Nitrogen Washout and Venous Gas Emboli During Sustained vs. Discontinuous High-Altitude Exposures

Rickard Ånell; Mikael Grönkvist; Ola Eiken; Mikael Gennser

INTRODUCTION: The frequency of long-duration, high-altitude missions with fighter aircraft is increasing, which may increase the incidence of decompression sickness (DCS). The aim of the present study was to compare decompression stress during simulated sustained high-altitude flying vs. high-altitude flying interrupted by periods of moderate or marked cabin pressure increase.

METHODS: The level of venous gas emboli (VGE) was assessed from cardiac ultrasound images using the 5-degree Eftedal-Brubakk scale. Nitrogen washout/uptake was measured using a closed-circuit rebreather. Eight men were investigated in three conditions: one 80-min continuous exposure to a simulated cabin altitude of A) 24,000 ft, or four 20-min exposures to 24,000 ft interspersed by three 20-min intervals at B) 20,000 ft or C) 900 ft.

RESULTS: A and B induced marked and persistent VGE, with peak bubble scores of [median (range)]: A: 2.5 (1–3); B: 3.5 (2–4). Peak VGE score was less in C [1.0 (1–2), $P < 0.01$]. Condition A exhibited an initially high and exponentially decaying rate of nitrogen washout. In C the washout rate was similar in each period at 24,000 ft, and the nitrogen uptake rate was similar during each 900-ft exposure. B exhibited nitrogen washout during each period at 24,000 ft and the initial period at 20,000 ft, but on average no washout or uptake during the last period at 20,000 ft.

DISCUSSION: Intermittent reductions of cabin altitude from 24,000 to 20,000 ft do not appear to alleviate the DCS risk, presumably because the pressure increase is not sufficient to eliminate VGE. The nitrogen washout/uptake rate did not reflect DCS risk in the present exposures.

KEYWORDS: decompression sickness risk, fighter aircraft, gas bubble formation, hypobaric DCS, in-flight refueling, nitrogen elimination, repeated altitude decompression.

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This study concerns decompression stress during simulated long-duration high-altitude flying in fighter aircraft, with special reference to effects of intermittent excursions to lower altitudes. Before the introduction of pressurized aircraft cabins, altitude decompression sickness (henceforth DCS denotes altitude decompression sickness) was a recognized risk in different types of high-altitude flying.[15] Even to date, cabin pressure in military aircraft is commonly kept low during high-altitude flying because, during military missions, the risks of DCS and hypoxia must be weighed against the risk of pulmonary barotrauma in case of rapid/explosive cabin decompression.[4,13,19] The risk of DCS depends not only on the cabin altitude per se, but also on the duration of altitude exposure and whether the pilot has been prebreathing 100% oxygen prior to the exposure, or is breathing oxygen during the altitude soujourn.[28] The threshold altitude for DCS in individuals not prebreathing oxygen vary between 18,000 and 25,000 ft (5486 and 7620 m) in different reports,[18,22,29] with a reported 5% DCS incidence after ≥4 h at 20,500 ft (6248 m) during oxygen breathing.[29] For tactical reasons, and since modern military aircraft commonly possess in-flight refueling capacity, demands for long-duration, high-altitude missions with fighter aircraft

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are increasing. Therefore, and because it has recently been found that U2 pilots who have experienced neurological DCS exhibit high incidence of subcortical brain lesions,[16] DCS warrants renewed interest. For instance, it is anticipated that fighter-aircraft missions lasting several hours may be undertaken at cabin altitudes between 22,000 and 25,000 ft (6706 and 7620 m), with intermittent refueling excursions to lower altitudes.

Information is limited and inconclusive as regards the influence of recurring high-altitude exposures on DCS risk, ranging from increased[9,20,22] to decreased[25] risk with repeated compared to single exposures. However, most of the references cited here concern single-altitude exposures repeated daily with a minimum sea-level interval of 15 to 17 h. Apart from the study by Pilmanis et al.,[25] very little information exists in the literature regarding the effects of a pattern of repeated changes in altitudes during a single high-altitude exposure. We reasoned that the degree of compression between altitude exposures might affect the evolution of gas bubbles in blood and other tissues and, therefore, also the risk of DCS.[12] Conceivably, excursions from high to moderate altitude while breathing gas containing a considerable fraction of nitrogen (N_2) may not generate sufficient pressure increments to crush gas bubbles formed at high altitude, but rather increase N_2 uptake and, therefore, facilitate bubble growth upon the next high-altitude exposure, although excursions to near sea level will eliminate gas bubbles formed at altitude.

Accordingly, the aim was to compare indices of decompression stress, in terms of venous gas emboli (VGE) and pulmonary washout/uptake of N_2 in three conditions: A) a continuous 80-min exposure to a simulated altitude of 24,000 ft (7315 m); B) four 20-min exposures to 24,000 ft interspersed by three 20-min intervals at 20,000 ft (6096 m); and C) four 20-min exposures to 24,000 ft interspersed by three 20-min intervals at 900 ft (274 m). The 20,000-ft level constitutes a possible cabin altitude for refueling. We hypothesized that VGE formation would be less, despite the fact that the net N_2 washout would be smaller in condition C than in the other two conditions, and that VGE formation would be similar in conditions A and B.

METHODS

Subjects

Eight healthy men participated as test subjects. Their mean (range) age and body mass index (BMI) were 43.7 (32–52) yr and 26.4 (23.6–32.5) $kg \cdot m^{-2}$, respectively. The subjects, who were recruited among fighter pilots ($N = 2$), divers ($N = 5$), and military high-altitude parachuters ($N = 1$), were all familiar with pressure-chamber exposures and well informed regarding DCS, although none of them had any personal history of DCS. All subjects were nonsmokers and had passed their annual physical and medical assessment prior to the study. The subjects gave their written, informed consent prior to enrolling, and were aware that they were free to prematurely terminate any single experiment, or to withdraw from the study at any time. The study was approved by the regional Human Ethics Committee in Stockholm, Sweden (approval no: 2016/480-31/2), and conformed to the Helsinki Declaration.

Equipment

Four-chamber cardiac images were obtained using a Philips CX50 Diagnostic Ultrasound System with a 1–5 MHz S5-1 linear array transducer (Philips Ultrasound Bothel, WA, USA). Cardiac impedance measurements were performed using a Physioflow PF07 Enduro (Manatec Biomedical, Paris, France). Capillary oxyhemoglobin saturation was measured using a Radical 7 monitor (Masimo Set, Rainbow, CA, USA) with a finger probe. A Poseidon Se7en rebreather was used for N_2 uptake and washout measurements (Poseidon Diving Systems AB, Göteborg, Sweden). A soda lime scrubber removed CO_2 in the breathing circuit (SofnoDive 797, Molecular Products Inc., Boulder, CO, USA). Surveillance of the subject and the chamber assistant was performed throughout the hypobaric trials with an audio/video system (JVC MI-5000, Victorcompany, Tokyo, Japan).

Procedures

The experiments were performed in the hypobaric chamber at the Royal Institute of Technology in Stockholm, Sweden. Prior to each experiment, the subject underwent a medical check-up to ensure that he was "fit to fly." Thereafter, the subject, who was dressed in shorts and gym shoes, was instrumented with pregelled electrodes for electrocardiography and impedance cardiography. He then performed 150 knee squats in 10 min to create a normalized baseline for venous bubble nuclei,[10] after which he was positioned on his left side in a horizontal decubitus position on a gurney inside the hypobaric chamber.

VGE were visualized from four-chamber cardiac ultrasound images. Prevalence of VGE was estimated from the cardiac images using the Eftedal-Brubakk 5-degree scale (0 = no visible bubbles, 1 = occasional bubbles, 2 = at least one bubble every fourth heartbeat, 3 = at least one bubble every heartbeat, 4 = at least one bubble/cm^2).[23]

Heart rate (HR) was derived from electrocardiography recordings with the electrodes in a precordial one-lead position. Cardiac stroke volume and output (CO) were determined using an electrical impedance cardiography system. Six impedance electrodes were placed at the base of the neck and the thorax. The impedance calibration procedure recommended by the manufacturer was conducted before each experiment, while the subject was resting supine. Capillary oxyhemoglobin saturation (S_pO_2) was monitored by use of a pulse oximeter, with the sensor placed on the left index finger.

During each experiment, the subject was wearing a nose clip and breathing via a mouthpiece. Whole body washout and uptake of N_2 was assessed continuously using a system described in detail elsewhere,[26] comprising a modified closed-circuit electronic rebreather in combination with custom-made computer software. Briefly, the system measures oxygen (O_2) partial pressure, temperature, and moisture in four different parts of the closed circuit. The elimination and uptake of N_2 was calculated

by measurement of total gas volume in the closed rebreather system, subtracting the calculated volumes of water vapor and O_2. Carbon dioxide (CO_2) was removed from the system by a soda lime scrubber. The rebreather system is a closed loop that was prefilled with a known volume of gas mixture with 21 kPa of O_2 before the subject exhaled to functional residual capacity and inhaled the prefilled gas from the rebreather. The system measured the O_2 content in the gas and the rebreather automatically injected additional O_2 on the inhalation side over time to keep a constant O_2 partial pressure of 21 kPa at all altitudes. The O_2 sensors (Poseidon Diving System PSR-11-39-MD) were calibrated before each experiment. A new scrubber was inserted in the breathing loop before each experiment.

Each subject was investigated in three different conditions (**Fig. 1**):

A) One 80-min continuous exposure to a simulated altitude of 24,000 ft
B) Four 20-min exposures to 24,000 ft interspersed by three 20-min intervals at 20,000 ft
C) Four 20-min exposures to 24,000 ft interspersed by three 20-min intervals at 900 ft

The three trials were conducted in alternate order and, for the individual subject, separated by ≥72 h. The rate of ascent and descent was 5000 ft · min^{-1} (1524 m · min^{-1}). During the initial ascent and final descent (from and to the 900-ft level), the subject was breathing ambient (chamber) air at simulated altitudes below 10,000 ft (3048 m), although to maintain normal O_2 saturation at altitudes of 10,000–24,000 ft, he was, during altitude transitions in this span, breathing a premixed gas containing 46.5% O_2 and 53.5% N_2 via an oro-nasal mask (VMASK, Hans Rudolph Inc., Shawnee, KS, USA) provided with a constant flow from a bottle of compressed gas. Once at 24,000 ft, after the initial ascent, the subject made an expiration to functional residual capacity and was then connected to the rebreather, which was prefilled with a known volume (3–4 L) of normoxic breathing gas (fractions of O_2= 52.5% and N_2=47.5%, i.e., Po_2 = 21 kPa, air temperature = 20°C). In the A and B trials, the subject continued to breathe via the rebreather throughout the altitude exposures. In those trials, normoxic breathing gases for 20,000 ft and 24,000 ft, respectively, were used to fill the rebreather in instances when the Boyle decompression/compression or N_2 washout/uptake made it necessary to adjust the bellows volume. During the C trial, the aforementioned rebreathing procedure was iterated during each 20-min period at 24,000 ft and, during the ascents and descents between 10,000 ft and 24,000 ft, the subject breathed the premixed gas (46.5% O_2) via an oro-nasal mask as described above, and chamber air for the initial ascent and final descent between 10,000 ft and 900 ft.

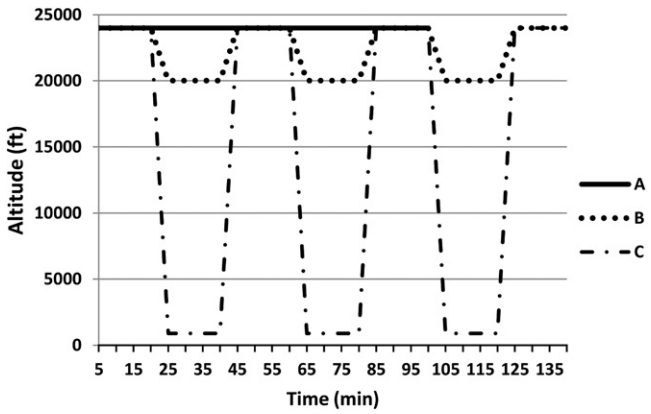

Fig. 1. Time-altitude profiles in conditions A, B, and C.

Every 15 min throughout each trial, the subject performed three knee bends while in the left-side horizontal decubitus position. VGE prevalence was assessed every 5 min and, in connection with this, the subject was asked for any symptoms and checked for signs of DCS. Levels of HR, stroke volume, CO, S_pO_2, and N_2 balance were measured/estimated continuously throughout each experiment.

An experimenter (medical doctor), accompanying the subject in the hypobaric chamber, performed the VGE and DCS assessments. End-point criteria for the altitude exposures were a persistent VGE score of 4 and/or symptoms/signs of DCS. In the C trial, another experimenter was managing the shifts of the subjects breathing gas from the rebreather to the mask and vice versa. Both inside experimenters were breathing 100% O_2 via a full-face diving mask (Atmosphere, Poseidon Diving Systems AB) and a demand valve during, and for 1 h preceding, each experiment. All experiments were surveilled continuously via a closed-circuit video/audio system by a medical doctor and an experimenter, both positioned outside the chamber.

Statistical Analyses

VGE scores are ordinal data. Thus, nonparametric tests should be used to assess the statistical significance of differences between the VGE scores. However, when more than two groups are compared, the most often used test, Friedman's test, has two major drawbacks. It is basically a sign test, which means that it has a relatively low power. The other problem is that there are no proper nonparametric post hoc tests. Therefore, a statistical procedure proposed by Baguley[2] was used. The VGE data for all three series were rank transformed and the ranks were tested using one-way repeated measures ANOVA; post hoc tests were carried out using the Tukey HSD test. The alpha level of significance was set a priori at 0.05.

For the N_2 exchange data, a single factor ANOVA was computed for each series and 95% confidence intervals for the average exchange rate were calculated for each 20-min time period. For the HR and CO data, a repeated measure ANOVA was used.

RESULTS

In all three conditions, the rates of ascent and descent were maintained at stipulated values, and in all experiments, chamber pressure was reached within 30 s from the expected time. At altitude, the subjects were connected to the rebreather and the data collection started in less than 3 min (mean: 1.5 min, range:

0.5–2.5 min). All but one subject completed all three experimental trials. One subject experienced knee pain after the last decompression to 24,000 ft during condition B; the symptoms were regarded as DCS related and the subject was subsequently given O_2 and recompressed to the surface. The pain disappeared promptly during recompression while returning to sea-level pressure. The overall incidence of DCS was 3.3%. This includes complete pretrial exposures.

VGEs were observed in the right ventricle in all subjects during conditions A and B, and in six of eight subjects during condition C. In series A, there was a continuous increase in VGE scores with time both during rest and in conjunction with the knee bends (**Fig. 2**). In series B, most subjects showed only small VGE scores during the first period at 24,000 and 20,000 ft, respectively. However, most of the subjects showed a gradual increase in VGE scores during the following periods at 24,000 ft and increased scores were also noted during the last period at 20,000 ft (Fig. 2).

One subject exhibited a different pattern in series B, with a high VGE score (EB 3) during the first knee bend at 24,000 ft, and maintained high VGE scores throughout the first period at 20,000 ft, but then exhibited a gradual decline in VGE scores and, during the last period at 24,000 ft, no bubbles were observed at rest. In series C, there were no bubbles observed in any of the subjects at the 900-ft level, although in several subjects, some occasional bubbles showed up at altitude, mostly during knee bends. (Fig. 2).

Comparing the median peak VGE scores both at rest and in conjunction with knee-bend provocations revealed a significant difference between the three conditions (**Table I**). There was also a significant difference between series C and series A and B, respectively, regarding the last VGE scores, but not between series A and series B (Fig. 2). No arterial bubbles were observed in any of the exposures.

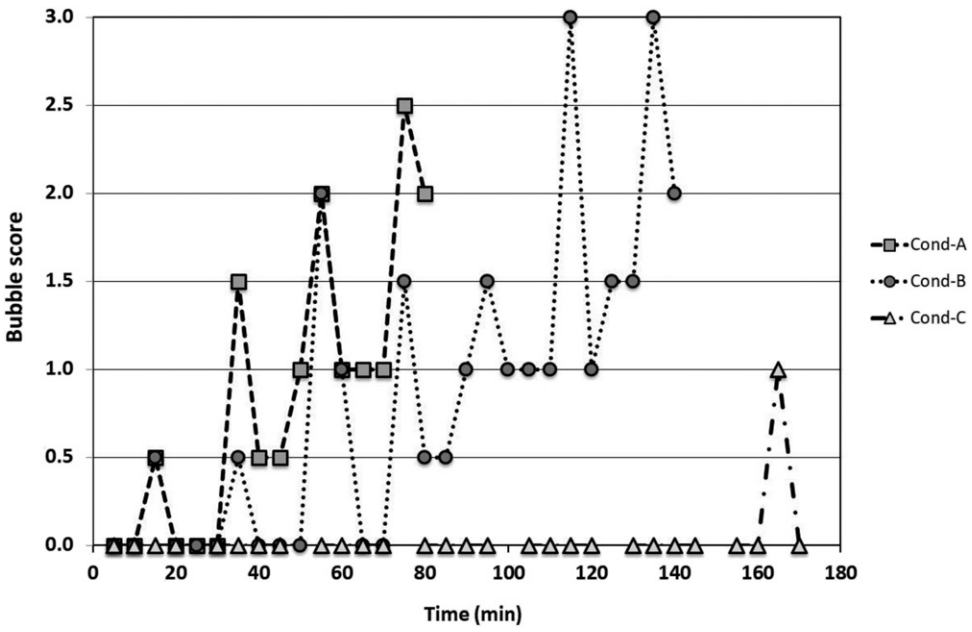

Fig. 2. VGE scores at rest and after knee bends in conditions A–C. Values are medians, $N = 8$.

N_2 washout was measured during all conditions. A gradually decreasing elimination rate was observed over time in condition A (**Fig. 3**). The average elimination rate (R) fell according to the equation $R = 15.45\exp(-0.029\ t)$, which gives a whole body half-time for N_2 washout of 24 min.

Due to technical problems during condition B, the initial washout curves (min 0–20) for three subjects could not be used. N_2 elimination was observed in the remainder of the subjects during the 0–20 min period and also during the second exposure at 24,000 ft. This was also the case for the first exposures at 20,000 ft. During the last exposure at 20,000 ft in condition B, no washout was found (average N_2 washout rate: 0.3 ± 8.3 mL · min^{-1}). However, more careful analysis of the N_2 movement showed one subject with a very high washout rate of 19.4 mL · min^{-1}. This was the subject who started to complain of knee pain. He had VGE scores between EB 3 and EB 4 during this period. Five of the seven other subjects showed an N_2 uptake during this period at 20,000 ft and the remaining two subjects had only very slow washout. When the data for the subject who developed DCS was excluded, the average N_2 exchange showed a washout of -2.5 ± 2.9 mL · min^{-1} (confidence interval: -5.1– 0.21 mL · min^{-1}) (**Fig. 4**), i.e., a slight gas uptake. The following period at 24,000 ft showed a significant N_2 washout (5.6 ± 3.4 mL · min^{-1}, confidence interval: 3.0–8.3 mL · min^{-1}).

The washout rate during the first 20 min in condition A (11.3 ± 3.6 mL · min^{-1}) was similar to the washout during the initial period at 24,000 ft in condition C (10.1 ± 4.1 mL · min^{-1}). The washout rate during the following three periods at 24,000 ft during condition C was only slightly less (8.1 ± 2.9 mL · min^{-1}). The average rate of N_2 uptake during the periods at 900 ft during condition C was 10.0 ± 3.0 mL · min^{-1} (**Fig. 5**).

In all conditions, HR decreased during the course of the experiment [$F(1,6) = 64,7$; $P < 0.001$]; in A from 72 ± 11 bpm to 63 ± 8 bpm, in B from 70 ± 10 bpm to 58 ± 7 bpm, and in C from 78 ± 14 bpm to 55 ± 8 bpm. Likewise, CO decreased during the course of each experiment [$F(1,6) = 50.0$; $P < 0.001$], with a relative reduction in A by $17 \pm 12\%$, in B by $20 \pm 9\%$, and in C by $31 \pm 12\%$.

DISCUSSION

Present results demonstrated that the incidence of VGE during an 80-min exposure to a simulated altitude of 24,000 ft (7315 m) was substantially reduced by intermittent 20-min excursions to 900 ft (274 m), but was, if anything, increased by 20-min excursions to 20,000 ft (6096 m). As regards

Table I. Statistical Evaluation of VGE During Conditions A–C.

	MEDIAN PEAK VALUE AT REST	MEDIAN PEAK VALUE (REST AND KNEE BENDS)	MEDIAN LAST VALUE
Condition A	2	2.5	2
Condition B	2.5	3.5	2.5
Condition C	0	1	0
ANOVA	$F(2,14) = 15.15; P < 0.001$	$F(2,14) = 26.6; P < 0.001$	$F(2,14) = 13.71; P < 0.001$
A/B (Tukey HSD)	n.s.	$P < 0.01$	n.s.
A/C (Tukey HSD)	$P < 0.01$	$P < 0.01$	$P < 0.01$
B/C (Tukey HSD)	$P < 0.01$	$P < 0.01$	$P < 0.01$

n.s. not significant.

N_2 washout/uptake, the three conditions exhibited different patterns, with an initially high and exponentially decaying rate of N_2 washout during continuous exposure to 24,000 ft, and alternating washout and uptake of similar magnitudes at 24,000 and 900 ft, respectively, in condition C. Condition B, by contrast, showed N_2 washout during each period at 24,000 ft as well as during the initial period at 20,000 ft, but a tendency for uptake, albeit not significant, during the last period at 20,000 ft.

Presuming that VGE is a valid marker of DCS risk,[7,12,18] these results suggest that when long-duration high-altitude flying is interrupted by excursions to lower altitude, the excursion altitude is critical for the DCS risk. During rapid reductions of the ambient pressure, VGE develop as a consequence of supersaturation of physically dissolved gas molecules, predominantly inert gas molecules such as N_2.[1,11] Therefore, it might be expected that during consecutive high-altitude exposures, the partial pressure of N_2 (PN_2) in venous blood and other tissues would gradually decrease as a consequence of pulmonary N_2 washout. Hence, VGE would be gradually less prone to develop for each consecutive high-altitude exposure, provided that the excursions to lower altitude were not of sufficient magnitude and duration to permit complete renitrogenation to basal level. Such a pattern of VGE development was clearly not observed in the present experiments. The most likely explanation for our finding that the peak prevalence of VGE was higher in condition B than in condition A and higher in conditions A and B than in C is that the pressure increments during the excursions from 24,000 to 20,000 ft were not capable of completely compressing venous gas bubbles formed at 24,000 ft. The excursions to 20,000 ft may, by contrast, have facilitated bubble growth by increasing venous PN_2. Thus, once bubbles have formed, they may grow not merely by expansion during the reductions of ambient pressure, but also by increased N_2 diffusion into the bubbles during the recurring periods of N_2 supersaturation in the blood in conjunction with excursions to lower altitude followed by return to high altitude. The lack of nitrogen exchange data for three of eight subjects during the first 20 min in condition B did not affect the comparisons made, since the focus was on the latter part of the exposures, where data for all subjects were available.

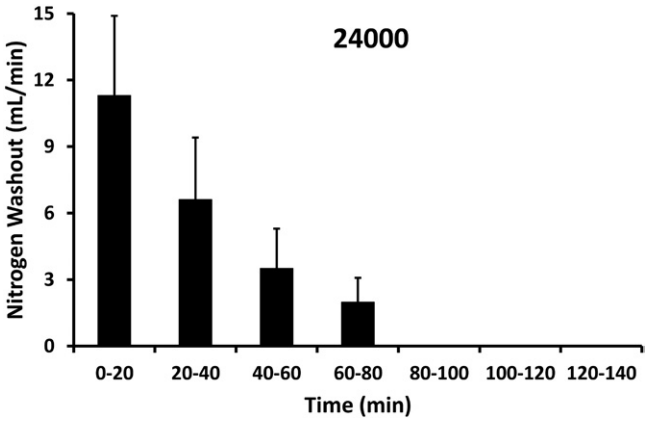

Fig. 3. Average nitrogen washout rate at 20-min intervals in condition A. Values are means (SD), $N = 8$.

Our finding that the excursions to 900 ft counteracted development of VGE at 24,000 ft is in keeping with the results of Pilmanis et al.[25] and supports the notion that complete compression of microbubbles is essential for the DCS-protective effects of excursions from high to lower altitude during long-duration high-altitude flights. Pilmanis and colleagues found that intermittent recompression from a 25,000-ft to 900-ft level reduced the incidence of DCS and VGE, regardless of whether the ground-level excursions were brief (no time at the 900-ft level) or lasted 30 min. The authors reasoned that the 30-min ground-level periods, during which the subjects were breathing air, were too brief to accomplish complete tissue renitrogenation. Given the difference in measured ventilatory N_2 exchange between condition B and C, it appears that it is not the amount of N_2 present at the latter part of the exposures that determines the amount of bubbling, since the N_2 amount was higher in the C condition. Rather, it appears to be whether the magnitude of the pressure increase during the intermittent compressions allows the bubbles to survive or not. Obviously, the subsequent time at high altitude will also play a role, especially in situations where the N_2 levels have been replenished during the time at low altitude.

This kind of repeated altitude exposures with short ground intervals exists, for example, in high-altitude parachute jumping in the Special Forces. From our and Pilmanis et al.'s[25] results, it appears that there might be a difference in DCS risk between the loadmasters, who are typically exposed either to constant low pressure or only to short intermittent recompressions, and the parachute jumpers, who are recompressed to sea level for longer intervals between jumps. During a session of repeated parachute jumping from 26,247 ft (8000 m) it was the loadmasters and not the jumpers who had symptoms of DCS (Ånell RKJ. Unpublished observations; June 2010). That the loadmasters sometimes perform strenuous physical work at altitude may also influence the DCS risk.

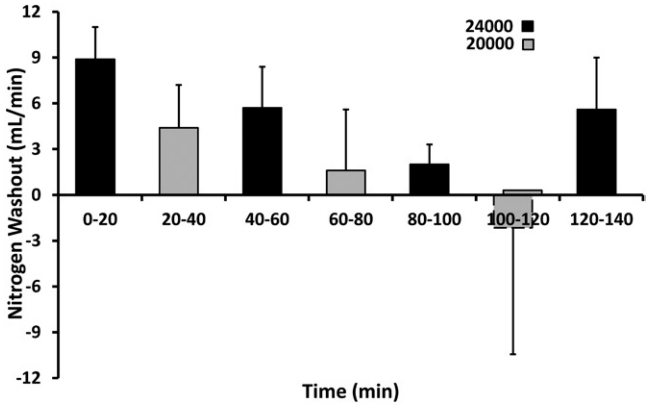

Fig. 4. Average nitrogen washout rates during the course of condition B. Hatched bar showing nitrogen uptake during the third period at 20,000 ft is without the subject who developed DCS. Values are means (SD), $N = 8$ for all time periods except for 0–20 min, where $N = 5$.

Notably, repeated compression and recompression patterns in yo-yo diving gave rise to a nearly 30-fold higher incidence of DCS than recreational dives, though the yo-yo dives were quite short and shallow.[30] It should of course be noted that during yo-yo diving the bubbles are compressed during the phase of the dive where the gas uptake occurs, and thus the two situations, yo-yo diving and repeated altitude exposures, are not directly comparable.

The rate of elimination and uptake of N_2 in response to reductions and elevations of ambient pressure, respectively, follow different time courses in different tissues, depending on the perfusion and N_2 solubility of the tissue, with tissues commonly being categorized as either fast, medium, or slow responders.[3,5,21] Several findings in the present experiments suggest that N_2 elimination from slow tissue compartments contributed significantly to VGE development. Thus, in all three conditions and in agreement with findings in previous studies,[25] VGE occurred after a certain latency period. In condition A, the incidence of VGE increased over time despite a decreasing rate of pulmonary N_2 washout, although in condition C, single VGEs were observed toward the end of the experiment, despite an approximate balance between pulmonary N_2 washout and uptake during the preceding high-altitude and near ground-level periods. In condition B, a tendency of an N_2 uptake during the third excursion to 20,000 ft resulted in an increased washout rate during the following 24,000-ft exposure. It thus appears that the pulmonary washout and uptake of N_2 predominately reflected changes of the fast and medium responding N_2 tissue stores. Presumably, release/diffusion of N_2 from slow tissue compartments contributed to gradual VGE growth during the experiment. The notion that slow tissue compartments play a major role in development of VGE and DCS is not novel.[8,25,27]

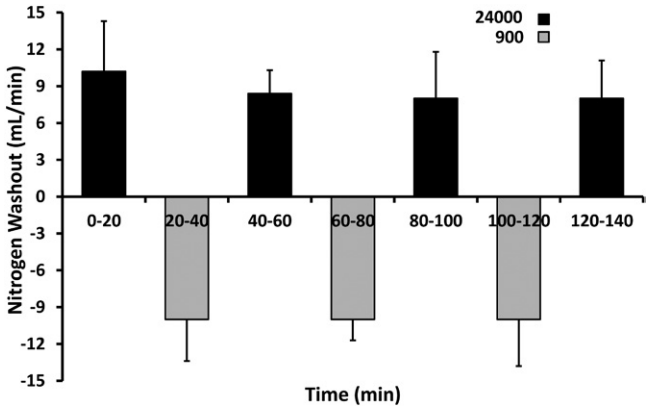

Fig. 5. Average nitrogen washout rates in condition C. Values are means (SD), $N = 8$.

The described reduction in CO and HR over time were probably due to the subjects lying down during the exposures and the initial stress decreasing over time. It cannot be excluded that this gradual reduction in cardiac output during the experiments contributed to the concomitantly decaying rate of pulmonary N_2 elimination in condition A. On the other hand, despite the decrease of cardiac output over time also in the B and C conditions, there was no apparent reduction in N_2 washout rate during the last 24,000-ft exposures.

N_2 solubility in water or watery tissue is such that an N_2 bubble with a volume of 10 μL will contain roughly the same amount of N_2 contained in 1 mL of blood, assuming identical PN_2 in the fluid and the gas phase. The potential for increased gas transport via bubbles has been commented on by others.[6] An experimental study measuring N_2 washout after a hyperbaric air exposure to 4 atm showed that the washout was significantly slower during isobaric shift to a helium:oxygen mixture compared to a similar gas shift in conjunction with decompression.[17] The investigators hypothesized that the more rapid N_2 washout during decompressions were due to bubble formation. The present experiment was not designed to test this hypothesis. However, it should be noted that the subject who complained of knee pain during his last exposure to 24,000 ft in condition B also had the highest bubble scores (3–4) and, during the previous period at 20,000 ft, had a high gas washout, although the other subjects showed a gas uptake or a very slight gas washout during this period. Thus, in this subject, the high bubble score correlated with a concomitant increase in N_2 washout, though the washout was not rapid enough to stop the occurrence of DCS symptoms. It was also noted that in the other subjects, the N_2 washout increased during the last period at 24,000 ft at the same time as the bubble scores increased. However, here it is uncertain whether the increase in washout was due to bubbles or to the fact that there had been a gas uptake during the previous 20-min period.

Two factors determined our decision to investigate the present B profile with excursions to 20,000 ft. Firstly, current Swedish regulations for high-altitude flying in fighter aircraft stipulates that any excursion to cabin altitudes below 22,000 ft, however brief, results in a resetting of the time elapsed at high altitude to zero as regards the risk of DCS. Secondly, as mentioned, the 20,000-ft level constitutes a possible cabin altitude for refueling fighter aircraft. Even though our results suggest that a flying pattern with the cabin altitude alternating between 24,000 and 20,000 ft is unsafe from a DCS perspective, it should be noted that in the present experiments the subjects were

always breathing a normoxic gas mixture, although in real-life conditions they would likely breath gas mixtures with higher Po_2, which would reduce the risk of VGE formation.[14,24] On the other hand, in a real-life scenario, total time at high altitude might be considerably longer and the peak cabin altitude might be somewhat higher than in the present experiments, in particular during missions conducted close to the Equator, which would increase the risk of VGE formation and hence the DCS risk.[13,29]

It remains to be investigated if, and to what extent, the risk of VGE formation and DCS can be reduced during long-duration high-altitude flying by breathing hyperoxic gas mixtures during and prior to the exposures and by altering the intermittent excursions to cabin altitudes lower than in the present experiments, but still realistic for refueling. In conclusion, the present study suggests that during long-duration flights with a cabin pressure corresponding to an altitude of 24,000 ft, intermittent reductions of cabin altitude to 20,000 ft do not appear to alleviate the DCS risk, presumably because the pressure increase is not sufficient to completely compress venous gas bubbles formed at 24,000 ft.

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