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Acute hypoxia in a simulated high-altitude airdrop scenario due to oxygen system failure

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Ottestad W, Hansen TA, Pradhan G, Stepanek J, Høiseith LØ, Kåsin JI. Acute hypoxia in a simulated high-altitude airdrop scenario due to oxygen system failure. *J Appl Physiol* 123: 1443–1450, 2017. First published August 24, 2017; doi:10.1152/jappphysiol.00169.2017.—High-Altitude High Opening (HAHO) is a military operational procedure in which parachute jumps are performed at high altitude requiring supplemental oxygen, putting personnel at risk of acute hypoxia in the event of oxygen equipment failure. This study was initiated by the Norwegian Army to evaluate potential outcomes during failure of oxygen supply, and to explore physiology during acute severe hypobaric hypoxia. A simulated HAHO without supplemental oxygen was carried out in a hypobaric chamber with decompression to 30,000 ft (9,144 m) and then recompression to ground level with a descent rate of 1,000 ft/min (305 m/min). Nine subjects were studied. Repeated arterial blood gas samples were drawn throughout the entire hypoxic exposure. Additionally, pulse oximetry, cerebral oximetry, and hemodynamic variables were monitored. Desaturation evolved rapidly and the arterial oxygen tensions are among the lowest ever reported in volunteers during acute hypoxia. P_{aO_2} decreased from baseline 18.4 (17.3–19.1) kPa, 138.0 (133.5–143.3) mmHg, to a minimum value of 3.3 (2.9–3.7) kPa, 24.8 (21.6–27.8) mmHg, after 180 (60–210) s, [median (range)], $N = 9$. Hyperventilation with ensuing hypocapnia was associated with both increased arterial oxygen saturation and cerebral oximetry values, and potentially improved tolerance to severe hypoxia. One subject had a sharp drop in heart rate and cardiac index and lost consciousness 4 min into the hypoxic exposure. A simulated high-altitude airdrop scenario without supplemental oxygen results in extreme hypoxemia and may result in loss of consciousness in some individuals.

NEW & NOTEWORTHY This is the first study to investigate physiology and clinical outcome of oxygen system failure in a simulated HAHO scenario. The acquired knowledge is of great value to make valid risk-benefit analyses during HAHO training or operations. The arterial oxygen tensions reported in this hypobaric chamber study are among the lowest ever reported during acute hypoxia.

acute hypoxia; altitude; blood gas; HAHO; hypoxic syncope

HIGH-ALTITUDE airdrop missions are carried out to deliver personnel and equipment into enemy territory. High-Altitude High Opening (HAHO) is a military operational procedure in which

parachutists exit the aircraft and deploy their parachutes at high altitude. Modern parachutes are efficient wings, and depending on exit altitude, wind direction, and speed, distances of more than 60 km (40 miles) can be attained by the parachutist. HAHO allows the deployment of military personnel from a significant standoff range, reducing the risk of detection by the enemy. HAHO operations are carried out at altitudes between 20,000 ft (6,096 m) and 35,000 ft (10,668 m) and require supplemental oxygen, putting personnel at risk for acute hypoxia in the event of oxygen equipment failure. During HAHO training in the Norwegian Army, incidents have been reported wherein the oxygen mask and hose have been accidentally disconnected due to interaction with the parachute during deployment. In a regular HAHO from 30,000 ft (9,144 m), parachutes are deployed 7–10 s into free fall, and are fully deployed at altitudes ranging from 28,000 to 29,000 ft (8,534–8,839 m). After deployment, return to a physiologically safe altitude is determined by the parachute's descent rate [\sim 1,000 ft/min (305 m/min)]. Exposure to severe hypoxia might be sustained if equipment failure were to occur. Hypoxic syncope could lead to loss of airway patency and potentially fatal outcome. In a scenario with a failed oxygen supply system, cut-away of the main parachute and rapid descent in free fall to a safe altitude is an option; however, this will increase other operational risks. The aim of the present study was to investigate the physiology, timing, and severity of ensuing hypoxia in a HAHO flight profile from 30,000 ft (9,144 m) simulating a complete failure of the oxygen supply system.

METHODS

Subjects. After regional ethics committee approval and written informed consent, nine volunteers were recruited from the Norwegian Special Operations Command. All were healthy nonsmokers, age 31(27–48) yr, weight 85 (75–95) kg, height 183 (174–193) cm, and a body mass index 26 (23–28) kg/m² [median (range)]. Subjects abstained from solid foods for 4 h, clear liquids 2 h, and physical exercise and any analgesics 24 h before the hypobaric exposure. None of the subjects were acclimatized to altitude before hypobaric exposure.

Hypobaric chamber and flight profile. Global positioning system data from 11 actual HAHO jumps from 30,000 ft (9,144 m) were reviewed to create a 30-min flight profile for this chamber experiment. The experiment was carried out in a hypobaric chamber (Aeroform

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Poole, Dorset, UK) at the Institute of Aviation Medicine, Oslo, Norway. The experiment was performed with one subject in the chamber at the time with the subject placed in the sitting position. The incidence of decompression sickness during hypoxia training at altitudes ranging from 25,000 to 35,000 ft is low. To facilitate denitrogenation and to decrease the risk of decompression sickness, a 60-min oxygen prebreathe started at ground level [1,017 (1,004–1,023) hPa], [763 (753–767) mmHg] [median (range)] (12, 18). The 60-min prebreathe complies with both standard operation procedures during hypoxia training in the Norwegian army and in NATO (1). The subjects breathed 100% oxygen using an oxygen mask (Gentex MBU 20, Gentex, Carbondale, PA) on a pressure demand regulator (CRU-73, Cobham Life Support, Davenport, IA). Approximately 40 min into the denitrogenation, pressure was reduced to 753 hPa (565 mmHg, 8,000 ft), simulating standard cabin pressure during flight. Baseline measurements for hemodynamics were completed, and a safety brief performed. When the 60-min prebreathe was completed, the chamber was decompressed from 753 hPa (565 mmHg) to 301 hPa (226 mmHg, 30,000 ft) at 4,000 ft/min. At an ambient pressure of 301 hPa (565 mmHg) while breathing oxygen, each subject was instructed to do 30 deep squats, and then to sit down, to simulate the workload associated with exiting the airplane. Immediately after seated rest we started a 15-s countdown, and the oxygen mask was removed by one of the attending anesthesiologists, and the regulator was switched off. The chamber was repressurized at 4,000 ft/min for 15 s to simulate the free fall phase before parachute deployment at a pressure of 314.9 hPa (236.2 mmHg) corresponding to 29,000 ft in the international standard atmosphere (2). The rate of descent was set to 1,000 ft/min for the remaining flight profile. Hemodynamic monitoring, oximetry, and blood gas sampling were continued to ground level. The pressure profile is illustrated in Fig. 1.

Arterial cannulation and blood sampling. An arterial catheter was placed in the left radial artery 30 min before the start of the chamber experiment. The arterial cannulation was performed with local infiltration anesthesia (xylocaine 1%). The catheter was filled with 0.1 ml heparin (100 IE/ml) to avoid clotting, and no extension tubing was attached. At 301 hPa (226 mmHg, 30,000 ft), while breathing oxygen, three blood gas samples were drawn for baseline measurements and brought out via the chamber lock for immediate analysis. The blood gas samples were drawn according to the time intervals illustrated in Fig. 1. Samples were immediately put on ice and brought out through the chamber lock every 4 min thereafter. All blood gas samples were analyzed using an automated self-calibrating blood gas analyzer (Radiometer ABL 90 FLEX, Brønshøj, Denmark), within 10 min of sampling. According to the manufacturer's user manual, the ABL 90 is validated for P_{aO_2} values as low as 1.9 kPa (14.3 mmHg).

Monitoring. Each subject underwent monitoring with pulse oximetry [finger probe (LNOP DC-I; Masimo, Irvine, CA)] from a Masimo Radical 7, software 7.3.1.1 (Masimo) placed on the right index finger. Data from the pulse oximeter were extracted using the TrendCom software (Masimo) at a 0.5-Hz resolution. Cerebral oximetry was performed using a near-infrared spectroscopy (NIRS) tissue oximeter (Invos 5100C cerebral/somatic oximeter; Somanetics, Troy, MI). Sensors (Adult SomaSensor; Covidien, Mansfield, MA) were attached to the left and right forehead (cerebral oximetry, ScO_2). Measurements from the cerebral oximeter were extracted via the serial port every 7–8 s. Cerebral tissue oximetry values are presented relative to baseline values at ground level breathing ambient air at the end of the experiment. Cardiac stroke volume was obtained by thoracic impedance (PhysioFlow PF07 Enduro; Manatec Biomedical, Paris, France). The chamber atmosphere was

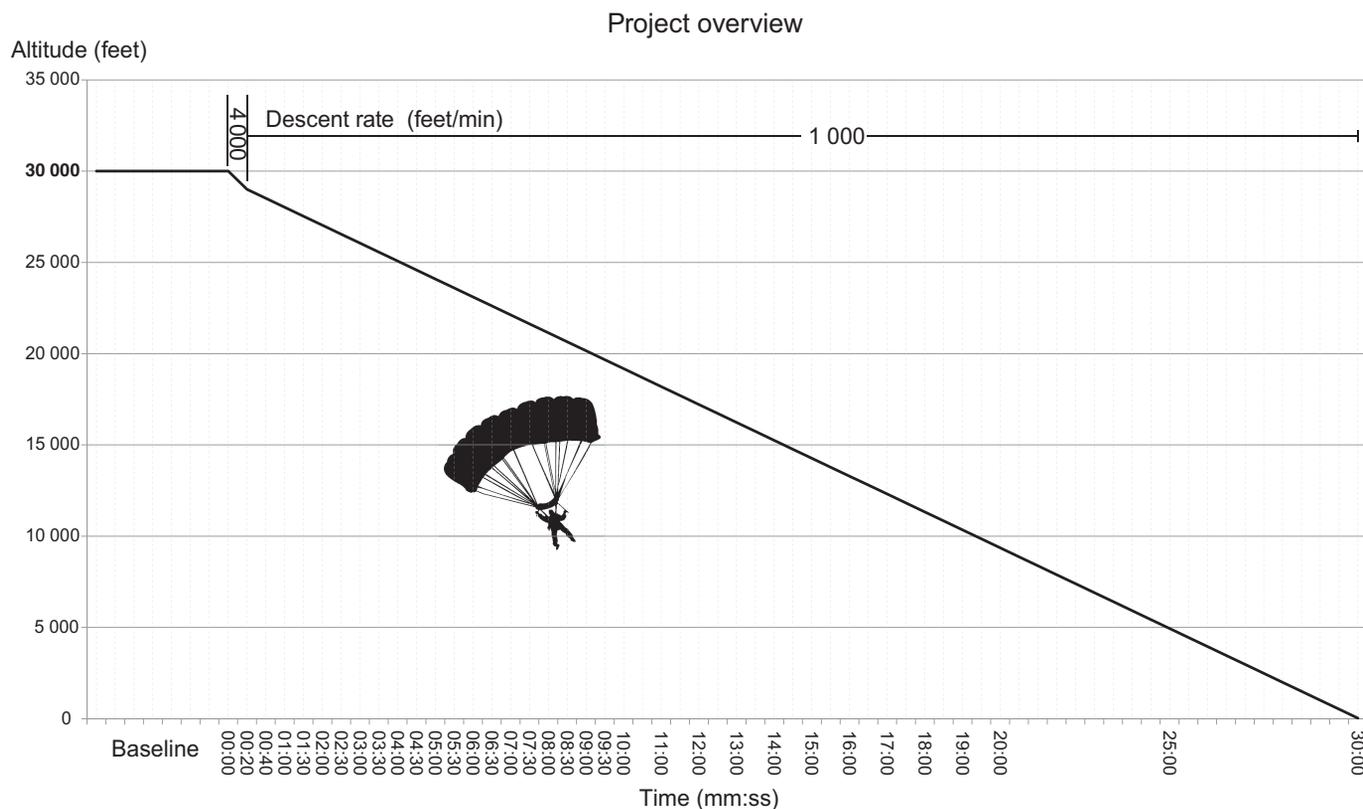


Fig. 1. The chamber flight profile. The first 15 s simulated the free fall phase before parachute deployment with a descent rate of 4,000 ft/min, followed by a descent of 1,000 ft/min after parachute deployment. Arterial blood was sampled at the indicated time points: every 20 s the first minute; every 30 s the next 9 min; every minute the next 10 min, and every 5 min the last 10 min.

Table 1. Minimum PaO₂ value for each person and the corresponding blood gas and oximetry values, while breathing ambient air

ID	Min PaO ₂	Time	Altitude	PaCO ₂	pH	P ₅₀	SaO ₂	ScO ₂	SpO ₂
1	3.1 (23.3)	210	25 900	3.8 (28.5)	7.46	3.1 (23.3)	51	45	35
2	2.9 (21.8)	180	26 400	3.7 (27.8)	7.50	2.9 (21.8)	51	54	28
3	3.5 (26.3)	210	25 900	3.4 (25.5)	7.55	2.8 (21.0)	63	69	55
4	3.3 (24.8)	210	25 900	3.6 (27.0)	7.46	3.0 (22.5)	57	53	39
5	3.0 (22.5)	180	26 400	3.9 (29.3)	7.47	3.0 (22.5)	48	46	20
6	3.7 (27.8)	120	27 350	3.0 (22.5)	7.55	2.9 (21.8)	67	71	60
7	3.2 (24.0)	60	28 400	3.6 (27.0)	7.52	3.0 (22.5)	54	69	62
8	3.4 (25.5)	180	26 400	3.2 (24.0)	7.51	2.9 (21.8)	59	65	49
9	3.7 (27.8)	90	27 900	3.6 (27.0)	7.55	2.8 (21.0)	67	63	65

Time in seconds, cerebral oximetry (ScO₂) and arterial oxygen saturation (SaO₂) in %, and all other values in kPa (mmHg). SpO₂, pulse oximetry.

monitored using a gas analyzer (Hitech Instruments ZIR 125, Eaton, Houston, TX). The gas sample was extracted ~10–15 cm behind the head of each test subject, using a flexible sample hose. The chamber was ventilated to maintain ambient oxygen and carbon dioxide within normal ranges.

Statistics. Unless otherwise specified, values are presented as mean (min–max). Regression analyses were performed using linear mixed-models (random intercept) with subject as random effect. Analyses were performed in JMP 11.2.1, (SAS Institute, Cary, NC). *P* values < 0.05 were considered statistically significant. The individual dissociation curves reported are strictly empirical and not based on any calculations or extrapolation of data.

Safety and scientific justification. HAHO training puts personnel at risk for decompression sickness, hypoxia, and potentially severe trauma due to parachute-related accidents. There is a need to better understand the physiological and occupational risks involved in the case of oxygen equipment failure during HAHO training. To ensure optimum medical safety, two anesthesiologists trained in emergency medicine were inside the hypobaric chamber during the experiment. The chamber personnel breathed 100% oxygen throughout the experiment after denitrogenation. Emergency procedures were briefed to all chamber personnel before each run in a standardized fashion. Existing evidence supports the notion that transient hypoxia is safe, and several studies report that even acute profound hypoxia is well tolerated in healthy subjects (4).

RESULTS

Eight subjects completed the entire flight profile, and they were alert and responsive throughout the entire exposure. All subjects reported symptoms of hypoxia ranging from light-headedness, blurred vision, paresthesia, labored breathing, euphoria, and confusion. *Subject 2* lost consciousness after 4 min of hypoxic exposure [PaO₂ = 3.3 kPa (24.8 mmHg), PaCO₂ = 3.7 kPa (27.8 mmHg), SaO₂ = 58%] at a pressure of 370 hPa (278 mmHg) corresponding to an altitude of 25,400 ft. He needed assistance to maintain a patent airway, and was given oxygen through a demand system. He breathed spontaneously and regained full consciousness after ~90 s of oxygen-breathing, when he resumed responsiveness to verbal commands.

Arterial oxygen tension. After oxygen system failure and start of the simulated descent to ground (recompression), PaO₂ decreased from baseline 18.4 (17.3–19.1) kPa, 138.0 (129.8–143.3) mmHg to a minimum value of 3.3 (2.9–3.7) kPa, 24.8 (21.8–27.8) mmHg, at a time of 180 (60–210) s, [median (range)] (*N* = 9). Minimum PaO₂ value with corresponding PaCO₂, SaO₂, p₅₀, and ScO₂ are shown in Table 1. The temporal patterns of PaO₂, PaCO₂, SaO₂, and ScO₂ for each subject are presented in Figs. 2 and 3. In Supplemental Material available with the online version of this article, we have provided the complete set of blood gas data, and a table with mean (SD) values.

Oxyhemoglobin dissociation curve. The p₅₀ calculated from the blood-gas analyses were tightly associated with PaCO₂ (Spearman's rho = 0.88; *P* < 0.001). In a linear mixed model with subject as random effect, and PaCO₂ as explanatory variable; p₅₀ decreased with 0.28 kPa (95% confidence interval: 0.26–0.30, *P* < 0.001) per kilopascal increase in PaCO₂ (*R*² = 0.86, *P* < 0.0001). There was a broad range of SaO₂ values for a specific PaO₂ value, reflecting the large variability in p₅₀ values and thereby the degree of left shift of the oxyhemoglobin dissociation curve (Fig. 4). At 21,000 ft, SaO₂ ranged from 55% to 91%. The calculated p₅₀ corresponding to the minimum PaO₂ for each subject is presented in Table 1. We plotted the measured PaO₂ and SaO₂ values from every time

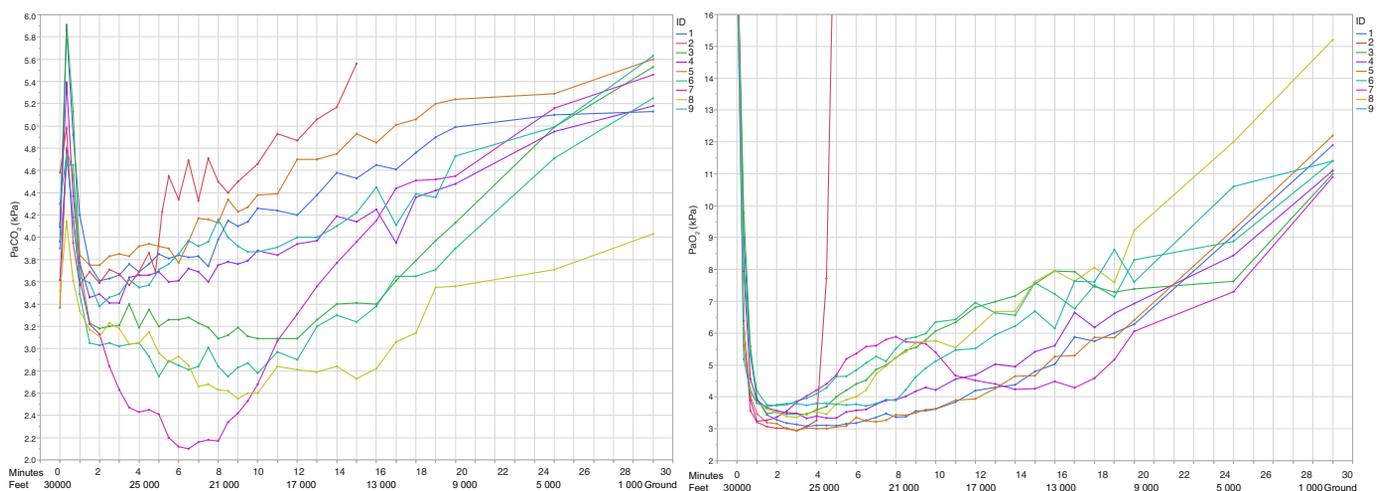


Fig. 2. PaO₂ and PaCO₂ through the simulated flight profile. *Subject 2* was given supplemental oxygen after ~4 min.

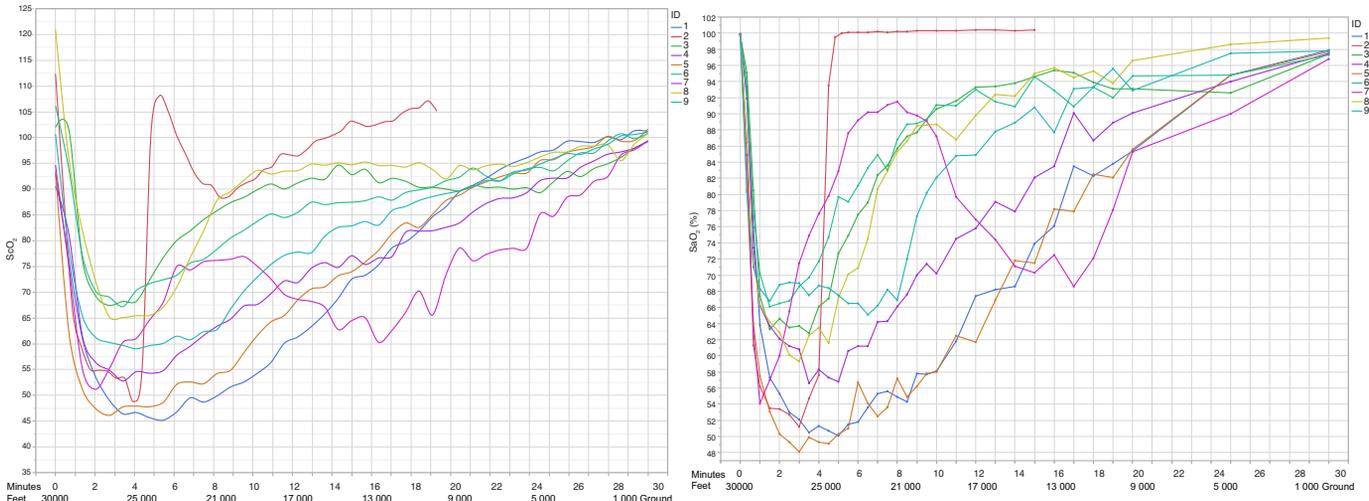


Fig. 3. SaO_2 and ScO_2 through the simulated flight profile. *Subject 2* was given supplemental oxygen after ~4 min.

point throughout the flight profile to illustrate the actual dissociation curve for each individual over the entire range of Pa_{O_2} values recorded. The subject who experienced syncope appeared to have the most leftward shifted dissociation curve during the initial phase (Fig. 4).

Relationship between Pa_{CO_2} , and Pa_{O_2} , SaO_2 , and ScO_2 . The respiratory response and corresponding Pa_{CO_2} changed rapidly due to the dynamic nature of our experiment. We explored the

effect of Pa_{CO_2} on Pa_{O_2} , SaO_2 , and ScO_2 at 7 and 15 min, corresponding to 22,000 and 14,000 ft respectively. At these two time points we recorded the widest range of Pa_{CO_2} values, in the context of both severe and moderate hypoxia; $Pa_{CO_2} = 3.46$ kPa (2.16–4.17), 26.95 (15.20 –31.28) mmHg with corresponding $Pa_{O_2} = 4.26$ kPa (3.22–5.61), 31.95 (24.15–42.08) mmHg and $Pa_{CO_2} = 4.05$ kPa (2.73–4.93), 30.38

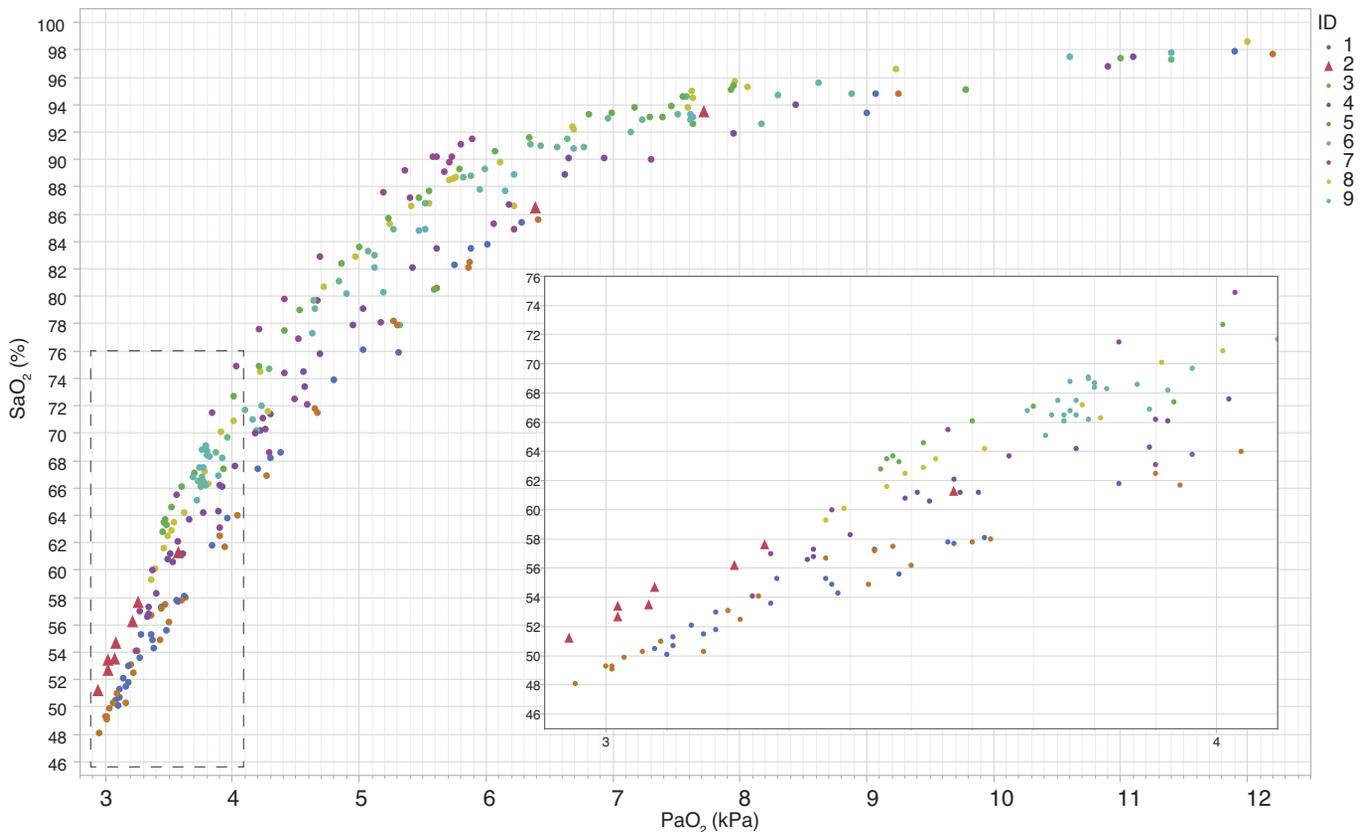


Fig. 4. Scatterplot of SaO_2 vs. Pa_{O_2} , illustrating the oxygen dissociation. The lowest values in the dashed rectangle have been highlighted for clarity. *Subject 2* experiencing syncope appeared to have the most leftward-shifted oxygen-hemoglobin dissociation curve.

(20.48–36.98) mmHg with corresponding $\text{PaO}_2 = 6.06$ kPa (4.26–7.62), 45.45 (31.95–57.15) mmHg [median (range)] ($N = 8$, at 7 and 15 min, respectively). Linear regression was performed to explore the relationship between PaCO_2 and PaO_2 , SaO_2 and ScO_2 . Subject 2 was excluded from the model. There was an inverse relationship between PaCO_2 and PaO_2 , SaO_2 and ScO_2 , but more pronounced during severe hypoxia (7 min) compared with moderate hypoxia (15 min) (Fig. 5).

Hemodynamic response. Among the eight subjects who completed the experiment without supplemental oxygen, heart rate increased from baseline [65 (41–90) beats/min] to a peak value at start of recompression [119 (96–154) beats/min] and gradually decreased back toward baseline values at 25 min [68 (52–89) beats/min] [median (range)]. Sampling of thoracic impedance data was unstable, and we lost signal in four subjects. In five subjects with uninterrupted signal acquisition, cardiac index (CI) increased from baseline [3.6 (2.6–4.4) $\text{l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$] to peak values at start of recompression [6.1 (5.0–7.6) $\text{l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$] and returned back toward baseline values at 25 min [3.2 (2.6–3.7) $\text{l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$] [median (range)]. The reduction in cardiac output through the hypoxic exposure seems to be mainly caused by a reduction in heart rate as stroke volume was quite stable. It should be noted that the hemodynamic response was not only a response to hypoxia, but also to the squats performed before the hypoxic exposure. Heart rate and cardiac index from the five subjects where stroke volume was successfully measured are presented in Fig. 6.

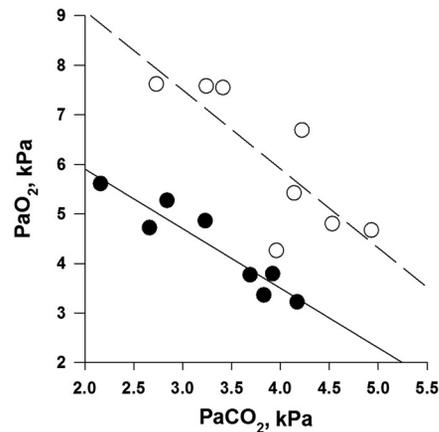
In subject 2, peak heart rate decreased from 136 beats/min at start of recompression to 55 beats/min at 4 min with loss of consciousness. Cardiac index decreased rapidly in the same time span from 5.6 to 1.7 $\text{l}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$.

DISCUSSION

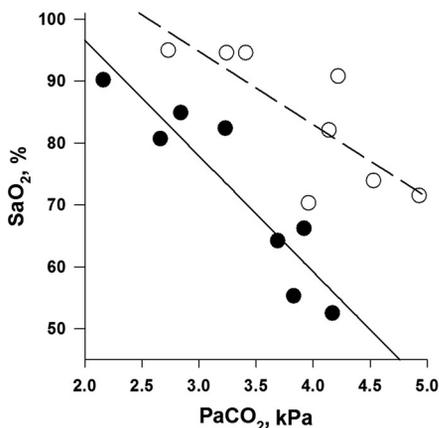
This study was initiated by the Norwegian Special Operations Command to examine the physiology and evaluate the risk of hypoxic syncope in the event of oxygen system failure during military HAHO training. In this chamber experiment we demonstrated rapid desaturation and severe hypoxemia when simulating a failure in the oxygen delivery system in a HAHO flight profile from 30,000 ft (9,144 m). Impressive compensatory mechanisms enabled eight of our subjects to maintain consciousness despite extreme hypoxia. To the best of our knowledge the attained PaO_2 readings in our subjects, 2.9–3.7 kPa (21.8–27.8 mmHg), are among the lowest arterial oxygen tensions reported in volunteers with no acclimatization to altitude (8). At an ambient pressure of 301 hPa (226 mmHg) corresponding to 30,000 ft (9,144 m), the inspiratory oxygen pressure is 5.0 kPa (37.5 mmHg), and alveolar oxygen tension falls below the level in mixed venous blood, resulting in reversal of the arterial-alveolar diffusion gradient for oxygen, leading to accelerated desaturation.

In one subject, loss of consciousness occurred at 25,400 ft (7,742 m), 4 min into the hypoxic exposure. Loss of consciousness seemed to be caused by a cardiovascular collapse, evident by a rapid fall in heart rate and cardiac output, followed by a sharp drop in cerebral oximetry values. The subject breathed spontaneously, but he needed assistance to maintain a patent airway, and he regained full consciousness after 90 s of oxygen breathing. Hypoxic incapacitation during military operations is

- 7 min: $\text{PaO}_2 = 8.3 - 1.2$ (95%CI -1.6 to -0.77)* PaCO_2 , $R^2 = 0.88$, $p < 0.001$
- 15 min: $\text{PaO}_2 = 12.3 - 1.6$ (95%CI -2.8 to -0.4)* PaCO_2 , $R^2 = 0.64$, $p < 0.017$



- 7 min: $\text{SaO}_2 = 134 - 19$ (95%CI -25 to -12)* PaCO_2 , $R^2 = 0.85$, $p = 0.001$
- 15 min: $\text{SaO}_2 = 130 - 12$ (95%CI -19 to -4.3)* PaCO_2 , $R^2 = 0.61$, $p = 0.022$



- 7 min: $\text{ScO}_2 = 112 - 13$ (95%CI -22 to -4.5)* PaCO_2 , $R^2 = 0.59$, $p = 0.026$
- 15 min: $\text{ScO}_2 = 123 - 11$ (95%CI -19 to -2.5)* PaCO_2 , $R^2 = 0.52$, $p = 0.044$

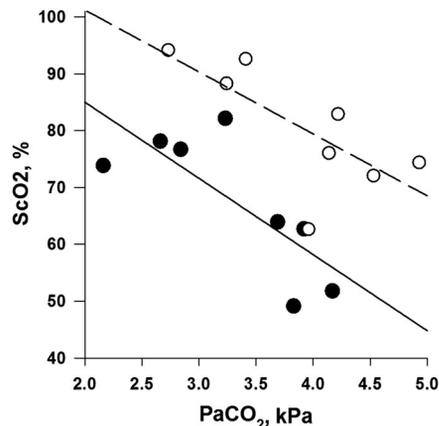


Fig. 5. Scatterplots of blood-gas analyses at 7 and 15 min with regression equations. Confidence intervals and P values are for the slope coefficients.

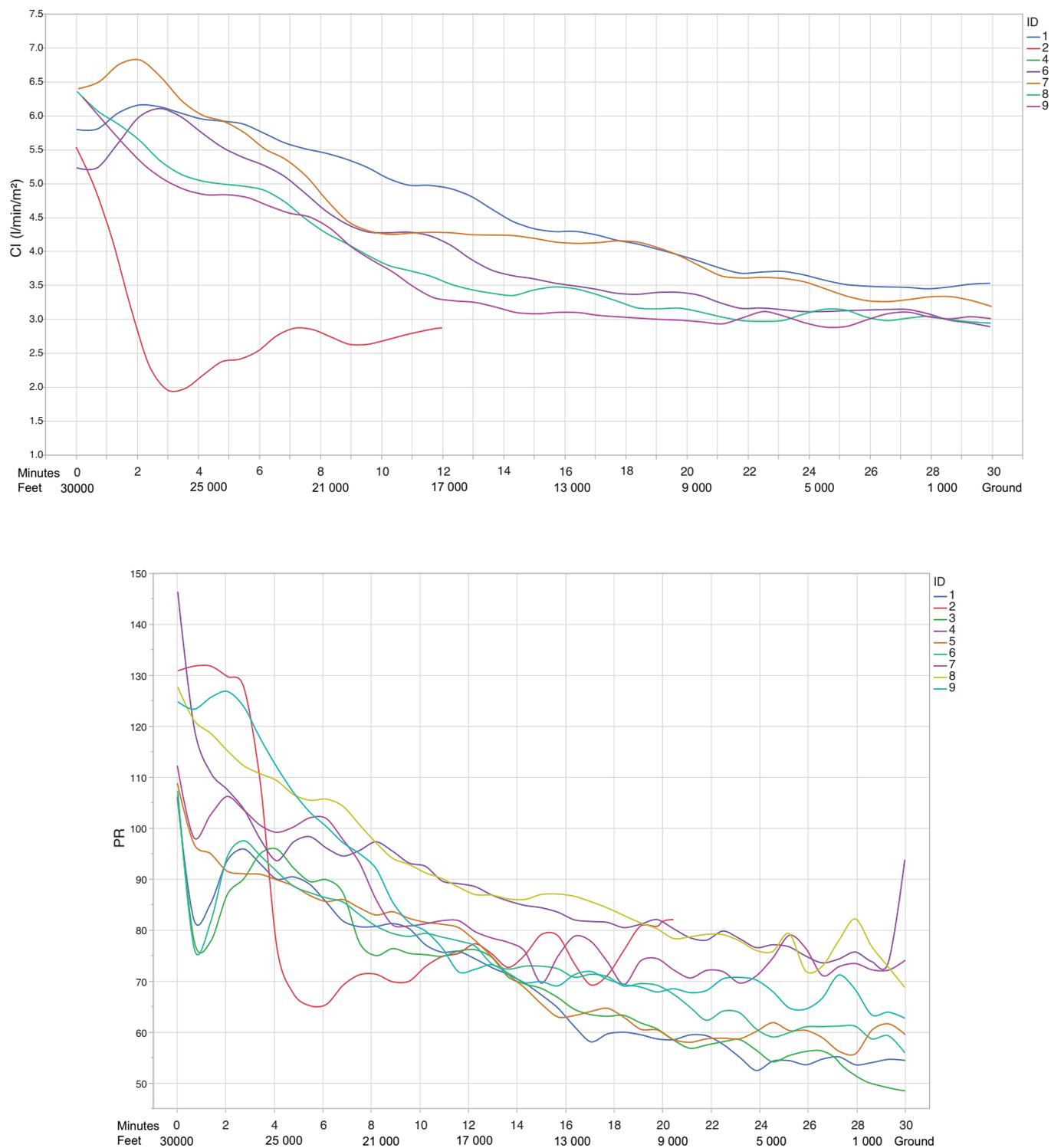


Fig. 6. Cardiac index and heart rate through the simulated flight profile.

not uncommon and represents a serious threat to aviators. Fatalities are rare but have been reported (5, 6). The risk of hypoxic syncope is difficult to assess and depends on degree of hypoxia, its duration, and individual responses. Westendorp et al. (19) reported hypoxic syncope with a short period of asystole in 2% of 120 hypobaric exposures at 20,000 ft (6,096 m); however, oxygen breathing was administered as soon as

heart rate decreased more than 20%. Robust assumptions about absolute risk of hypoxic syncope in this flight profile cannot be made due to our small number of exposures. However, the rapid desaturation and severe hypoxemia observed in this flight profile and loss of consciousness in one of our subjects justifies a major concern for the parachutists' safety in the event of oxygen system failure.

Hypoxia triggers the carotid chemoreceptors sparking of a brisk respiratory response with ensuing hypocapnia and respiratory alkalosis (10, 13), shifting the oxyhemoglobin dissociation curve to the left, thereby increasing hemoglobin affinity, evident by a decrease in p_{50} value. The classic alveolar gas equation is not valid when inspired oxygen pressure is < 5 kPa (38 mmHg), as it will predict a negative P_{aO_2} (6a). However, in steady state, the alveolar gas equation predicts decreasing P_{aO_2} with increasing P_{aCO_2} , compatible with our results. We found a negative correlation between P_{aCO_2} and P_{aO_2} , SaO_2 and ScO_2 . Hypercapnia has been demonstrated to counter hypoxic symptoms and improve both cognitive and oculometric performance in the context of moderate hypoxia (13, 16). The proposed underlying mechanisms are hypercapnic cerebral vasodilation and enhanced tissue oxygen delivery. Hypocapnia will induce cerebral vasoconstriction, hence reducing cerebral perfusion (3). However, there are conflicting data in the context of hypobaric hypoxia (9, 16). The effects of P_{aCO_2} on cerebral oxygenation may thus be competing, as hypocapnia may both increase P_{aO_2} , but also decrease cerebral blood flow. In our experiment during severe acute hypoxia the effect on P_{aO_2} seems to dominate, as high ScO_2 values tended to be associated with high P_{aO_2} and low P_{aCO_2} levels. This effect appeared to explain the biphasic course of *subject 7*, who between 6 and 8 min into the flight profile had high P_{aO_2} and ScO_2 values and extremely low P_{aCO_2} values. Later in the run, P_{aCO_2} increased and P_{aO_2} and ScO_2 decreased. The subject who experienced loss of consciousness had among the lowest nadir values of P_{aO_2}/ScO_2 and among the highest recorded P_{aCO_2} values. There seems to be a hypoxic threshold where hypoxic vasodilatation overrides the cerebral vasoconstrictive effects of hypocapnia (9, 11). However, we have not measured cerebral blood flow directly, and utilizing cerebral oximetry as a surrogate introduces a major limitation to the conclusions that can be drawn from this small study (7, 15). The impact of the ventilatory response on the SaO_2 was impressive. This is clearly demonstrated in *subject 7* with a $SaO_2 = 90\%$ at 21,000 ft (6,400 m) and a decrease to 54% at 13,000 ft (3,962 m), with corresponding $P_{aCO_2} = 2.2$ kPa (15.5 mmHg) and 4.2 kPa (31.5 mmHg), respectively. Hyperventilation with ensuing hypocapnia increased both arterial oxygen saturation and cerebral oximetry values, and potentially improved tolerance to severe hypoxia.

We were not able to completely reproduce the complex reality of a HAHO procedure in the hypobaric chamber. In a real-life HAHO scenario, the parachutists will be in the upright position suspended in a parachute harness, which represents a severe hemodynamic challenge in the context of hypoxia-induced bradycardia and concomitant loss of consciousness (14). Suspension trauma and impingement caused by the harness will restrict venous return from the lower extremities and decrease cardiac preload. Suspended in a parachute harness with a failed oxygen supply, the parachutists' ability to spontaneously recover is limited, and under these circumstances we believe that hypoxic syncope might lead to a fatal outcome. Our experiment was done during seated rest, and the workload associated with steering of the parachute, and a potential effort to solve problems with the oxygen system in flight, could not be adequately simulated. It is reasonable to assume that all these factors will further increase the risk of hypoxic syncope

compared with the conditions in our controlled chamber experiment.

Conclusions. Failure in oxygen delivery systems during high-altitude airdrops at 30,000 ft (9,144 m) will lead to rapid desaturation and severe hypoxemia. Hypoxic syncope occurred within 4 min in one of our subjects and illustrates the marginal window of opportunity to solve problems in-flight during oxygen supply failure. However, when heart rate and cardiac output are maintained, healthy, fit subjects will transiently tolerate extremely low oxygen tensions. Loss of consciousness occurred in 1 of 9 exposures. We urge personnel engaged in HAHO training to carefully consider the risk-benefit of training at altitudes above 25,000 ft, due to the risk of hypoxic syncope in the event of equipment failure. Proper training in emergency procedures related to problems with oxygen equipment should be implemented in HAHO training.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

W.O., T.A.H., L.Ø.H., and J.I.K. conceived and designed research; W.O., L.Ø.H., and J.I.K. performed experiments; W.O., T.A.H., G.N.P., J.S., L.Ø.H., and J.I.K. analyzed data; W.O., T.A.H., G.N.P., J.S., L.Ø.H., and J.I.K. interpreted results of experiments; W.O., L.Ø.H., and J.I.K. prepared figures; W.O., T.A.H., L.Ø.H., and J.I.K. drafted manuscript; W.O., T.A.H., G.N.P., J.S., L.Ø.H., and J.I.K. edited and revised manuscript; W.O., T.A.H., G.N.P., J.S., L.Ø.H., and J.I.K. approved final version of manuscript.

REFERENCES

1. Functional requirements for physiological protection during high altitude parachuting operations. In: *STANAG 7056*. NATO, 1997.
2. *Standard Atmosphere ISO 2533:1975*. International Organization for Standardization, 1975.
3. Ainslie PN, Subudhi AW. Cerebral blood flow at high altitude. *High Alt Med Biol* 15: 133–140, 2014. doi:10.1089/ham.2013.1138.
4. Bickler PE, Feiner JR, Lipnick MS, Batchelder P, MacLeod DB, Severinghaus JW. Effects of acute, profound hypoxia on healthy humans: implications for safety of tests evaluating pulse oximetry or tissue oximetry performance. *Anesth Analg* 124: 146–153, 2017. doi:10.1213/ANE.0000000000001421.
5. Cable GG. In-flight hypoxia incidents in military aircraft: causes and implications for training. *Aviat Space Environ Med* 74: 169–172, 2003.
6. Chiang K-T, Yang C-S, Chiou W-Y, Chu H. Repeated hypoxic syncope in a helicopter pilot at a simulated altitude of 18,000 feet. *Aviat Space Environ Med* 83: 609–613, 2012. doi:10.3357/ASEM.3273.2012.
- 6a. Cruickshank S, Hirschauer N. The alveolar gas equation. *Contin Educ Anaesth Crit Care Pain* 4: 24–27, 2004. doi:10.1093/bjaceaccp/mkh008.
7. Davie SN, Grocott HP. Impact of extracranial contamination on regional cerebral oxygen saturation: a comparison of three cerebral oximetry technologies. *Anesthesiology* 116: 834–840, 2012. doi:10.1097/ALN.0b013e31824c00d7.

8. Grocott MP, Martin DS, Levett DZ, McMorrow R, Windsor J, Montgomery HE; Caudwell Xtreme Everest Research Group. Arterial blood gases and oxygen content in climbers on Mount Everest. *N Engl J Med* 360: 140–149, 2009. doi:10.1056/NEJMoa0801581.
9. Imray CH, Brearey S, Clarke T, Hale D, Morgan J, Walsh S, Wright AD; The Birmingham Medical Research Expeditionary Society. Cerebral oxygenation at high altitude and the response to carbon dioxide, hyperventilation and oxygen. *Clin Sci (Lond)* 98: 159–164, 2000. doi:10.1042/cs0980159.
10. López-Barneo J, González-Rodríguez P, Gao L, Fernández-Agüera MC, Pardal R, Ortega-Sáenz P. Oxygen sensing by the carotid body: mechanisms and role in adaptation to hypoxia. *Am J Physiol Cell Physiol* 310: C629–C642, 2016. doi:10.1152/ajpcell.00265.2015.
11. Ogoh S, Sato K, Nakahara H, Okazaki K, Subudhi AW, Miyamoto T. Effect of acute hypoxia on blood flow in vertebral and internal carotid arteries. *Exp Physiol* 98: 692–698, 2013. doi:10.1113/expphysiol.2012.068015.
12. Rice GM, Vacchiano CA, Moore JL, Jr, Anderson DW. Incidence of decompression sickness in hypoxia training with and without 30-min O₂ prebreathe. *Aviat Space Environ Med* 74: 56–61, 2003.
13. Richardson DW, Kontos HA, Shapiro W, Patterson JL Jr. Role of hypocapnia in the circulatory responses to acute hypoxia in man. *J Appl Physiol* 21: 22–26, 1966.
14. Roggla G, Moser B, Roggla M. Suspension trauma. *Emerg Med J* 25: 59, 2008. doi:10.1136/emj.2007.049197.
15. Scheeren TWL, Schober P, Schwarte LA. Monitoring tissue oxygenation by near infrared spectroscopy (NIRS): background and current applications. *J Clin Monit Comput* 26: 279–287, 2012. doi:10.1007/s10877-012-9348-y.
16. Stepanek J, Pradhan GN, Cocco D, Smith BE, Bartlett J, Studer M, Kuhn F, Cevette MJ. Acute hypoxic hypoxia and isocapnic hypoxia effects on oculometric features. *Aviat Space Environ Med* 85: 700–707, 2014. doi:10.3357/ASEM.3645.2014.
18. Webb JT, Pilmanis AA. Fifty years of decompression sickness research at Brooks AFB, TX: 1960–2010. *Aviat Space Environ Med* 82, Suppl: A1–A25, 2011. doi:10.3357/ASEM.2576.2011.
19. Westendorp RG, Blauw GJ, Frölich M, Simons R. Hypoxic syncope. *Aviat Space Environ Med* 68: 410–414, 1997.

