen [19] reported 13 cases of DCS in 9,018 pressure exposures in 320 compressed-air workers at the Great Belt Tunnel in Denmark. Pressures ranged from 126-396 kPa. The first seven cases occurred within three days, and six of these occurred on the same day in three consecutive shifts. Nine out of 13 cases occurred among new starters within the first five pressure exposures. However, decompression procedures were changed after the first seven cases of DCS, and this makes it impossible to assess any acclimatization effect.

Sayer et al. [20] reported 27 incidents of decompression illness (DCI) during four years of recreational diving at the Bikini Atoll. One of these occurred in a dive guide, the other 26 in customers. Diving depth at the Bikini Atoll is typically 50-55 msw, with air as bottom gas and typically 80% oxygen in balance nitrogen during the shallow part of decompression. Authors estimated DCI incidence to 1.31 per 1,000 dives (1.81 and 0.16 per 1,000 dives for customers and dive guides, respectively). The study is difficult to interpret, as the cases of DCI are not independently verified and only a single case of DCI occurred in the dive guide group. The authors do not detail how the number of dives were estimated, but the text suggests that these are based on extrapolation of the average number of divers arriving per week. The authors speculate that the difference in DCI incidence between divers and customers could be due to acclimatization. Customers would not be acclimatized to deep air diving when arriving at Bikini in contrast to dive guides. The report does not detail which day in the dive series the DCI cases occurred, so further interpretation of this study is not possible.

Self-assessed health

In a previous study [21] Doolette reported the use and validity of a standardized questionnaire designed to assess health effects of diving. The responses are summarized in a numerical "Diver Health Score" (DHS). DHS may range 0-30, and a score higher than 8 has been shown to predict decompression illness among divers presenting to recompression clinics [21]. Doolette and Gorman [22] reported an increase of one DHS unit per 1% increase in estimated DCS incidence. In a later study Doolette [23] reported the findings of a health survey submitted to Australian tuna farm divers participating in multiday diving (2-29 dives). The diving exposure was quantified by means of electronic dive logs, and "decompression stress" was estimated based on the USN probabilistic model [24]. The authors reported that mean decompression-related health status did not change significantly during the high number of long multiday series of occupational diving (Figure 5). No cases of

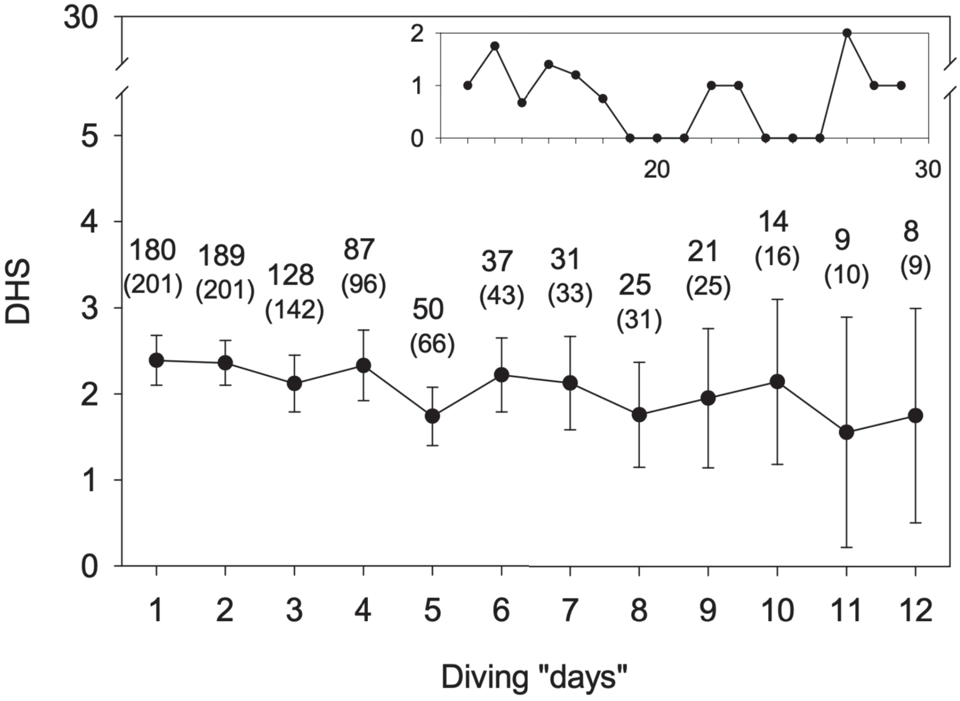

FIGURE 5: Subjective health assessment summarized as a health score (DHS, Y-axis) in a group of 201 divers.

Diving days (*X*-axis) are either succeeding or one day apart. Mean +/- 95% CI. Numbers over each point is number of DHS scores. DHS scores are missing in a few cases – the total number of cases is provided in parenthesis. Inserted graph shows DHS score for longer exposure periods (one to five cases). From [23]. With permission.

DCS occurred in the multiday series of diving. Some caution should be raised, as the mean DHS was low (approximately two DHS units) in this cohort. Further, the external validity remains to be proven as van der Hulst and Buzzacott [25] were unable to demonstrate any association between DHS and estimated DCS incidence in a sample of 18 occupational divers in the New Zealand recreational diving industry.

Venous gas embolism

Assessment of any acclimatizing effect of multiday diving on VGE is difficult unless the hyperbaric exposure is standardized and described in sufficient detail. Five studies [15,26-29] met these criteria and are described in further details as "standardized dives."

Standardized dives

Eckenhoff and Hughes [15] did not observe any change in VGE score (Doppler, Kisman-Masurel grading [30]) in 15 subjects exposed to 12 consecutive days of controlled, simulated dives to 148 fsw (555 kPa) for 28 minutes. VGE was monitored in 15-minute intervals for two hours after each dive.

Zanchi et al. [26] reported the findings from a study on 16 subjects diving four consecutive days to 18 meters for 47 minutes. They were monitored by transthoracic echocardiography in 20-minute intervals for two hours after the dive; VGE was scored by the Eftedal and Brubakk grading system [31]. Odds ratio (OR) for having high bubble grade (Grade > III) compared to Day 1 decreased as a function of dive days and reached 0.37 (CI 0.20-0.70) on Dive Day 4, suggesting acclimatization to VGE.

Bilopavlovic et al. [27] reported a study on 16 divers diving four consecutive days to 18 meters for 47 minutes. VGE was measured by transthoracic echocardiography in 20-minute intervals for two hours after finished dives on Day 1 and Day 4. The authors did not observe any difference in VGE when comparing Days 1 and 4.

Marinovic et al. [28] reported a study on 10 subjects diving three consecutive days on air and three consecutive days breathing 36% oxygen in balance nitrogen (Nitrox 36) to 18 meters for 47 minutes. A pause of at least two weeks separated the profiles. VGE was measured by transthoracic echocardiography 20 and 40 minutes after the dives. Though significantly more VGE was observed after the air dives compared to the nitrox dives, there was no sign of acclimatization and the amount of VGE remained unchanged during the three days of exposure.

Souday et al. [29] completed a study on 10 men and two women participating in three simulated dives to 28 msw (376 kPa) for 55 minutes. The subjects breathed compressed air ("air dive") during two and oxygen-enriched air ("EAN dive" 36% O_2) during one of these exposures. The purpose of this study was to investigate the effect of EAN breathing on the amount of VGE after a finished dive. VGE was measured every 30 minutes for 90 minutes by pulsed Doppler on the pulmonary artery and scored according to the Spencer scale [32]. To qualify for the final two test dives the participants presented VGE score ≥2 after the initial air dive. Qualified subjects were then allocated to a double-blinded crossover design with one air and one EAN dive. The authors do not specify the interval between the dives except a statement that "a minimum of 24 hours delay between the dives were required." The main finding was a significantly lower VGE score after the EAN dive compared to the air dive. As an additional finding the authors state that the VGE score was lower after the second air dive compared to the first. Median VGE score was 1 immediately after surfacing in both of the air dives. However, median bubble grade was consistently lower 30 to 90 minutes after the second air dive (Grade 2) compared to the first air dive (Grade 3). The authors provide no confirmation on whether this difference was statistically significant.

Not standardized dives

Dunford et al. [33] reported Doppler-detected VGE in a group of 67 recreational divers participating in 281 dives during six diving trips lasting six to eight days each. These dives were not controlled, and the diving depth and time would vary. The divers were monitored only once during a 20- to 40-minute period after the finished dive and not necessarily every day. Some divers skipped dives in the middle of the period, but this was not logged. Doppler scores were categorized as high bubble grade (HBG) with Spencer [32] grades 2-4. Exposure severity was calculated based on a probabilistic model estimating a conditional probability for DCS (P_{DCS}) based on data from the dive computers. HBG was, as expected, significantly correlated to exposure severity. However, for a given P_{DCS} the incidence of HBG was lower on trip Days 5-8 compared to trip Days 1-2 ($p<0.001$), suggesting acclimatization as a function of days of diving.

Fife et al. [34] reported the occurrence of Doppler-detected VGE in a group of divers participating in multiday repetitive diving as part of archaeological studies. Working depths ranged 140-180 feet (43-55 meters). Each diver made two 20-minute dives per day with a five- to six-hour surface interval six days per week. Twenty divers were monitored for VGE after 240 man-dives. They reported that there was no statistically significant trend from Day 1 through Day 6 over the four weeks.

Breedijk et al. [35] completed a study on 15 workers participating in a Dutch tunneling project. VGE measurements by means of Doppler were completed one and two hours after a finished exposure. VGE was scored according to the Kisman-Masurel grading system [30]. The workers breathed compressed air during the hyperbaric exposure at 11.4 meters (213 kPa) and oxygen during decompression. Four subjects completed measurements on two consecutive days with 304-315 minutes of bottom time, but the difference in bottom time for each diver was only two minutes comparing Day 1 and Day 2. Median bubble grade in rest was 1 (range 0-1) and after movement 2 (range 2-3). VGE in rest Day 2 was decreased in one subject, unchanged in one and increased in two subjects compared to Day 1. VGE after movement Day 2 was decreased in one subject and unchanged in three subjects compared to Day 1. None of these differences were statistically significant.

Marinovic et al. [36] reported the results from a study on nine divers participating in a technical diving course. They completed one dive per day for six consecutive days to a maximum diving depth of 55 meters. Breathing gas and bottom time varied from one dive to another, but the dives on Days 3 and 4 were identical. VGE (grading system not detailed) was monitored with transthoracic echocardiography 60 minutes after a finished dive. VGE was significantly higher ($p<0.05$) after the second and third dive (median grade 2 for either) compared to the first and fourth dive (median grade 0 and 1, respectively).

Ljubkovic et al. [37] examined seven recreational divers by means of echocardiography after participation in diving exercises. The divers, breathing a mixture of oxygen, helium and nitrogen (trimix) completed one dive per day for three consecutive days. The trimix blending was not equal from dive to dive. The report does not detail exact diving depth and bottom time, but the graphical presentation suggests approximately 65 meters for 15 minutes. VGE was measured 45, 60 and 90 minutes after each finished dive and graded according to Eftedal and Brubakk [31]. The median VGE score was Grade 3 at 60 minutes post-dive after each day of diving but was lower on Day 3 compared to Day 1 after 45 and 90 minutes (3 and 2 vs. 4 and 3, respectively). However, this reduction was not statistically significant. Interpretation of the results is limited by the fact that exposure was not identical for each day of diving.

Marinovic et al. [38] and Obad et al. [39] reported incidence of VGE in a group of seven divers participating in one dive each day for six successive days. The divers were breathing gas mixtures of helium, nitrogen and oxygen (trimix). VGE was measured by echocardiography 60 minutes after the dive and graded according to the Eftedal and Brubakk [31] grading system. Diving depth, bottom time and breathing gas mixtures were different from one day to another, but all divers were exposed to the same dive profile for any day. VGE score was significantly lower ($p<0.05$) on Days 4-6 compared to Days 1-3. Due to the fact that the profiles were slightly different from one day to another it cannot be resolved as to whether this decline could be ascribed to the different dive profiles of acclimatization or a combination of these factors.

Thom et al. [40] reported a study on 16 divers diving to 18 meters for 47 minutes for four consecutive days. The primary objective of the study was to measure microparticle concentration and neutrophil activation after diving. VGE was measured every 20 minutes for two hours with transthoracic echocardiography and scored according to a modified Eftedal and Brubakk [31] scale. Resting median bubble score was 3 at 20 minutes after surfacing and declined gradually to 1 after two hours following the first dive. The authors state that the pattern of VGE reduction was similar after Dives 2-4, but do not provide further data to allow comparison.

Wong [41] reported the incidence of DCS and VGE (Kisman-Masurel Doppler scores [30]) in Western Australian (Broome) drifting pearl divers. VGE measurements were completed after simulated dives – testing decompression profiles – as well as field testing during actual diving. Regarding field measurements the report states that "For the non-rotational profiles, the bubble grades tended to peak on day 3, with an average grade II – at the end of the day. However, on day 4, they dropped down to grade I+ and remained at I+ to day 8." This study was not considered eligible for inclusion due to lack of details.

Animal studies

Decompression sickness

There are fewer animal studies on the effect of acclimatization on decompression outcome, but Montcalm-Smith et al. [42] published a carefully designed study to investigate this phenomenon. Sprague-Dawley rats were exposed to simulated (dry) dives. The study was completed in two phases. Phase I was designed to explore the effects of four different acclimatization dives on a succeeding test dive. Findings were compared to a control group not acclimatized at all before the test dive. The test dive was a 175-fsw (638-kPa) dive for 60 minutes. DCS and death were monitored as the outcome measure. The test dive induced extensive injuries, as demonstrated by the approximate 60% incidence of DCS and 40% mortality. Two protocols (acclimatization dives for one or two weeks to 70 fsw (316 kPa) significantly reduced DCS incidence (OR 0.34 and 0.39 respectively, $p<0.05$) but did not affect death rate (Figure 6). Acclimatization dives to 40 fsw (224 kPa) for one or two weeks had no significant effect on either DCS or death. In a second phase the test dive was preceded by various configuration of acclimatization dives to 70 fsw (316 kPa). Two groups were exposed to acclimatization dives either with or without staged decompression; one group was exposed to a single acclimatization dive; and a fourth group was not acclimatized before the test dive (control group). None of the exposures significantly reduced mortality. A single exposure was not sufficient to protect the animals from DCS. The lower DCS incidence in the group acclimatized to 70-fsw dives with decompression stops just failed to reach statistical significance compared to the control group (OR 0.51, $p=0.0544$). This study strongly suggests a protective effect of acclimatization dives on DCS incidence in rats and that the depth of the acclimatization dives is important.

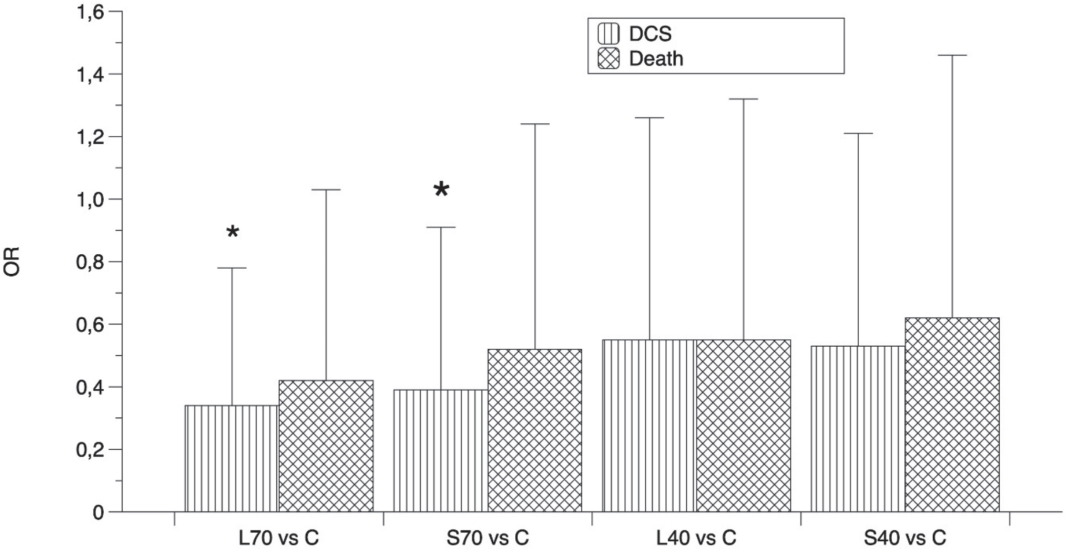

FIGURE 6: Odds ratio for DCS versus death

Odds ratio for DCS (bars with vertical lines) and death (bars with hash) after a 175-fsw/60-minute test dive in four groups of acclimatized rats vs Control (C).
Long acclimatization period of nine daily dives to 70 fsw (L70) or 40 fsw (L40).
Short acclimatization period of four daily dives to 70 fsw (S70) or 40 fsw (S40).
OR +upper 95% CI. *: P<0.05. Data from Montcalm-Smith et al. [42]

Ward et al. [43] reported findings from a study on rabbits exposed to a simulated test dive to 2 ATA (203 kPa) for 30 minutes and decompressed to a subatmospheric pressure of 0.21 ATA (21 kPa) breathing oxygen. In a group of seven unacclimatized rabbits all experienced DCS. In another group of 13 rabbits exposed to four acclimatization dives to 1.5 ATA (152 kPa) before the test dive, only three rabbits showed signs of DCS. The reduction DCS incidence is statistically significant (Barnard's exact test, p<0.01†). The results are not extensively detailed, as they have been published only as an abstract.

Lehner et al. [44] examined DCS incidence and VGE in eight sheep exposed to two simulated test dives to 4.6 ATA (466 kPa). These dives were either completed by a direct ascent or a five-minute "safety stop" at 1.45 ATA (148 kPa). The design was a crossover exposure, so four sheep started with the direct ascent dive and completed the dive with a safety stop two days later. The other four sheep made the dives in reverse order. All sheep were acclimatized with five dives to increasing maximum pressure (4.0-4.8 ATA) before the first of the two test dives. The authors state that acclimatization significantly reduced DCS incidence, but had no effect on VGE score. However, the results are published in an abstract only and do not allow detailed review.

Nazarkin [45] published a study in Russian for which an abstract in English language is available [46]. Cats were subjected to gradually increased exposure time at 8 atm (811 kPa). Acclimatization allowed extension of bottom time from one to five minutes without development of symptoms.

Aver'yanov [47] reported the findings of a study on five dogs participating in daily four-hour hyperbaric exposures breathing compressed air. The experiments were designed to determine the minimum pressure (threshold level) required to cause DCS. Pressure was either increased or decreased by 20 kPa/day. Three dogs were initially exposed to 243-304 kPa and pressure was increased by 20 kPa/day. In these three dogs the threshold pressure reached 344-426 kPa after six to 10 days of acclimatization. In another group of two dogs, the first exposure was 405 kPa. This caused DCS in both dogs. When pressure was reduced by 20 kPa/day for the succeeding four days, a threshold pressure of 304-345 kPa was reached. No statistical analysis was provided; however, the data suggests that a gradual increase in hyperbaric exposure will cause an acclimatizing effect. Contrary, a too-high initial pressure exposure seems to cause a sensitizing effect on successive hyperbaric exposures.

Hills [48] examined DCS incidence in a series of goat experiments. In one of the series ("second method") four goats were exposed to 20 simulated dives to 40-85 fsw (224-362 kPa) with varying depths in the last decompression stop. The report does not detail the exact interval between the dives, but one of the goats demonstrated a particularly low DCS incidence compared to the others. The author claimed that this goat was acclimatized to the extent that the results of the decompression profile testing could not be used. The results are regrettably not presented in a way that allow confirmation of whether this claimed acclimatization was restricted to one animal or could be a general phenomenon.

VGE

As previously mentioned, Lehner et al. [44] examined VGE incidence in eight sheep following a test dive to 4.6 ATA (466 kPa). Five acclimatization dives did not significantly affect VGE incidence.

Bassett [49] reported the findings of a study on two mongrel dogs exposed to 32 simulated dives to 100 fsw (408 kPa) in a pressure chamber. They were instrumented by caval vein flow probes and a thoracic ultrasound probe for measurement of VGE by Doppler after finished exposure. In this study he was unable to observe any acclimatization effect of preceding dives on the extent of VGE. It should be noted that the study was not designed to identify any acclimatization effect, and insufficient data is presented to allow independent review.

Havnes et al. [50] examined VGE by echocardiography in four groups of rats breathing compressed air in a pressure chamber. Because the primary objective was to measure endothelial function by means of aorta tension measurements, the animals had to be sacrificed after the dive. Group A served as a control group; Group B was exposed once to a 700-kPa dive; Group C was exposed to 400 kPa on Day 1 and 700 kPa on Day 2; Group D animals were exposed to 550 kPa on Day 1 and 700 kPa on Day 2. In Group B, four of the six rats (67%) had high bubble grade (Grade 5), comparable to the findings in Group C with high bubble grade in five of the eight rats (63%). However, in Group D only two of seven rats (29%) had high bubble grades after the last dive. Though the differences in these incidence rates did not reach statistical significance, the data suggest that the first hyperbaric exposure in Group C (400 kPa) was insufficient to exert an acclimatizing effect on the dive day. A better-powered study would be useful to investigate whether a threshold exists for an acclimatizing effect.

DISCUSSION

The question of acclimatization has been repeatedly discussed in individual manuscripts, but a comprehensive literature review has not yet been published. The leading textbook in diving physiology and medicine [4] briefly mentions the topic in the introductory chapter on compressed-air work, but the subject is not discussed further in relationship to decompression tables or decompression sickness.

Acclimatization during caisson work has been well described as presented in this review [8-13]. The results may be affected by selection bias – workers experiencing DCS may tend to leave hyperbaric work (healthy worker effect) and this is difficult to monitor properly. However, three studies [8-10[have addressed this concern by means of subgroup analysis and have demonstrated that acclimatization affects DCS incidence independent of any healthy worker effect. The consistent direction of results in a large number of studies gives strong support to the fact that acclimatization may reduce DCS incidence in caisson work. The combination of a large number of compressions combined with a relatively high DCS incidence (typically 1-10%) during caisson work has allowed studies with high statistical power. In contrast it is difficult to reach sufficient power using DCS as the outcome measure when experimental studies [15] and large epidemiological surveys [14] adhere to standard decompression profiles with low DCS incidence.

We have identified only one study on humans designed to identify acclimatization to multiday diving. Eckenhoff and Hughes [15] observed less itching after consecutive days of hyperbaric (dry) exposure. However, the question remains open as to whether this could be due to adaptation (having less awareness of symptoms) rather than a physiological acclimatization. No change in VGE was observed during the course of multiple days of exposure in that study.

The low incidence of DCS in recreational and occupational diving (typically fewer than 1/1000 dives) makes it difficult to use epidemiological data to assess the extent of acclimatization. The conflicting results of the work of Dunford et al. [14] illustrates this. However, the case series reported by Elliott et al. and Thalmann [16,18] support that workup dives provide acclimatization to succeeding He-O_2 dives. These case series shared a high DCS incidence (30-40%) in unacclimatized divers. The single study publishing self-assessed health outcome of multiday diving did neither observe any acclimatizing nor see a sensitizing effect [23].

The question of acclimatization to diving was extensively discussed in a workshop in 1991 [51]. The workshop included a number of presentations describing diving practice and DCS incidence in recreational and occupational diving. Richardson and Shreeves presented the results from a survey submitted to representatives from dive resorts and liveaboard operators present at the 1991 DEMA show. Eighteen dive resorts, nine liveaboard boats and seven training organizations responded. The operators reported that the average diver spent five days of diving and completed 2.2 dives/day. Accordingly, multiday diving was a rather common practice in this part of the recreational diving industry. Only 19% of the operators practiced multiday skip – a mandatory day off diving during the stay. In spite of this the reported DCS incidence was as low as 0.002%. Gilliam reported experience from one year of operation (77,680 man dives) of a cruise ship with accommodation capacity for 160 recreational divers. On average the customers made three dives per day and dived for four consecutive days. Seven cases of DCS (0.009%) occurred; none of the professional staff nor guests using dive computers suffered DCS. However, notably, no hits occurred during the first two days of diving. Fife and co-workers reported the findings in a group of 62 scientific divers participating in a nautical archaeological work. They completed 7,523 air scuba dives in a five-year period. The divers made typically two 20-minute dives per day for five to six days a week. Various decompression protocols were used. A total of three cases occurred (0.04%). DCS incidence in recreational diving was reported to be 0.02% (range 0.005-0.15%) in a recent literature review [52]. The DCS incidence in multiday diving reported in this workshop [51] seems to be in the same order as recreational diving in general and does not support the notion of any sensitizing effect of multiday diving. However, it is difficult to draw any firm conclusion due to the heterogeneity of DCS data in recreational diving. The workshop [51] included eight presentations related to commercial diving. However, none of these presented data of multiday diving or DCS incidence related to such diving. Many of the diving contractors explained that they had modified U.S. Navy Dive Tables, but none advised for multiday skip.

Acclimatization to DCS has been demonstrated in rats [42], goats [48], cats [45], sheep [44], rabbits [43] and dogs [47]. Regrettably, only the study of Montcalm-Smith et al. [42] was properly designed, controlled and reported to allow independent assessment of the findings. The only animal study not demonstrating any acclimatizing effect was the one by Bassett [49] studying VGE in dogs. However, this study was not designed to answer this question.

The animal studies reporting VGE after successive days of hyperbaric exposure are not conclusive [44,49,50]. The same holds true for human studies. Five studies on humans favor the hypothesis of acclimatization [26,29,33, 36,38), while another six found no significant trend in VGE score as a function of days of diving [15,27,34, 35,37,40]. It should be mentioned that only the three studies of Dunford et al., Eckenhoff and Hughes, and Zanchi et al. [15,26,33] did either control or monitor diving exposure to an extent allowing assessment of exposure severity. Of these three studies two showed acclimatization using VGE as the outcome measure [26,33]. The validity of VGE measurements as a surrogate measure for DCS likelihood has been debated since it was first introduced in the 1970s, and Doolette has summarized some of the concerns [53]. Detailed guidelines for VGE monitoring have been published to ensure standardized, comparable and appropriately powered studies [54,55]. Only three studies [15,26,27] have measured VGE with sufficient short interval and for a sufficient period of time to comply reasonably to the standard suggested by Blogg [54]. None of the studies were sufficiently powered to detect minor changes in VGE. How, ever, these deficiencies will rather tend to underestimate any acclimatizing or sensitizing effect than to exaggerate them.

The modification of VGE occurrence by factors such as exercise, vibration and nutritional antioxidants has been reviewed by Madden et al. [56]. Acclimatization may well act through the same mechanisms as these factors, but studies must be carefully designed to isolate the effect of each factor. An example of interaction of multiple factors would be the study of Pontier and Castagna [57]. They reported the results of VGE Doppler monitoring of 22 military divers for 90 minutes following a simulated test dive to 400 kPa for 30 minutes. The test dive was completed twice: before and after a 90-day period of physical training and open-sea air diving. Bubble grades were significantly decreased after the dive training period. The design does not allow conclusions as to whether reduction in VGE score was due to acclimatization caused by multiday diving, physical training or a combination.

The mechanism underlying acclimatization remains unclear. Acclimatization may deplete micronuclei as potential seeds for later bubble growth. Crushing of micronuclei by raised pressure is supported by gelatin experiments [58] but was demonstrated by much higher pressure and compression rate than the exposures relevant for most human diving. Crushing of nuclei is thus a possible, though speculative, mechanism underlying acclimatization. Ward et al. [59] showed that rabbits demonstrating DCS would have a complement system activated by air bubbles in contrast to those not having DCS. Decomplementing the rabbits would make them less sensitive for DCS but after sufficient time for recomplementing they would again be sensitive to DCS. Acclimatization could potentially affect the complement system in a way that protects from DCS.

Another potential mechanism of acclimatization would be modification of the oxidative stress response induced by diving. Obad et al. [39] examined a group of seven recreational divers participating in technical diving exercises to 55-80 meters. The divers made one dive per day for six consecutive days while breathing helium-nitrogen-oxygen and nitrogen-oxygen mixtures. The dives were not standardized. Endothelial function was measured by means of flow-mediated dilatation (FMD), while plasma was analyzed for antioxidant capacity (ferric reducing antioxidant power) and a marker of oxidative stress (thiobarbituric acid-reactive substance) before and after the first, third and sixth dive. Each dive decreased FMD and antioxidant capacity. Pre-dive FMD and antioxidant capacity were decreased while oxidative stress was increased on Day 6 compared to Day 1. The results suggest that the oxidative stress, depleted antioxidant capacity, and reduced endothelial function caused by diving are not fully reversed the next day. Multiday diving could potentially enhance this response. However, diving-induced responses to immersion, changes in pressure, and oxidative stress are incompletely understood [60].

Acclimatization could alternatively be considered as a stress response with similarities to that observed after heat shock. Heat shock protein 70 (HSP70) has been measured in many experimental studies of hyperbaric exposure, and expression is increased in rabbits and rats subjected to DCS [61,62]. Su et al. [61] examined rabbits exposed to 6 ATA (608 kPa) for 90 minutes. Rabbits experiencing DCS after this exposure expressed pulmonary, hepatic and cardiac HSP70 similar to another group exposed to heat shock only. These results suggest a similar stress response of DCS and heat shock. Djurhuus et al. suggested that compression or pressure per se rather than decompression stimulated HSP 70 expression [63]. This would offer an alternative explanation of the acclimatizing effects of multiday diving.

Molecular techniques allow insight into the effects of diving on gene transcription. Chen et al. [64] investigated gene expression and signal transduction in pulmonary tissue of rats after hyperbaric exposure. Four groups were studied: Two of the groups were exposed to nine acclimatization dives for two weeks immediately preceding a sham dive or a test dive. Two control groups were exposed to a test dive or sham without any acclimatization dives. The authors observed activation of the cellular ERK pathway and upregulation of the egr-1 transcription in rats with DCS irrespective of whether they had been acclimatized. The only statistical difference in gene transcription between acclimatized and control animals with DCS was an attenuation of the egr-1 upregulation in the acclimatized rats. Eftedal et al. [65] studied blood transcriptome in 10 subjects before and after three consecutive days of diving to 18 meters for 47 minutes. They reported downregulation as well as upregulation of genes and showed that acclimatization may affect gene transcription. Neither of these studies can fully explain the molecular basis for acclimatization, but they suggest a promising method for future studies to allow for better insight.

The optimal strategy for acclimatization is unresolved, but the reports by Elliott [16], Havnes et al. [50], Montcalm-Smith et al. [42], Rose [11] and Walder [9] would favor acclimatization to a pressure close to target depth of the succeeding dives.

Neither military decompression tables from Sweden [66], United Kingdom [67], United States [7] nor the commercial decompression tables from Canada [68], France [69] or Holland [70] require a day off diving after a certain number of consecutive days of diving (multiday skip). To the best of our knowledge, the requirement for a multiday skip has been formalized in the Norwegian decompression tables only [1]. The practice of workup dives is commonly applied in military deep diving such as the NATO exercise "DeepDivex" (author experience). Thalmann [17] recommended that acclimatization should be taken into account when testing decompression procedures.

The contrast of acclimatization would be sensitization – increasing the risk for an unfavorable outcome as a function of multiday diving. There is no scientific data supporting such a notion. We found two statements suggesting that sensitization takes place. Gilliam [51] reported that all DCS occurred after the first two days of recreational diving provided by a particular operator. A similar statement was made by Wong [41], but neither provided data to support the conclusion.

Limitations

To our knowledge this is the first systematic review of acclimatization to diving. However, the conclusions are affected by the methodological concerns of many studies. There are no randomized controlled studies, and except for one animal study [42] even the experimental studies have concerns related to confounding factors such as inclusion bias, standardization of hyperbaric exposure, and outcome monitoring. It is recognized that the review process, and in particular the assessment of level of evidence, is subject to confirmation bias since the work was completed by a single author rather than a group.

CONCLUSION

We have presented a systematic review of health outcomes of multiday hyperbaric exposure. We wanted to assess whether preceding hyperbaric exposures would provide acclimatization or sensitization to DCS, self-perceived health, or VGE. The majority of human and animal studies suggests a protective (acclimatization) effect on DCS incidence and no significant effect on self-perceived health. The effects on VGE are less consistent, though the majority of studies suggest a reduction of VGE scores after multiday diving. Acclimatization is probably best achieved by exposure to a pressure similar to the target of the succeeding dives. None of the included studies suggests a sensitizing effect of multiday exposure. There is insufficient data to explain by which mechanism preceding dives exert acclimatization. ■

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Conflict of interest

The author is a consultant in diving medicine for a number of in-shore and offshore diving contractors as well as offshore oil and gas operators. He is the principal author of the Norwegian Diving- and Treatment Tables.

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