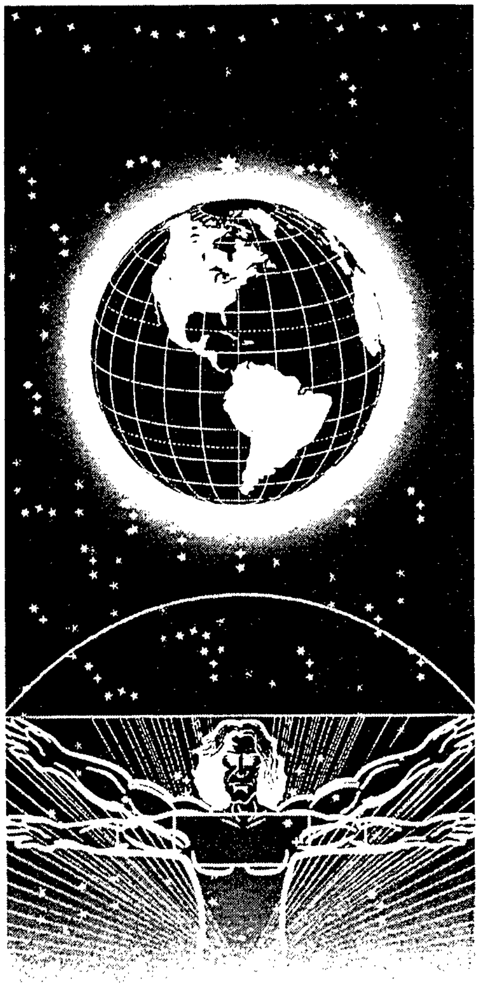
AFRL-HE-BR-TR-2002-0212



UNITED STATES AIR FORCE RESEARCH LABORATORY

GENDER NOT A RISK FOR ALTITUDE DECOMPRESSION SICKNESS RISK

James T. Webb
Nandini Kannan
Andrew Pilmanis

HUMAN EFFECTIVENESS DIRECTORATE
BIODYNAMICSC AND PROTECTION DIVISION
PROTECT SYSTEMS BRANCH
2485 Gillingham Dr.
Brooks AFB, Texas 78235-5105

October 2002

NOTICES

ANDREW PILMANIS, Ph.D.
Contract Monitor

WESLEY BAUMGARDNER, Ph.D.
Chief, Biodynamics and Protection Division

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-01-0188

1. REPORT DATE *(DD-MM-YYYY)*
30-11-2002

2. REPORT TYPE
Final

3. DATES COVERED *(From - To)*
1Oct1995-30Nov2002

4. TITLE AND SUBTITLE
GENDER NOT A FACTOR FOR ALTITUDE DECOMPRESSION SICKNESS RISK

5a. CONTRACT NUMBER
F-33615-92-C-0018 & F-41624-97-D-6004

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER
62202F

6. AUTHORS
James T. Webb, Ph.D., Nandini Kannan, Ph.D., and Andrew A. Pilmanis, Ph.D.

5d. PROJECT NUMBER
7184

5e. TASK NUMBER
58

5f. WORK UNIT NUMBER
01

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Wyle Laboratories, Life Sciences, Systems and Services Inc.
2485 Gillingham Drive
San Antonio, TX 78235-5105

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
High Altitude Protection Research
Protection Systems Branch
Air Force Research Laboratory
2485 Gillingham Drive
San Antonio, TX 78235-5105

10. SPONSOR/MONITOR'S ACRONYM(S)
AFRL/HEPR

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
AFRL-HE-BR-TR-2002-0212

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for Public Release; distribution is unlimited.

13. SUPPLEMENTARY NOTES
This report will be published in Aviation, Space, and Environmental Medicine as a peer-reviewed article in 2003, Volum 74.

14. ABSTRACT
INTRODUCTION. We conducted 25 altitude chamber decompression exposure profiles incorporating both genders in a prospective attempt to clarify the role of gender in DCS susceptibility. METHODS. The 291 human subjects were exposed (961 subject-exposures) to simulated altitude for up to 8 h, using zero to 4 h of preoxygenation. Subjects breathed 100% oxygen, rested or performed mild or strenuous exercise while decompressed, and were monitored for precordial venous gas emboli (VGE) and DCS symptoms. RESULTS. No differences (P=0.24) in DCS incidence were observed between males (49.5%) and females (45.3%). Higher DCS incidence ($P < 0.001$) was observed in the heaviest males, females with the highest body fat, and in subjects with the highest body mass indices and lowest levels of fitness. CONCLUSION. No differences in altitude DCS incidence were observed between males and females under our test conditions. No apparent need exists for changes in procedures, training, or equipment to enhance protection from DCS based on gender.

15. SUBJECT TERMS
decompression sickness, gender, fitness, body mass index, age, weight, venous gas emboli

16. SECURITY CLASSIFICATION OF: a. REPORT	b. ABSTRACT	c. THIS PAGE	17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
U	U	U	UU	13	James T. Webb
					19B. TELEPHONE NUMBER *(Include area code)* 536-3439

Standard Form 298 (Rev. 8/98)
Prescribed by ANSI Std. Z39.18

GENDER NOT A FACTOR FOR ALTITUDE DECOMPRESSION SICKNESS RISK

James T. Webb, Nandini Kannan, and Andrew A. Pilmanis

ABSTRACT: INTRODUCTION. Early, retrospective reports of the incidence of altitude decompression sickness (DCS) during altitude chamber training exposures indicated that females were more susceptible than males. We hypothesized that a controlled, prospective study would show no significant difference. METHODS. We conducted 25 altitude chamber decompression exposure profiles. A total of 291 human subjects, 197 males and 94 females, underwent 961 exposures to simulated altitude for up to 8 h, using zero to 4 h of preoxygenation. Throughout the exposures, subjects breathed 100% oxygen, rested or performed mild or strenuous exercise, and were monitored for precordial venous gas emboli (VGE) and DCS symptoms. RESULTS. No significant differences in DCS incidence were observed between males (49.5%) and females (45.3%). However, VGE occurred at significantly higher rates among men than women under the same exposure conditions, 69.3% and 55.0% respectively. Females using hormonal contraception showed significantly greater susceptibility to DCS than those not using hormonal contraception during the latter two weeks of the menstrual cycle. Significantly higher DCS incidence was observed in the heaviest males, in females with the highest body fat, and in subjects with the highest body mass indices and lowest levels of fitness. CONCLUSION. No differences in altitude DCS incidence were observed between the sexes under our test conditions, although males developed VGE more often than females. Age and height showed no significant influence on DCS incidence, but persons of either sex with higher body mass index and lower physical fitness developed DCS more frequently.

INTRODUCTION

The increased role of females in military aviation was addressed by the Presidential Commission on the Assignment of Women in the Armed Forces initiated by President Bush in 1992 (34). Susceptibility to decompression sickness (DCS) was among the questions posed about male-female differences in response to military aerospace environmental stresses.

It is generally accepted that DCS symptoms are caused by evolved gas emboli (bubbles) which apply direct pressure on nerves and other tissues, block small blood vessels, and interact with proteins in blood. Although pain is the most common symptom of DCS, other signs and symptoms include skin, neurologic and respiratory manifestations. These symptoms range from barely noticeable to life threatening and constitute an avoidable threat to mission accomplishment.

The evolved gas emboli result from nitrogen, dissolved in our tissues and blood at ground level, becoming supersaturated during a subsequent decompression. Since fats dissolve at least 5 times the nitrogen volume that would dissolve in water or blood, a higher fat content implies a greater total nitrogen content in body tissues. Due to females' higher body fat content, a typical female will contain more dissolved nitrogen than a typical male of the same weight, possibly implying greater need for denitrogenation in females or greater propensity to develop DCS symptoms.

Although several retrospective studies (3,33) have indicated that gender is a significant factor in DCS susceptibility, some prospective research chamber studies (8,12,21) have not supported those results. Other factors have also been implicated as influencing susceptibility to DCS. Increasing age and higher body fat have long been cited as factors which increase susceptibility to DCS (6,18).

A prospective research program at Brooks Air Force Base was initiated using standardized altitude research chamber methodology to answer questions regarding susceptibility based on gender and other individual variables. Exposure profiles were designed with diverse altitudes, exposure durations, and other parameters, thus ensuring that any patterns of susceptibility were not a function of specific exposure conditions.

METHODS

All protocols were reviewed and approved by the Brooks AFB Institutional Review Board. The voluntary, fully-informed consent of the subjects used in this research was obtained in accordance with AFI 40-402 (Protection of Human Subjects in Biomedical and Behavioral Research). The profiles for susceptibility comparisons were chosen from the Air Force Research Laboratory's Altitude Decompression Sickness Research Database at Brooks AFB, TX, where all exposures were accomplished in the same research altitude chamber between March, 1994 and August, 2001 by the same investigators, using the same endpoint/termination criteria. To be included in the analyses comparing incidence of DCS, each altitude exposure profile had to involve subjects of both genders and result in a DCS incidence of 5% to 95% DCS in both males and females. The requirement to be in this range of DCS response was established to ensure that severity of the profiles was sufficient to elicit some, but not overwhelming DCS.

Subjects and Experimental Procedures. Subjects (n=291; 197 males and 94 females) participated in 25 altitude exposure profiles involving 961 exposures as described in Table I. The five profiles to altitudes below 6,096 m (20,000 ft, 102 exposures; Table I, Profiles 1-5) were only used for determination of the zero-preoxygenation altitude DCS and venous gas emboli (VGE) threshold probit curves. Those profiles did not result in at least 5% DCS in both males and females as stipulated for comparison of DCS incidence. Data from 859 of the 961 exposures during 20 altitude exposure profiles (Profiles 6-25; 150 males and 70 females; 3.9 exposures per subject) were used for comparisons of DCS susceptibility based on gender and other individual variables.

All subjects were nonsmokers for the 2 years preceding exposure, passed an appropriate subject physical, and were otherwise representative of the USAF rated aircrew population. They were not allowed to participate in scuba diving, hyperbaric exposures, or flying for at least 72 h before each scheduled altitude exposure. Peak oxygen uptake (VO_{2peak}), a measure of aerobic fitness, was determined with a SensorMedics® 2900z (Yorba Linda, California) metabolic measurement system as each subject performed dual-cycle ergometry or with a treadmill test (2-min stages) to a mean RQ of at least 1.1 and ACSM test termination guidelines (1) or by estimation of VO_{2max} using the Air Force Fitness Assessment cycle ergometry test[1]. Body fat was measured using a three-site caliper method (1).

Prior to each altitude exposure, a medical monitor conducted a short physical examination of that day's 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 1,524 m (5,000 ft) simulated altitude in the altitude chamber at a rate of 1,524 m/min for an ear and sinus check. Time spent at 1,524 m was less than 5 seconds.

[1] In accordance with Air Force Instruction 40-501, The Air Force Fitness Program, 1 October 1998.

TABLE I. EXPOSURE CONDITIONS AND EXPOSURE N

Profile #	Notes	Altitude M (ft)	Pressure mm Hg	Exposures, N Male	Exposures, N Female	Preox min	Duration h	Activity at altitude
1	* (29)	3,505 (11,500)	493	22	20	0	8	EVA
2	* (30)	4,572 (15,000)	429	10	0	0	6	EVA
3	* (30)	5,029 (16,500)	404	10	0	0	6	EVA
4	* (30)	5,517 (18,100)	378	10	10	0	6	EVA
5	* (30)	6,035 (19,800)	352	10	10	0	6	EVA
6	*† (32)	6,462 (21,200)	332	20	20	0	6	EVA
7	*† (32)	6,858 (22,500)	314	20	20	0	6	EVA
8	† (32)	6,858 (22,500)	314	20	22	0	6	Rest
9	† (¶¶)	6,858 (22,500)	314	26	4	15	4	Moderate
10	†‡ (¶¶)	6,858 (22,500)	314	31	9	0	4	EVA
11	*† (32)	7,254 (23,800)	297	10	9	0	6	EVA
12	*† (20,32)	7,620 (25,000)	282	24	11	0	4	EVA
13	†§ (¶¶)	7,620 (25,000)	282	33	7	90	4	EVA
14	† (¶¶)	7,620 (25,000)	282	21	10	30	4	Moderate
15	†¶ (2)	9,144 (30,000)	226	39	10	60	4	AEVA
16	† (31)	9,144 (30,000)	226	32	31	240	4	EVA
17	† (31)	9,144 (30,000)	226	32	32	90	4	EVA
18	†** (31)	9,144 (30,000)	226	31	32	90	4	EVA
19	† (¶¶)	9,144 (30,000)	226	21	10	75	4	Rest
20	† (28)	10,668 (35,000)	179	37	36	75	3	Rest
21	†¶ (¶¶)	10,668 (35,000)	179	33	10	265	3	AEVA
22	†¶†† (¶¶)	10,668 (35,000)	179	31	10	265	3	AEVA
23	†¶‡‡ (¶¶)	10,668 (35,000)	179	35	9	265	3	AEVA
24	† (¶¶)	12,192 (40,000)	141	28	12	90	1.5	Rest
25	†§§ (¶¶)	12,192 (40,000)	141	26	5	90	1.5	Rest

Parenthetical numbers in the second column refer to published references
* Exposures used to determine zero-preoxygenation DCS threshold
† Exposures used to determine if individual variables effect change in DCS and VGE incidence
‡ Breathing gas 40% nitrogen, 60% oxygen
§ Prebreathe and exposure with 93% Oxygen, 4.2% Argon, and 2.8% Nitrogen
¶ Prebreathe (preoxygenation; preox) began with 10 min of exercise at approximately 75% of VO_{2peak})
** Prebreathe (preoxygenation; preox) began with 15 min of exercise at approximately 75% of VO_{2peak})
†† Staged-decompression at 5,486 m (18,000 ft) for 240 min breathing 100% oxygen
‡‡ Staged-decompression at 5,486 m (18,000 ft) for 240 min breathing 62% Argon and 28% Oxygen
§§ Rate of ascent averaged 24,384 mpm (80,000 fpm)
¶¶ Air Force Research Laboratory Altitude Decompression Sickness Research Database
Altitudes shown to nearest 100 feet. Rest = seated or supine; EVA = extravehicular activity simulation mild exercise as described by Webb et al. (1996); AEVA = EVA exercises performed while adynamic, not walking between exercise stations while decompressed or during prebreathe; Cycle= moderate leg ergometry (30% of VO_{2peak})

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. Breathing gas for preoxygenation (when accomplished), ascent, and altitude exposure was 100% oxygen (aviator's breathing oxygen; normal analysis 99.7-99.8% oxygen) unless noted in Table I.

The subjects were decompressed at 1,524 m/min (unless noted in Table I) until reaching the scheduled altitude (Table I) and remained at that altitude for at least 1.5-h or until another end-point (see below) was reached. During each exposure, the subjects performed exercises (27,32; see Table I) or remained at rest. Subjects were monitored for VGE at regular intervals.

Endpoints. Endpoints of the exposures were: 1) completion of the scheduled exposure (1.5 to 8 h); 2) development of constant DCS pain as reported by the subject (joint awareness or "fullness" and intermittent, mild pain with no impairment of function or performance were not considered DCS); 3) development of DCS signs or symptoms other than constant DCS pain as reported by the subject or observed by changes in behavior, gait, or other mental/physical performance; or 4) observation of gas emboli in the left ventricle. 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 or change in well-being and a list of symptoms was posted in plain view inside the chamber[2].

Data Collection and Analysis. Precordial echo-imaging for gas emboli was accomplished three to five times per h using a Hewlett-Packard® SONOS 500 or 1000 Echo Imaging System (Andover, Massachusetts). The subjects lay on a horizontal examining table on their left side or remained in a seated position. 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. Grading of VGE employed a modified 4-grade Spencer Scale where Grade 1 are infrequent VGE and Grade 4 VGE are of sufficient magnitude to overwhelm the heart sounds (23). Each VGE monitoring session was video taped and onset times for each level of VGE were recorded to provide information on exposure severity independent of DCS incidence.

For development of the altitude VGE and DCS threshold curves, data obtained after 4 h were deleted to allow comparison between altitudes at equal exposure times of 4 h. For comparison of VGE and DCS incidence between genders, conditions of preoxygenation, exposure altitude, exposure duration, and activity at altitude were identical as shown in Table I.

Use of hormonal contraceptives is defined here as use of oral or parenteral hormones as a method of contraception. Use of specific hormones was not evaluated due to the diversity of use and low N.

Chi Square analysis was used to test for differences in DCS incidence between genders. A Probit analysis (using the SAS Statistical Package) was used to develop curves relating incidence and altitude, and corresponding 95% confidence intervals (11,32).

RESULTS

Incidence of DCS and VGE under variable conditions. The conditions of this study resulted in a mean DCS incidence of 48.0% during 859 subject-exposures by 150 males and 70 females. There were no differences in DCS incidence in any of the profile comparisons or in the total group of 550 male exposures (49.5% DCS) vs. 309 female exposures (45.3% DCS; Table II) ($P > 0.24$). The 69.3% VGE observed during the male exposures was higher (Chi Square = 17.48; $P < 0.001$) than the 55.0% VGE

[2] Pain or tightness in a joint or muscle, headache, visual difficulties, light headedness, dizziness, unusual weakness or fatigue, chest pain, tightness in chest, coughing, difficulty breathing, skin itching or tingling, or any change in how you feel.

observed during the female exposures. Grade 4 VGE showed an even larger difference between males (38.0%) and females (17.2%; Chi Square = 40.48; P < 0.001).

The data shown in Figure 1 as examples of onset rate equivalence between genders were chosen because they represent the largest number of male and female subjects accomplishing identical exposures in nearly identical numbers (Profiles 17 and 20 in Table I). With gender as the only variable, there were no differences between the onset rates of DCS or final incidence of DCS during the exposures: 1) 4 h at 9,144 m (30,000 ft; Profile 17) with mild exercise following 90 min of preoxygenation; or 2) 3 h at 10,668 m (35,000 ft; Profile 20) while resting following 75 min of preoxygenation.

Altitude Threshold of DCS. Figure 2 shows male, female, and combined-gender threshold curves for altitude DCS. The probit curves (11) for males and females indicate no difference in DCS susceptibility based on gender. This is shown in Figure 2 as seen by the confidence bands for the curve representing both genders. The combined-gender subject pool yielded a 5% DCS threshold at 19,500 ft and a 50% incidence at 23,200 feet.

Treatment of DCS. The 48.0% incidence of DCS symptoms during the 859 exposures included 32 which required hyperbaric oxygen (HBO) therapy to successfully resolve or was employed as a precautionary treatment. There was no significant difference between the rate of male exposures (18; 6.8% of the 263 male exposures with DCS) and female exposures (14; 10.1% of the 139 female exposures with DCS) requiring HBO (Chi Square = 1.29, N.S.). The ratio of U.S. Navy Treatment Table V vs. VI treatments was also not significantly different between males (9 vs. 9) and females (9 vs. 5) (Chi Square = 0.65; N.S.).

Menstrual Cycle and Hormonal Contraception vs. DCS Incidence. The effect of the menstrual cycle on female susceptibility to DCS was evaluated by examination of 269 female subject-exposures with reliable menstrual cycle data. Of these, 120 subject-exposures involved hormonal contraception. Those using hormonal contraception were more likely to develop DCS (52.5%) than those not using hormonal contraception (40.3% DCS; Chi Square = 4.01; P < 0.05). There was no difference in DCS during the first two weeks of the cycle based on use of hormonal contraception (Chi Square = 0.01; see Fig. 3); however, if only those exposed during the last half of their menstrual cycle are compared, those using hormonal contraception had approximately double the DCS incidence (59.6%; N=52) of those not using hormonal contraception (31.7%; N = 60) (Chi Square = 8.81; P < 0.005). The higher incidence of DCS during the last two weeks of the menstrual cycle by those using hormonal contraceptives is not significantly greater than the incidence in male subjects. However, the 31.7% DCS observed during exposures of those not on hormonal contraceptives in last two weeks of their menstrual cycle is significantly less than the 49.5% observed during all male exposures (Chi Square = 6.86; P< 0.01).

Height. Neither male or female exposures showed a relationship between height and DCS incidence when compared separately. However, when the exposures representing the tallest third of each gender were compared with the exposures representing the shortest third, significance (P < 0.01) was reached in comparisons of VGE and Grade 4 VGE. The tallest subjects in a combined group of males and females showed a trend toward greater DCS susceptibility (Chi Square 3.36; P = 0.067).

Weight. The males representing the heaviest third of the male exposures developed more VGE, Grade IV VGE, and DCS than the lightest third (Table II; P < 0.05). Female exposures did not show a significant relationship, although when all exposures representing the heaviest third of each gender were compared with the lightest third, significantly more VGE, Grade IV VGE, and DCS (P < 0.05) were evident in the heavier group.

BMI [Body Mass Index; weight in kg/(height in m)^2]. Both male and female exposures representing the highest third by BMI developed more DCS than the third with the lowest BMI (Table II; $P < 0.05$) as reflected in the combined group.

Body Fat. Female exposures representing the highest third by body fat had a higher incidence of DCS ($P < 0.05$). This difference was not matched when comparisons were made between VGE in the highest and lowest third of females or between male exposures (Table II) ro in comparisons of higher and lower thirds of males and females segregated by body fat.

TABLE II. GENDER VS. DCS AND VGE INCIDENCE

Variable, Mean ± S.D.; Range (N)		VGE, %	Gr4VGE, %	DCS, %
Male Subject-Exposures (550)		69.3†	38.0†	49.5
Height, cm	177.8 ± 7.3; 160 - 203 (550)	69.3	38.0	49.5
Tallest third	185.9 ± 4.1; 182 - 203 (182)	73.1	40.1	54.4
Shortest third	170.0 ± 3.8; 160 - 174 (180)	67.2	36.7	45.6
Weight, kg	82.7 ± 11.0; 49.5 - 131.4 (550)	69.3†	38.0†	49.5
Heaviest third	94.7 ± 8.0; 86.8 - 131.4 (183)	76.5*	44.3*	61.7*
Lightest third	71.4 ± 4.9; 49.5 - 77.7 (184)	63.6	34.2	39.7
BMI	26.1 ± 2.8; 17.5 - 34.9 (550)	69.3†	38.0†	49.5
Highest third	29.1 ± 1.5; 27.4 - 34.9 (183)	72.7	41.0	59.0*
Lowest third	23.1 ± 1.5; 17.5 - 24.9 (182)	69.8	40.1	43.4
Body Fat, %	16.8 ± 5.1; 5.7 - 31.8 (489)	68.7	37.2	50.5
Highest third	22.3 ± 2.2; 19.4 - 31.8 (165)	66.7	38.2	50.3
Lowest third	11.2 ± 2.7; 5.7 - 14.6 (167)	67.7	39.5	47.9
Age, y	30.9 ± 5.7; 19.9 - 43.8 (550)	69.3†	38.0†	49.5
Oldest third	37.6 ± 2.2; 34.3 - 43.8 (183)	77.6*	47.5*	53.6
Youngest third	24.5 ± 2.0; 19.9 - 27.6 (182)	56.0	26.9	45.6
$VO_{2peak/max}$	42.6 ± 6.8; 25.5 – 62.6 (500)	67.8†	37.0†	47.4
Highest third	50.1 ± 4.2; 45.3 – 62.6 (166)	59.0	28.3	38.0
Lowest third	35.5 ± 3.0; 25.5 – 39.8 (168)	70.8*	41.7*	50.6*
Female Subject-Exposures (309)		55.0	17.2	45.3
Height, cm	165.2 ± 6.6; 147 - 179 (309)	55.0	17.2	45.3
Tallest third	171.8 ± 3.3; 168 - 179 (117)	58.1	21.4	43.6
Shortest third	159.3 ± 4.7; 127 - 147 (127)	50.4	14.2	45.7
Weight, kg	63.1 ± 7.9; 45.9 - 85.9 (309)	55.0	17.2	45.3
Heaviest third	72.2 ± 4.2; 67.0 - 85.9 (102)	59.8	18.6	51.0
Lightest third	54.4 ± 3.2; 45.9 - 59.4 (103)	46.6	12.6	41.7
BMI	23.1 ± 2.3; 17.9 - 29.4 (309)	55.0	17.2	45.3
Highest third	25.7 ± 1.1; 24.3 - 29.4 (100)	64.0	22.0	49.0*
Lowest third	20.5 ± 1.1; 17.9 - 22.1 (102)	53.9	15.7	32.4
Body Fat, %	22.2 ± 4.4; 14.0-31.4 (240)	58.3	16.7	46.3
Highest third	27.0 ± 2.0; 24.5 - 31.4 (79)	55.7	13.9	55.7*
Lowest third	17.3 ± 2.1; 14.0 - 19.3 (83)	57.8	24.1	38.6
Age, y	29.0 ± 5.9; 19.5 - 43.4 (309)	55.0	17.2	45.3
Oldest third	36.0 ± 3.5; 30.4 - 43.4 (103)	62.1*	25.2*	38.8
Youngest third	22.9 ± 1.4; 19.5 - 25.1 (104)	42.3	7.7	49.9
$VO_{2peak/max}$	35.6 ± 5.1; 25.1 – 54.6 (260)	58.1	18.1	46.2
Highest third	41.2 ± 3.6; 37.6 – 54.6 (88)	52.3	20.5	35.2
Lowest third	30.2 ± 1.9; 25.1 – 33.3 (86)	60.5	14.0	54.7*

BMI = Body Mass Index; weight in kg/(height in m)^2 $VO_{2peak/max}$ in ml/min/kg

* $P < 0.05$ (Chi Square); shown on highest value within each gender

† $P < 0.05$ (Chi Square); shown on highest value between genders

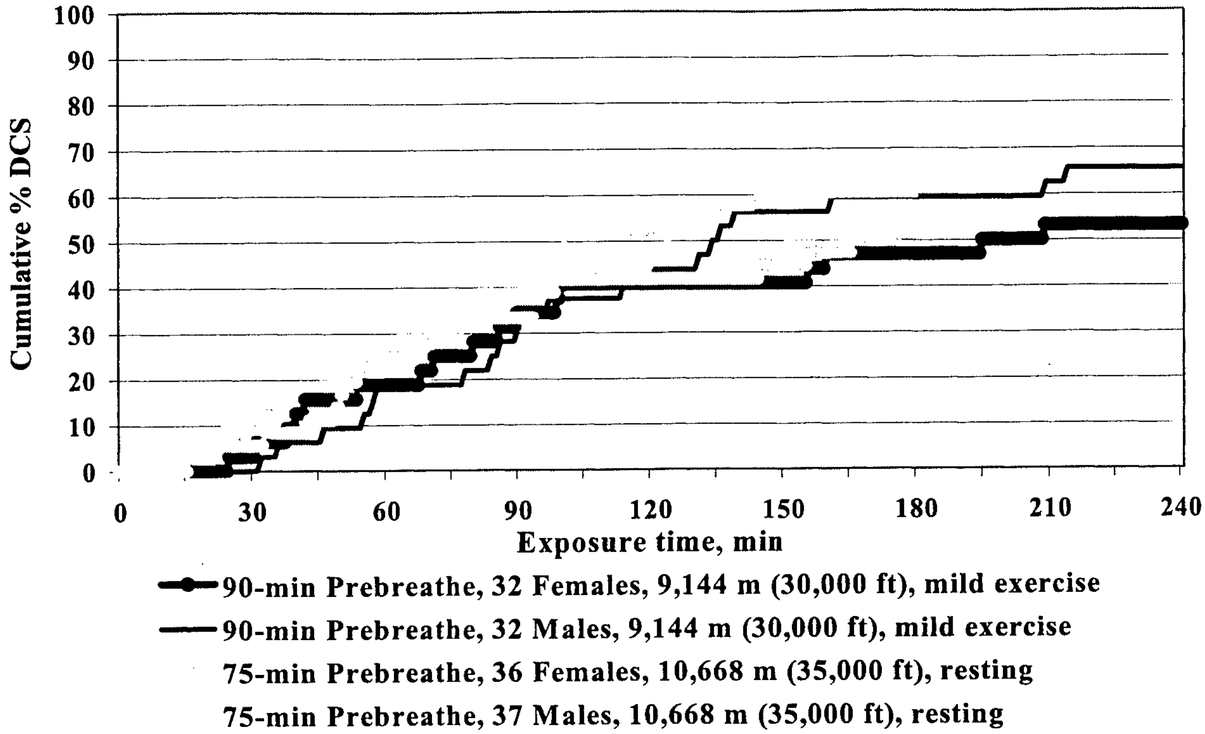


Fig. 1 Cumulative DCS Incidence in Male and Female Subjects at 9,144 m (30,000 ft) and 10,668 m(35,000 ft)

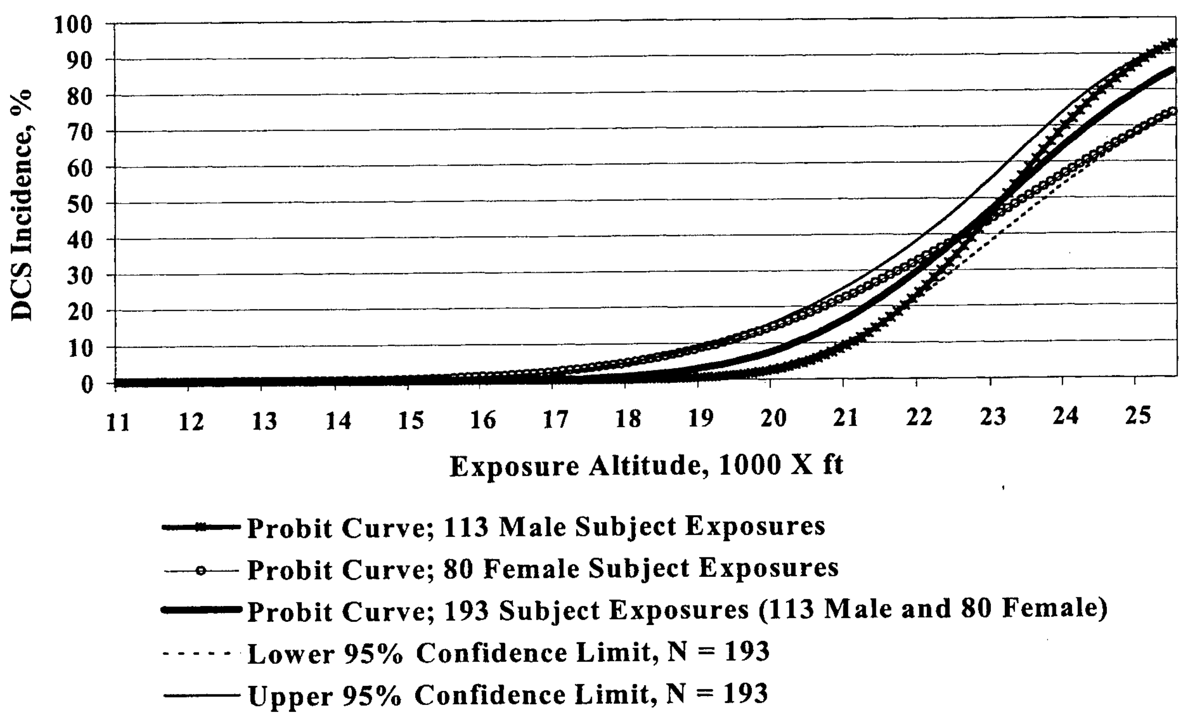


Fig. 2 Zero-Preoxygenation Altitude Threshold Curves for DCS and VGE.
Data from, in part, (29,30,32). Probit analysis based on Finney (11).

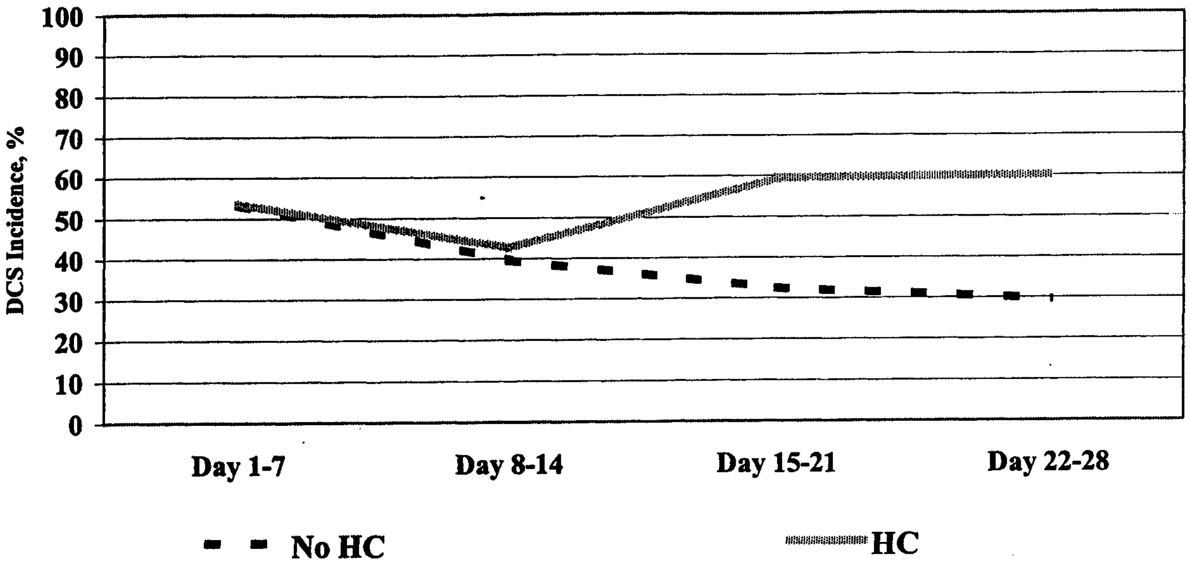


Fig. 3 Female DCS Susceptibility vs. Menstrual Cycle Week and Use of Hormonal Contraceptives
HC = Hormonal Contraceptive use, N = 120; Control N = 149

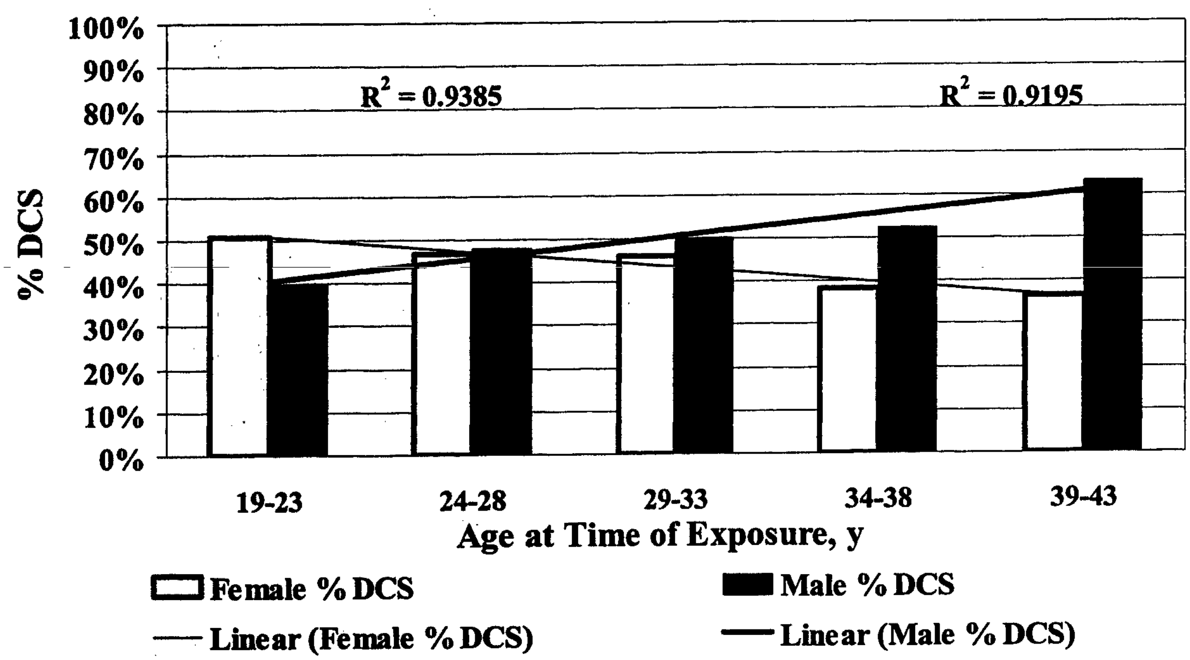


Fig. 4 Age vs. DCS Incidence

Age. The difference in age of the females at the time of their subject-exposures vs. the males was less than two years. The male exposures representing the oldest third of the 550 male exposures did not develop significantly more DCS than the youngest third (Table II). However, the male exposures within the oldest 5-y group (39-43 y) as shown in Fig. 4 resulted in a higher level of DCS ($P < 0.03$; Fig. 4) than the male exposures in the youngest 5-y group (19-23 y). The trend lines based on 5-y age groups indicate positive correlation of age with DCS (Fig. 4; MS Excel Linear Regression Trendline; $R^2 > 0.91$); males showing greater incidence of DCS with increasing age and females showing an inverse relationship. Due, in part, to the opposite slope of male and female trendlines for age group vs.

DCS incidence, there was no difference between the oldest and youngest groups consisting of both males and females. However, during both male and female subject exposures, VGE and Grade 4 VGE were more prevalent in the oldest vs. youngest third of the age groupings ($P < 0.05$; Table II).
Aerobic Fitness. Males showed significant differences between occurrence of VGE, Grade 4 VGE, and DCS between the upper and lower third of fitness levels as determined by VO_{2peak}. Females showed a difference only in DCS incidence yielding a higher ($P < 0.0007$) DCS incidence for the 132 male and female lesser fit subjects than the 94 better fit male and female subjects.

DISCUSSION

The altitudes and other environmental parameters included in this study were chosen to allow considerable variation in response due to the effect of any of the measured variables, maximizing the potential for detection of differences in DCS incidence. The 48% DCS incidence in 859 exposures resulted from a diverse array of conditions which should preclude any one environmental parameter from having undue influence on the determination of gender or anthropometric effects on DCS susceptibility. The finding of no difference between male and female altitude DCS incidence agrees with some earlier reports (8,12,15,21). However, previous findings of greater female susceptibility during training chamber exposures (3,4,33) require discussion.

Reports of DCS during U. S. Air Force training chamber exposures may have been influenced by a number of factors. First, briefings before training chamber exposures, conducted to inform the trainees of proper procedures and hazards of hypoxia and DCS, were not fully standardized. This allowed some briefings to have gender-specific impact on the trainees, in particular, briefings to female nurses that stated their greater DCS susceptibility. Second, motivation of trainees to report symptoms may be related to their career field. Until 1989, personnel experiencing neurologic DCS symptoms were usually grounded permanently. Even mild limb pain DCS symptoms during chamber training were cause for fear of grounding in the mostly male aircrew population. Pilot trainees, being highly motivated to avoid grounding, had little incentive to report symptoms. In contrast, a large majority of the flight nurses who received chamber training from 1968 to 1986, took the course as auxiliary training and did not plan to participate regularly in flight activities. Consequently, they were not in jeopardy of losing flight pay or career plans if grounded. Therefore, fear of grounding was not a factor for most nurses. Hence, the gender difference in DCS incidence during this period may actually have been more a function of reporting than of physiologic differences related to gender. This is upheld by the paucity of official reports of DCS in the mostly male U-2 community despite much higher incidence of DCS revealed when anonymity was assured (Bendrick et al., 1996).

To better understand the reporting issue, we completed a retrospective analysis of computerized records of hyperbaric oxygen treatment resulting from over 19,000 training chamber exposures accomplished by pilot trainees from 1978 to 1991. Over 550 of those pilots (2.75%) were females. Each pilot trainee completed at least two exposures during the first portion of their pilot training program. If the incidence of DCS requiring hyperbaric therapy was the same for these 19,000 pilot trainees as it was for all USAF altitude chamber trainees during an analogous period (0.207% female DCS versus 0.048% male DCS) (33), 1 female and 9 male trainees should have developed DCS requiring hyperbaric therapy. None of these pilot trainees, male or female, were treated with hyperbaric oxygen therapy for their DCS symptoms. Concern about potential grounding may have contributed to the lack of reports. In addition, any pilot trainee with symptoms would have been given ground-level oxygen until arrival at a hyperbaric treatment facility. Since no hyperbaric treatment facilities were co-located with pilot training bases during that time, the delay between report of symptoms and initiation of treatment would likely have been at least two hours. During that time, most or all of the symptoms from such an exposure could have resolved (14); hence no record of hyperbaric oxygen treatment. As reviewed by Bassett (4), this was not the case for most female trainees (mostly nurses) who received altitude chamber training at Brooks AFB, TX where hyperbaric therapy was immediately available.

While the rate of onset of symptoms during altitude exposures (Fig. 1) and the total incidence of DCS during long and varied exposures (Table II) are of interest, the altitude threshold of symptoms is also a factor in determining the influence of gender in DCS susceptibility. The threshold altitudes for 50% DCS in males and females were nearly identical at approximately 7,071 m (23,200 ft; Fig. 2), reinforcing the lack of difference in DCS incidence between genders when all subject-exposures are compared with gender as the only variable. The DCS probit curve indicates approximately 15% DCS (Fig 2) at 6,401 m (21,000 ft), within about 4% of Kumar et al. (1990), who found an incidence of 11.5% DCS in 78 exposures of male and female subjects to 6,401 m without preoxygenation. Under the same conditions reported here, the DCS risk prediction from the Air Force Research Laboratory's Altitude DCS Risk Assessment Computer model (Pilmanis et al., 2000) is 14%.

The 50% risk of DCS at 7,163 m (23,500 ft; Table I, Profile 11) in our data contrasts with the commonly-stated DCS threshold altitude of 7,620 m (25,000 ft). The 7,620-m ceiling in current military[3] and civilian[4] guidance is based on WWII data which used exposure termination criteria which exceeded currently acceptable criteria. Despite considerable DCS incidence reported by male and female subjects during our research exposures simulating training scenarios, DCS has only been occasionally reported during USAF unpressurized trainer (T-37) missions. However, the duration of these training missions to altitudes exceeding 6,401 m (21,000 ft) is usually less than 30 min. The reporting incidence following cross-country flights, where exposure to altitudes above 6,401 m exceeds 30 min, may be low because of perceived severe career consequences as discussed by Bendrick et al. (5).

Other civilian, and military unpressurized aircraft have operational missions and performance capabilities which exceed 6,401 m (21,000 ft). Some unpressurized aircraft in testing will have a ceiling above 7,620 m (25,000 ft). Although standard oxygen equipment will prevent hypoxia, unpressurized cruise above 7,620 m will present both male and female crewmembers with a DCS hazard (26,32).

The significantly higher levels of VGE and Grade 4 VGE observed during male exposures does not appear to relate to % body fat. The greater muscle mass in males may allow greater muscle tension to develop in muscle and associated connective tissue, promoting higher levels of gas emboli formation in the low-pressure venous system within these tissues. With less muscle mass, females develop less joint and connective tissue tension, hence lower pressure differentials in these areas. Lower pressure differentials may result in lower cavitation potential which should result in formation of fewer bubbles in females. Although the group of females representing the higher third of percent body fat had a higher level of DCS (Table II), their incidence of DCS was not higher than the group of males representing the higher third of percent body fat.

The frequency of HBO treatments required for male cases of DCS versus female cases of DCS in this set of subject-exposures was not significantly different ($P > 0.05$). This finding concurs with the altitude DCS treatment frequencies reported by Rudge and Shafer (21) and diving survey data (24) but not with other reports (7,33). Although the data set was much larger for the studies which showed a greater requirement for treating females vs males with HBO following altitude chamber training, the

---

[3] USAF Air Force Instruction 11-202V3, General Flight Rules, 9 February 2001

[4] Federal Aviation Regulation Parts 91.211 and 121.327-333

current data were derived from prospective research chamber exposures where subject briefing and procedures were standardized before data collection.

Our data from 149 female exposures by subjects not using hormonal contraception (Fig 3.) agree with other reports (10,13,17,22) in showing a reduction in susceptibility from week one through week four of the menstrual cycle. Although there is a strong correlation (MSExcel linear regression trendline; $R = 0.91$), a comparison of first vs. last week's DCS incidence is borderline significant (Chi Square = 3.84; $P < 0.05004$).

The data from 52 female exposures for subjects using hormonal contraception in the last two weeks of their menstrual cycle show greater susceptibility to DCS (Fig. 3; $P = 0.003$) than exposures by the 61 females not using hormonal contraception. This difference may relate to effects of hormonal contraceptives on fluid balance. Our observation of increasing susceptibility as the menstrual cycle progresses from menses for those using hormonal contraception is in contrast with analogous data from SCUBA diving females who showed higher DCS incidence during menses (9).

Height was a positive factor ($P < 0.05$) in development of more VGE (Chi Square = 7.49) and Grade 4 VGE (Chi Square 29.79) when upper and lower thirds of all 859 subject-exposures were compared. The same relationship was not evident within male or female exposures analyzed separately. This finding was different from Motley et al. (18), who reported that males with greater height developed DCS more frequently. Weight was a positive factor during male and all exposures for greater incidence of VGE, Grade 4 VGE, and DCS in agreement with Behnke's (6) report of correlation between increasing weight and DCS susceptibility. BMI appeared to reflect the positive relationship between higher male weight and higher DCS incidence and greater female body fat content and higher DCS incidence in agreement with previous reports (6,18). The higher DCS incidence associated with lower levels of aerobic fitness may relate to a lower relative degree of vascularization and potential effects on denitrogenation in the less fit subjects.

The finding that increasing age in males is related to increased incidence of DCS (Fig. 4) is in general agreement with previous reports (18,25). Since increasing age is associated with decreased cardiac index (cardiac output per m^2 of body surface area), older men may require more denitrogenation time to achieve the same degree of protection against DCS. This relationship was, in general, reversed during female subject exposures (Fig. 4).

CONCLUSIONS

The lack of difference in DCS incidence experienced by male and female human subjects during identical, prospective, decompression profiles is contrary to previous findings from retrospective analyses of training chamber exposures. The altitude threshold for 50% DCS during zero-preoxygenation exposures is below the 7,620 m (25,000 ft) allowed for unlimited flight without preoxygenation under USAF and FAA regulations. Although few cases of DCS have been reported as a result of zero-preoxygenation exposure to altitudes below 7,620 m, the incidence of such exposures lasting for sufficient time to result in symptoms may soon show a large increase coincident with evolving aircraft capabilities.

The finding that female subject-exposures resulted in a lower incidence of VGE and Grade 4 VGE is consistent with previous reports on bubble formation in males and females. In contrast with previous reports, females did not require HBO treatment to relieve DCS symptoms more frequently than males.

Females showed nearly identical susceptibility to DCS during the first two weeks of the menstrual cycle, regardless of hormonal contraceptive use. DCS incidence during the latter two weeks is higher for those using hormonal contraceptives, although not in comparison with male DCS incidence.

Height was a significant factor in susceptibility to develop VGE or Grade IV VGE only in comparisons of the tallest third of both genders with the shortest groups. Weight was a significant factor for males with the heaviest third developing more VGE, Grade IV VGE, and DCS. Although females did not show a significant relationship between weight and DCS incidence, the combined upper third of both genders had higher incidence of VGE and DCS than the lower third. BMI was a factor showing a positive relationship with VGE and DCS. The female group with the highest body fat % developed DCS more frequently than the female group with the lowest body fat %, although not more frequently than the male group with the highest body fat %.

Increasing age of male subjects was only a significant factor in DCS susceptibility when the exposures of the 39-43-yr-old group was compared with the 19-23-yr-old group. The oldest third of each gender developed more VGE and more Grade 4 VGE than the youngest third. Higher aerobic fitness was shown to be a significant factor in protection from DCS for both males and females.

These prospective results are not in agreement with previous reports of gender-related susceptibility derived from retrospective analyses. The lack of difference in DCS susceptiblity based on gender as documented herein implies that procedures, equipment (personal or aircraft), and training of male and female aircrew should not require differentiation based on susceptibility to DCS.

ACKNOWLEDGMENTS

This research was sponsored, in part, by the Air Force Research Laboratory, Brooks AFB, TX, (USAF Contracts F-41624-97-D-6004, and F-33615-92-C-0018), USSOCOM, NAVAIR, and by NASA Contract T-82170 and by the Defense Women's Health Research Program (Study NR A-6778). We appreciate the technical support of Ms. Heather O. Alexander, and Ms. Michele D. Fischer. Opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the United States Air Force.

REFERENCES

1. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription (5th Ed.). Baltimore: Williams and Wilkins. 1995.
2. Balldin UI, Pilmanis AA, Webb JT. The effect of simulated weightlessness on hypobaric decompression sickness. Aviat Space Environ Med 2002;73:773-778.
3. Bassett BE. Decompression sickness in female students exposed to altitude during physiological training. AsMA Ann Sci Mtg Preprints. 1973;241-2.
4. Bassett BE. Twelve year survey of the suceptibility of women to altitude decompression sickness. AsMA Ann Sci Mtg Preprints. Anaheim, CA. 1980;12-13.
5. Bendrick GA, Ainscough MJ, Pilmanis AA, Bisson RU. Prevalence of decompression sickness symptoms in U-2 pilots. Aviat Space Environ Med 1996;67:199-206.
6. Behnke AR. Decompression sickness: Advances and interpretations. Aerospace Med 1971;42:255-66.
7. Davis JC, Sheffield PJ, Schuknecht L, Heimbach RD, Dunn JM, Douglas G, Anderson GK. Altitude decompression sickness: Hyperbaric therapy results in 145 cases. Aviat Space Environ Med 1977;48:722-30.
8. Dixon GA, Krutz RW Jr, Fischer JR. Decompression sickness and bubble formation in females exposed to a simulated 7.8 psia suit environment. Aviat Space Environ Med 1988;59:1146-9.
9. Doyle K, Baek PS, De Long ER, Uguccioni DM, Dear G de L, Stolp BW, Dovenbarger JA, Moon RE. Menstruation as a risk factor for decompression illness (DCI) in female scuba divers taking oral contraceptives (OC). Undersea Hyperb Med 24(Suppl):A143, 1997.

10. Dunford RG, Hampson NB. Gender-related risk of decompression sickness in hypperbaric chamber inside attendants: A case control study. (Abstract) Undersea BioMed Res 1992;19(Suppl):37.
11. Finney DJ. Probit Analysis, 3rd Ed. London. Cambridge University Press. 1971;333pp.
12. Horrigan DJ Jr, Waligora JM, Gilbert J, Edwards B, Conkin J, Stanford J Decompression in space. In: The Physiological Basis of Decompression. (Ed. RD Vann). 1989;425-437.
13. Krause KM, Webb JT, Pilmanis AA. The effect of menstruation day on decompression sickness (DCS). (Abstract) Aviat Space Environ Med 1998;69:199.
14. Krause KM, Pilmanis AA. Effectiveness of ground-level oxygen in the treatment of altitude decompression sickness. Aviat Space Environ Med 2000;71:115-8.
15. Krutz RW Jr, Webb JT, Dixon GA. Determining a bends-preventing pressure for a space suit. 26th Annual SAFE Symposium Proceedings. 1988;36-9.
16. Kumar KV, Waligora JM, Calkins DS. Threshold altitude resulting in decompression sickness. Aviat Space Environ Med 1990;61:685-9.
17. Lee VM, St. Leger Dowse M, Bunting AJ, Edge CJ. The menstrual cycle and decompression illness – What are the risks? Undersea Hyperbaric Med 1998;25[Suppl]:11.
18. Motley HL, Chinn HI, Odell FA. Studies on bends. J Aviat Med 1945;16:210-34.
19. Pilmanis AA, Petropoulos L, Kannan N, Webb JT. Altitude decompression sickness (DCS) risk prediction research. Proceedings of the HFM Symposium on "Operational Medical Issues in Hypo and Hyperbaric Conditions", NATO RTO, 16-20Oct00, Toronto, Canada.
20. Pilmanis AA, Webb JT, Kannan N, Balldin UI. The effect of repeated altitude exposures on the incidence of decompression sickness. Aviat Space Environ Med 2002;73:525-31.
21. Rudge FW, Shafer MR. The effect of delay on treatment outcome in altitude-induced decompression sickness. Aviat Space Environ Med 1991;62:687-90.
22. Rudge FW. Relationship of menstrual history to altitude chamber decompression sickness. Aviat Space Environ Med 1990;61:657-9.
23. Spencer MP. Decompression limits for compressed air determined by ultrasonically detected blood bubbles. J Appl Physiol 1976;40:229-35.
24. St. Leger Dowse M, Bryson P, Gungy A, Fife W. Comparative data from 2250 male and female sports divers: Diving patterns and decompression sickness. Aviat Space Environ Med 2002;73:743-9.
25. Sulaiman ZM, Pilmanis AA, O'Connor RB. Relationship between age and susceptibility to decompression sickness. Aviat Space Environ Med 1997;68:695-8.
26. Webb JT, Balldin UI, Pilmanis AA. Prevention of decompression sickness in current and future fighter aircraft. Aviat. Space Environ. Med. 1993;64:1048-50.
27. Webb JT, Fischer MD, Heaps CL, Pilmanis AA. Exercise-enhanced preoxygenation increases protection from decompression sickness. Aviat. Space Environ. Med. 1996;67:618-24.
28. Webb JT, Krause KM, Pilmanis AA, Fischer MD, Kannan N. The effect of exposure to 35,000 ft on incidence of altitude decompression sickness. Aviat. Space Environ. Med. 2001;72:509-12.
29. Webb JT, Olson RM, Krutz RW Jr, Dixon GA, Barnicott PT. Human tolerance to 100% oxygen at 9.5 psia during five daily simulated eight-hour EVA exposures. Res Aviat Space Environ Med 1989;60:415-21.
30. Webb JT, Pilmanis AA. Breathing gas of 100% oxygen compared with 50% oxygen, 50% nitrogen reduces altitude-induced venous gas emboli. Aviat Space Environ Med 1993;64:808-12.
31. Webb JT, Pilmanis AA, Fischer MD, Kannan N. Enhancement of preoxygenation for decompression sickness protection: Effect of exercise duration. Aviat Space Environ Med [In Press; Manuscript 82059].
32. Webb JT, Pilmanis AA, O'Connor RB. An abrupt zero-preoxygenation altitude threshold for decompression sickness symptoms. Aviat. Space Environ. Med. 1998;69:335-40.
33. Weien RW, Baumgartner N. Altitude decompression sickness: Hyperbaric therapy results in 528 cases. Aviat Space Environ Med 1990;61:833-6.
34. Women in Combat. Report to the President. [Presidential Commission on the Assignment of Women in the Armed Forces]. Brassey's (US). Maxwell Maxmillan Co. 1993.