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Enclosed please find a copy of my Master's Thesis proposal, written in fulfillment of requirements for graduating my Master of Public Health program.

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**A PROPOSAL TO STUDY GENDER DIFFERENCES IN THE RATES OF  
DECOMPRESSION SICKNESS**

**By**

**GREGG ALEXANDER BENDRICK, M.D., M.S.**

**PROJECT PROPOSAL**

**Presented to Faculty of The University of Texas**

**Health Science Center at Houston**

**School of Public Health**

**in Partial Fulfillment**

**of the Requirements**

**for the Degree of**

**MASTER OF PUBLIC HEALTH**

**THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT HOUSTON  
SCHOOL OF PUBLIC HEALTH  
Houston, Texas  
May 1994**

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**Submitted: 18 March 1994**

**A PROPOSAL TO STUDY GENDER DIFFERENCES IN THE RATES OF  
DECOMPRESSION SICKNESS**

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The University of Texas  
Health Science Center at Houston  
School of Public Health, 1994**

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**Decompression sickness is the clinical syndrome associated with evolution of nitrogen bubbles in the blood and body tissues upon exposure to an acute reduction in barometric pressure. Because nitrogen is more soluble in fatty substances than in water, adiposity has long been considered a risk factor for the development of decompression sickness. Due to the physiologic differences between the sexes, women have an average eight per cent more body fat than men, so it is possible that women have a greater likelihood of developing decompression sickness. Several studies in the scientific literature seem to support this hypothesis, but they have been associated with such drawbacks as selection and reporting bias, retrospective approach, and the lack of an objective diagnostic modality for the syndrome of decompression sickness.**

**Because there has been no well-controlled prospective study which assesses the gender-specific rates of decompression sickness, an epidemiologic approach is proposed by which a symptom-based questionnaire is anonymously distributed to Air Force pilots after exposure to hypobaric pressures in an altitude**

chamber during routine physiologic training. The gender-specific rates will then be assessed, and a Chi-square analysis will determine whether or not women manifest a significantly higher rate of symptoms than men. By confining questionnaire distribution to a specific population, selection and reporting bias due to personality profile will be minimized.

If no significant difference is found, the Air Force can implement without difficulty specific directives for women to fly combat aircraft. If a significant difference is found, the Air Force will be obligated to communicate such risk to those pilots prior to entry into the career field. In either case it is doubtful that gender differences in decompression sickness could be legitimately used to categorically exclude women from combat flying assignments.

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## ABBREVIATIONS

USAF	United States Air Force.....	1
DCS	Decompression Sickness.....	1
ATF	Advanced Tactical Fighter.....	5
EVA	Extravehicular Activity.....	10
AFB	Air Force Base.....	14
SCN	Survey Control Number.....	18
HAPF	High Altitude Protection Function.....	19
IRB	Internal Review Board.....	22
AFMOA	Air Force Medical Operations Agency.....	23
STINFO	Scientific and Technical Information Office.....	23

## **SECTION I**

### **INTRODUCTION**

#### ***Overview***

Although female pilots have been flying in the United States Air Force (USAF) since 1976, they have been specifically excluded from flying combat aircraft until recently, when early in the Clinton administration the Department of Defense was directed to remove such restrictions. Some concerns, however, have been raised about the physiologic differences between men and women in the context of the aerospace combat environment. One such a problem is that of decompression sickness (DCS) associated with the sudden loss of cabin pressurization at high altitude, and there is some evidence in the scientific literature that women have a greater predisposition to decompression sickness than men (26). While others may question these findings, the issue is far from resolved, and certain methodological problems make accurate assessment of the problem currently difficult. But if the Air Force is to effectively carry out its combat mission without undue risk to its female pilots, the question of gender difference in DCS susceptibility should be answered. Since there are currently no well-controlled studies which adequately address this question, the following study to prospectively ascertain the gender-specific rates of DCS, using a symptom-based questionnaire, is proposed.

#### ***Background***

Decompression sickness is the clinical syndrome of pain and/or functional impairment associated with the evolution of nitrogen bubbles in the blood and

tissues upon exposure to reduced ambient air pressure (3, 10, 18, 31). Since ambient air is approximately seventy-nine per cent nitrogen, a certain amount of nitrogen is dissolved in all body tissues at any given time. Upon a reduction in the pressure of the ambient air, dissolved nitrogen "washes out" from the tissues and diffuses into the blood, where it travels to the lungs and is expired. If the decompression is rapid, or if the change in pressure is great, the amount of nitrogen released into the blood may exceed the capacity for absorption and elimination. Nitrogen can then evolve into free gas and form bubbles, similar in nature to the bubble formation seen when one opens a bottle of champagne. The blood, literally, boils. Continued decompression may cause expansion of the bubbles with significant physiologic effects. Skin and joint symptoms may result from the mechanical effects of bubbles directly on tissues such as nerve endings and tendon sheaths. Cardiopulmonary symptoms may result from the intravascular effect of bubbles in the circulation of the lungs, and neurologic signs may result from the spontaneous formation of bubbles in neural tissue such as the brain and spinal cord. Intravascular bubble formation can also initiate complement activation as well as platelet aggregation, precipitating the release of prostaglandins and other vasoactive substances. Disrupted circulation potentially leads to ischemia and infarction, and if not reversed, incapacitation, hemodynamic instability, and organ system failure may ensue (21).

Bason and Yacovone reported on the manifestations of altitude-induced decompression sickness in the Navy (4). Joint and limb pain was present in nearly seventy-one per cent of these patients, and was the most common presenting symptom. Other symptoms, in decreasing order of frequency, included extremity paresthesia, numbness and tingling, visual disturbances, fatigue, paralysis, pruritus, skin mottling, dyspnea, slurred speech, and difficulty forming words (4).

Such symptoms of decompression sickness are often divided into two major types based on the site of pain and/or impairment. Type I involves pain in the joints ( the "bends") or skin manifestations such as mottling or pruritus (the "niggles"). Type II involves pulmonary manifestations (the "chokes"), neurologic deficits, vestibular deficits (the "staggers"), or hemodynamic instability ("shock"). Type II DCS is obviously more serious, and carries a much poorer prognosis (21).

Treatment of either type initially entails delivery of 100% oxygen, while definitive therapy is hyperbaric oxygen. Hyperbaric oxygen therapy involves placing the patient in a hyperbaric chamber where a schedule of compressions above atmospheric pressure, followed by decompressions back to atmospheric pressure, almost always eradicates the nitrogen bubbles, and is usually accompanied by the resolution of symptoms. Specific supportive therapies, such as intravenous fluids, ventilatory assistance, analgesia, and cardiac monitoring may also be necessary (21).

Intravascular bubbles of the heart and major blood vessels can be detected by Doppler ultrasonography. In this procedure, which is still a research tool only, the amount of bubbles are graded from zero (no bubbles) to four (excessive bubbles). Though there is usually an association between intravascular bubble formation and the symptoms of decompression sickness, the two phenomena are not synonymous, and a person may demonstrate one without the other. One study in fact revealed that symptoms were present in only thirty-nine per cent of those subjects with bubbles detectable by ultrasound (25). It is possible that bubbles form in different tissues at different times, and that symptoms are specifically related to extravascular bubbles rather than the intravascular bubbles seen on ultrasound. Since it is the signs and symptoms of decompression sickness which dictate treatment, not bubble formation per se, the clinical manifestation of symptoms is of

the utmost importance.

With the aid of computers, mathematical modeling has been applied in an effort to identify specific predictors leading to DCS development (30, 36, 37). Obesity, for example, has long been considered a risk factor for decompression sickness (21). Since decompression sickness is associated with the formation of nitrogen bubbles, and the formation of nitrogen bubbles is related to the partial pressure of nitrogen in the tissues, a reduction of the initial partial pressure of nitrogen would predictably lead to a lower likelihood of developing decompression sickness. Furthermore, nitrogen is approximately five times more soluble in hydrophobic substances, such as fat, than in water (9), and regional blood flow to the adipose tissues is only about sixteen per cent of the total cardiac output (27). Therefore an individual with excess adiposity will have a larger total amount of dissolved nitrogen than someone with less body fat. Because of decreased regional blood flow, it will likewise take that individual a longer period of time to eliminate that nitrogen to a specific level while prebreathing pure oxygen prior to a known altitude exposure. Conversely, the individual with greater body fat will have a higher partial pressure of nitrogen in the blood and body tissues at any given time of the prebreathing protocol. If these two individuals are simultaneously exposed to hypobaric decompression, the person with greater body fat will have, at least in theory, a higher likelihood of developing decompression sickness.

Due to the physiologic differences between the sexes, women have an average of eight per cent more body fat than men. In the Air Force this is reflected in the standards for maximum body fat allowance found in Air Force Regulation 35-11 "The Air Force Weight Management Program". Whereas for men under the age of thirty it is twenty per cent (twenty-four per cent over the age of thirty), for women it is twenty-eight per cent (thirty-two per cent over the age of thirty). Because of this

increased body fat percentage it is possible that women have a greater likelihood of developing decompression sickness than men. It is this reasoning which has been the impetus to various reports in the literature analyzing specific differences between body fat and gender in relation to susceptibility to decompression sickness, more about which will be discussed shortly.

To date there have been nineteen deaths due to altitude-induced decompression sickness, the last of which occurred as late as March 1987 (17). The operational rate of reported DCS in USAF aircraft had been 0.2-0.3 events per 100,000 flying hours for the period 1977-1988. In 1989, however, this rate increased to over 0.5 events per 100,000 flying hours, due likely to increased awareness and the removal of selected disincentives to reporting (23). Even though a single DCS mishap at a critical time can have potentially significant consequences, this reported incidence admittedly does not seem to warrant much attention. Yet reported rates and actual rates may be different. For example, the U-2 aircraft flies at altitudes over 60,000 feet with a cabin altitude over 29,000 feet. One would expect a higher incidence of DCS among U-2 pilots, and published reports indeed indicate an approximate rate of 7.8 per 100,000 flying hours (35). Yet in a recent anonymous survey of 232 active-duty and retired U-2 pilots, almost 65% reported at least one symptom of DCS at some point in their career (8). Currently the F-15 fighter flies at altitudes near 50,000 feet. This aircraft has, on average, one to three unintentional decompressions per squadron per month, due most frequently to failure of the canopy seal (24). Given the fact that the Advanced Tactical Fighter (ATF) may cruise at altitudes above 50,000 feet, with cabin altitudes exceeding 20,000 feet (39), this problem clearly warrants closer attention if female aircrew are unknowingly facing increased risk.

## ***Review of the Literature***

Philp and Gowdey published a report in 1964 which used a rat animal model to investigate the relationship between body fat and susceptibility to nitrogen bubble formation (29). They found that both the incidence and severity correlated with the overall amount of body fat. Obviously nothing could be said regarding the clinical symptoms of decompression sickness. One drawback of this study, however, is that it utilized hyperbaric compressions with decompression back to normobaric conditions, similar to the experience of deep sea scuba diving. These findings cannot be simply extrapolated to the hypobaric environment because bubble formation at altitude is less likely for several reasons: 1) the critical radius needed to achieve bubble formation is more, making bubble formation less likely; 2) carbon dioxide is a larger component of bubbles at altitude, resulting in greater diffusability and presumably greater dissolution; 3) preoxygenation prior to exposure to altitude results in a lower partial pressure of nitrogen; and 4) "recompression" to ground-level pressure favors bubble collapse (22). Likewise, a review of the Hypobaric Decompression Sickness Databank shows the incidence of altitude-induced DCS is different from what would be predicted from calculations based on a diving model (12, 13). For these reasons the decompression sickness upon exposure to hypobaric conditions is fundamentally different from that experienced in the hyperbaric environment encountered in scuba diving.

In 1971 Allen and Bancroft performed a study which again looked at the question of body fat and decompression sickness, this time with altitude-induced decompression in humans (2). They showed that men with greater than twelve per cent body fat had a higher incidence of decompression sickness when exposed in an altitude chamber than those with less than twelve per cent body fat. This difference, however, disappeared when the two groups prebreathed one hundred

per cent oxygen for a total of four hours beforehand (2).

At a scientific meeting in 1973 Bassett reported a review of altitude chamber training records demonstrating a greater incidence of DCS in women (5). In it there were 7 cases of DCS in 3190 exposures in women, compared with 2 cases in 9056 exposures in men, representing a ten-fold increased risk (0.22% vs. 0.02%). In 1980 he presented a follow-up report revealing a total of 21 cases in 5791 exposures for women compared with 17 cases in 18,920 exposures for men (6), representing a four-fold increased risk (0.36% vs. 0.09%).

However, the male and female groups in these reports were not comparable because most of the females were flight nurses undergoing initial chamber training whereas most of the males were experienced aircrew members undergoing "refresher" physiologic training. Pilots are required to undergo a Flying Class I physical examination prior to entry into pilot training. This exam has very restrictive physical standards, and deviations from them are virtually never waived. Nurses on the other hand undergo Flying Class III physical examinations, which are much less restrictive, and minor deviations from set standards are frequently waived. Hence there is a physical standard difference between the two groups which could readily affect susceptibility to decompression sickness.

Later, Dixon and coworkers reported their experience with volunteers exposed to hypobaric pressures in the context of designing the spacesuit for shuttle and space station operations (15, 16). In their reports five of thirty women experienced DCS whereas only one of thirty men did so. The authors reported no correlation between body fat percentage and DCS, but they unfortunately did not report the body fat percentage figures, nor is it clear whether or not this correlation even included the male population. An unexpected finding, however, was that all five women who experienced DCS were in the menses or early phase of their

menstrual cycle, whereas only eight of twenty-five women who did not experience DCS were in a such a phase. Due to the limitations of the study, no conclusions could be drawn.

In a paper published in 1990 Frederick Rudge reviewed the records of 81 females treated in various Air Force hyperbaric chambers for altitude chamber-induced decompression sickness (32). He found that the number of DCS cases declined linearly relative to the start of the patient's last menstrual period. The correlation coefficient in fact was 0.988, indicating a very good linear relationship. Since this was simply a retrospective observational study no conclusions could be drawn, and the author refused to speculate on possible physiologic mechanisms. However, if a gender difference were related solely to differences in body fat, this result is difficult to explain.

In a follow-on study Schirmer and Workman reported the results of a survey regarding time of menses, which was distributed to women undergoing physiologic training at thirteen different altitude chambers in the Air Force (33). They retrieved 508 questionnaires, which was approximately thirty-three per cent of the population eligible to respond. They found that trainees who did not experience DCS were evenly distributed along the menstrual cycle. Unfortunately, however, they did not report whether anyone did experience DCS, or if they did, its relationship to the menses.

In the meantime Weien and Baumgartner reported the results of hyperbaric therapy in 429 cases of altitude chamber-induced decompression sickness (40). This was in effect an historical cohort study, as data were also available on persons who were exposed to decompression but did not develop DCS. Cases were self-reported and had required hyperbaric oxygen therapy. The authors discovered a DCS rate of 48.08 per 100,000 exposures for males, compared with

206.87/100,000 exposures for females. This is a relative risk of 4.30 (99.9% Confidence Interval: 4.190 to 4.413). Because of the strong statistical power generated by this study, it is persuasive evidence favoring increased susceptibility of women to decompression sickness.

However, the concerns mentioned earlier again apply here. The majority of females were flight nurses while the majority of males were operational aircrew. In the Air Force, Type I DCS with no residual symptoms requires only a 72 hour "grounding" period to monitor for the recurrence of symptoms. If the member has no deficits he or she is returned to flying status by the local flight surgeon. Type II DCS, however, even if fully resolved, results in a permanent disqualification from flying duties unless waived by the Office of the Air Force Surgeon General. Most pilots do not clearly understand this distinction, and generally feel that any report of DCS symptoms could permanently threaten their flying career. Along with the psychological consequences this would entail, there is the loss of financial support resulting from flight pay and the pilot "bonus". Thus there is a reluctance among pilots to report decompression sickness unless the problem is overwhelming and/or incapacitating. On the other hand many flight nurses undergoing physiologic training are not assigned to active flying billets; "getting wings" is one aspect of professional career development in Air Force nursing. Even when flight nurses are assigned to active flying slots, it is usually for only a few years and they are returned to non-flying duties. Nurses, furthermore, do not get a pilot "bonus" when they fly. Thus there is not the disincentive toward reporting DCS that one finds with the pilots. Likewise, because of their medical training and choice of career, flight nurses may attach greater significance to symptoms suggestive of DCS, and may therefore be more likely to report them (38). If the majority of nurses are female and the majority of pilots are male, a spurious difference in gender-

specific DCS rates could be found.

Most recently Kumar and associates published a retrospective review examining, among other things, risk factors development of decompression sickness in the context of high altitude research for the space program (25). The study population included 164 astronauts (37 women and 127 men) all of whom had passed an Air Force Flying Class III physical examination. In contrast to prior studies, those individuals who developed symptoms of DCS were less likely to be women (Odds Ratio: 0.40; 95% Confidence Interval: 0.13 - 1.28). Due to the small sample size this finding did not achieve statistical significance, but demonstrated no evidence supporting a greater risk of DCS in women. Although the women in this study were older, less active, and had a higher body mass index than the men, these factors were presumably taken into account using a logistic regression model which gave the "adjusted" odds ratios reported by the authors. They conclude that the question of gender difference in the risk of DCS warrants further study because women will be working in the markedly reduced pressures of the Extravehicular Activity (EVA) space suits.

In regard to this study, however, there is the question of how cases were determined. For instance, the authors state, "The subjects were encouraged to report any symptom ... at once. Further, they were questioned periodically about the presence of symptoms ... all symptoms classified as DCS were defined as cases" (25). But in the very next sentence they state that it is difficult to distinguish musculoskeletal pain from discomfort due to the spacesuit in an operational setting. They do not state whether all such pain was diagnosed as DCS for this study, or if the diagnosis was applied equally to both men and women. Neither do they state who exactly was making this diagnosis-- a chamber technician, an aerospace physician, or the subjects themselves. Women entered this investigation at a later

point in the study than men, so if there was a "learning curve" in regard to what types of pain are operational and what types are DCS, the women would show a lower rate of DCS. Likewise it is not clear whether the periodic questioning about symptoms was standardized, as in a set questionnaire format, or whether it varied from one chamber operator to the next.

Secondly, there was a potential for reporting bias on the part of the participants. The female astronauts clearly realized that they were in a career field which in the past had been dominated by men. A personality profile for women in this field could make them, as a group, less likely to report minor musculoskeletal pain for fear of giving the impression of not being able to endure the physical stresses that men endure. This potential for underreporting would be exacerbated if women also felt that reporting minor symptoms would jeopardize the mission at hand. If all DCS "cases" included any pain symptoms, whether major or minor, and if women reported minor pain less frequently than men, women would appear to have lower rates of DCS. As the authors state in their paper, a more reliable assessment of DCS would be test aborts, but unfortunately they did not report the gender-specific rates for test aborts.

A third point to consider in analyzing this study is the potential for making a Type II error, i.e. concluding there is no gender difference when one actually exists. Using a standard formula for the determination of the sample size, which will be elaborated later, one would need 118 subjects in each group, for a total of 236, to determine no difference with only 90% confidence in avoiding a Type II error. This requirement would obviously increase if one wanted to avoid the Type II error with greater, e.g. 95%, confidence. With only thirty-seven women, the authors had less than a third of the females needed for adequate assessment of a negative finding. So although no association was observed in this study, this lack of association

could be the result solely of random variation and does not necessarily mean no association exists.

### ***Summary of Literature Review***

As one can see, there has been a fair number of studies looking at the question of gender, adiposity, and risk of decompression sickness. It appears there is evidence that women indeed have a greater susceptibility to decompression sickness than men, and this is possibly related to gender differences in body fat. However, virtually all of these studies have been retrospective in nature, with the associated problems of selection and reporting bias. The lack of an objective method for accurately diagnosing DCS is another problem. The result is that to date there has been no prospective, well-controlled study assessing the gender-specific rates of decompression sickness.

### ***Purpose***

The purpose of this study, therefore, is to conduct a prospective, controlled study assessing the gender-specific rates of DCS. To do this a questionnaire asking about symptoms of decompression sickness will be distributed to USAF pilots after exposure to hypobaric pressures in an altitude chamber. The gender-specific rates will then be assessed, and the risk ratio will determine whether or not women manifest a higher rate of DCS symptoms than men. By confining questionnaire distribution to a specific population, i.e. Air Force pilots, reporting bias due to personality profile or the negative ramifications of reporting will be controlled. If there is no significant difference, as determined by the Chi-square analysis, the Air Force will have good evidence refuting various reports in the scientific literature that women have a greater susceptibility to decompression sickness. If women do show a greater rate of DCS, they would need to be properly informed of such risk prior to entry into the particular career field, e.g. fighter or

high-altitude reconnaissance aircraft. It is doubtful that any such increased risk would present a sufficiently valid reason to restrict women from these career fields altogether.

## **SECTION II**

### **METHODS**

#### ***Altitude Chamber Training***

During their initial training pilots undergo physiologic training in which the effects of high altitude on human physiology are encountered first-hand. Things such as adequate "clearing of the ears", symptoms of hypoxia, rapid decompression, visual changes, and the experience of trapped gas in the gastrointestinal tract are experienced through a specific flight profile in a multiplace altitude (hypobaric) chamber. After entry into operational flying, all active aircrew undergo physiologic "refresher" training once every three years, or upon change to a different weapon system. The refresher profile achieves an maximum altitude equivalent of 35,000 feet. This is immediately followed by rapid descent to 8000 feet to simulate a parachute free fall in an ejection scenario. A rapid ascent to 25,000 feet to simulate a slow leak canopy seal problem ensues, and at 25,000 feet the subjects intentionally experience hypoxic symptoms. The profile then descends to 18,000 feet, where effects of altitude on visual acuity are demonstrated, after which the participants are returned to ground level (20). The various altitude chambers located at various bases throughout the continental United States, including Brooks Air Force Base (AFB), conduct such refresher training profiles on a regular, recurring basis.

#### ***Questionnaire Development***

There is no standard questionnaire for ascertaining decompression sickness in the Air Force, and so development of one is necessary. The development and

distribution of surveys is governed by Air Force Regulation 30-23, "Air Force Personnel Survey Program," which concerns primarily the mechanics of survey production. The content will be based on known presentations of decompression sickness, such as those tabulated by Bason and Yacavone mentioned earlier (4). Obviously, the questionnaire will ask about symptoms specific to decompression sickness. Questions about hypoxia, for example, will not be asked because hypoxic symptom recognition is a formal part of the altitude chamber flight profile.

There are four confounding variables which could influence the survey results, and should be taken into consideration in questionnaire design: age, personality, menses, and obesity. In order to compare the population ages of the males and females the age of the respondent will be asked. The questionnaire should only be distributed to pilots, not all aircrew, but it is possible that mistakes will be made, so a question verifying aeronautical rating will be asked. Because of some of the findings noted in the literature, a questions regarding time of menses will be asked. And finally, participants will be asked if they are on the weight management program.

In order to ease data processing, as well as enhance reliability, questions will be asked to yield binomial, i.e. yes/no, data (1, 19). The response rate to the questionnaire will likewise be of interest (28). Such rates on well-done surveys run typically around seventy per cent, and it is doubtful a rate higher than this will be attained. One way to track results will be the inclusion of a response statement on the questionnaire which indicates the intended options of the participant. That is, the respondents can say whether they do or do not wish to complete the survey. The explicit granting of such a choice does not decrease the rate of response, and may in fact increase accuracy (34). Another aspect which may affect response rate is the length of the survey. Respondents may be more likely to answer a short

survey than a long one (8), so only the most relevant and necessary diagnostic questions will be asked. Respondents will not be asked to elaborate on symptoms. A proposed questionnaire is shown in the appendix.

### **Sample Size**

The equation for sample size in the comparison of two proportions, which is essentially what this project is designed to do, is as follows (11):

$$n = \left[ \frac{z(\alpha) [2P(1-P)]^{1/2} + z(\beta) [P(f)(1-P(f)) + P(m)(1-P(m))]^{1/2}}{D} \right]^2$$

For  $n$  = sample size for each group (male group and female group)

$z$  =  $z$  statistic for the standard normal distribution at the confidence level of the stated alpha and beta error, respectively

$P$  = the proportion of the general population which will experience decompression sickness after exposure to the maximum altitude of the altitude chamber "flight"

$P(m)$  = the proportion of males who will experience DCS

$P(f)$  = the proportion of females who will experience DCS

$D$  = the proportional increase (or decrease) in the risk of DCS for females

The alpha error for this project will be arbitrarily chosen to be 95%, making the  $z$ -statistic for a two-tailed test 1.96. The beta error will be 90%, making the  $z$ -statistic for a one-tailed test -1.28. The proportionate difference in the DCS rate of females will be conservatively chosen to be a fifty per cent increase over that of the males. In other words, a sample size is achieved to detect as little as a fifty per cent increased likelihood of developing decompression sickness, or  $D = 50\% \times (P)$ . The assumption will also be made that the general population risk of decompression sickness is equal to that of males. What is not known reliably is the proportion of males who actually develop symptoms. In a report by Baumgartner and Weien,

the gender-specific incidence rates for Type I altitude chamber exposures were 0.00147 for males and 0.0048 for females (7). Performance of the necessary calculations yields a sample size requirement of 4561 for each gender group, for a total of 9122 participants. Clearly this figure is too large for a realistic expectation of accomplishment. On the other hand, if the figure used in the estimation by Kumar and coworkers (20%) is chosen (25), the sample size requirement becomes 357 for each group, for a total of 714. This number is clearly more feasible. In fact the first phase of this project is designed specifically to establish the proportion "P", based on the questionnaire.

Because of logistical constraints, and because sample size is dependent upon the proportion of respondents positive for decompression sickness, a proportion value necessitating a sample population greater than approximately five hundred participants will not be feasible. Using the above equation it is seen that this number correlates with a proportion of 0.15, i.e. a rate of fifteen per cent yields a sample size requirement of 510 per group (total 1020). Therefore, in order to proceed with the second phase of this study, the observed proportion in the first phase must be at or above fifteen per cent.

### ***Project Management***

As mentioned, this study will be accomplished in two phases. Phase I will be a feasibility study, and will involve questionnaire distribution to pilots undergoing physiologic refresher training at the Armstrong Laboratory, Brooks AFB, Texas. Because of the demographics of the USAF pilot population, most of these pilots will be male. If the proportion of pilots reporting DCS symptoms is sufficiently high enough to warrant further investigation, i.e. greater than or equal to fifteen per cent, Phase II will be implemented, which involves questionnaire distribution to all female pilots undergoing physiologic refresher training at any of thirteen USAF

physiologic training centers throughout the continental United States. Phase I will also determine such things as the response rate of the survey, and the logistical feasibility of this method of research. Phase II will answer the specific question: Is the incidence of DCS symptoms higher in female pilots than in male? By confining questionnaire distribution to pilots only, rather than all aircrew, and by making the assumption that all pilots have a similar personality profile in regard to the anonymous reporting of symptoms, differences in reporting due to training or personality profile will be minimized.

The key objectives for Phase I of this project are:

- 1) questionnaire development;
- 2) development of a data collection sheet for easy entry of data into a computerized database;
- 3) approval by the appropriate USAF authority, including the attainment of a survey control number (SCN);
- 4) development of a technician briefing sheet which adequately addresses the purposes and procedures of this study to ensure correct distribution to altitude chamber participants;
- 5) compilation of the surveys, response cards, and return envelopes into individual packets for ease of distribution;
- 6) actual distribution of the questionnaires to participants;
- 7) retrieval of questionnaires through the mail;
- 8) entry of the data into a computerized database;
- 9) analysis of the data for validity and statistical significance;
- 10) generation of a report.

Phase II of the project will then entail:

- 1) approval/disapproval to initiate Phase II of the project from the

- appropriate USAF authority;
- 2) bulk package mailing of the surveys to the twelve USAF physiologic training units located outside the San Antonio area;
  - 3) retrieval of completed surveys through the mail;
  - 4) data entry for Phase II;
  - 5) data analysis for Phase II;
  - 6) report generation for Phase II containing specific conclusions and recommendations;
  - 7) distribution of the Phase II report to the appropriate USAF authorities;
  - 8) closeout of the project.

Accomplishment of these objectives will involve the services of a number of personnel, as shown in the responsibility matrix (Figure I). The project director has the primary responsibility for oversight and completion of the project. If possible, an administrative assistant would be a tremendous asset, but if unavailable, such duties would fall upon the project manager. The basic research staff will be from the High Altitude Protection Function (HAPF) at the Armstrong Laboratory, and will be consulted on development of the questionnaire and data collection sheets, as well as on the data analysis for both Phase I and Phase II of the project. They will thereby ensure quality performance of these objectives. The clinical staff will be a physician with expertise in aerospace medicine who will likewise be consulted on the questionnaire development as well as analysis of the data. To ensure a thorough and valid statistical analysis, a statistician will be consulted on both phases of the project. Finally, the altitude chamber technicians will be the key link between the investigators and the study population; they will deliver the questionnaire packets and will give basic instructions to the participants regarding completion of the questionnaire.

**FIGURE 1**  
**RESPONSIBILITY MATRIX**

	A	B	C	D	E	F	G	H	I
1	P		C	C				C	
2	P		C						
3					P	P			P
4	P						C		
5		P							
6							P		
7		P							
8	P								
9								P	
10	P								
11					P	P			P
12		P							
13		P							
14	P								
15								P	
16	P								
17		P							
18	P								

**P = Primary Responsibility**

**C = Consultant**

**KEY OBJECTIVES**

1. Develop Questionnaire
2. Develop Data Sheet
3. Approval (Obtaining SCN)
4. Technician Briefing Sheet
5. Package Compilation
6. Distribution
7. Retrieval
8. Data Entry
9. Data Analysis
10. Report Generation
11. Approval ("Go/No-Go")
12. Package Mailing
13. Retrieval
14. Data Entry
15. Data Analysis
16. Report Generation
17. Report Distribution
18. Closeout

**KEY PERSONNEL**

- A. Program Director
- B. Administrative Assistant
- C. Basic Research Staff
- D. Clinical Staff
- E. Internal Review Board
- F. Local Commander
- G. Altitude Chamber Technician
- H. Statistician
- I. Office of the Air Force Surgeon General

## **Budget**

This study will require resources in several categories, including office space, equipment, communications, consummable office supplies, and postage. Some type of office will obviously be necessary, along with access to a bulk mailbox to retrieve mail. This office may be a shared one if necessary, and will be used to house a computer/printer, write out the questionnaire, input and analyze the data, retrieve questionnaires, and generate final reports for both phases of the project. In order to accomplish such taskings, equipment needs include a computer, preferably IBM-compatible, with a letter-quality printer, appropriate software, and access to copy services.

A local phone line will be necessary for inter-office communications between the principal investigator and the consultants. Access to a long-distance line will be necessary to communicate with the twelve physiologic training units outside the San Antonio area, should Phase II of the project be implemented.

Consummable office supplies include paper, ink cartridges for the printer, pens, staples and the like. Postage will be a major needed resource. A survey of the type proposed here is not considered "Official Business" for the Department of Defense; therefore each return envelope must be stamped or metered. Likewise, upon implementation of Phase II, bulk mailings of adequate numbers of survey packets to the various USAF altitude chambers will be necessary.

A summary of the resources needed by category is listed in the "Budget Summary" table (Table I). Because salaries and costs vary from time to time, the precise amount in dollars is not listed. Upon initiation of the project this budget summary will be given to the unit resource manager for conversion into monetary units.

**TABLE 1**  
**BUDGET SUMMARY**

<b>1) Personnel</b>	
a) Program Director (part-time)	240 hours
b) Administrative Assistant (part-time)	310 hours
c) Basic Research Staff (part-time)	22 hours
d) Clinical Staff (part-time)	20 hours
e) Internal Review Board (IRB) Approval	10 hours
f) Local Commander (part-time)	2 hours
g) Altitude Chamber Technician (part-time)	4 hours
h) Statistician (part-time)	40 hours
i) Office of the Air Force Surgeon General (part-time)	2 hours
<b>2) Space</b>	
a) Office (200 square feet; shared)	36 months
b) Bulk Mailbox (with address listing)	36 months
<b>3) Equipment</b>	
a) IBM-Compatible Computer (availability)	36 months
b) Letter-Quality Printer (availability)	36 months
c) Copy Services (availability)	4000 copies
d) Microsoft Word <sup>®</sup> Software (or equivalent availability)	36 months
e) Epi-Info 6.0 Software (or equivalent availability)	2 months
<b>4) Communications</b>	
a) Local Phone Line (availability)	36 months
b) Long-Distance Phone Line (domestic)	200 minutes
<b>5) Consumable Office Supplies</b>	
a) Printer Paper	500 sheets
b) Printer Ink Cartridges (black)	2 cartridges
c) Large (8.5" X 11") Envelopes	1000
d) Business-Sized Return Envelopes	1000
e) Stapler (heavy-duty, business)	1 large
f) Staples	500
<b>6) Postage</b>	
a) 1000 Large (8.5" X 11") Envelopes	First Class Domestic
b) 1000 Business-Sized Return Envelopes	First Class Domestic
c) Twelve 24" X 24" X 24" Cardboard Boxes	Priority Domestic

### **Schedule**

A proposed schedule for accomplishing various key objectives is shown in the Gantt chart (Figure 2). Timely completion of the respective tasks will depend greatly on the number of potential participants, i.e. male and female pilots undergoing refresher physiologic training each month, as well as other factors such as timely approval of the developed document, and the response rate of the questionnaire. This schedule is therefore tentative at best, and modifications may have to be made to account for "slippage" of scheduled milestones.

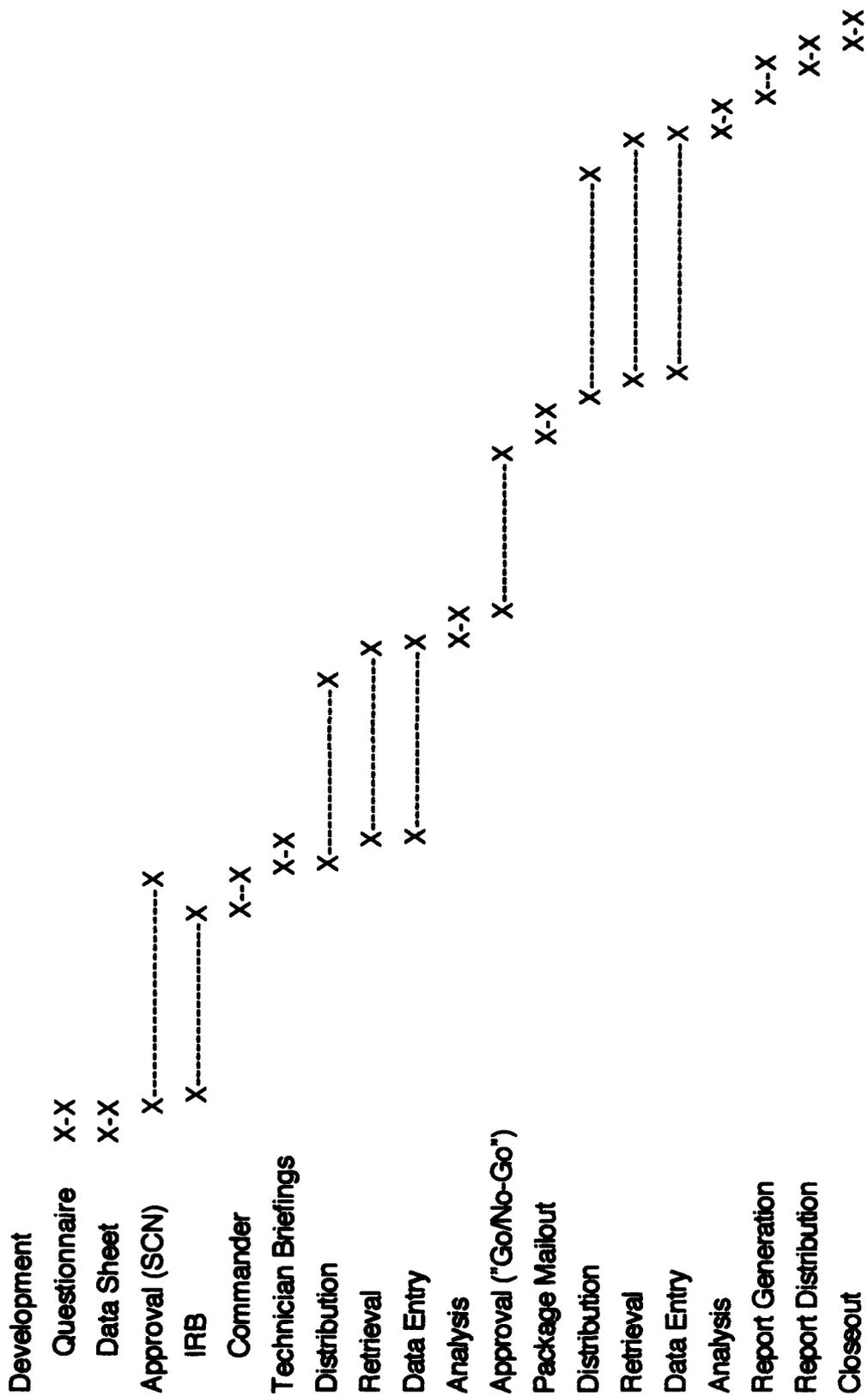
### **Information Management**

In accordance with the Privacy Act of 1974 the confidentiality of respondent information must be assured, as well as the fact that participation is voluntary and without the threat of adverse action if participation is refused. Such statements will be included on the front sheet of the questionnaire, and at the top and bottom of each page of the questionnaire.

Specific results and conclusions will be compiled in a formal report and forwarded to the Office of the Air Force Surgeon General, Air Force Medical Operations Agency (AFMOA), for review and appropriate action. Before public release of this information, review and approval must be first obtained by a local authority, such as the unit Public Affairs Office, or for publication in technical or professional journals, the Scientific and Technical Information Office (STINFO). A STINFO release is accomplished by means of an Air Force form on which appropriate approval signatures are obtained. If approved, it is intended that the data from this study will be presented at an annual scientific meeting of the Aerospace Medical Association, and submitted for publication in their peer-reviewed journal *Aviation, Space and Environmental Medicine*.

**MONTHS**

0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36



**FIGURE 2  
GANTT (TIME-TASK) CHART**

## **SECTION III**

### **RESULTS**

The mean age of each gender group will be compared using the pooled t-test analysis. If any respondent indicates an aeronautical rating other than pilot, that survey will be considered invalid and will not be included for analysis. Likewise, because a fundamental assumption of this thesis is that susceptibility to decompression sickness is related to adiposity, any respondent who indicates that they are on the weight management program, i.e., the individual exceeds Air Force standards for body fat, that survey will also be considered invalid and will be excluded from analysis. Data on time of menses will not be used for stratification, but will nevertheless provide an interesting observation to compare with those found in the literature. Any respondent answering in the affirmative on any of questions five through fifteen of the questionnaire will be considered a case of decompression sickness. Data will be summarized in a table as shown (Table 2).

The results will be presented in a 2X2 table, as shown in the "Results" figure (Figure 3). As mentioned previously, the risk of decompression sickness will be computed for both males and females, and the relative risk will be assessed. Statistical significance will be accomplished using the Chi-square test. Display of results and statistical analysis will be accomplished using conventional spreadsheet and database software, such as Epi Info 6.0 (14).

**TABLE 2**  
**DATA SUMMARY SHEET**

	FEMALES	MALES
1) Number of Questionnaires Distributed	( )	( )
2) Number Retrieved:	( )	( )
3) Number Invalidated (total):	( )	( )
a) Number Declining Participation:	( )	( )
b) Number Non-Pilot:	( )	( )
c) Number on Weight Management Program:	( )	( )
4) Number Valid for Analysis (total):	( )	( )
5) Age:		
a) Mean:	( )	( )
b) Median:	( )	( )
c) Minimum:	( )	( )
d) Maximum:	( )	( )
e) Standard Deviation:	( )	( )
6) Number Positive for Decompression Sickness:	( )	( )
7) Percentage Positive for Decompression Sickness:	( )	( )
8) Gender-Specific Rate/1000 Exposures:	( )	( )

**FIGURE 3**  
**RESULTS DISPLAY**

	+ DCS	- DCS	
FEMALES	A	B	R
MALES	C	D	S
	M	N	T

1) GENDER-SPECIFIC RATES OF DECOMPRESSION SICKNESS:

$$\text{FEMALE} = \frac{A}{A+B}$$

$$\text{MALE} = \frac{C}{C+D}$$

2) RELATIVE RISK =  $\frac{A}{A+B} \times \frac{C+D}{C}$

3) CHI-SQUARE STATISTIC =  $\frac{T(AD - BC)^2}{R \times S \times M \times N}$ ; DEGREE OF FREEDOM = 1

SIGNIFICANCE ASSIGNED IF P-VALUE LESS THAN 0.05

## **SECTION IV**

### **DISCUSSION**

#### ***Limitations***

The preceding review of the literature shows that there are three components involved in the assessment of decompression sickness: 1) the identification of microbubbles, 2) the manifestation of symptoms, and 3) reporting of such symptoms to medical authority. Circulating microbubbles can be assessed by means of Doppler ultrasound, though this method is less useful for detecting extravascular microbubbles. Likewise, several reasons for the lack of reporting among aircrew, particularly pilots, have been covered. This study will focus on the second component, the experience of symptoms, by asking the question: Is the incidence of DCS symptoms in female pilots higher than that of male pilots after altitude chamber training?

This study will have several faults. One problem with any epidemiologic approach to studying decompression sickness is the lack of an objective method of diagnosis; there is no gold standard. Ultrasonic detection of circulating microbubbles is one step in this direction, but as mentioned earlier, its sensitivity and specificity for clinical manifestations are very low. At best there is presently what amounts only to a case definition for DCS, exemplified as any positive response to the questions listed in the questionnaire shown in the appendix. This lack of a clear endpoint accounts to some extent for the disparate results seen in the literature. But with the lack of any more powerful instruments, and with a need to address the gender difference in rates, the proposed questionnaire will offer one

method of approaching this issue. A second weakness of this study, consequently, is the reliance on the subjective data obtained in survey-type research. That is, cases are self-diagnosed. There is no easy way around this problem, and unfortunately it remains a fact inherent in the nature of clinical study. A third potential weakness, and the greatest threat to the study's feasibility, is the lack of adequate numbers of female pilots currently undergoing refresher physiologic training. It is entirely possible that five hundred female pilots may not be available during the timeframe proposed, though the increasing numbers of women entering flight training may alter this situation somewhat.

### ***Future Directions***

A final aspect of this study which should not be overlooked is the fundamental assumption on which the proposed gender difference in DCS susceptibility rests-- the difference in body fat. There were two studies mentioned in the review of the literature which demonstrated a temporal association between menses and DCS symptoms. Body fat clearly affects the volume of retained nitrogen, with a resultant effect presumably on nitrogen elimination rates and bubble formation, but the demonstration of intravascular bubbles has only a tenuous relationship to the manifestation of symptoms, and differences in DCS rates related to body fat are undoubtedly attenuated by an appropriate prebreathing protocol with one hundred per cent oxygen. It is possible that changes in prostaglandin metabolism at the time of the menses may affect the link between bubble formation and symptom manifestation. But before one may speculate on the pathogenesis of DCS differences, differences in the incidence of DCS between males and females must be demonstrated; this has yet to be done.

## **SECTION V**

### **CONCLUSIONS**

The gender-specific rates of altitude-induced decompression sickness will be ascertained using a symptom-based questionnaire. Reporting bias and other factors affecting the onset of decompression sickness have been minimized to the greatest extent possible. If no significant difference is found the Air Force can implement directives for women to fly combat aircraft without difficulty. If a significant difference is found the Air Force will be obligated to communicate such risk to those pilots prior to entry into the career field. Research into mechanisms affecting susceptibility would then be warranted. Because of the scope and severity of the problem, it is doubtful that gender differences in the rates of decompression sickness could be legitimately used to categorically exclude women from flying in combat.

## APPENDIX

### DECOMPRESSION SICKNESS SYMPTOM SURVEY

Capt. Gregg A. Bendrick, M.D., M.S.

ARMSTRONG LABORATORY  
BROOKS AFB, TEXAS 78235

#### PRIVACY ACT STATEMENT

In accordance with AFR 12-35, paragraph 8, the following information is provided as required by the Privacy Act of 1974.

**Authority:** 10 USC 8012, Secretary of the Air Force; powers and duties; delegation by; implemented by AFR 30-23, Air Force Personnel Survey Program.

**Purpose:** To obtain confidential information about the health status of active duty aircrew undergoing high-altitude physiologic training.

**Routine Use:** To provide health information to Air Force medical investigators regarding the health status of altitude chamber trainees. In no case will data be analyzed by individual response, and no respondent will be identified by name, social security number or any other identification means. Confidentiality is assured. Responders who do provide identifying information will not be at risk for adverse administrative action related to any information they may provide.

**Participation:** Participation in this survey is voluntary. No adverse action will be taken against any member who elects not to participate in any or all of this survey.

FOR OFFICIAL USE ONLY (When filled in)

Personal information, if provided, will not be released without consent of the individual.

## DECOMPRESSION SICKNESS SURVEY

This is a survey about the symptoms of decompression sickness which *may* be associated with your altitude chamber flight. This survey is anonymous and completely voluntary. If, however, you do not wish to complete this survey, please check the following line and return the blank survey in the return envelope provided. This lets us know you at least received this survey, and choose not to participate.

Thank-you, but I do not wish to complete this survey.

If you do choose to complete this survey, please do not do so until at least 24 hours have passed since the completion of your chamber ride. Please do not skip any questions. The last page contains room for elaborating any question(s), and/or comments; use additional sheets if desired. When completed, please return the survey in the return envelope provided. You do not necessarily need to use a No. 2 lead pencil when checking off the answers. We have tried to "streamline" this survey as much as possible, and we think you will find it goes pretty quickly.

Thank-you very much for your time and effort.

1. WHAT IS YOUR AGE?  YEARS

2. WHAT IS YOUR GENDER?  
 MALE  FEMALE

3. WHAT IS YOUR AERONAUTICAL RATING?

- PILOT
- NAVIGATOR/WEAPON SYSTEMS OPERATOR
- BOOM OPERATOR
- ENLISTED AIRCREW
- FLIGHT SURGEON
- FLIGHT NURSE
- OTHER (Please list): \_\_\_\_\_

4. ARE YOU CURRENTLY ON THE WEIGHT MANAGEMENT PROGRAM (WMP)?  
 YES  NO

Personal information, if provided, will not be released without consent of the individual.

FOR OFFICIAL USE ONLY (When filled in)

FOR OFFICIAL USE ONLY (When filled in)

Personal information, if provided, will not be released without consent of the individual.

**EITHER DURING YOUR CHAMBER RIDE, OR WITHIN 24 HOURS  
AFTER YOUR CHAMBER RIDE:**

5. DID YOU EXPERIENCE DECOMPRESSION SICKNESS, i.e. THE "BENDS"?  
 YES  NO
6. DID YOU EXPERIENCE PAIN, DISCOMFORT, OR A DULL ACHE IN ANY OF  
YOUR JOINTS (elbows, shoulders, knees, wrists, hips, etc.)?  
 YES  NO
7. DID YOU EXPERIENCE ANY SKIN SENSATIONS, SUCH AS A FEELING OF  
BUGS CRAWLING ON YOUR SKIN, SEVERE ITCHING, OR SKIN MOTTLING  
(color changes)?  
 YES  NO
8. DID YOU EXPERIENCE ANY NUMBNESS OR TINGLING?  
 YES  NO
9. DID YOU EXPERIENCE WEAKNESS, MARKED FATIGUE, OR MALAISE  
CLEARLY BEYOND WHAT WOULD BE EXPECTED, AND WAS NOT DUE TO  
EXCESSIVE EXERCISE, POOR SLEEP, ETC.?  
 YES  NO
10. DID YOU HAVE TROUBLE BREATHING OR DIFFICULTY CATCHING YOUR  
BREATH, WHICH WAS NOT RELATED TO YOUR OXYGEN DELIVERY  
SYSTEM?  
 YES  NO
11. DID YOU EXPERIENCE PARALYSIS (inability to move) YOUR ARM OR YOUR  
LEG?  
 YES  NO
12. DID YOU EXPERIENCE TROUBLE SPEAKING, SLURRED SPEECH, OR  
DIFFICULTY FORMING WORDS?  
 YES  NO
13. DID YOU EXPERIENCE TROUBLE WITH YOUR VISION, SUCH AS BLURRED  
VISION, DOUBLE VISION, OR TUNNEL VISION?  
 YES  NO

Personal information, if provided, will not be released without consent of the individual.

FOR OFFICIAL USE ONLY (When filled in)

FOR OFFICIAL USE ONLY (When filled in)

Personal information, if provided, will not be released without consent of the individual.

14. WERE YOU DIAGNOSED AS HAVING DECOMPRESSION SICKNESS (the "bends") BY A FLIGHT SURGEON AFTER YOUR CHAMBER RIDE?

\_\_\_\_\_ YES                      \_\_\_\_\_ NO

15. WERE YOU TREATED FOR DECOMPRESSION SICKNESS AFTER YOUR CHAMBER RIDE (e.g. ground-level oxygen or hyperbaric chamber treatment)?

\_\_\_\_\_ YES                      \_\_\_\_\_ NO

IF YOU HAVE ANY ADDITIONAL COMMENTS, OR ELABORATION OF A PARTICULAR QUESTION, PLEASE WRITE THEM HERE:

**XX  
THANK YOU VERY MUCH FOR PARTICIPATING IN THIS SURVEY  
XX**

Personal information, if provided, will not be released without consent of the individual.

FOR OFFICIAL USE ONLY (When filled in)

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## VITA

Gregg Alexander Bendrick was born in Chicago Heights, Illinois, on 2 June 1962. He is the son of Alexander Joseph and Shirley Philipak Bendrick. After graduating from Marian Catholic High School in Chicago Heights, he attended the University of Chicago, where he received his Bachelor of Arts degree in Biological Science in 1984. In 1986 he received the Master of Science degree in the Program of the Liberal Arts and Sciences Basic to Human Biology and Medicine. He graduated the Pritzker School of Medicine at the University of Chicago in 1988, after which he completed a Transitional-Year Residency at Saint Joseph Mercy Hospital in Pontiac, Michigan. He was commissioned an officer in the United States Air Force Reserve on 5 March 1985, and entered extended active duty in 1989, serving initially as an Emergency Services Physician at Misawa Air Base, Japan. He then transferred to Yokota Air Base, Japan where he served as a flight surgeon. In 1993 he was selected for postgraduate training in aerospace medicine, and entered the University of Texas at San Antonio to earn a Master of Public Health degree, in fulfillment of first-year requirements for this program.

He is married to Kathleen Tajiri, an Air Force pediatrician who is currently completing postgraduate training in Allergy/Immunology at Wilford Hall Medical Center in San Antonio. They have one daughter, Yuri Bendrick Tajiri.

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This thesis was typed by the author.