

Decompression Sickness Risk in Parachutist Dispatchers Exposed Repeatedly to High Altitude

Desmond M. Connolly; Timothy J. D'Oyly; Stephen D. R. Harridge; Thomas G. Smith; Vivienne M. Lee

- INTRODUCTION:** Occurrences of severe decompression sickness (DCS) in military parachutist dispatchers at 25,000 ft (7620 m) prompted revision of exposure guidelines for high altitude parachuting. This study investigated residual risks to dispatchers and explored the potential for safely conducting repeat exposures in a single duty period.
- METHODS:** In this study, 15 healthy men, ages 20–50 yr, undertook 2 profiles of repeated hypobaric chamber decompression conducting activities representative of dispatcher duties. Phase 1 comprised two ascents to 25,000 ft (7620 m) for 60 and then 90 min. Phase 2 included three ascents first to 25,000 ft for 60 min, followed by two ascents to 22,000 ft (6706 m) for 90 min. Denitrogenation was undertaken at 15,000 ft (4572 m) with successive ascents separated by 1-h air breaks at ground level.
- RESULTS:** At 25,000 ft (7620 m), five cases of limb (knee) pain DCS developed, the earliest at 29 min. Additionally, multiple minor knee “niggles” occurred with activity but disappeared when seated at rest. No DCS and few niggles occurred at 22,000 ft (6706 m). Early, heavy, and sustained bubble loads were common at 25,000 ft, particularly in older subjects, but lighter and later loads followed repeat exposure, especially at 22,000 ft.
- DISCUSSION:** Parachutist dispatchers are at high risk of DCS at 25,000 ft (7620 m) commensurate with their heavy level of exertion. However, the potential exists for repeated safe ascents to 22,000 ft (6706 m), in the same duty period, if turn-around times breathing air at ground level are brief. Older dispatchers (>40 yr) with functional right-to-left (intracardiac or pulmonary) vascular shunts will be at risk of arterialization of microbubbles.
- KEYWORDS:** decompression sickness (DCS), high-altitude parachuting, parachutist dispatcher, venous gas emboli (VGE).

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In 2017, two Royal Air Force parachutist dispatchers on the same sortie, at 25,000 ft (7620 m), developed symptoms of severe decompression sickness (DCS). This prompted a safety investigation and subsequent evidence-based review of procedures, resulting in revised guidance on altitude exposure limitations and denitrogenation requirements for high altitude parachuting.¹⁷ The core features of these more conservative procedures are summarized in **Table I**. Of note, exposure to a jump altitude of 25,000 ft was limited to a single daily decompression lasting no longer than 60 min, following an obligatory 60-min denitrogenation period. This was required to be the final event of the day. Requirements were less restrictive for altitudes up to 22,000 ft (6706 m). The guidance was informed by risk estimation using the U.S. Air Force Research Laboratory (AFRL) Altitude DCS Risk Assessment Computer (ADRAC) model.²⁶ A “mild” level of physical activity was assumed, while

recognizing that the predicted risk of DCS, based on laboratory studies, would likely over-estimate the operational risk. The guidance was introduced in November 2018, highlighting that risk of DCS at provocative altitudes remained nonzero and emphasizing the importance of minimizing physical work and exposure duration.

The current research study was required to validate the effectiveness of the revised guidance, in terms of satisfactorily

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Table I. Royal Air Force Revised 2019 Guidance on Altitude Exposure Limits and Denitrogenation Requirements for High-Altitude Parachuting.

ALTITUDE (ft PA*)	DENITROGENATION TIME (min)	SINGLE EXPOSURE LIMIT (min)	CUMULATIVE EXPOSURE LIMIT (min)	PREDICTED DCS RISK (%)
>12,000 to 18,000	None	90	200	Up to 1–2%
>18,000 to 22,000	30	90	120	Up to 2%
>22,000 to 25,000	60	60	Single exposure only	Up to 7%

*PA = pressure altitude.

mitigating the residual risk of DCS in parachutist dispatchers, by conducting representative hypobaric chamber exposures. It was also considered that the more conservative approach might enable repeated exposures in the same duty period and that this should be explored at 25,000 ft and 22,000 ft.

Traditionally, repeated decompression to provocative altitudes has been regarded to increase risk of DCS. However, available recent data on risk with repeat exposure are limited and historical reports are contradictory.¹⁴ On the one hand, a second ascent to an altitude over 18,000 ft (5486 m) within 3 h has been stated to “greatly increase the chance of decompression sickness occurring, even if the first exposure was asymptomatic.”¹⁶ On the other hand, repeated brief exposures, interleaved with intermittent recompression for 1 h at ground level, clearly exhibit decreased risk compared with sustained dwell at altitude for an equivalent cumulative duration.²⁴ The current work adds to the existing body of knowledge on repeat exposure, evaluating longer dwells at altitude interleaved with similar recompression periods at ground level.

Thus, the aims of this study were to:

- Evaluate the risk of DCS specific to parachutist dispatchers (thereby requiring inclusion of representative levels of physical activity at altitude);
- Evaluate current UK exposure limitations for high-altitude parachuting;
- And assess the potential to conduct safely repeated high altitude ascents in a single duty period.

METHOD

Subjects

The study adhered to the principles of the Declaration of Helsinki. The research was funded by the UK Ministry of Defence (MOD) and the experimental protocol was approved in advance by the MOD Research Ethics Committee, an independent body constituted and operated in accordance with national and international guidelines.

Volunteers were briefed individually and provided written informed consent prior to medical screening. This encompassed all of the following: fitness for hypobaric decompression and hypoxia familiarization; factors predisposing to DCS; conditions that could be confused with DCS at altitude; suitability for magnetic resonance imaging (MRI); and conditions associated with white matter hyperintensities (WMH), including past history of concussive head injury with disturbance or loss of consciousness. A detailed physical examination was followed

by an electrocardiogram, urinalysis, and hemoglobin estimation. Smokers were excluded, as smoking is linked with increased severity of DCS symptoms,² besides influencing vascular endothelial function.³ Volunteers with a body mass index (BMI) greater than 30 were excluded, as excess weight and BMI may be associated with increased risk of DCS, particularly in men.^{1,32} A history of neurological or respiratory DCS was also exclusive, but past limb pain DCS was not.

Volunteers underwent outpatient contrast transthoracic echocardiography (CTTE) screening at the Royal Brompton Hospital, London, UK, to exclude right-to-left intracardiac (patent foramen ovale, PFO) or pulmonary vascular shunt. A trivial PFO observed only upon Valsalva maneuver was considered acceptable. A total of 28 volunteers were screened, with 9 (32%) showing evidence of a right-to-left shunt, comprising 6 with low grade PFOs at rest, 2 with a pulmonary shunt, and 1 with both. Thus, seven volunteers (25%) had a right-to-left intracardiac shunt at rest and three had a pulmonary shunt (11%). Thereafter, volunteers underwent Fluid Attenuated Inversion Recovery (FLAIR) MRI screening to exclude excess pre-existing subcortical WMH, using a 3.0 Tesla Philips Achieva MRI scanner (Koninklijke Philips N.V., Amsterdam, Netherlands) at the Sir Peter Mansfield Imaging Centre, University of Nottingham, UK. The threshold for study entry was defined as no more than five punctate subcortical lesions, in accordance with recent UK altitude studies.^{9,10} Thus, 2 volunteers, exhibiting 8 and 53 subcortical WMH, were excluded.

The resulting study cohort comprised 15 healthy civilian men, ages 18–50 yr, recruited by advertisement. This reflected the 95% male population of UK military parachutist dispatchers at the time of protocol submission. The single-sex cohort avoided possible confounds related to hormonal changes influencing DCS risk during the ovarian cycle,^{7,20,31} as well as sex differences in vascular endothelial function influencing biomarker responses (reported separately).¹⁵ The mean (\pm SD) age of participating subjects was 38 ± 11 yr. However, this misrepresents the age distribution of the cohort. By chance, the cohort comprised 5 young men in their third decade of life (mean 24 yr, range 20–28 yr) and 10 older men in their fifth decade (mean 46 yr, range 41–50 yr), enabling consideration of the influence of age between these subcohorts. Additional biometric data for the entire cohort (mean \pm SD) were: height = 1.82 ± 0.07 m; weight = 82.2 ± 8.4 kg; and body mass index = 24.9 ± 2.4 kg \cdot m⁻².

Equipment

Decompressions were conducted in the high-performance hypobaric chamber of QinetiQ's Altitude Research Facility at

MOD Boscombe Down, Wiltshire, UK, at an elevation of 406 ft (124 m) above mean sea level. Chamber occupants' 100% oxygen was supplied via Mk 17F pressure-demand breathing gas regulators (Honeywell Normalair-Garrett Ltd, Yeovil, UK). An Affinity 70C Ultrasound System (Koninklijke Philips N.V.) was used for 2D + Doppler echocardiography. Physiological monitoring employed noninvasive finger photoplethysmography (Finometer, Finapres Medical Systems, Amsterdam, Netherlands) for blood pressure, heart rate, and derived cardiovascular indices, and digital pulse oximetry (Kontron 7840, Kontron Instruments Ltd, Watford, UK) for peripheral oxygen saturation (S_pO_2). Breath-by-breath respired breathing gas composition was analyzed with an LR12000 mass spectrometer (Logan Research UK Ltd, Rochester, UK), calibrated repeatedly at ground level and altitude using various dry gas mixtures of known composition (BOC Gases Ltd, Guildford, UK). Data were recorded continuously using PC-based digital data acquisition systems (PowerLab with LabChart software, ADInstruments, Castle Hill, Australia). All pressure transducers, pneumotachographs, syringe volumes, flow meters, strain gauges, and temperature sensors employed were calibrated for each experiment.

Design

The study was conducted in two phases. Phase 1 (P1) experiments comprised two consecutive hypobaric chamber ascents to 25,000 ft (7620 m; P1A1 and P1A2), the first for 60 min and the second for 90 min, each preceded by 60 min of denitrogenation breathing 100% oxygen at 15,000 ft (4572 m). Phase 2 (P2) experiments comprised three consecutive ascents (P2A1, P2A2, and P2A3), the first of which was identical to P1A1. The subsequent two ascents were both to 22,000 ft (6706 m) for 90 min, each preceded by 30 min of denitrogenation at 15,000 ft. Pre-exposure denitrogenation is generally regarded as effective at altitudes up to 16,000 ft (4877 m),²⁷ and staged denitrogenation enables conservation of oxygen relative to denitrogenation at lower altitudes. The phase order was governed by the anticipation that the DCS risk associated with three ascents in Phase 2 would be greater than the two-ascent profile in Phase 1. Successive ascents were separated by breaks lasting 60–75 min breathing air at ground level. The altitude profiles for each Phase are shown in **Fig. 1**.

DCS endpoint criteria were managed conventionally,²⁵ except that it soon became clear that subjects could experience minor knee discomfort during activity that quickly settled once seated at rest. Such mild and transient symptoms ("niggles"), when present only during activity, were recorded but were not regarded as study endpoints, even if they recurred during subsequent bouts of activity. However, symptoms consistent with DCS immediately curtailed the experiment, including those that originated during activity and either persisted or progressed at rest, or any discomfort rated subjectively with a score greater than 4 out of 10. Intermittent symptoms recurring at rest over a 30-min period would also have prompted curtailment but did not occur. Symptoms that improved at rest but did not resolve entirely, prior to the next scheduled activity,

curtailed the experiment at that point. Thus, no subjects commenced a later spell of activity with residual discomfort from the previous one. The same medical officer, an experienced aerospace medicine practitioner, supervised all exposures to ensure consistency in diagnosis.

The response to decompression stress was evaluated using precordial 2D + Doppler echocardiography ("echo") conducted every 15 min at altitude. Apical four-chamber views were obtained to enable grading of venous gas emboli (VGE) bubble loads passing through the right side of the heart. Any left-sided bubbles would immediately curtail an experiment. A single experienced investigator graded all echos to avoid interrater inconsistency. Audible Doppler grades 1–4 were treated conventionally in accordance with the Spencer scale.²⁹ These were augmented by additional visual grades 4+, 4++, and 4+++ according to the subjective appearance of heavy VGE loads passing through the right heart, where 4+++ equates to visual obscuration of intracardiac anatomy (modified Spencer grade 5). Overall, this approach mirrored use of the Expanded Eftedal-Brubakk scale.²²

Subjects conducted activities throughout that were intended to represent the physical workload of a busy parachutist dispatcher. Activity at ground level reflected unloading and subsequent aircraft embarkation of 20 parachutes, each weighing 25 kg. During the hour of denitrogenation at 15,000 ft, six brief sets of activity were conducted, each representing movement along a "stick" of seated parachutists to monitor their pre-breathe status. Finally, at the dispatch altitude, activities simulated assisting heavily laden parachutists to stand before doing right- and left-sided, top-to-toe equipment checks on each in turn, followed by overarm movements to represent retrieval of static lines post-dispatch. Precise actions and repetitions are detailed in **Table II**. Limb movements were balanced to load both sides equally.

Procedure

Subjects underwent instruction on hazards associated with altitude exposure, were familiarized with the altitude chamber, breathing gas regulator, and oxygen mask, and experienced hypobaric hypoxia familiarization at 25,000 ft (7620 m). They were required not to have been exposed to hypobaric or hyperbaric environments (e.g., flying, diving, parachuting, mountaineering) in the 72 h prior to decompression, nor for 24 h afterwards. They were asked to avoid alcohol and unusually strenuous physical exertion for 48 h prior to decompression and 24 h afterwards. They were also asked to declare any illnesses and injuries that occurred during the research program. All subjects completed Phase 1 before undertaking Phase 2 some months later.

Subjects arrived at the chamber at 0800 h for brief medical confirmation of fitness to proceed (ability to clear ears and review of fitness since medical screening). They were reminded about DCS symptoms and to report any symptom at altitude as soon as it occurred. They were encouraged to maintain normal hydration and nutrition by drinking and eating freely whenever at ground level during the day.

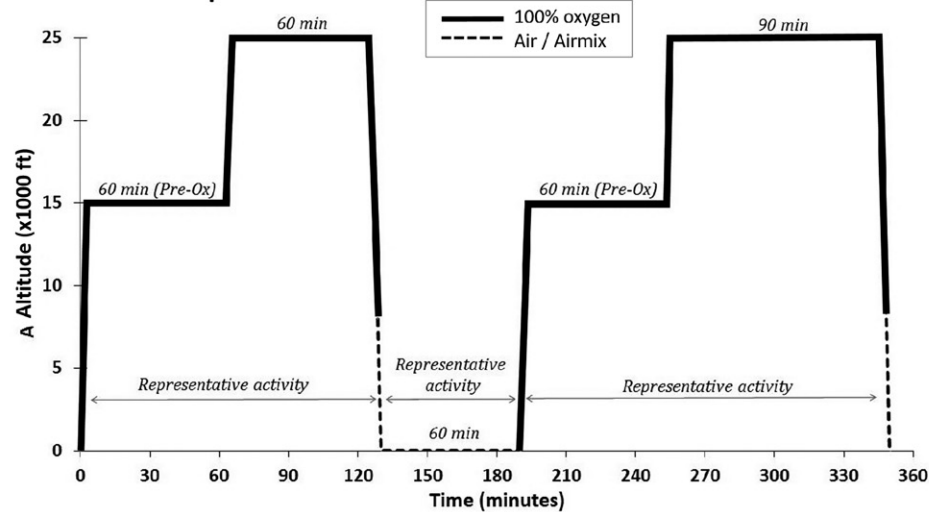
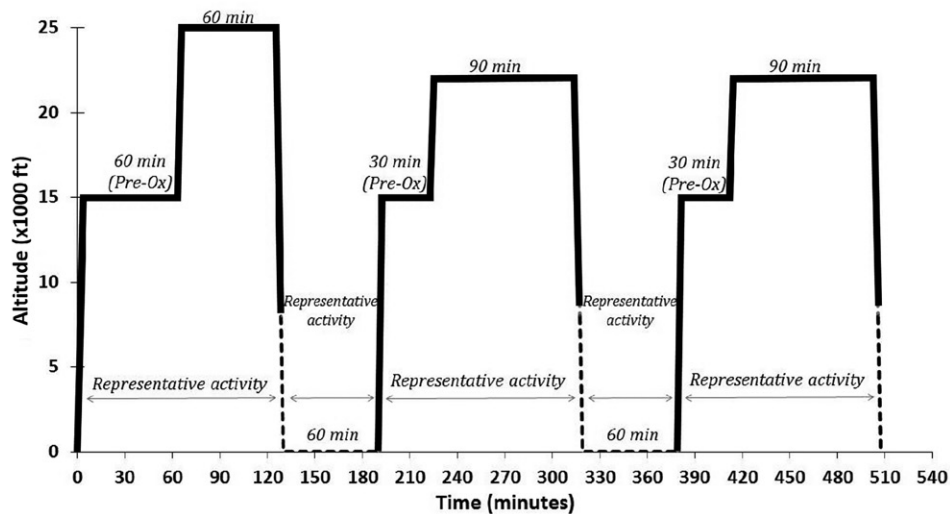
Phase 1: Two-ascent profile**Phase 2: Three-ascent profile**

Fig. 1. Ascent profiles for Phase 1 (two ascents) and Phase 2 (three ascents). All ascent and descent rates were $5000 \text{ ft} \cdot \text{min}^{-1}$. Oxygen breathing commenced at the start of each ascent. Subjects were switched from breathing 100% oxygen to breathing air at 8000 ft in the descent. Air breaks at ground level lasted a minimum of 60 min (as shown) and maximum 75 min, typically 65–70 min.

Subjects wore RAF-type aircrew t-shirts, flying coveralls, cloth type G hat and a P/Q oxygen mask, modified with a port to allow sampling of breathing gas composition by respiratory mass spectrometry. The aircrew t-shirt and coveralls were intentionally loose to facilitate echocardiography. Activity

conducted 25 min prior to ascent, and again 10 min prior, represented prepositioning and embarkation of parachutist equipment (Table II). The subject then sat in the altitude chamber, donned the hat and mask, and was instrumented with physiological monitoring equipment and the mass spectrometer

Table II. Representative Parachutist Dispatcher Activities Conducted at Different Stages of Simulated Flight.

TIMING	ACTIVITY / REPETITIONS	DURATION	FREQUENCY
At ground level prior to each ascent.	Lift 25 kg load from ground level to chest for 10 s, move it 5 m, then lower. Complete 20 repetitions.	5 min	Two bouts starting at 25 min and 10 min prior to ascent.
During denitrogenation at 15,000 ft.	Stand, squat with 'thumbs up', stand. Side step and repeat. Complete four repetitions, alternating sides.	1 min	At rate of six bouts per hour of denitrogenation.
At maximum altitude, every 15 min starting upon arrival at plateau.	Stand, strop 'pull up' x2 (right and left). Squat, stand, 1/4 turn, squat, stand. Repeat eight times. Followed by: Overarm "line retrieval" movements, moving carabiners along a rail. Eight repetitions (four right, four left).	4 min 1 min	Repeated every 15 min following echocardiography (four bouts per hour).

sampling line. The expiratory port of the mask was fitted with an expiratory hose and antiviral filter. This arrangement imposed no meaningful additional breathing resistance over use of the mask alone.

Accompanying investigators viewed a “slave” monitor displaying the subject’s echo image. Echos were conducted with the subject sitting still at rest but leaning slightly to the left, such that the left lateral chest wall was supported against a cushioned rail, to facilitate image acquisition. A practice echo at ground level allowed identification of optimal transducer placement. Each echo lasted about 5 min, with grading conducted first with the subject sitting quietly at rest, and then while gently moving all major articulations of each limb in turn to dislodge any gas emboli.

Initial ascents were identical in both Phases (P1A1 and P2A1) and generally commenced before 1000 h, with accompanying investigators completing an additional 30 min of denitrogenation beforehand. As ascent commenced, the subject’s inspiratory hose was connected to the breathing gas supply, delivering 100% oxygen with safety pressure. All ascents and descents were conducted at $5000 \text{ ft} \cdot \text{min}^{-1}$. Safety pressure was de-selected at 12,000 ft (3658 m) in the ascent, when the regulator applies safety pressure automatically. The subject could stand to conduct activity representing checks of parachutist pre-breathe (Table II), undertaking six such episodes before completion of 1 h at 15,000 ft (4572 m). Also, four echos were completed at 15,000 ft, occupying the last 5 min of each 15 min at that altitude.

After 60 min at 15,000 ft, the chamber ascended to 25,000 ft where it remained for 1 h, managed as four 15-min test epochs. Each epoch comprised 5 min of simulated dispatcher activity, representative of preparation and dispatch of eight parachutists (Table II), followed by 5 min of rest (minimizing limb movements), and a final 5 min echo. Thus, each echo completed one 15-min cycle of activity-rest-echo before beginning the next 15-min test epoch. After precisely 60 min at 25,000 ft, the chamber was recompressed to ground level, with 100% oxygen de-selected at 8000 ft (2438 m).

The subject spent the next hour breathing air at ground level. Echos were repeated upon arrival at ground level and at 15-min intervals until VGE were no longer seen. At 25 min prior to the next ascent, and again 10 min prior, further representative parachute preparation and embarkation activities were repeated (Table II).

In Phase 1, the second ascent (P1A2) mirrored the first, except that dwell time at 25,000 ft was extended to 90 min, divided into six 15-min test epochs. A second in-chamber investigator accompanied the subject for this ascent, and was replaced by a third part-way through the exposure, to ensure that no investigator remained at 25,000 ft for longer than 60 min. In Phase 2, denitrogenation at 15,000 ft in the second ascent (P2A2) was limited to 30-min duration with representative activity, followed by 90-min dwell at 22,000 ft (6706 m), again with six 15-min test epochs. Upon completion of the second ascent and second ground-level interval as before, a third ascent (P2A3) was conducted that was identical to the second.

A different in-chamber investigator accompanied the subject for each ascent to 22,000 ft in P2A2 and P2A3.

Ground-level dwell times between ascents never exceeded 75 min, and usually occupied 65–70 min. Following completion of the final ascent in each phase, subjects were monitored with 15-min echos until all VGE had disappeared, then remained under medical supervision for 1 h before being released from the facility. When an experiment was curtailed due to DCS, the chamber was recompressed immediately to ground level at $5000 \text{ ft} \cdot \text{min}^{-1}$ and the subject continued to breathe 100% oxygen at ground level for 1 h, having confirmed well-being and symptom resolution following recompression.²³ Thereafter, the ambulatory subject was monitored at the facility for a further hour. A subject experiencing DCS in Phase 1 remained eligible to return for Phase 2. No subjects or investigators experienced post-descent symptoms.

Apart from transient fluctuations with ascent and descent, ambient temperature in the chamber generally remained between 20–24 °C, minimizing any influence of temperature on either risk of DCS or vascular endothelial function.¹¹

Analysis

The statistical analysis of data from small-scale DCS studies is challenging and the utility of inferential analysis is limited. DCS symptom occurrences are reported descriptively. VGE loads are ranked according to a nonlinear ordinal scale that limits the utility of statistical analysis. Hence, VGE scores for each test epoch in consecutive ascents are presented graphically as “heat maps”, ranked by subject age, first as the maximum VGE grade from any single limb, and second as the total VGE score from all four limbs (maximum contribution score of 4 from any one limb). To evaluate the influence of age, mean maximum VGE scores and mean combined scores, were calculated for the entire cohort and for the younger and older subcohorts, employing a score of 5 for obscuration of cardiac anatomy. Survival plots were derived for the two phases, where survival was defined as continued absence of DCS plus absence of grade 4 VGE. A 2×2 contingency matrix was used to assess the relationship between grade 4 VGE and DCS occurrences using accumulated data from the three ascents to 25,000 ft (7620 m), evaluated statistically using Fisher’s Exact Test.

RESULTS

All 15 subjects completed Phase 1. Due to an unrelated injury while exercising, 1 later withdrew, leaving 14 subjects for Phase 2. One of these was withdrawn following his first ascent in Phase 2 after experiencing brief, self-limiting palpitations at ground level. He remained well but did not participate further.

There were 5 diagnoses of DCS at 25,000 ft (7620 m), all lower limb (knee) pain bends affecting older subjects, comprising 2 (of 15) in P1A1 (incidence 13%), at 29 and 37 min of exposure; 1 (of 13) in P1A2 (8%), at 60 min; and 2 (of 14) in P2A1 (14%), at 44 and 60 min. All involved knee

pain/discomfort that began during activity and persisted (static limb pain DCS) or worsened (progressive limb pain DCS) once seated at rest (Table III, serials 1–5). All cases improved with descent and had resolved upon arrival at ground level. All were managed breathing 100% oxygen for 1 h at ground level with no sequelae. One experienced DCS twice, i.e., in both P1A1 and P2A1, affecting different knees on each occasion (Table III, serials 2 and 4). There were no cases of DCS at 22,000 ft (6706 m) in Phase 2.

Additionally, six other subjects in Phase 1 experienced either mild knee pain/discomfort only during activity, being absent at rest, or trivial knee discomfort toward the end of an ascent (Table III, serials 6–11). These knee niggles varied in character but were either transient or trivial, and hence were not considered sufficient to allow diagnosis of DCS. Thus, 9 of 15 subjects in Phase 1 (60%) experienced a degree of knee discomfort at some point during the experiment, with 3 diagnosed as DCS and 6 with niggles. Similarly, 5 of 14 (36%) in Phase 2 experienced knee discomfort, 2 diagnosed with DCS and 3 with niggles.

No arterialized gas emboli were observed in the left cardiac chambers at any time. Individual VGE data for Phase 1 are shown in Fig. 2, ranked in order of increasing subject age, as the

maximum VGE grade observed in any limb, and as the cumulative VGE score from all four limbs (where each limb has a maximum permissible score of 4). Corresponding data for Phase 2 are shown in Fig. 3.

VGE loads generally preceded and became heaviest in limbs that developed knee pain or niggles, with rapid, early progression to very heavy loads, from multiple limbs, preceding all DCS occurrences during initial ascents to 25,000 ft in both phases. However, there were also heavy VGE loads in both phases that were never associated with symptoms (“silent bubbles”). Grade 4 VGE preceded all 5 occurrences of DCS; of the remaining 37 exposures, 18 generated grade 4 VGE and 19 did not (Fisher exact test value = 0.0532). While not quite achieving statistical significance, the data suggest that DCS was unlikely in the absence of substantial VGE loads. The positive predictive value of grade 4 VGE for subsequent DCS was poor, at only 0.217. This is low but would probably have increased with further DCS diagnoses had exposure duration extended beyond 60 min, since VGE were detected early and their intensity increased rapidly and remained high.⁴ On the other hand, the negative predictive value of absence of grade 4 VGE was 1.0 (100%), indicating ongoing absence of risk of DCS and consistent with expectation.⁵

Table III. Details of Limb Pain DCS Diagnoses and Minor Knee Symptoms (“Niggles”) Reported Only During Activity (Absent at Rest) or Regarded as Trivial.

SERIAL	PHASE	ASCENT	AGE	DCS OCCURRENCES
1	1	1	43	Discomfort right knee above/behind patella, grade 2-3/10, when seated after second session of activity. Persisted as dull ache during second echo. Static limb pain DCS diagnosed at 29 min. Discomfort eased below 15,000 ft in descent, absent at 13,500 ft.
2	1	1	48	Worsening left peripatellar knee pain, maximum grade 3/10 during third bout of activity. Eased to popliteal fossa discomfort 1/10 when at rest then progressed and worsened over next 2-3 min. Progressive limb pain DCS diagnosed at 37 min. Discomfort eased at 20,000 ft in descent, absent at 17,000 ft. (See also P2A1, serial 4)
3	1	2	48	Third activity, discomfort left tibial tuberosity. Absent at rest but recurred and worse with next activity, grade 4/10. Eased once sitting but persisted, grade 2-3/10, as band across insertion of patellar tendon. Diagnosed static limb pain DCS at 60 min that resolved with descent below 12,000 ft.
4	2	1	48	Mild, bilateral, activity-related ache in knees, R = L, during second and third activity sessions. At 37 min mild right knee discomfort, grade 2/10, then worsening right knee and hamstring pain, 4/10. Progressive limb pain DCS diagnosed at 44 min. Improved with descent from 18,000 ft through 16,500 ft, ‘hardly anything’ at 15,000 ft and absent at 11,000 ft. Note opposite side to knee bend in P1A1 (Serial 2).
5	2	1	50	Vague discomfort anterior right knee and near quadriceps insertion after fourth activity, with minimal discomfort once at rest, grade 1/10. Static by start of descent at 60 min. Diagnosed static right limb pain DCS. Improving by 15,000 ft in descent and resolved at 5000 ft.
SERIAL	PHASE	ASCENT	AGE	MINOR KNEE “NIGGLES”
6	1	1 & 2	26	P1A1, third activity, mild left knee pain at end of squats, nil at rest. Bilateral on final activity, fading over 1-2 min at rest. Recurred with activity in P1A2, medial aspect both patellae over joint line, but progressively easier with each activity session. Only during squats, nil at rest, absent at ground level.
7	1	1	28	Single ‘twinge’ right quadriceps insertion on final squat of last activity.
8	1	1	41	Vague sense of pressure, anterior left knee, last 3-4 min of P1A1; 0.5/10.
9	1	1	42	Progressive bilateral knee pain during last few squats of final activity. Around patellar tendon bilaterally plus left-sided mild anterior knee pain. Eased at rest. Did not recur on second ascent.
10	1	2	43	Mild left anterior knee pain, either side of patella, when standing from squat during last two periods of activity. Nil at rest
11	1	2	45	Sense of knee “fullness” bilaterally, only during squats for last two activity sessions. Nil at rest.
12	2	1	41	Right thigh/calf ache and pressure over patellar tendon, last two sessions of activity, grade 1/10. Eased at rest and no recurrence
13	2	1 & 3	43	Slight altered sensation left knee during final activity of P2A1, grade 1/10. Nil at rest. P2A3 final echo, mild aches both knees. Absent at GL.
14	2	2 & 3	48	Bilateral trivial ache over tibial tuberosities for last 30 min of P2A2 and P2A3. Eased with mobilization at ground level.

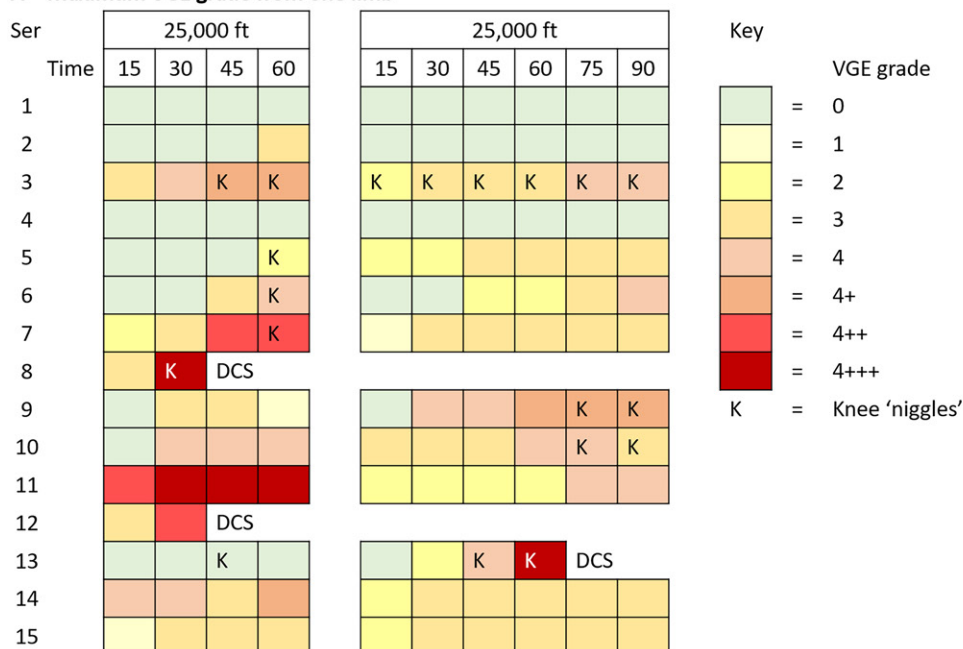
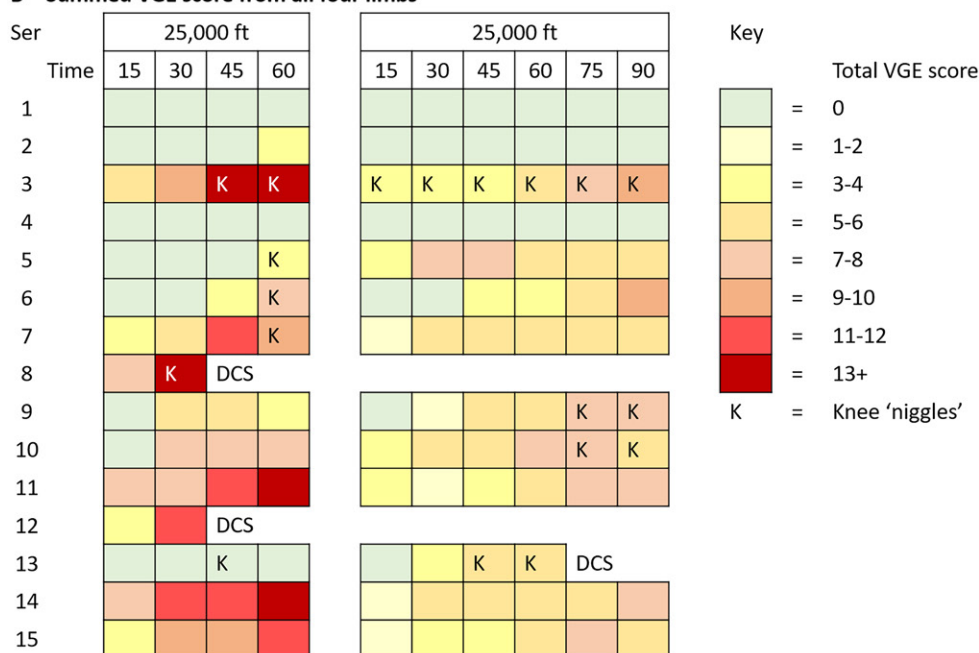
A – Maximum VGE grade from one limb**B – Summed VGE score from all four limbs**

Fig. 2. VGE data from Phase 1, ranked by age for 5 subjects in their 20s (serials 1–5) and 10 > 40 yr of age (serials 6–15): A. Maximum VGE grade from a single limb; B. Summed VGE score of all four limbs (each limb contributing a maximum score of 4).

Considering the influence of repeat exposure, contrary to expectation, individuals' VGE loads appeared slightly lighter and later in P1A2 compared to P1A1, except for 3 subjects who generated more VGE on the second ascent (Fig. 2, serials 5, 9, and 13). In Phase 2 (Fig. 3), far lighter and later VGE loads were evident at 22,000 ft in P2A2 relative to 25,000 ft in P2A1, with the clear exception of subject serial 13, a fit long-distance runner who was apparently reluctant to give up his nitrogen during the initial ascents in either phase. This is misleading. He may

have denitrogenated very effectively, without generating VGE, during his first ascent, but developed greater propensity toward bubble formation on the second ascent, following 1 h breathing air at ground level. Still fewer VGE were seen during P2A3 relative to P2A2. The overall impression from Figs. 2 and 3 is of a beneficial influence of prior altitude exposure to mitigate VGE loads during subsequent ascents.

Considering the influence of altitude, unsurprisingly, exposure to 22,000 ft in P2A2 was associated with lower maximum

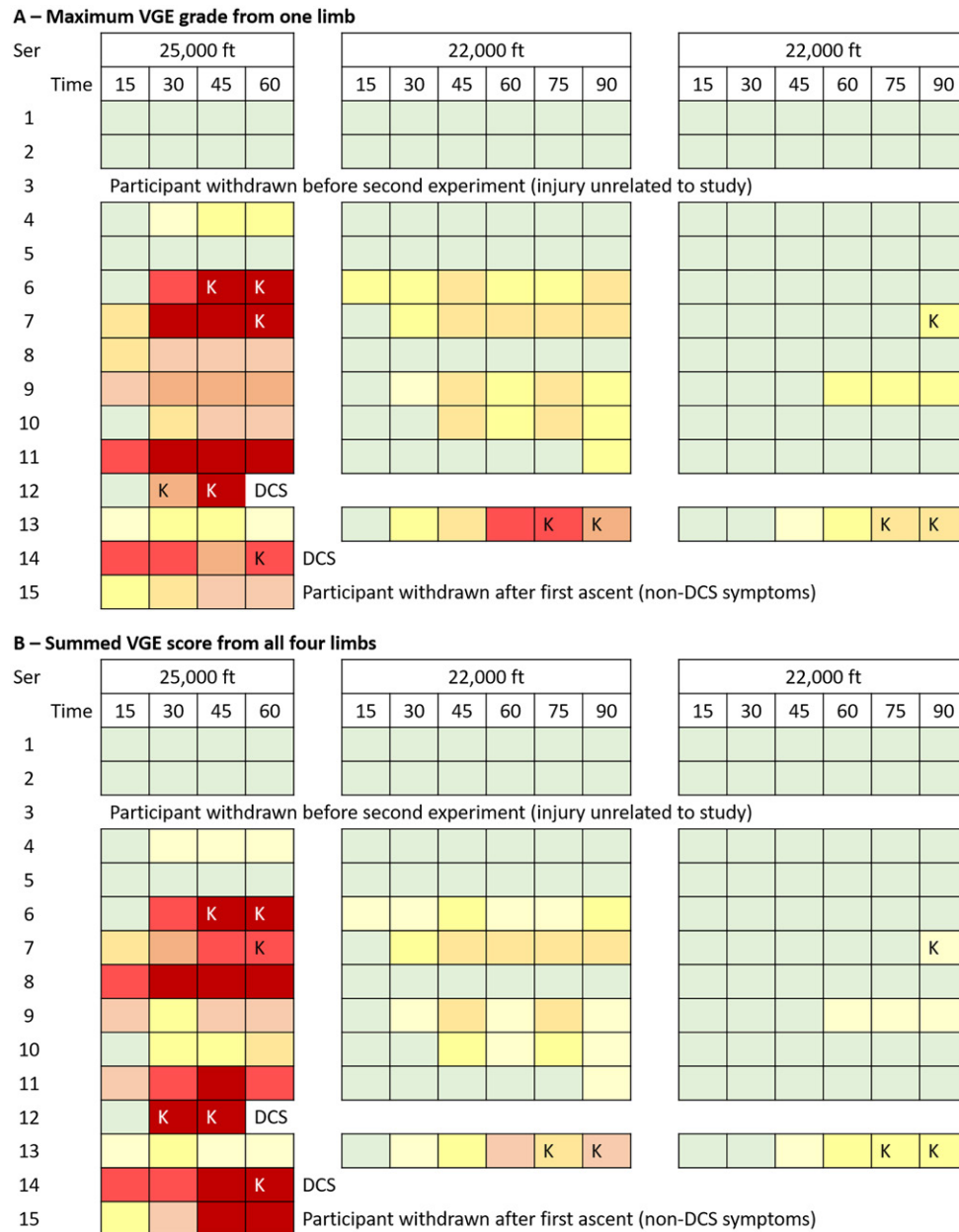


Fig. 3. VGE data from Phase 2, ranked by subject age: A. Maximum VGE grade from a single limb; B. Summed VGE score of all four limbs. For keys, see Fig 2.

grades of VGE from any single limb, and substantially lighter total VGE scores from all four limbs, than the second ascent to 25,000 ft in P1A2. For all ascents to 25,000 ft, in both phases, VGE loads tended to become heavier with longer duration exposure. This was far less evident during repeat ascents to 22,000 ft in Phase 2; the trend was still there, but bubble loads remained light. Survival curves were derived to enable further comparison of the response to decompression stress between phases and ascents, where “survival” was defined as continuing absence of both DCS and grade 4 VGE (**Fig. 4**). These illustrate well the relatively benign nature of repeat exposures to 22,000 ft in Phase 2 compared with the exposures to 25,000 ft. In contrast, survival during repeat exposure to 25,000 ft in Phase 1

(P1A2) appears little better than the initial exposures to 25,000 ft in either phase, with the slope of the survival curve only slightly shallower in P1A2.

Regarding age, younger volunteers (<30 yr) produced fewer and later VGE, and often none at all, whereas older subjects (>40 yr) produced early, heavy, and persistent bubble loads, from multiple limbs, notably during initial exposures in both phases. While such data are generally unsuitable for parametric analysis, in this instance average VGE scores very effectively highlight the gross disparity with age. **Fig. 5** shows mean maximum VGE grades and cumulative scores segregated into disparate younger (<30 yr) and older (>40 yr) subcohorts, the former exhibiting very few bubbles while the latter generate many.

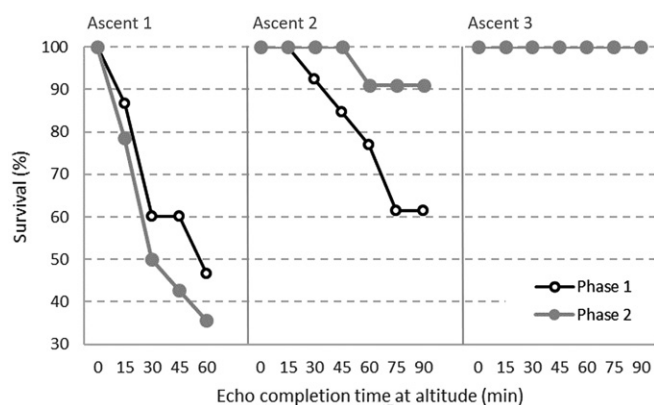


Fig. 4. Proportion of subjects commencing an ascent who “survive,” where survival is defined as continued absence of decompression sickness together with absence of grade 4 venous gas emboli.

DISCUSSION

In this study, the consistent 13–14% incidence of DCS within 1 h of initial exposure to 25,000 ft, following denitrogenation for 60 min, exceeds the 5% laboratory threshold suggested as a surrogate for acceptable operational risk.³³ Cumulative DCS incidence data from Phase 1 and Phase 2 are shown in **Fig. 6** relative to ADRAC predictions for various levels of exertion. The plots indicate an incidence of DCS associated with heavy exertion at altitude and suggest further cases should be expected if exposure is extended beyond 60 min. Levels of activity in this study are considered representative of military parachutist dispatchers, and the greater risk associated with heavy exertion would readily explain sporadic occurrences of severe DCS at high altitude. Any future use of the ADRAC model to predict DCS risk

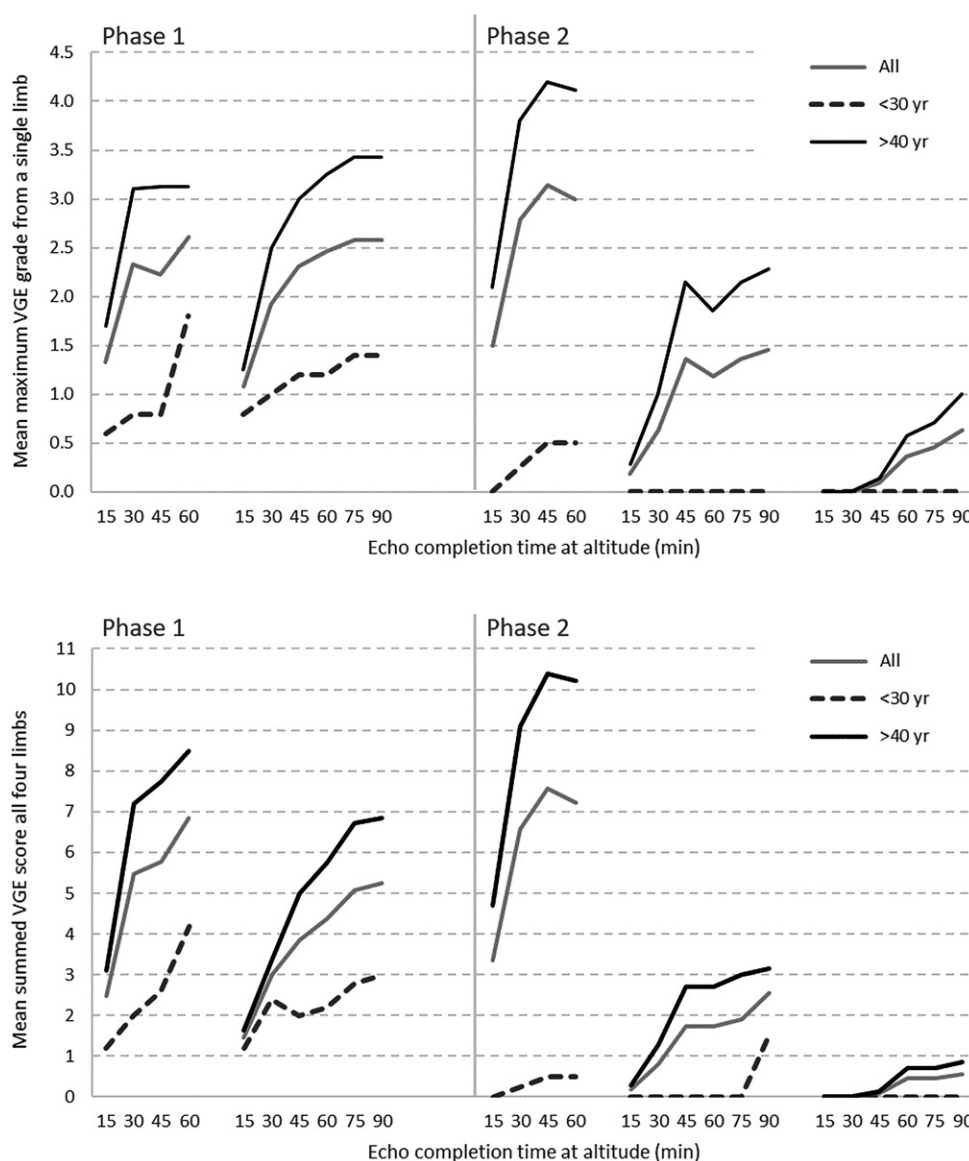


Fig. 5. Average VGE grades emphasize the disparity between younger (very few bubbles) and older (masses of bubbles) subcohorts. Upper graph: mean maximum VGE grade from a single limb (allowing maximum VGE score of 5 for obscuration of right heart anatomy). Lower graph: mean summed VGE scores from all four limbs. Data for both phases, for all subjects, and segregated into younger (<30 yr, $N = 5$) and older (>40 yr, $N = 10$) subcohorts.

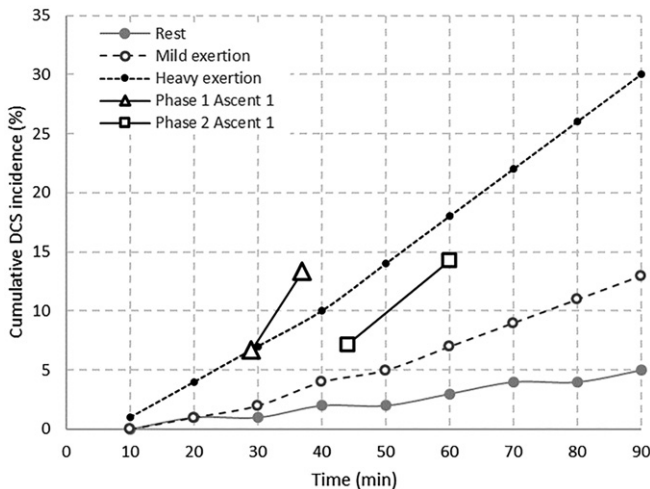


Fig. 6. Cumulative DCS incidence data for initial exposures to 25,000 ft in Phase 1 (triangles, $N = 15$) and Phase 2 (squares, $N = 14$), shown relative to predicted incidence at rest and with mild and heavy exertion, following denitrogenation for 60 min, using the US Air Force Altitude DCS Risk Assessment Computer (ADRAC) model. Phase 1 diagnoses at 29 and 37 min; Phase 2 diagnoses at 44 and 60 min. The data indicate that parachutist dispatcher activity is best represented to ADRAC as “heavy” exertion.

in dispatchers should represent their activities as “heavy” exertion, rather than “mild”.

While occurrences of knee niggles were mostly trivial, with some representing minor musculoskeletal symptoms, others were undoubtedly decompression-related. Some squats associated consistently with mild discomfort at altitude were symptom-free when repeated at ground level following planned recompression. This was most evident in the individual described at Table III, serial 6, who experienced repeated episodes of discomfort for the last two sessions of activity in P1A1 and all six bouts of activity in P1A2. In retrospect, this individual might reasonably have been diagnosed with limb bend DCS. In the event, diagnostic consistency was maintained throughout the study, whereby DCS was not diagnosed in the absence of symptoms at rest. In this context, reports of knee niggles reflect low-grade symptoms that were not at all troublesome and would probably go unreported or unnoticed if they occurred during flight, particularly during busy periods of activity.

Early, heavy VGE loads were generated from multiple limbs at 25,000 ft (7620 m), particularly in those over 40 yr of age (Figs. 2 and 3), suggesting a strong propensity toward development of DCS.¹⁹ While onset and progression of VGE were a little slower with repeat exposure in P1A2 (Figs. 3 and 4), some (older) individuals still produced heavy VGE loads on their second ascents, in one case preceding DCS (Fig. 2). Thus, the repeat exposure to 25,000 ft was not benign. However, the general appearances of Figs. 2 and 3 indicate decreasing VGE loads in response to repeated decompression stress, implying carry-over of protection from oxygen breathing during earlier ascents, as long as intervening air breaks on the ground are sufficiently brief. Depletion of bubble micronuclei may contribute in some subjects, but clearly not those who produce more VGE

the second time around. VGE loads during repeat ascents to 22,000 ft (6706 m) in Phase 2 were particularly light, suggesting that repeat ascents to 22,000 ft may be achievable with minimal additional risk providing turn-around times on the ground are brief (Figs. 3 and 4). It is therefore possible that prior exposure to 22,000 ft could mitigate the risk of DCS during subsequent ascent to 25,000 ft, with relevant independent variables likely to include the total time spent breathing 100% oxygen on earlier ascent and the duration of the air break between ascents, such that replenishment of nitrogen in the tissues remains incomplete. As in diving, the order of exposures would be important but, unlike repeated dives, to minimize the risk of altitude DCS, the ascent imposing greatest decompression stress should be conducted last while the gap between ascents should be minimized.

While denitrogenation at altitudes up to 16,000 ft (4877 m) may be effective, one individual in this study produced low grade VGE toward the end of the initial pre-breathes at 15,000 ft (4572 m), consistent with previous reports.³³ Any tissue bubbles present at 15,000 ft should be expected to enlarge upon further ascent to 25,000 ft, and, consistent with expectation, this subject progressed rapidly to grade 4 VGE soon after arrival at 25,000 ft. Staged denitrogenation for high altitude parachuting should be conducted at altitudes that avoid bubble generation.

Exercise promotes bubble formation, with subsequent bubble growth depending on the levels of exertion and decompression stress.¹³ In the current study, periods of physical exertion at the simulated jump altitude were relatively brief and of modest intensity but involved repetitive squats with knee flexion beyond 90° followed by full extension, generating the associated mechanical stresses around knee joints. This activity clearly predisposed to knee pain DCS and niggles, particularly affecting the soft tissues around the patella and patellar tendon. Susceptibility to knee bend DCS may be modifiable by adjusting the nature of the activities undertaken at the jump altitude to reduce the stress on knees especially. Nonetheless, other risk factors being equal, maintaining a similar general level of exertion is likely to retain a comparable residual risk of more severe (neurological or respiratory) DCS, even if sparing the knees. In contrast, none of the investigators accompanying subjects to 25,000 ft experienced either DCS or niggles, despite moving about the chamber, bending, kneeling, sitting, and standing at different times, and adopting a variety of postures to accomplish the echos. Their activities were less intensive and less repetitive, and their risk of DCS mitigated by the extra 30 min of denitrogenation.

Individuals >42 yr of age are at increased risk of DCS,³⁰ while age also influences propensity to generate heavy loads of VGE.⁶ Data from the current study are consistent with these findings. Older dispatchers undertaking physical work at altitude, including assisting parachutists to stand and adjusting their equipment, are likely to perform brief strains that transiently promote a right-to-left shunt across a PFO, if one is present. In older dispatchers particularly, the early appearance, and persistence at altitude, of heavy VGE loads must then incur some risk of arterialization of gas. While PFOs have attracted

considerable attention over the last three decades with regard to risk of right-to-left shunt and arterial embolization, pulmonary vascular shunts have been largely ignored but may be quite common. For both this study and a previous UK study of DCS,⁸ approximately 10% of volunteers screened by CTTE had evidence of an extra-alveolar pulmonary shunt allowing micro-bubbles to bypass the pulmonary filter. Transpulmonary arterio-venous passage of gas may also be promoted by exertion,¹² and arterialization of VGE may also occur through normal lungs at rest.²¹ Dispatchers are often experienced (older) parachute jump instructors who may be at increasing risk of arterialization over time, as their propensity to develop VGE increases with age.

With early recompression to ground level, minor symptoms of DCS may be expected to resolve completely during the descent. Traditionally, these cases have been managed breathing 100% oxygen at ground level for 2 h with a very low risk of symptom recurrence,^{18,28} although the evidence underpinning this regime is unclear.²³ In this laboratory, providing symptoms at altitude have resolved fully following descent, such cases have been managed by breathing oxygen for 1 h at ground level, followed by observation for another hour. No symptom recurrences or adverse sequelae have been observed.

The main limitation of the current work, common to all human studies of DCS risk, is the small subject sample, offset to some degree by the repeated measures approach. Other limitations are the absence of female subjects, which we intend to address specifically in a follow-on study, and a lack of diversity in this predominantly Caucasian sample. The subjects' health status is broadly representative of military parachutist dispatchers, except that volunteers are prescreened for right-to-left vascular shunts and pre-existing WMH. The unusual age distribution of volunteers was entirely fortuitous but enabled some consideration of the influence of age, directly relevant to the population of military dispatchers, which includes more experienced parachute jump instructors. On the other hand, unfortunately, data were unavailable for any individuals in their fourth decade (30–39 yr). Another limitation is loss of subjects due to withdrawal during and between experiments. Other constraints common to DCS studies include the challenges of consistently high-quality echocardiography, within and between both subjects and imagers, and associated difficulty with consistent bubble grading. Nonetheless, highly reproducible environmental exposures were achieved, minimizing sources of bias.

In summary, parachutist dispatchers are at considerable risk of DCS following aircraft depressurization owing to their high levels of physical activity. Prediction of dispatchers' risk of DCS using the USAF ADRAC model should assume that their level of exertion is "heavy" and interpret the associated risk accordingly. At 25,000 ft, older dispatchers (>40 yr) are liable to generate early, heavy, and sustained VGE loads, with attendant risk of arterialization of bubbles through any functional intracardiac or pulmonary right-to-left shunt. On the other hand, repeated high-altitude parachuting sorties at slightly more modest altitudes (22,000 ft) in the same duty period may be safe, with carryover benefit of oxygen breathing to successive sorties,

providing turn-around times breathing air at ground level are brief. Staged denitrogenation should be avoided at altitudes that risk bubble generation prior to final depressurization of the aircraft cabin.

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REFERENCES

- Allen TH, Maio DA, Bancroft RW. Body fat, denitrogenation and decompression sickness in men exercising after abrupt exposure to altitude. *Aerosp Med.* 1971; 42(5):518–524.
- Buch DA, El Moalem H, Dovenbarger JA, Ugucioni DM, Moon RE. Cigarette smoking and decompression illness severity: a retrospective study in recreational divers. *Aviat Space Environ Med.* 2003; 74:1271–1274.
- Celermajer DS, Sorensen KE, Georgakopoulos D, Bull C, Thomas O, et al. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. *Circulation.* 1993; 88(5):2149–2155.
- Conkin J, Foster PP, Powell MR, Waligora JM. Relationship of the time course of venous gas bubbles to altitude decompression illness. *Undersea Hyperb Med.* 1996; 23:141–149.
- Conkin J, Powell MR, Foster PP, Waligora JM. Information about venous gas emboli improves prediction of hypobaric decompression sickness. *Aviat Space Environ Med.* 1998; 69:8–16.
- Conkin J, Powell MR, Gernhardt ML. Age affects severity of venous gas emboli on decompression from 14.7 to 4.3 psia. *Aviat Space Environ Med.* 2003; 74:1142–1150.
- Conkin J. Gender and decompression sickness: a critical review and analysis. Houston (TX): NASA Johnson Space Center; November 2004. NASA Technical Report, NASA/TP-2004-213148.
- Connolly DM, Lee VM, D'Oyly TJ. Decompression sickness risk at 6553 m breathing two gas mixtures. *Aviat Space Environ Med.* 2010; 81(12):1069–1077.
- Connolly DM, Lee VM, Hodgkinson PD. White matter status of participants in altitude chamber research and training. *Aerosp Med Hum Perform.* 2018; 89(9):777–786.
- Connolly DM, Lupa HT. Prospective study of white matter health for an altitude chamber research program. *Aerosp Med Hum Perform.* 2021; 92(4):215–222.
- Donald AE, Charakida M, Falaschetti E, Lawlor DA, Halcox JP, et al. Determinants of vascular phenotype in a large childhood population: the Avon Longitudinal Study of Parents and Children (ALSPAC). *Eur Heart J.* 2010; 31(12):1502–1510.

12. Eldridge MW, Dempsey JA, Haverkamp HC, Lovering AT, Hokanson JS. Exercise-induced intrapulmonary arteriovenous shunting in healthy humans. *J Appl Physiol*. 2004; 97(3):797–805.
13. Foster PP, Feiveson AH, Boriek AM. Predicting time to decompression illness during exercise at altitude, based on formation and growth of bubbles. *Am J Physiol Regul Integr Comp Physiol*. 2000; 279(6): R2317–R2328.
14. Furr PA, Sears WJ. Physiological effects of repeated decompression and recent advances in decompression sickness research: a review. Warrendale (PA): Society of Automotive Engineers 1988. Technical Paper Series # 881702.
15. Hashimoto M, Akishita M, Eto M, Ishikawa M, Kozaki K, et al. Modulation of endothelium-dependent flow-mediated dilatation of the brachial artery by sex and menstrual cycle. *Circulation*. 1995; 92(12):3431–3435.
16. Heimbach RD, Sheffield PJ. Decompression sickness and pulmonary overpressure accidents. In: DeHart RL, editor. *Fundamentals of Aerospace Medicine*, Chapter 7. Philadelphia (PA): Lea and Febiger; 1985:139.
17. Hodgkinson PD, Green NDC. Evidence based revision of pre-oxygenation and altitude exposure guidelines for high altitude parachuting. *Aerosp Med Hum Perform*. 2019; 90(3):189.
18. Krause KM, Pilmanis AA. The effectiveness of ground level oxygen treatment for altitude decompression sickness in human research subjects. *Aviat Space Environ Med*. 2000; 71:115–118.
19. Kumar KV, Calkins DS, Waligora JM, Gilbert JH III, Powell MR. Time to detection of circulating microbubbles as a risk factor for symptoms of altitude decompression sickness. *Aviat Space Environ Med*. 1992; 63:961–964.
20. Lee V, St Leger Dowse M, Edge C, Gunby A, Bryson P. Decompression sickness in women: a possible relationship with the menstrual cycle. *Aviat Space Environ Med*. 2003; 74:1177–1182.
21. Ljubkovic M, Marinovic J, Obad A, Breskovic T, Gaustad SE, Dujic Z. High incidence of venous and arterial gas emboli at rest after trimix diving without protocol violations. *J Appl Physiol*. 2010; 109(6): 1670–1674.
22. Møllerløkken A, Blogg SL, Doolette DJ, Nishi RY, Pollock NW. Consensus guidelines for the use of ultrasound for diving research. *Diving Hyperb Med*. 2016; 46(1):26–32.
23. Muehlberger PM, Pilmanis AA, Webb JT, Olson JE. Altitude decompression sickness symptom resolution during descent to ground level. *Aviat Space Environ Med*. 2004; 75:496–499.
24. Pilmanis AA, Webb JT, Kannan N, Balldin U. The effect of repeated altitude exposures on the incidence of decompression sickness. *Aviat Space Environ Med*. 2002; 73:525–531.
25. Pilmanis AA, Webb JT, Kamian N, Balldin UI. The risk of altitude decompression sickness at 12,000 m and the effect of ascent rate. *Aviat Space Environ Med*. 2003; 74:1052–1057.
26. Pilmanis AA, Petropoulos LJ, Kannan N, Webb JT. Decompression sickness risk model: development and validation by 150 prospective hypobaric exposures. *Aviat Space Environ Med*. 2004; 75:749–759.
27. Pilmanis AA, Webb JT, Balldin U. The impact of high levels of nitrogen in the breathing gas and in-flight denitrogenation on the risk of decompression sickness (DCS) during simulated altitude exposure. Wright-Patterson AFB (OH): U.S. Air Force Research Laboratory Report; April 2005. Report No.: AFRL-HE-BR-TR-2005-0036.
28. Rudge FW. The role of ground level oxygen in the treatment of altitude chamber decompression sickness. *Aviat Space Environ Med*. 1992; 63: 1102–1105.
29. Spencer MP. Decompression limits for compressed air determined by ultrasonically detected blood bubbles. *J Appl Physiol*. 1976; 40(2):229–235.
30. Sulaiman ZM, Pilmanis AA, O'Connor RB. Relationship between age and susceptibility to altitude decompression sickness. *Aviat Space Environ Med*. 1997; 68:695–698.
31. Webb JT, Kannan N, Pilmanis AA. Gender not a factor for altitude decompression sickness risk. *Aviat Space Environ Med*. 2003; 74:2–10.
32. Webb JT, Pilmanis AA, Balldin UI, Fischer JR. Altitude decompression sickness susceptibility: influence of anthropometric and physiologic variables. *Aviat Space Environ Med*. 2005; 76:547–551.
33. Webb JT, Pilmanis AA, O'Connor RB. An abrupt zero-preoxygenation altitude threshold for decompression sickness symptoms. *Aviat Space Environ Med*. 1998; 69:335–340.