An abrupt zero-preoxygenation altitude threshold for decompression sickness symptoms

**ABSTRACT**

INTRODUCTION. The altitude threshold for decompression sickness (DCS) symptoms has been variously described as being 18,000 ft (5,487 m) to above 25,000 ft (7,620 m). Safety and efficiency of aerospace operations require more precise determination of the DCS threshold. METHODS. One hundred fifteen male human-subjects were exposed to simulated altitude (11 at 11,500 ft; 10 at 15,000 ft; 8 at 16,500 ft; 10 at 18,100 ft; 10 at 19,800 ft; 20 at 21,200 ft; 20 at 22,500 ft; 10 at 23,800 ft, and 16 at 25,000 ft) for up to 4 h. All breathed 100% oxygen beginning with ascent. Subjects were monitored for precordial venous gas emboli (VGE) and DCS symptoms. Probit curves representing altitude versus incidence of DCS symptoms and VGE allowed estimation of respective risk. RESULTS. VGE were first observed at 15,000 ft with increasing incidence at higher altitudes; over 50% at 21,200 ft and at least 70% at 22,500 ft and above. DCS symptoms were first reported at 21,200 ft with an incidence of 5%. At 22,500 ft, the DCS incidence climbed to 60%. CONCLUSION. The 5% threshold for zero-preoxygenation altitude DCS symptoms is at 21,000 ft and an abrupt increase in DCS symptom incidence with increased altitude.

**SUPPLEMENTARY NOTES**

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An Abrupt Zero-Preoxygenation Altitude Threshold for Decompression Sickness Symptoms

JAMES T. WEBB, M.S., PH.D., ANDREW A. PILMANIS, M.S., PH.D., AND ROBERT B. O’CONNOR, M.S.

DECOMPRESSION sickness (DCS) is caused by the evolution of gas bubbles in human tissues during decompression to altitude. The bubbles, composed primarily of nitrogen, not only must be formed, they must be in critical locations and be of sufficient size and/or number to result in a clinical manifestation. Altitude DCS symptoms range from joint pain to neurological dysfunction and respiratory distress. Preoxygenation (breathing 100% oxygen prior to exposure to remove nitrogen) provides protection from DCS symptoms.

Definition of the altitude at which DCS symptoms become a risk factor has great importance for a variety of operational and aircraft design reasons. A well-defined threshold affects unpressurized military and civil aircraft flight planning, airdrop training and operations, design of future extravehicular activity pressure suits, and design of next-generation fighter cockpit pressurization systems.

Reports of threshold altitudes for DCS symptoms (without preoxygenation) vary between 18,000 ft and 25,000 ft (5,487 m). Reasons for this variation include: definition of the term “threshold”; differences in breathing mixtures; varying endpoint criteria for symptoms reporting; and wide separation of exposure altitudes. The term “DCS threshold” as used in this paper is defined as a 5% incidence of DCS, where DCS is further defined as incidence of decompression-related symptoms including neurologic, respiratory, skin, pain not in joints, and joint pain which is constant or affects performance (24). Determination of the altitude DCS threshold using progressive altitude exposures under rigorous hypobaric research conditions has not been reported.

Previous zero-preoxygenation studies in this laboratory indicated that venous gas emboli (VGE) were not observed at 11,500 ft (3,505 m); 8-h exposures; 20 and had an incidence of 20% at 15,000 ft (4,572 m; 6-h exposures; 23). Both studies used 100% oxygen during ascent, exposure, and descent and both employed mild exercise during exposure. The results suggest that the 5% threshold for detection of VGE is between 11,500 ft and 15,000 ft. These same studies did not observe any DCS symptoms at or below 19,800 ft (6,035 m), the highest altitude tested. This paper describes results of exposures at altitudes between 20,000 ft and 25,000 ft using otherwise identical procedures as the studies on VGE below 20,000 ft. The continuum of data from the present study and data from the two previous studies (20,23) allows depiction of the relationship between altitude and VGE and DCS from sub-threshold altitudes to altitudes where greater than 50% incidence was observed.

METHODS

Subjects and Experimental Procedures

Male subjects (124; nonsmokers for the preceding 2 yr) participated in the three studies as described in Table I. The voluntary, fully informed consent of the subjects used in this research was obtained in accordance with AFI 40-402. All subjects passed an appropriate subject physical, and were otherwise representative of the USAF rated aircrew population. They were not allowed to par-

From KRUG Life Sciences Inc., San Antonio, TX 78214 (J. T. Webb); and Air Force Research Laboratory, Flight Stress Protection Division, Brooks AFB, TX 78235-5104 (A. A. Pilmanis and R. B. O’Connor).

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Address reprint requests to: James T. Webb, Ph.D., who is a Lead Scientist with KRUG Life Sciences, Inc., 13818 Chittim Oak, San Antonio, TX 78232.

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TABLE 1. EXPOSURE ALTITUDES, NUMBER OF SUBJECTS EXPOSED, AND EXPOSURE DURATION.*

<table>
<thead>
<tr>
<th>Feet</th>
<th>Meters</th>
<th>mmHg</th>
<th>psia</th>
<th>Subject N</th>
<th>Exposure Time h</th>
</tr>
</thead>
<tbody>
<tr>
<td>11,500</td>
<td>3,505</td>
<td>493</td>
<td>9.5</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>15,000</td>
<td>4,572</td>
<td>429</td>
<td>8.3</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>16,500</td>
<td>5,029</td>
<td>404</td>
<td>7.8</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>18,100</td>
<td>5,517</td>
<td>378</td>
<td>7.3</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>19,800</td>
<td>6,035</td>
<td>352</td>
<td>6.8</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>21,200</td>
<td>6,462</td>
<td>333</td>
<td>6.5</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>22,500</td>
<td>6,858</td>
<td>314</td>
<td>6.1</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>23,800</td>
<td>7,254</td>
<td>297</td>
<td>5.8</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>25,000</td>
<td>7,620</td>
<td>282</td>
<td>5.5</td>
<td>25</td>
<td>4</td>
</tr>
</tbody>
</table>

* Exposure pressure was maintained at the mmHg shown above. Altitudes are shown to the nearest 100 ft. † Data from exposures at 11,500 ft are from Webb et al. (20). ‡ Data from exposures between 15,000 ft and 20,000 ft are from Webb and Filtmanis (23). § Data from exposures above 20,000 ft are from the current study.

participate in SCUBA diving, hyperbaric exposures, or flying for at least 72 h before each scheduled altitude exposure.

Prior to each altitude exposure, a medical monitor conducted a short physical examination of subjects to identify any signs of illness or other problem which would endanger the subject or bias the experimental results. In addition, each subject was taken to 5000 ft (1524 m) simulated altitude in the altitude chamber at a rate of 5000 ft · min⁻¹ for an ear and sinus check. Time spent at 5000 ft was less than 5 s.

A neck-seal respirator made by Intertechnique® (Plaisir Cedex, France) was used for oxygen delivery. It provided a slight, 2 cm of water, positive pressure which reduced the opportunity for inboard leaks of nitrogen from ambient air. This respirator is also more comfortable than the standard aviator's mask. Although no preoxygenation was accomplished, breathing gas for ascent and altitude exposure was 100% oxygen (aviator's breathing oxygen; normal analysis 99.7—99.8% oxygen). Two full inspiration/expiration cycles were completed after donning the mask immediately before ascent, to reduce the nitrogen concentration in the mask and in the conducting airways.

The subjects were decompressed at 5000 ft · min⁻¹ until reaching the scheduled altitude (Table 1) and remained at that altitude for at least 4 h or until another end-point (see below) was reached. During each exposure, the subjects performed three sets of mild arm exercises each h which simulated extravehicular activity (EVA) workload (10). The exercises each lasted 4 min and consisted of the following: 1) Hand-cranked cycle ergometer, 24 rpm, 4 Newtons, alternating arms each two revolutions; 2) Torque Wrench, 25 ft-lbs held for 5 s in each of 5 positions, alternating arms; 3) Rope pull, resistance of 17 kg, one pull from shoulder height to waist level each 5 s. To provide relief from boredom and more closely emulate operational distractions, action-oriented movies were shown to the subjects during the hypobaric exposures.

Endpoints and DCS Grading

Endpoints of the exposures were: 1) completion of the scheduled exposure (4 to 8 h); 2) development of Grade 2 DCS joint pain; 3) development of DCS signs or symp-


toms other than joint pain; or 4) observation of gas emboli in the left heart. Subjects were not questioned about how they felt during the altitude exposures. However, they did receive a briefing on the morning of each exposure which emphasized their responsibility to report any DCS symptoms to chamber personnel, and a list of symptoms was posted in plain view inside the chamber. DCS joint pain was graded as follows: Grade 1—intermittent, mild to moderate pain, intermittent or constant joint awareness or "fullness"; Grade 2—constant, tolerable, mild to moderate pain (24).

Data Collection and Analysis

Precordial echo-imaging for gas emboli was accomplished three times per h using a Hewlett-Packard® SONOS Echo Imaging System (Andover, MA). The subjects lay on a horizontal examining table on their left side. The ultrasound probe, via an entry port in the chamber wall, was positioned at the subject's third intercostal space on the left side for a parasternal, short-axis view of the heart. This view allowed clear observation of all four chambers of the heart while the probe was aimed at the apex of the right ventricle. The echo-image provided guidance and visual feedback for probe orientation to allow reception of the best image and ultrasound signals. Sequential articulation of each limb during the observation period facilitated movement of VGE to the vena cava and right atrium. Each VGE monitoring session was video taped and onset times for each level of VGE and DCS were recorded to provide information on exposure severity independent of DCS incidence. Data on VGE and DCS obtained after 4 h were deleted to allow comparison between altitudes at equal exposure times of 4 h.

Chi Square analysis was used to test for differences in DCS incidence between altitudes. A Probit analysis (using the SAS Statistical Package) was used to develop curves relating incidence and altitude, and corresponding 95% confidence intervals. The Probit analysis (8) procedure calculates maximum-likelihood estimates of regression parameters and threshold response rates for discrete event data. Here, altitude was the independent variable. The response, or dependent variable, was DCS or VGE. Probit analysis requires use of discrete subjects at each altitude. This results in use of a larger number.
of subjects than if the same subjects could have been exposed to all of the altitudes. The Probit analysis thus provides a better estimate of the incidence vs. altitude curves and their respective confidence intervals, also presented as curves. Additionally, it provides a more reliable method of developing these curves than ordinary least squares regression.

RESULTS

Fig. 1 shows a sharp increase in percentage of subjects with DCS symptoms between 21,200 ft and 22,500 ft. The difference was significant (p < 0.01) when comparing incidence at 21,200 ft with any higher altitude tested. The 5% DCS threshold determined by Probit analysis was 20,500 ft (rounded from 20,493 ft), with 95% confidence limits ranging from 18,942 ft to 21,307 ft. The 50% DCS risk level from the Probit curve was at 23,155 ft (22,606 ft to 23,729 ft). Although the curves were not extended beyond 25,000 ft due to lack of data at the higher altitudes, the Probit curve began to level above 22,500 ft as incidence approached 100%. Fig. 1 also shows an increasing risk of VGE with altitude, reaching 50% incidence at 19,776 ft (18,488 ft to 20,831 ft; from Probit curve).

Fig. 2 indicates 20–75% DCS within 2 h at altitudes above 21,200 ft. VGE levels at 21,200 ft reached 20% in 1 h and 40% within 2 h. Although about 30 min of exposure resulted in only 10% DCS at 22,500 ft (Fig. 2), the corresponding level of VGE was 50% (Fig. 3). Neurologic, respiratory, and other serious* symptoms increased in incidence with altitude: 0% at 21,200 ft, 10% at 22,500 ft, 10% at 23,800 ft, and 24% at 25,000 ft. The symptoms observed at 25,000 ft included two which required hyperbaric oxygen (HBO) therapy to resolve; one subject developed chokes and another had lymphatic symptoms which occurred well after the exposure. Although the other 4 serious symptoms, along with the 10 cases of mild joint pain, all resolved on descent, it is not known whether these symptoms would have resolved with continued exposure, continued at their same severity, or become more serious.

DISCUSSION

The specific physical or physiologic mechanism responsible for the abrupt increase in DCS incidence is speculative. The rapid increase in incidence of DCS between 21,200 ft and 22,500 ft may reflect an increase in rate of bubble growth at this altitude range. The in vitro experiments of Olson and Krutz (14) indicated a substantial increase in bubble size between 18,000 ft (5,487 m) and 25,000 ft relative to growth below or above those altitudes (Fig. 4).

A comparison of bubble size (14) and supersaturation with nitrogen during decompression from 14,000 ft (4,267 m) to 31,800 ft (9,700 m) is also shown in Fig. 4. A 0.9-mm in vitro bubble at sea level pressure was shown to increase to approximately 1.2 mm at 14,000 ft and 3.1 mm at 33,500 ft (10,200 m). The relative saturation of nitrogen also increases with greater slope over this altitude range. Eq. 1 shows the relative saturation of nitrogen, \( PrN_2 = \frac{760 - 47 - 40}{760} \cdot 0.78 = 525 \text{ mmHg} \) at sea level pressure (760 mmHg), where \( P_r \) = barometric pressure at any altitude (17). The partial pressure of nitrogen in tissues that denitrogenate slowly will remain at or very near the initial saturated level of 525 mmHg throughout decompression. By approximately 20,800 ft (6350 m) the partial pressure of nitrogen in atmospheric air has decreased to half the nitrogen partial pressure in the slowly denitrogenating tissues (Fig. 4). Thus, these slow tissues are highly supersaturated and bubble formation and growth may be accelerated, causing an abrupt onset of symptoms in the 21–22,000 ft altitude range. Coincidentally, the incidence of VGE at 22,500 ft and higher altitudes is significantly higher than at 21,200 ft. Thus, the VGE data support the concept of a non-

*Joint pain which could impact function is defined here as a serious symptom along with neurologic, respiratory, multiple-site symptoms and any symptoms requiring hyperbaric oxygen therapy.
Fig. 2. DCS incidence as a function of exposure time.

Fig. 3. VGE incidence as a function of exposure time.
linear increase in severity of exposure with increased altitude as shown in Fig. 1 and 3.

Relative Saturation of Nitrogen = F1N2/(0.78+P3)

The sharp increase in VGE observed at 22,500 ft is relevant to plans for future fighter aircraft, such as the F-22 and EuroFighter. These aircraft are designed to be capable of cruise at an altitude of 60,000 ft (18,288 m) or higher with a 5-psid cockpit (15). This will expose the aircrew to a cockpit altitude of 22,500 ft. During the past several decades, current and previous aircraft with 5-psid pressurization systems were limited to 50,000 ft (15,240 m) or below. When the 5-psid differential was added to the 1.69 psi at 50,000 ft, the cockpit pressure surrounding the pilot was equivalent to about 20,200 ft (6,157 m). In normal operations, including combat, these aircraft rarely exceeded 40,000 ft (12,192 m; cockpit altitude about 16,800 ft, 5,121 m) for more than a few minutes. Thus, the potential for developing VGE at the level described here was very minimal. In addition, decompression was rare and, when it occurred, it was usually to altitudes below 40,000 ft.

Approximately 75% of the subjects exposed to 22,500 ft (6,858 m), in this study, developed VGE within the first 60 min of exposure (Fig. 3). Although higher incidence of VGE per se may not be reason for concern, the presence of VGE relates to the consequences of subsequent decompression. If pilots cruising at 60,000 ft in a 5-psid fighter cockpit (22,500 ft cockpit altitude) for 45–60 min were subsequently decompressed to 60,000 ft due to loss of pressurization, growth of the existing “silent” bubbles would provide a potential for rapid onset of symptoms (19). The situation described above is similar to the conditions resulting in an incident discussed by Fryer (9). He described an incident of fatal DCS (Fatality IX) caused by exposure to 25,000 ft for only 25 min followed by further decompression to 40,000 ft (12,192 m). The respiratory symptoms became evident “almost at once” and, despite immediate descent, the crewmember later collapsed and died from severe neurologic and cardiopulmonary symptoms.

Breathing mixture affects incidence of VGE and, there-
DCS symptoms by U-2 pilots was recently documented by Bendrick et al. (3).

Other civilian (4), and military unpressurized aircraft have operational missions and performance capabilities which exceed 21,000 ft, including AC-130H gunships. The new CV-22 tiltrotor Osprey will be unpressurized and will have a ceiling of 26,000 ft (7,925 m) (1). Although standard oxygen equipment will prevent hypoxia, unpressurized cruise above 21,000 ft will present crews of these craft with a DCS hazard as presented herein and recalled in a survey of pilots with 20,000–25,000 ft exposure experience dating to World War II (22). With a planned cruise time of only 1 h at 22,500 ft, a 10% incidence of DCS symptoms (Fig. 3) is likely. These findings are also applicable to civil aviation endeavours and soaring activities capable of considerable cruise/loiter time. The civil activities are governed by Federal Aviation Administration Federal Aviation Regulation Parts 91.211 and 121.327–333 which do not stipulate time limits for exposures above 21,000 ft. Performance of unpressurized private and light commercial aircraft has improved sufficiently to allow routine cruise well above 21,000 ft.

CONCLUSIONS

A 5% threshold for DCS symptoms was concluded to be 20,500 ft under the conditions of this study. Reconsideration of current military and civilian altitude exposure guidance is recommended. Suggested issues include: 1) use of 100% oxygen during all flight where crewmembers are exposed to greater than 16,000 ft; 2) recognition of DCS hazard above 21,000 ft; 3) restriction of time above 21,000 ft to no more than 30 min when no preoxygenation is used; 4) use of preoxygenation to reduce the potential for DCS symptom development when operating above 21,000 ft.

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