To the Graduate Council:

I am submitting herewith a dissertation written by John Timothy Lightfoot entitled "The Interaction of Strength and Aerobic Fitness on Sympathetic Nervous System Activity in Simulated Weightlessness and Reentry." I have examined the final copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Education.

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THE INTERACTION OF STRENGTH AND AEROBIC FITNESS ON SYMPATHETIC NERVOUS SYSTEM ACTIVITY IN SIMULATED WEIGHTLESSNESS AND REENTRY

A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

John Timothy Lightfoot

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DEDICATION

To Kellye, my wife. Because you were always my silent partner,
at least half of the credit is yours.

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ABSTRACT

The purpose of this study was to investigate the interactive effects of various levels of aerobic fitness and leg strength on the plasma catecholamine concentrations during simulated weightlessness and reentry. Twenty-four male subjects (30.8±3.9 years old, 178.9±4.9 cm, and 81.0±10.2 kg) were classified into four groups by their aerobic capacity and leg strength . If the subject's VO_2max was ≤50 ml O_2/(kg·min) or ≥45 ml O_2/(kg·min), he was classified as high fit (HF) or low fit (LF), respectively. Using a Cybex dynanometer, if the subject could lift ≥103% or ≤97% of his bodyweight with each leg, he was classified as high strength (HS) or low strength (LS), respectively. The subjects underwent a 90 min., -6° head-down tilt (HDT), preceded by a 20 minute baseline period and followed by a lower body negative pressure (LBNP) test to -50 mm Hg. Heart rate (HR), plasma norepinephrine (NE) and epinephrine (E) levels were measured. Mean arterial pressure (MAP) was calculated using systolic and diastolic blood pressures. During the first 15 minutes of HDT, there were no changes in NE, E, or HR in any of the groups. During 90 minutes of HDT, there were no differences in E and NE levels among the groups. NE responses during LBNP were not different among the groups. While the E responses of the HFHS, LFHS, and LFLS groups to LBNP increased similarly, E levels in the HFLS group did not change during LBNP. The low fit, high strength group (LFHS) exhibited a significantly higher MAP during LBNP than the other three groups. The head-down tilt responses indicate that early exposure to head-down tilt does not result in a load on the cardiac baroreceptors sufficent to trigger changes in sympathetic nervous activity and heart rate. The data also indicate that the sympathetic nervous system response to head-down tilt does not differ in individuals with different combinations of aerobic fitness and strength levels. The similar increases in NE in all the subjects during LBNP

suggested that the stress did not recruit trained systems in the subjects (stress specificity). Similarity of E responses during LBNP in the LF and HFHS groups was also attributed to stress specificity. The LBNP protocol did not stress the HFLS group sufficently to increase the E levels during LBNP. The increased MAP in the LFHS group during LBNP was speculated to be due to an augmentation of blood pressure with high strength levels. The augmentation could be due to increased muscle tone in the LFHS group.

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CHAPTER I

INTRODUCTION

For almost three decades, humans regularly explored the environment of outer space. Transporting humans to outer space and returning them without harm was a great challenge. With this challenge came questions about the effect of the space environment upon space travelers. While many questions have been answered and many humans have been exposed to the weightless condition of space and returned safely, multitudes of new concerns and questions arise with our continuing exploration of space.

Exposure to weightlessness causes the human body to undergo profound changes in cardiovascular function (92). When a person that has been exposed to weightlessness is returned to earth, these "weightless adaptations" can actually impair the body's ability to function (132). Characterization and quantification of these adaptations is imperative for determining how to best negate the detrimental effects of space travel.

Adaptation to a weightless envirionment is thought to occur in at least three phases: an immediate acute phase lasting for approximately 15-30 minutes after initial exposure to weightlessness; an intermediate phase which follows the acute phase and lasts 6-24 hours; and a long-term chronic phase which follows the intermediate phase (93, 126). Research has concentrated upon the latter part of the intermediate phase and on the chronic adaptation to weightlessness (40, 42, 45, 53, 63, 64, 65, 66, 71, 72, 80, 130, 131). Very little research has been focused on the immediate effects of insertion into weightlessness and the early part of the intermediate adaptation phase.

Vorobyov, et al. (131) postulated that the sympathetic nervous system was primarily responsible for adaptation of the cardiovascular system to the weightless environment. Sympathetic nervous system activity has also been suggested as an important part of the reflex mechanism responsible for the

body's ability to readjust to normal gravity (70). However, progress in clarifying the sympathetic nervous system's role in adaptation to weightlessness and high gravitational levels has been slow because of the difficulty in quantitatively determining sympathetic activity during spaceflight and reentry.

Studies using plasma catecholamine levels as indicators of sympathetic nervous activity during the first 90 minutes of simulated weightlessness are sparse. Research has focused on catecholamine fluctuations occurring after a hour of simulated weightlessness (42, 80, 83). These studies do not measure any changes that may occur within the first 30 minutes of exposure to simulated weightlessness. If the cardiovascular system undergoes any adaptation to simulated weightlessness within the first 90 minutes of exposure and the sympathetic nervous system plays a major role in this adaptation, then the importance of quantifying the sympathetic nervous system's responses during this period is further underlined.

The technical constraints of flight have understandably reduced the ability of researchers to collect data on the acute and intermediate phases of weightless adaptations (67). Necessarily, laboratory simulations of weightlessness have been employed in terrestrial studies of the physiological responses to weightlessness. The most popular methods of weightless simulation used by researchers have included supine bed rest, water immersion, and more recently, head-down tilt. Nixon, et al. (93) noted that the use of different methods of simulating the weightless condition has led to disagreements in the literature about physiological responses to weightlessness simulations. While much early literature used water immersion and bedrest as weightless simulations, head-down tilt is currently believed to promote physiological changes that are more consistent with the actual adaptations that occur in a weightless environment (93). This fact limits discussion of physiological adaptations to weightlessness to those studies employing head-down tilt.

The cardiovascular adaptations that occur after a period of exposure to weightlessness are detrimental to the body's ability to cope with the stress of terrestrial gravity (32, 60). Exposing an individual to a gravitational force of greater magnitude than that which he is adapted may lead to a phenomenon known as decreased orthostatic tolerance. Decreased orthostatic tolerance has been commonly seen in astronauts returning from the weightless environment of space (10). Reduced orthostatic tolerance manifests itself as an inability of the cardiovascular system to perfuse the brain with blood. This reduced cranial perfusion results in presyncopal symptoms which may further progress to actual syncope if left untreated.

Passive standing, head-up tilting, lower body negative pressure and centrifugation producing higher gravity levels (+Gz-acceleration) have all been used to provoke and measure responses to orthostatic stress. Lower body negative pressure has been the most popular method of provoking physiological responses to orthostatic challenges because of the ability to finely control the stress and eliminate confounding muscle contractions present in passive standing and head-up tilt tests. While centrifugation and lower body negative pressure elicit similar physiological responses, evidence of their comparability does not exist (49, 60). Therefore, results garnered from studies where centrifugation was the primary orthostatic challenge used may not be comparable to results from studies which use lower body negative pressure.

It is not known why some individuals have a reduced lower body negative pressure tolerance. It has been suggested that individuals with high aerobic fitness may be more susceptible to decreased orthostatic tolerance following exposure to a weightless environment than individuals with low aerobic fitness (115). Researchers have postulated that the lower catecholamine levels in endurance-trained individuals may be a contributing factor to this response (70). However, this suggestion is not without controversy. In direct oppostion to this hypothesis, a recent abstract by Sather, et al. (105)

indicates that aerobic fitness has no influence upon adaptation to orthostatic stress.

The astronauts of the National Aeronautics and Space Admininistration have been associated with an image of good health and high fitness levels. If aerobic fitness does negatively influence orthostatic tolerance, even moderate levels of aerobic fitness may be predisposing our spacecrews to the possibility of syncope upon reentry. Therefore, clarification of the effect of high aerobic levels on weightless adaptations and orthostatic responses is very important.

Conversely, it has been theorized that individuals with high strength might better be able to tolerate the increased +Gz forces of reentry and a return to terrestrial gravity (125). Information on this intriguing possibility is virtually non-existant. Preliminary studies have indirectly suggested that strength training may increase orthostatic tolerance (71, 115), whereas another study indicates that strength training does not increase orthostatic tolerance (18). No study has been reported which has considered a possible interaction between the effects of aerobic and strength training on orthostatic tolerance.

Therefore, the purposes of this study were: 1) To measure catecholamine responses during simulated weightlessness and simulated reentry (orthostatic stress); and 2) to compare these responses in groups of men who have (a) high aerobic fitness and low strength, (b) high strength and low aerobic fitness, (c) both high aerobic fitness and high strength, and (d) neither high strength nor high aerobic fitness.

Specifically, the following hypotheses were tested:

1) There will be no difference between the groups' catecholamine levels during head-down tilt.

2) There will be a decrease in catecholamine levels and heart rate within the first 15 minutes of head-down tilt in all groups.

3) Individuals with high levels of aerobic fitness will exhibit diminished catecholamine levels and blood pressure during lower body negative pressure as compared to individuals with low levels of aerobic fitness.

4) Individuals with high levels of leg strength will not exhibit diminished catecholamine or blood pressure responses during lower body negative pressure as compared to individuals with low leg strength levels.

CHAPTER II

REVIEW OF THE RELATED LITERATURE

Physiological Responses to Spaceflight

Spaceflight subjects humans to an environment where little or no gravitational force acts on them. This condition has been known as zero-g or weightlessness but has been more accurately described as microgravity (92, 132).

When a human is exposed to microgravity, physiological changes occur that trigger compensatory reflexes (92). Although some of the adaptation mechanisms and reflexes are not known, certain facts about the body's response to microgravity have been elucidated. The facts have been gathered through the spaceflights conducted by the Soviet Union and by the United States' National Aeronautics and Space Administration (NASA).

Physiological adaptations associated with spaceflight first became known during the Mercury and Gemini programs. Because of operational constraints, only electrocardiograms, respiration, and oral temperature were recorded during flight (10). In light of the limited inflight data, the primary means of elucidating the effects of weightlessness and reentry on man's physiological systems was comparing postflight data with preflight data (60). Due to the constraints on biological data collection, the primary contribution of the Mercury program was that it showed that man could survive and work in space (10). Gemini, while providing more physiological data, was still hampered by operational constraints. While not specific, Gemini data did indicate that some cardiovascular changes possibly took place during flight (10). These changes were characterized by a loss of exercise capacity, orthostatic tolerance, and red cell mass (10, 33, 92).

The bulk of our knowledge about physiological changes that occur during spaceflight has come from NASA's Apollo and Skylab programs and the

Soviet Union's Soyuz/Salyut program. The most evident physiological change that occurred upon exposure to microgravity was noted early in the Apollo program. All crewmen except one during the Apollo program reported fullness of the head and rounding of the features (10, 92). The fullness of the head was believed to be a result of the lack of gravity and the resulting translocation of body fluids toward the head (10, 62, 92, 132). This effect was also noted during the Russian spaceflights (131) and during Skylab (123). Vorobyov reported that the cephalid fullness usually was transient and diminished at the end of the first week (131). Associated with this fullness of the head and features during weightlessness, it was noted that calf and thigh circumferences were reduced (92, 123, 131, 132). This was attributed to a transfer of approximately 1.5-2 liters of body fluids headward during the first 24 hours of exposure to microgravity (67, 92).

All of the cardiovascular adaptations that were observed during the American and Soviet spaceflights were postulated to be a direct result of the cephalid blood shift which resulted in an increased venous return and preload (131). Berry (10) noted that, during the Apollo program, heart rates tended to stablize at lower-than-preflight levels. However, Russian scientists have recently noted that with long periods of time in weightlessness, heart rate tends to increase, rising to a plateau after approximately two months of exposure to microgravity, (131). Vorobyov, et al. also noted that during the first week of exposure to microgravity, stroke volume increased which led to a slightly increased cardiac output (131). Also noted by Soviet scientists was a large range of decreases in peripheral resistance (11-64%) upon acute exposure to microgravity (131). In addition to causing an increase in stroke volume and cardiac output soon after exposure to microgravity, the increase in venous return was thought to cause a diuresis in response to increased right atrial pressure (39). This in turn was postulated to lead to a decrease in plasma volume during spaceflight (10, 15, 32, 92, 131). The decrease in plasma volume after long term

exposure to microgravity compensated for the increase in thoracic and cephalid fluid volume (10). These cardiovascular adaptations are postulated to maintain a stable blood pressure during the central hypervolemia resulting from microgravity. No significant changes in blood pressure have been recorded during any spaceflight, both American and Soviet (104).

The observation of cardiovascular change during weightlessness led some researchers to postulate that the sympathetic nervous system's activity was modified as a result of exposure to microgravity (32, 45, 60, 92). Catecholamines were not measured in any spaceflights before Skylab to derive an index of sympathetic activation during weightlessness and test this postulation. Skylab crewmembers' urine was analyzed for the catecholamines epinephrine and norepinephrine after each flight (74). Skylab data indicated that epinephrine and norepinephrine were decreased during exposure to microgravity, with occasional peaks in norephinephrine exhibited at various points (74, 92). These peaks occurred because of the exercise regimes of the astronauts (60, 74).

All inflight data gathered in our young space program are very valuable but must be viewed with caution. In the early years of the space program, data collection was limited. Several limitations are apparent in considering spaceflight data (16). The number of subjects that have been subjected to microgravity has been small. The majority of the subjects have been male, 35-45 years old, and physically fit. Flight constraints have often necessarily made biological data collection of secondary importance. Thus, data collection at times did not go as planned or collect what was intended (16, 60, 92). These concerns have led to the development and use of laboratory simulations of weightlessness (41).

Microgravity Simulations

Weightlessness is difficult to reproduce within Earth's 1-G environment. Jets flying Keplerian arcs can produce weightless conditions for periods of time

approaching only 45 seconds (16, 92, 103, 132). Laboratory simulations provide the strictly controlled conditions needed for rigorous scientific study.

The near impossibility of producing weightlessness on Earth has led to simulations which evoke the physiological changes observed with insertion into weightlessness. Several microgravity simulation methods have been employed: bed rest, water immersion, head-down tilt, lower body positive pressure, and volume expansion with saline (16, 103). These methods, with the exception of volume expansion, attempt to remove the hydrostatic pressure gradient imposed by gravity on the circulatory system (103). Although imperfect, the simulations do remove the majority of the hydrostatic pressure gradients and provoke what is thought to be one of the primary physiological events that occurs upon exposure to weightlessness: an initial thoracic and cephalid hypervolemia (14, 16). This initial thoracic and cephalid hypervolemia is also provoked by volume expansion (94).

Bed rest was extensively used in the early years of the space program as an analog of microgravity. Blomqvist and Stone noted that there were over 500 studies done world-wide on bed rest between 1921 and 1978 (16). Bed rest, though widely used, fell out of favor when some reports suggested that bed rest did not mimic the physiological responses of the microgravity environment as closely as head-down tilt (93).

Another method used for simulating weightlessness has been water immersion (16, 37, 103). Although this is a viable simulation of microgravity, methodological difficulties such as hygiene, the need for precise water temperature, and maceration of the subject's skin during immersion have made water immersion difficult to use (103).

Water immersion has a more powerful and immediate effect on fluid redistribution than bed rest, head-down tilt, or weightlessness (14, 16). Although water immersion promotes a cephalid fluid shift, it is believed that the shift observed is of much greater magnitude than that exhibited during microgravity

(16, 93). Nixon, et al. speculated that the larger cephalid shift during water immersion may be caused by an increased thoracic pressure gradient and a compression of the submerged tissues (93).

Volume expansion with saline (94) and lower body positive pressure (22, 94) have also been used as simulations of weightlessness. Unfortunately, these analogs offer methodological difficulties and have not proven to be any more applicable than other simpler methods.

As early as 1895, Hill used head-down tilt to examine changes in body reactions (59). Application of head-down tilt as a weightless simulation was used as early as 1968 by Russian scientists (71). However, not until Kakurin, et al. (63) published their study on the validity of different head-down tilt angles as analogs of microgravity, did the method gain tentative acceptance among Western scientists. As a weightless simulation, Kakurin, et al. concluded that head-down tilt angles from -4° to -12° produced physiological responses closer to those of actual spaceflight than did horizontal bed rest (63).

At approximately the same time, Volicer, et al. published a study on the effects of -5° head-down tilt on metabolism (130). In their study, Volicer, et al. suggested that head-down tilt was a more valid model than bed rest for simulating weightlessness because metabolic results with head-down tilt closely resembled those seen during spaceflight (130). In a comprehensive study further validating head-down tilt, Nixon, et al. (93) noted that head-down tilt provided a closer model of the actual time-course and physiological responses to microgravity than did either bed rest or water immersion. Currently, head-down tilt is the method most widely used as an analog of weightlessness (16).

Researchers using head-down tilt have used a variety of tilt angles. Kakurin, et al. (63) recommended any angle between -4° and -12°. However, with steeper angles, (i.e. -8° and greater), some researchers have noted severe

cranial congestion (63, 133). Therefore, many studies now use between -4° and -6° to elicit the fluid shifts common to insertion into microgravity (93).

Physiological Responses to Head-Down Tilt

Because head-down tilt is thought to closely mimic the weightless state, many studies have been done on its effects on the body. As a consequence, many of the preliminary observations made during the American and Soviet space programs have been reexamined.

Upon exposure to head-down tilt, as with microgravity, there is a significant shift of fluid from the lower extremities to the thorax (15, 27, 51, 63, 64, 65, 66, 72, 77, 93, 127). Nixon estimated this fluid shift by measuring decreases in leg volume and noted that approximately 0.9 liters of body fluid had shifted headward after 30 minutes of exposure to head-down tilt (93). After two hours of head-down tilt, they observed a further decrease in leg volume of 0.4 liter (93). These figures corresponded approximately to what had been noted in spaceflight (67).

It has been reported that central venous pressure increases due to the central hypervolemia occurring after initial exposure to head-down tilt (42, 80, 83, 93). Even though the majority of the papers reported an increased central venous pressure with head-down tilt, the time course of this increase was different in the various studies. Goldsmith, et al. (42) noted that central venous pressure increased after l5 minutes of head-down tilt and then stabilized. Nixon, et al. (93) noted that the increase in central venous pressure occurred after 30 minutes and was stable after 90 minutes. However, Katkov, et al. (65) reported that central venous pressure actually decreased non-significantly in the first hour of head-down tilt and did not increase until the second hour of tilt, (from 3.6 mm Hg to 4.6 mm Hg). However, it is agreed that central venous pressure increases with head-down tilt and then is stable, generally within the first six hours of head-down tilt (93). This increase and plateau in central venous pressure has

been considered an acute physiological change which reflects an early adaptation to head-down tilt (72).

The increase in central venous pressure is thought to increase the pressure in the right atrium, the right ventricle (80), and the pulmonary tree (40, 64, 65). It is tempting to infer that the increase in right heart pressure and pulmonary pressure might lead to increases in left heart pressures, but Lollgen, et al (80), noted that this inference is not valid. They explained that while there was a slight increase in left ventricular pressure in their study, it was not significant and did not occur until 15 minutes after the increase in central venous pressure. Lollgen, et al. (80) pointed out that the right and left hearts have different compliances. They noted, that with the initial shift of blood with head-down tilt, the blood is most likely to be stored in the more compliant right heart and pulmonary vessels. This has been validated by studies that have implanted catheters in the pulmonary artery and directly measured increases in pulmonary artery pressure soon after exposure to head-down tilt (40, 63). Recently, Tomaselli, et al. (127) have postulated that blood is stored in the pulmonary tree as soon as 30 minutes after head-down tilt begins.

Nixon, et al. (93) reported that with exposure to head-down tilt, no change in left ventricular contractile state occurred. However, Gazenko, et al. (40) noted a decrease in left ventricular distensibility and contractility with head-down tilt. Gazenko, et al. (40) went on to note that contractile parameters returned to baseline 55-60 minutes after the beginning of the head-down tilt. These reports of variation in contractility could be due to the different experimental protocols employed in the various studies. Gazenko, et al. (40) preceeded their head-down tilt treatment with head-up tilt. This treatment used by Gazenko, et al. could have affected their head-down tilt observations. Nixon, et al. (93) did not have any treatments preceding head-down tilt and the tilt was six hours long. Therefore, Nixon et al.'s (93) results may be the most accurate representation of contractility states during weightlessness.

If the Frank-Starling mechanism were employed, the reported increase in venous return and central venous pressure (42, 80, 83, 93) would be expected to increase stroke volume in response to the central hypervolemia. However, if the reasoning of Lollgen, et al. (80) is correct, the hypervolemia of weightlessness may not be of sufficient magnitude to trigger this mechanism. The increase in thoracic fluid may be sequestered in the right heart and pulmonary tree until the fluid regulating systems of the body take over. These speculations have led to controversy concerning the true pattern of stroke volume after insertion into microgravity. Several studies reported an increase in stroke volume with head-down tilt (58, 66, 83). Lollgen, et al. (80) reported a non-significant increase in stroke volume (8%) while Nixon, et al. (93) and Katkov et al. (65) reported no change in stroke volume. These discrepancies have not been resolved.

Another cardiovascular parameter that has been reported to react in different patterns with insertion into head-down tilt is heart rate. Actual heart rate data during the early period of head-down tilt have been conflicting. Several authors have reported no differences in heart rate with initial exposure to head-down tilt (3, 42, 53, 65, 80, 82, 83, 130). Nevertheless, significant heart rate reductions were noted by Hill, et al. (58), Convertino and Benjamin (27), Tomaselli, et al. (127), and Nixon, et al. (93). Where it has been observed, the decreases in heart rate have been noted to be short-term with restoration of baseline values occurring within one hour (127) to six hours (93).

While the majority of studies have either reported no change or a small decrease in heart rate during head-down tilt, one report (66) noted an increase in heart rate using a tilt angle of -20°. While acknowledging that this finding was different than previous findings, the authors could not discredit or explain the data.

One might be tempted to speculate that head-down tilt angle determines the heart rate response. However, upon review of the studies that found no

change in heart rate (3, 40, 42, 53, 66, 80, 82, 83, 130), tilt angles ranged from -5° to -30°. Tilt angles employed in the studies which found a decrease in heart rate (27, 58, 93, 127) varied from -6° to -30°. Tilt angles of the same range elicited different heart rate responses in different studies.

Observations on cardiac output have followed the stroke volume data closely. Authors reporting an increase in stroke volume during initial head-down tilt (58, 64, 83, 127), have also reported an increased cardiac output. London, et al. (82), did not report stroke volume data but noted an increased cardiac index with initial head-down tilt. Those studies reporting little or no change in stroke volume (65, 80, 93) have also reported no change in cardiac output.

Any changes that take place in heart rate during the same period of head-down tilt do not appear to be of significant magnitude to offset the effects of stroke volume changes on cardiac output. In all three studies noting no change in stroke volume and cardiac output (65, 80, 93), Nixon et al. (93) reported a significant decrease in heart rate, while Katkov et al. (65) and Lollgen, et al. (80) reported no change in heart rate. The studies reporting an increase in stroke volume and cardiac output vary on whether heart rate decreases (58, 127), increases (66), or stays the same (82, 83) during the acute period of exposure to microgravity.

As with several manned spaceflights (103), several studies have reported no change in systolic or diastolic blood pressure (3, 82, 83), mean arterial pressure (42, 80, 93), or pulse pressure (82) with head-down tilt. A few studies, however, have not confirmed these observations. Some authors have observed that blood pressure decreases during the early stage of head-down tilt (53, 66, 130). Volicer, et al. (130) and Hargens, et al. (53) both reported that the blood pressure returned to baseline after the initial decrease. Katkov et al.'s (66) report of a decrease in arterial pressure was puzzling because of the observed increases in heart rate and stroke volume with the head-down tilt. Katkov, et al. did not report total peripheral resistance, but suggested that a

decrease in peripheral resistance may have caused the decrease in arterial pressure (66). Vorobyov, et al. (131) have reported a decrease in total peripheral resistance with exposure to microgravity. This led to a partial explanation of the decrease in blood pressure noted in these studies (53, 66, 130). However, in contradiction to these observations was one study (127) which noted an increase in arterial pressure after 15 minutes of head-down tilt. Tomaselli, et al. (127) observed an increase in total perpheral resistance and arterial pressure during the early period of head-down tilt.

The role of the sympathetic nervous system in the adaptation to head-down tilt has been questioned (45). Lollgen, et al. (80), and Goldsmith, et al. (42) showed no change in plasma norepinephrine levels during head-down tilt. In addition, Lollgen, et al. (80), showed no change in plasma epinephrine and dopamine levels. Goldsmith, et al. (42) concluded that the loading on the cardiopulmonary baroreceptors that occurs with head-down tilt did not affect catecholamine levels. However, London, et al. (83) reported that catecholamine levels decreased when subjects were tilted head-down -10°. However, Goldsmith, et al. (42) questioned the reliability of London, et al.'s extremely high resting catecholamine values. Goldsmith, et al. (42) speculated that London, et al.'s catecholamine values may have unusually high because of subject anxiety. Any reduction noted by London, et al. (83), Goldsmith, et al. observed, was probably due to subject relaxation. No report has focused on sympathetic activity within the initial 30 minutes of tilt.

Orthostatic Tolerance

The cardiovascular adaptation that occurs with an exposure to microgravity can lead to cardiovascular dysfunction upon return to terrestrial gravity (15). This dysfunction may be severe enough to prevent the cardiovascular system from maintaining arterial blood pressure during standing. This is commonly known as decreased orthostatic tolerance. Convertino, et al. (28) succinctly defined orthostatic tolerance as "the capacity of the

cardiovascular reflexes to maintain arterial pressure so an individual can tolerate the upright, stationary posture." Decreased orthostatic tolerance has been noted to be marked by increased venous pooling in the lower extremeties, increased heart rate and decreased pulse pressure (10), and is particularly evident after exposure to microgravity (10, 32, 60, 92, 132).

Recently, Tomaselli, et al. (128) reported that responses to lower body negative pressure were changed after a period of 60 minutes of -6° head-down tilt. They noted that the ability of the cardiovascular system to withstand orthostatic stresses was dependent on the previous state of the system. Similar observations of reductions in orthostatic and G- tolerance after use of a laboratory simulation of microgravity have been reported in connection with another head-down tilt study (51) and in conjuction with water immersion and bedrest studies (12, 13, 16, 44, 50, 61, 70, 104, 129).

The reduction of orthostatic tolerance after a period of exposure to microgravity has been postulated to be caused by several mechanisms. Goodall, et al. (45) postulated that a decrease in sympathetic nerve activity during weightlessness predisposed the body to decreased orthostatic tolerance. Sandler, et al. (104), and Greenleaf, et al. (50) both speculated that the decrement in orthostatic tolerance was caused by an absence of baroreceptor stimulation during microgravity exposure. Triebwasser, et al. (129) postulated that exposure to microgravity caused a loss of hydrostatic pressure in the vascular beds which led to a loss of vascular tone and accounted for the decreased orthostatic tolerance. While these are all plausible explanations, a stronger argument is that the decrease in circulatory blood volume, inherent in chronic cardiovascular adaptation to weightlessness, was the major factor in the reduction of orthostatic tolerance (132).

The body axis that is parallel to the gravitational force that is applied determines the direction the hydrostatic pressure is applied to the circulatory column and the severity of the orthostatic challenge to the body's homeostatic

mechanisms. A standard gravitational nomenclature has developed (Figure 1) to denote the anatomical direction of the force (16). Commonly, three axes of gravitational forces on the body are denoted. Gravitational forces which act from

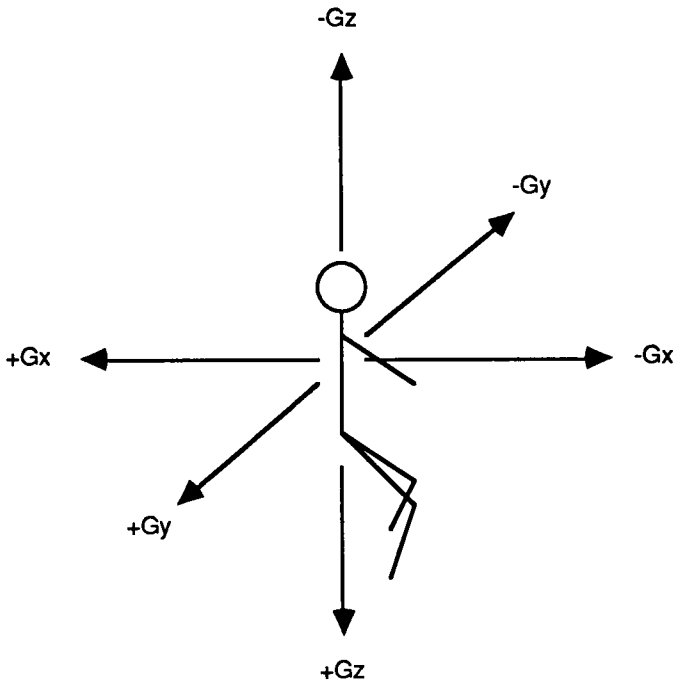

Figure 1. Gravitational vectors acting on the body.

the anterior to the posterior portion of the body are denoted Gx forces. If the force is from the front to back it is termed +Gx; forces from back to front are -Gx forces. Gravitational forces acting upon the long axis of the body (from head to foot) are called Gz forces. When the force is applied from the head to the feet it is termed +Gz; forces acting from the feet toward the head are termed -Gz. The last G force, Gy, acts on the body from side to side. Gravitational forces acting from right to left are +Gy and forces acting from the left to right are -Gy forces.

The magnitude of the gravitational force is expressed as multiples of terrestrial gravity at sea level and denoted by preceding the gravitational force symbol by the multiple, (e.g. +3Gx is three times terrestrial gravity acting from the front to back of the body), (16).

Laboratory Methods of Orthostatic Challenge

Data collection during conditions of high gravitational forces such as reentry is technically and operationally infeasible (67). Therefore, most of the data pertaining to man's adaptation to gravitational forces after a period of insertion in microgravity has been collected immediately postflight or in laboratory simulations (10, 60).

Probably the simplest test used to evaluate orthostatic responses was the stand test (60). This test involved a five minute control period followed by a five minute passive stand. The subject stood with his heels six inches away from the wall, in a relaxed manner (60). Electrocardiograms and blood pressure were recorded during the test. Unfortunately, this test lacked fine control of the stress. Nevertheless, it was the orthostatic stress test used in the early Apollo program (60).

Head-up tilt was another method used to initiate the venous pooling of fluid in the lower extremities (16). The ability to tilt the body to different angles provided more control over the severity of the stressor. However, the restraint system necessary to keep the subject secure on a tilt table and the position of the calf muscle during tilt has caused concern about possible compression and contraction of the leg musculature. These factors could provide augmented venous return and confound results (60, 70).

The most popular method of provoking venous pooling in the lower extremities has been lower body negative pressure (LBNP). With this method, the subject is supine and sealed in a chamber from the iliac crest to the feet. The air pressure in the box is then reduced according to an appropriate protocol.

Tomaselli (126) listed several reasons why lower body negative pressure has been favored over other methods.

1. It is comfortable and acceptable to the subject.
2. The stress is quantifiable, reliable, and reproducible.
3. The rate of production and degree of central hypovolemia can be easily controlled and readily adjusted.
4. Multiple levels of orthostatic stress can be presented.
5. Impounded blood can be relocated whenever and as quickly as desired.
6. The effects of altered hydrostatic gradients are not a consideration.
7. Lower body negative pressure can be performed during weightless simulation studies without requiring alteration in body position between baseline and experimental measurements.
8. The technique can be used to test orthostatic tolerance in a microgravity environment.

Actually reproducing high G-forces is also possible with the use of a centrifuge. The subject is seated in a gondola attached to a long arm and then spun about (50). While this actually produces high gravitational forces, human centrifuges are very large and expensive to run. This has limited the use of this modality.

Physiological Responses to Orthostatic Stress

While all of the aforementioned methods induce venous pooling (70, 89), differences in elicited responses for these modalities have been suggested (49, 60), especially in men. Shvartz noted a low correlation between standing and head-up tilt tests, suggesting difficulty in comparing results between the two modalities (110). Greenleaf, et al. (49) noted that in male subjects who had been heat acclimated, head-up tilt tolerance was increased, whereas centrifugation tolerance was not. Hoffler, et al. (60) noted that responses to lower body negative pressure, while qualitatively the same as responses to head-up tilt, differed in magnitude. Baisch, et al. (5) also voiced this concern in a

recent review. Therefore, results from studies using different methods of producing venous pooling may not be comparable.

Application of lower body negative pressure to the body causes an increase in transmural pressure and a pooling of body fluid in the lower extremities with an increased filtration into the extravascular spaces (11, 16, 89, 136). The negative pressure which acts internally upon the circulatory system varies according to the specific tissue (89). The pressure applied to the subcutaneous tissue is approximately 95% of the externally applied pressure. Pressures applied to the muscular tissue are also variable, being only 80-90% of external pressure (25, 89).

Musgrave, et al. (89) found that when subatmospheric pressure was applied to the lower extremities, an increase in fluid content of the leg resulted. With exposure to -40 mm Hg for one, three, and five minutes, total leg volume changed by 513, 573 and 614 mls., respectively. The peak change in leg blood volume was measured as an increase of 3.16% of baseline. These values are comparable to results obtained by Raven, et al. (97), Smith, et al. (114), Smith and Raven (115), higher than values reported by Baisch, et al. (5), Raven, et al. (98), Wolthius, et al. (136), and lower than that reported by Montgomery, et al. (86). Wolthius, et al. (136) noted that differences between leg volume changes may be due to different measurement methodology. Musgrave, et al. (89) used total leg water plethysmography whereas other authors (5, 97, 98, 114, 115, 136) have used single band Mercury-in-silastic strain gauges and electrical impedance (86). Wolthius, et al. (136) doubted the ability of the mercury strain gauges to reproduce the results derived using total leg water plethysmography. However, the differences noted in leg volume change and venous pooling are also dependent upon length of time and magnitude of pressure applied at the time of measurement (5). In short, differences in the literature may be explained by different measuring methodologies and protocols used. However, it is

generally agreed that there is an increase in leg volume with increased levels (decreased pressure) of lower body negative pressure.

A sequestering of body fluids in the lower extremities caused by decreased transmural pressure results in a decreased central venous pressure (11, 43, 88, 94). Goldsmith, et al. (43) reported a fall in central venous pressure of 46% at an unspecified magnitude of lower body negative pressure. They reported further decrements in central venous pressure with further decreases in lower body negative pressure (43). Norsk, et al. (94), in a recent abstract reported central venous pressure falling from 7.5±0.5 mm Hg to 2.0±0.5 mm Hg at -30 mm Hg lower body negative pressure. This decrease in central venous pressure leads to decreases in right heart pressures (80), left heart filling pressure (40), and end diastolic volume (1). The increased pooling of fluids in the lower extremities during lower body negative pressure and the decreased central venous pressure result in a decreased stroke volume (1, 5, 11, 46, 79, 85, 86, 88, 97, 98, 114, 119, 136) and a decrease in cardiac output (5, 11, 46, 58, 79, 80, 88, 97, 98, 115, 119, 136).

Researchers have noted a Starling effect at smaller magnitudes of lower body negative pressure (e.g. -8, -16, and -30 mm Hg). There is a decreased filling pressure, end-diastolic volume, and stroke volume without other compensatory mechanisms, such as heart rate, being recruited (1, 97). Other authors have also noted little change in heart rate in the early stages of lower body negative pressure, (5, 43, 86, 88, 98).

With lower negative pressures (e.g. -40 and -50 mm Hg), central venous pressure continues to decrease (43). Goldsmith, et al. (43) stated that this fall in central venous pressure unloads the cardiopulmonary receptors and participates in the activation of the sympathetic nervous system. The increase in sympathetic drive has several consequences. An increase in sympathetic activity could lead to an increase in cardiac contractility, heart rate, total peripheral resistance (70) and a decrease in venous pooling (46). Several

authors have observed a compensatory increase in heart rate with greater magnitudes of lower body negative pressure (11, 43, 46, 58, 79, 85, 88, 97, 98, 114, 115, 119, 136).

Mean arterial pressure is determined by three items: heart rate, stroke volume, and total peripheral resistance (52). With further increases in the magnitude of lower body negative pressure, cardiac output continues to decrease in the face of an increasing heart rate (5, 11, 46, 58, 79, 80, 88, 97, 98, 115, 119, 136). However, in spite of the continued decline of cardiac output, Baisch, et al. (5) noted that mean arterial pressure remains relatively stable during lower body negative pressure preceding syncope. Some researchers concluded that the stability of mean arterial pressure during lower body negative pressure preceding syncope was due to an increase in total peripheral resistance (11, 88, 98). Bevegard, et al. (11) reported that five to nine minutes after the onset of lower body negative pressure, total peripheral resistance and vascular resistance increased. This was also observed in several other studies (79, 97, 98).

Plasma catecholamine levels have been used as an index of sympathetic nervous system activity (38, 73). Several studies report catecholamine levels during lower body negative pressure experiments (43, 47, 91, 105, 106). Generally, the reports support an increase in catecholamine levels with increasing magnitude of lower body negative pressure. Graboys, et al. (47), in the first study published on plasma catecholamine levels during lower body negative pressure, found an increase in plasma catecholamines with lower body negative pressure. The type of catecholamines measured was not specified, but from the values given, it is assumed that norepinephrine was the catecholamine of interest. Graboys, et al. (47) also noted that their results, while being the first reported with lower body negative pressure, compared well with values derived from head-up tilting and passive standing. Other studies have reported, at different levels of lower body negative pressure, increases in

plasma norepinephrine (47, 91). Sather, et al. (105) measured the peak plasma norepinephrine values during a maximum lower body negative pressure tolerance test and reported values that seemed to be different from baseline. However, statistics verifying whether or not the peak values were different than those at baseline were not reported in the abstract. Quantification of epinephrine levels during lower body negative pressure has not been reported in the literature.

The cardiovascular changes that occur with the onset and continuation of lower body negative pressure maintain arterial pressure for a short period of time. However, with increasing duration and magnitude of lower body negative pressure, the compensatory reflexes are overcome and blood perfusion of the cerebral cortex is severely reduced (88). This leads to syncope. As mentioned before, greater magnitudes of lower body negative pressure cause further decreases in cardiac output and stroke volume without any further increases in heart rate or peripheral resistance (87). Murray, et al. (88) noted that during lower body negative pressure to syncope, heart rate only exceeded 100 beats per minute in only two subjects.

Immediately preceding syncope, venous tone increases, leading to an increased central venous pressure (88). This increase in venous tone may be caused by an increase in sympathetic nervous system activity. Robertson, et al. (100) reported that at syncope, plasma norepinephrine values were only increased two-fold. Nevertheless, the increase in central venous pressure is probably offset by vasodilatative effects of a tremendous increase in plasma epinephrine as has been reported by Robertson, et al. (100) just prior to syncope. Further compounding the body's struggle is an unexplicable decrease in heart rate seen just before syncope (55, 88). At this point, arterial pressure starts to drop (55) and progression to syncope from this point is very rapid (55, 88).

Several researchers have tried to elucidate the mechanisms which predispose some individuals to reduced orthostatic tolerance. It has been established that age (75) or sex (109) do not have any effect on orthostatic tolerance. Klein, et al. (68) observed that height was inversly related to orthostatic tolerance because of the taller circulatory column in a tall individual. Shvartz, et al. (111) noted that individuals susceptible to orthostatic syncope had a decreased functioning of the sympathetic nervous system. Baisch, et al. (5) also concluded that individuals who had high orthostatic tolerance had a high level of sympathetic activity that led to increased peripheral resistance. However, when Loeppky, et al. (78) used propranolal to block the beta-adrenergic receptors during a head-up tilt test, he noted that the heart rate adjustment to head-up tilt was only partially blocked. He suggested that the parasympathetic nervous system also influenced orthostatic responses. Harrison, et al. (55) and Shvartz, et al. (111) also pointed out that intolerant individuals exhibited a lower circulating blood volume than orthostatic tolerant individuals.

Exercise Training and Orthostatic Responses

The effect of exercise training on gravitational and orthostatic responses has been a topic of much research and controversy for many years. Several studies and reports have been completed that suggest that individuals with high aerobic levels exhibit impaired +Gz and orthostatic responses (7, 9, 20, 44, 70, 85, 90, 98, 99, 114, 115, 117, 118, 125, 129)

Stegemann, et al. (117) tested 50 subjects using head and neck negative and positive pressure. Half of the subjects were untrained; the other half consisted of trained runners, swimmers, and soccer players. Stegemann, et al. observed that the blood pressure gain system in the athletic groups was reduced. They thought that this reduction was caused by a change in the baroreceptor loop. While not speculating on any mechanisms, they did state that, "Endurance training reduces the effectiveness of the blood pressure control

system." However, this study did not test the subjects' maximum oxygen consumption, a commonly used indicator of aerobic fitness. This eliminated any possibility of actually comparing fitness levels between the groups.

Lack of quantification of aerobic fitness was again obvious in Stegemann, et al.'s next study (118) that tested endurance athletes' and control individuals' orthostatic responses after a six hour immersion with exercise and an eight hour immersion without exercise. In both treatments, non-athletes tolerated the orthostatic challenge better than did the athletes. Whereas no non-athlete had syncope during a head-up tilt test following immersion, six of the 16 athletic subjects fainted. Stegemann, et al. again speculated that the athletes' diminished orthostatic responses were due to a decreased effectiveness of the blood pressure control system (118). While the methods used in this study have been shown not to be the best simulations of microgravity and high G situations, the conclusions added fuel to the growing controversy. These results were reemphasized by Goldwater, et al. (44), who also concluded in their abstract that athletes had less orthostatic tolerance because of reduced blood pressure regulation.

These findings were reaffirmed by Myhre, et al. (90) who found that runners' lower body negative pressure tolerance was 42% less than non-runners. They also found that after dehydration, runners still had lower orthostatic tolerance than non-runners and speculated that this was due to greater fluid shifts in runners. Klein, et al. (70) also suggested that this was a cause of athlete's decreased orthostatic responses.

In 1977, Klein, et al. published a review on whether or not endurance training for spacecrews was advantageous. Klein, et al. (70), after reviewing several research studies, concluded that aerobically trained individuals showed unfavorable responses to orthostasis. Klein, et al. (70) further speculated that these responses were further decreased when the individual was submitted to microgravity or laboratory simulations.

These opinions were confirmed in a series of studies conducted by Raven. In 1984, Raven, et al. found that the compensatory reflexes that guard against hypovolemia were reduced by endurance training (98). They noted that leg compliance in both highly fit (VO_2max=70.2±2.6 ml O_2/(kg·min)) and average fit (VO_2max=41.3±2.9 ml O_2/(kg·min)) subjects was the same. The average fit subjects exhibited higher heart rates, total peripheral resistances, and systolic blood pressures during lower body negative pressure at -50 mm Hg than did highly fit subjects. These facts suggested that average fit subjects tended to exhibit more stable cardiovascular adjustments to lower body negative pressure than did highly fit subjects and that leg compliance was not a factor in orthostatic responses.

Raven and Smith (99) partially elucidated these responses in a 1984 study which again found leg compliance the same in fit (VO_2max=62.5±1.9 ml O_2/(kg·min)) and unfit (VO_2max=35.4±2.8 ml O_2/(kg·min)) subjects. After an infusion of an alpha-receptor agonist (phenylephrine hydrochloride), Raven and Smith assessed alpha-receptor sensitivity in the subjects. They noted that the unfit subjects seemed to have less sensitive alpha-receptors, resulting in a lower peripheral resistance in these subjects. Derivation of a baroreflex index of sensitivity showed that baroreflex sensitivity was negatively correlated to fitness levels. Raven and Smith (99) suggested that the high pressure baroreceptors were altered by training. These findings were further validated in a follow-up publication in 1985 by Smith and Raven (115). These studies showed that the baroreceptor response was attenuated in endurance trained subjects. They also speculated that the autonomic nervous system of endurance trained individuals favored the parasympathetic nervous system and this led to decreased orthostatic responses.

Mangseth, et al. (85) noted that they believed the difference between the aerobically trained individuals that exhibited syncope and the untrained individuals who did not exhibit syncope was due to a deficit in peripheral

resistance regulation caused by decreased sympathetic activity. Several studies have shown a reduction of sympathetic activity during submaximal work after an aerobic training program (23, 24, 134, 135). However, no difference in resting plasma catecholamine levels has been reported between aerobically trained individuals and untrained individuals. (23, 134). A comparison of plasma catecholamine levels in trained and untrained individuals subjected to low levels of stress, (electrical shock, cold water hand immersion, and standing), was made by Claytor (23). No difference was noted between the trained and untrained subjects' plasma catecholamine levels at rest or during any of the stressors (23). The author noted that the stresses used in the study may not have been of sufficent magnitude to provoke great catecholamine changes or that, possibly, the attenuation of sympathetic nervous system activity with training was stress specific.

Not all of the cross-sectional data have shown a decrement in orthostatic tolerance in individuals with high VO_2max values. Allen, et al. (2) who tested all their subjects on a tilt table noted no difference in treadmill scores between fainters and non-fainters. Montgomery, et al. (86) noted that athletic females had better lower body negative pressure tolerance than did non-athletic females. However, oxygen consumption was not measured in any of the subjects, so quantitative assessment of the relationship of maximal oxygen consumption values to lower body negative pressure tolerance was not possible.

Shvartz (108) tested 18 men on various physical performance tests: a mile run, pull-ups, push-ups, and sit-ups. He found no relation between the mile run times and orthostatic responses during head-up tilt. Sit-up scores correlated well with orthostatic responses, suggesting abdominal strength influenced orthostatic responses.

Klein, et al. (69) showed that physical conditioning did not necessarily influence orthostatic responses. They tested two groups of men: 12 were

trained endurance athletes and 12 were non-athletes. The groups showed significant differences in VO_2max but no difference in head-up tilt tolerance.

Sather, et al. (105) tested fit subjects ($VO_2max > 50$ ml $O_2/(kg \cdot min)$) versus unfit subjects ($VO_2max < 50$ ml $O_2/(kg \cdot min)$) using lower body negative pressure. They found no statistical difference in lower body negative pressure tolerance between the groups.

All studies reviewed thus far have been cross-sectional in design. Longitudinal studies on the effect of aerobic training on orthostatic tolerance are limited. The longitudinal studies that are available deal mainly with heat acclimation and +Gz tolerance.

Cooper and Leverett in 1966 (29) found that there was no decrement in +Gz tolerance with five weeks of conditioning (running). Shvartz (107) found no difference in tilt tolerance with seven weeks of bench stepping exercise in 12 men.

In 1984, Convertino, et al. (28) trained eight subjects on an ergometer for eight days at two hours per day at 65% VO_2max. The subjects were exposed to head-up tilt tests before and after the training. Convertino, et al. (28) found an 8.3% increase in VO_2max, an 8.1% decrease in resting heart rate, and a 12.2% increase in plasma volume after the training. Head-up tilt duration increased an average of six minutes but the increase was not significant. Convertino, et al. (28) concluded that short-term endurance training non-significantly enhanced tilt tolerance because of the increase in plasma volume.

Epperson, et al. (35) trained eight men aerobically for 13 weeks. After training, there was a 7.5% increase in VO_2max. There was no change in +Gz tolerance in the subjects.

Greenleaf, et al. (48) trained 16 women aerobically for eight days. The women trained at different environmental temperatures, but at constant relative humidity (42%). The training was preceded by two weeks of centrifuge tests and maximum oxygen consumption tests to eliminate the possibility of a learning

effect confounding the data. Two centrifuge runs and maximal oxygen consumption tests were conducted after the training. Greenleaf, et al. (48) found that there was no difference in G tolerance after ergometer training. However, no difference in pre- and post- VO_2peak was found. The authors recognized that the training intensity may not have been sufficent to elicit training effects. Because classical training effects were not exhibited, conclusions concerning the effect of training on G-tolerance from these data are limited.

In another study, Greenleaf, et al. (49) heat acclimated six women and four men with ergometer exercise for 12 days at 44%-49% of VO_2peak at 40° Centigrade, relative humidity = 42%. No change in VO_2peak was noted pre- and post-training, while there was a significant decrease in exercise heart rate with training. There was no difference in G tolerance in either the men or women, pre- or post-training. There was no difference in tilt tolerance in the women, but a two-fold greater tilt tolerance was observed for the men after training. Greenleaf, et al. (49) stated that there was no obvious explanation for the different tilt responses between the men and women. However, again, because of the low intensity of exercise performed, care should be taken when speculating about the effects of endurance training on either G or orthostatic tolerance. Nevertheless, it should be noted that head-up tilt tolerance did increase after physical exercise bouts in this study.

Shvartz, et al. (111), in a study delineating differences between fainters and non-fainters, found no decrement of orthostatic tolerance with aerobic training. Their study employed 50% of VO_2max workloads in both hot and cool temperatures. Decreases in heart rate during submaximal work were observed as were increases in VO_2max after training.

Strength Training

It has been suggested that increased strength levels may increase orthostatic tolerance (125). Henry (57) noted that high abdominal and thigh

strength increased head-up tilt tolerance. Shvartz (107) also observed an increase in head-up tilt responses in a group of men subjected to strength exercises (pull-ups and dips) for seven weeks.

In 1968, Korobkov, et al. (71) subjected five runners and five weight lifters to a 40 day head-down tilt preceded and followed by head-up tilt tests. They found that both groups had a loss of central blood volume that led to decreased head-up tilt responses in both groups. However, Korobkov, et al. noted that the weightlifters tolerated the head-up tilt better and had less fluctuations in blood pressure than did the runners during the head-up tilt test. They suggested that the weightlifters had a greater venous stability caused by an increase in muscle tone.

Another study that has investigated the effects of weight training on orthostatic tolerance was done by Smith and Raven (115). They found that the baroreflex response to lower body negative pressure was augmented in weightlifters. This augmentation led to more stable cardiac parameters during lower body negative pressure. Smith and Raven speculated that this was the result of a training induced sympathetic dominance in the weightlifters (115). Unfortunately, this study lacked an appropriate strength testing modality. Since the lower body was exposed to negative pressure during lower body negative pressure testing, it seems that a test of lower body strength should have been used. Nevertheless, Smith and Raven used hand-grip strength to quantify the individual's strength levels (115).

The only longitudinal weight training study that has considered any effects on lower body negative pressure tolerance was recently reported by Buchanan, et al. (18). Twenty-one subjects' lower bodies were strength trained for 12 weeks. Buchanan, et al. (18) reported that there was no change in lower body negative pressure responses after the strength training.

Several studies have been conducted assessing the effect of strength-training programs on G-tolerance in fighter pilots (7, 8, 34, 35, 35, 120,

121). Epperson, et al. (35) trained three groups of subjects: one group was trained aerobically, another group was trained with weights, and the last group served as controls. They found that the runners and controls increased their G-tolerance four seconds per week but that the weightlifters increased their G-tolerance 16 seconds per week. This suggested that strength training augmented the learning effect in some manner in the weightlifters.

In a more complete study, Epperson, et al. (36) found that G-tolerance increased 53% with a 12 week weight-training program. They found that abdominal and bicep exercises were correlated with G-tolerance. Balldin (7) in another study, also found similar increases in G-tolerance after a strength-training program. Balldin noted that the mechanisms for the increase in G-tolerance after strength training were not known, but speculated that it might be due to an increased sympathetic drive in individuals after weight training. However, there are no data to support this speculation.

Tesch, et al. (121) found a 39% increase in G-tolerance after a strength training program. Tesch, et al. speculated that the increase in G-tolerance was due to an ability to perform the muscle tensing techniques for longer periods of time after training. Tesch, et al (121) noted that this was the only viable explanation because neither gains in muscle hypertrophy or mass were observed.

Several studies have emphasized the importance of the abdominal muscles during orthostatic challenges (2, 57, 107). To test these findings, Balldin, et al. (8) trained 15 pilots for 11 weeks using an isometric abdominal muscle training program. They found no increase in G-tolerance after the training program. However, only ten of the subjects completed 50% or more of the training. This fact confounded the results and any conclusions that could be inferred from the training.

One must be careful in inferring an increased orthostatic tolerance after weight training using these studies. All of the subjects in each of these studies used abdominal and leg tensing techniques designed to increase G-tolerance during all centrifugation tests. Even though these techniques were used pre- and post-test, Burton (19) pointed out that there was also a learning effect associated with the tensing techniques. As the subjects practiced the tensing techniques, their G-tolerance increased (19). Also, Greenleaf, et al. (49) have suggested that responses to centrifugation and orthostatic tests are different. Therefore, the question of whether strength-training will increase orthostatic tolerance is still unresolved.

Interaction of Strength and Aerobic Training

The controversy of whether athletic training is a detriment to orthostatic responses has touched many areas. The United States Air Force recently issued a directive (21) which limits active fighter pilots to no more than 20-30 minutes of aerobic fitness activity per day and encourages the use of weight training. This directive suggests an interesting question: "Can the effects of strength training offset any detrimental effects of aerobic conditioning?" No study has addressed any possible interaction of aerobic conditioning and strength training.

Summary

Spaceflight and the return to terrestrial gravity have profound effects upon the human cardiovascular system (92). Upon insertion into simulated microgravity, there is an increase in central venous pressure (93), right heart filling pressure (80), and pulmonary pressure (65). There is a slight increase in stroke volume and cardiac output (65) while heart rate either stays stable or decreases slightly (83, 127). There is a slight decrease in total peripheral resistance (131). After 15-30 minutes, stroke volume, cardiac output, and heart rate begin to return to baseline values, with central venous pressure

approaching baseline after 90 minutes (93). This acute adaptation is completed between six and 24 hours and is thought to be partially caused by sequestering of the increased thoracic volume in the pulmonary tree (127). Because of this sequestering, plasma volume decreases. Activity of the sympathetic nervous system is not known within the initial 30 minutes of head-down tilt.

Exposure to increased gravity after a period of microgravity is marked by a decreased orthostatic tolerance (10, 60). This decrease in orthostatic responses is manifested as a decrease in central venous pressure, heart filling pressures, stroke volume, and cardiac output (132). A decrease in central venous pressure is thought to lead to an increase in sympathetic nervous system activity which increases heart rate, heart contractility, and total peripheral resistance to maintain arterial pressure (5). With continued exposure to orthostatic stress, cardiac output continues to fall. This leads to a failure of the compensatory reflexes and syncope occurs (88).

The data concerning the relationship of high aerobic fitness to orthostatic responses are inconsistent. Numerous cross-sectional studies point to a decrease in orthostatic tolerance with high oxygen consumption values. The decrement in orthostatic responses is thought to be due to a lack of blood pressure gain when subjected to an orthostatic challenge (118). The training induced attenuation of sympathetic nervous system activity has also been postulated as an additive factor (70), but no evidence exists to support this theory.

Few longitudinal studies on the effects of aerobic conditioning on orthostatic responses have been completed. These studies indicate that no decrease in orthostatic responses is evident after an aerobic conditioning program (29).

It has been suggested that strength training regimens might increase orthostatic responses (125). Few studies have been done on this topic and the results are inconsistant. Cross-sectional studies suggested that weight training

stabilized the cardiovascular responses to orthostatic stress (71, 115). However, longitudinal results showed no change in orthostatic responses after a strength training program (18).

No study has considered the interaction of aerobic fitness and high strength levels on orthostatic responses.

CHAPTER III

METHODS

Overview

Twenty-four male subjects were classified by aerobic fitness and strength characteristics into four groups. Each subject was asked to come to the laboratory on four occasions. A complete physical examination, leg strength tests, and all paper work were completed at the first visit. The second visit consisted of the maximal treadmill test. An equipment and protocol orientation along with underwater weighing took place during the third visit. The last visit consisted of the experimental protocol which had four phases: 1) supine rest, 2) head-down tilt, 3) lower body negative pressure, and 4) recovery. Heart rate, blood pressures, calf circumference changes and plasma catecholamine levels were measured during the procedure and compared using repeated measures statistical analysis.

Recruitment of Subjects

Twenty-four male subjects volunteered for this study. The subjects were recruited from the work force at Kennedy Space Center (KSC) and the surrounding areas. At the beginning of the study, potential subjects were obtained from the subject pool at the Biomedical office at KSC. These potential subjects were sent a letter (Appendix A) inviting them to participate in the study. Also, posters announcing the need for subjects were placed in several places at KSC and in health clubs in the area. Individuals responding to the letters or posters were given a thorough explanation of the project on the telephone. If the individual continued to express interest in being a subject, a preliminary visit was scheduled.

Prior to each visit, the subject was sent a letter reminding him of his appointment (Appendix B) and informing him of the procedures which would take place during the upcoming visit. It was emphasized to the individual that he should maintain his usual lifestyle and activity level for the duration of his participation.

Selection of Subjects

Physical Examination. To participate in the study, the subject had to meet qualification criteria for strength and cardiovascular fitness. These variables were measured at the first and second visits.

Before the first visit, the subject was sent a packet (Appendix C) that included a reminder of the physical examination, instructions on how to get to the laboratory, a copy of the Privacy Act, a consent form to be signed before the treadmill test, and medical history forms. At this preliminary visit, each potential subject viewed a video presentation showing all procedures to which he would be subjected. The subject was then asked to read and sign the consent form for the main protocol (Appendix D).

After the consent forms were signed, a blood sample was taken from the subject for analysis. The blood samples were chemically assayed for glucose, blood urea nitrogen, lactate dehydrogenase, aspartate amino transferase, cholesterol, creatinine, uric acid, total bilirubin, and high density lipoprotein by laboratory technicians at KSC. White and red blood cell counts, along with hematocrit, hemoglobin, mean cell volume, and blood differentials were quantified using whole blood.

The subject then gave a urine sample for analysis. The specific gravity, color and character were checked. Using a Chemstrip dipstick, a technician

then tested the urine for leukocytes, nitrite, pH, protein, glucose, ketones, urobilinogen, bilirubin, and blood.

The medical history forms were checked, and while the subject was standing and lying, blood pressures were taken. A 12-lead resting ECG was performed to screen for ECG abnormalities. Upon completion of the ECG, a physician performed a physical examination and a pulmonary function test using a Collins Eagle One spirometer. Using the results of the pulmonary function test, the physical examination, the blood analysis, and the urine analysis, the physician then determined whether the subject should undertake the treadmill test to maximal aerobic capacity.

Strength Testing. After the preceding tests, the subject was given a leg strength test. This test employed a Cybex isokinetic dynamometer (Lumex, Inc.), which was calibrated daily. Davies (31) suggested using the strength of the quadriceps muscle group as an index of leg strength. To test this muscle group, the subject sat on the Cybex, and the action of the specified muscle group was isolated using large Velcro straps across the chest, abdomen and lower thigh. The lower leg was attached to the dynamometer arm using a Velcro strap. The Cybex speed was set at 60 degrees per second, which was recommended by Davies (31) as the best speed for testing strength. The subject was asked to extend and flex his leg maximally four times. Each extension and flexion produced a torque curve which was read by the Cybex data reduction computer. The computer then derived the highest torque produced from the four extensions and flexions. The extension score was then divided by the subject's bodyweight to give a percentage of bodyweight lifted. Strength testing was done on both legs.

These scores were used to determine the strength classification of the subject. If the percentage of body weight scores for both of the subject's legs were over 103%, the subject was classified as high strength. If the subject's percentage of bodyweight scores were both below 97%, the subject was classified as low strength. While it is admitted that these strength criteria are in part based on practical experience and communication with several athletic trainers familiar with the strength testing field, no other guidelines for leg strength testing are available in the published scientific literature. Similar guidelines as those noted above were presented by Davies (31) and represented the only published guidelines on total leg strength indexes.

Cardiovascular Fitness Determination. After the Cybex test, the date and time for the subject's treadmill test were arranged with the subject. The subject was asked not to eat anything two hours prior to the treadmill test. The treadmill protocol used during the second visit was a modified Bruce maximal treadmill protocol (Appendix E). This treadmill protocol was a graded test which consisted of increases in speed and grade until maximal exertion.

During the treadmill test, heart rate was monitored using the Frank ECG system (Figure 2). Five electrodes were placed in the same transverse plane on the anterior surface of the subject. Leads A and I were placed on the left and right midaxillary lines, respectively. Lead C and the Common lead were located on the left and right midclavicular line, respectively. Lead E was placed on the inferior margin of the sternum. All anterior leads were placed 3-4 cm below the nipples. Lead H was placed at the base of the neck, lead M at the level of the anterior electrodes and lead F directly above the iliac crest. The right paraspinal line was used to position the three posterior leads laterally.

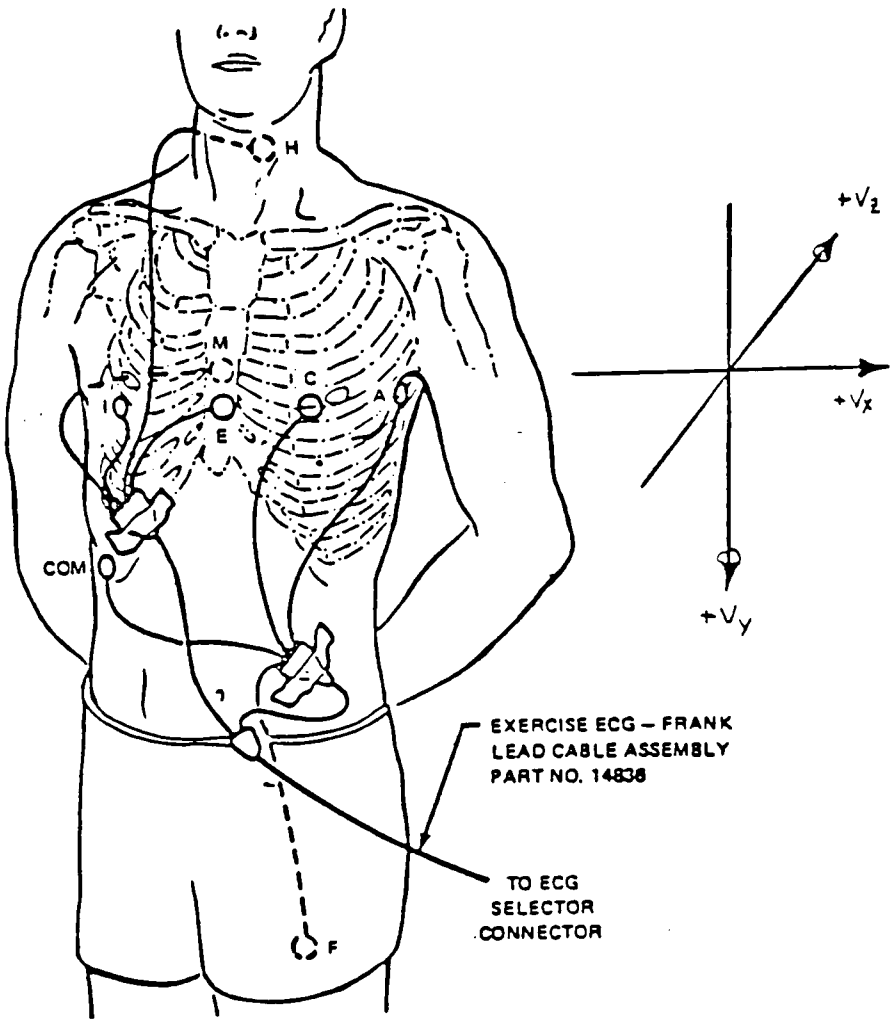

Figure 2. Frank Lead System

The heart rate was monitored with a Del Mar Avionics Exer Stress Monitor, Model 3000 and a Hewlitt-Packard oscilloscope. These signals were branched to two different outputs. The heart rate and S-T segment depression values were routed to a Beckman Metabolic Measurement Cart (MMC) which also collected and analyzed all gas parameters. The MMC then fed these data to a Computer Automation LSI-2 data acquisition unit which routed the data to three different areas: 1) to a Computer Automation DM Series monitor for minute-by-minute display, 2) to a Beehive International Model P1600 printer for hard-copy print-out, and 3) to a Pertec, Incorporated, 10 megabyte hard disk storage unit.

All ECG parameters were also routed from the Avionics unit to an interface and then into an electronic patchboard. This facilitated routing of the ECG parameters to three outputs for continuous monitoring by the test technician. The ECG parameters were fed to a Brush Mark 200 eight-channel horizontal recorder, a Brush Mark 200 eight-channel vertical recorder, and an Ampex PR2230 14 channel analog magnetic tape storage unit.

Blood pressure was automatically monitored using a custom built system integrating an Electronics for Medicine sphygmomanometer and an automatic pump. The signals from the cuff microphone were amplified and then routed to the electronic patchboard. This allowed blood pressure to be monitored continuously on the horizontal Brush recorder and recorded on the magnetic tape storage unit.

Oxygen consumption was monitored using open circuit spirometry in conjunction with the Beckman Metabolic Measurement Cart (MMC) using the Exercise Metabolic Program. Gas parameters measured and calculated by the MMC were expired volume, expired and inspired oxygen fractions, expired and inspired carbon dioxide fractions, maximal oxygen consumption per minute,

maximum oxygen consumption per kilogram per minute, maximum carbon dioxide production, respiratory exchange ratio and respiratory rate.

The maximal treadmill test was used to derive maximum oxygen consumption in milliliters per kilogram per minute (VO_2max ml O_2/(kg·min)). If the subject's VO_2max was less than or equal to 45 ml O_2/(kg·min), the subject was classified as low fit. If the subject had a VO_2max of 50 ml O_2/(kg·min) or greater, he was classified as high fit.

Subject Classification. Using the VO_2max and the Cybex leg strength scores, each subject was classified into one of four groups:

1) High fit, High strength (HFHS) - those subjects with a VO_2max greater than or equal to 50 ml O_2/(kg·min) and a Cybex score greater than or equal to 103% of body weight on each leg.

2) High fit, Low strength (HFLS) - those subjects with a VO_2max greater than or equal to 50 ml O_2/(kg·min) and a Cybex score less than or equal to 97% of body weight on each leg.

3) Low fit, High strength (LFHS) - those subjects with a VO_2max of less than or equal to 45 ml O_2/(kg·min) and a Cybex score greater than or equal to 103% of body weight on each leg.

4) Low fit, Low strength (LFLS) - those subjects with a VO_2max of less than or equal to 45 ml O_2/(kg·min) and a Cybex score of less than or equal to 97% of body weight on each leg.

Equipment and Procedure Orientation and Underwater Weighing

Before the underwater weighing, the subject was given an orientation to the laboratory equipment and procedures that would be used during the head-down tilt and lower body negative pressure test. This orientation was designed to familiarize the subject with all sensations and timelines used during

the final procedure so that any psychological influences upon the experimental variables would be minimized. The orientation consisted of a complete verbal description of the protocol and methods of instrumentation. The subject was then placed on the tilt table and in the lower body negative pressure chamber. The chamber was sealed at the level of the subject's iliac crest with plyboard contoured to fit the subject. This was then covered with a thin rubber material to minimize air leaks. The subject was tilted head-down six degrees for a maximum of five minutes. Then, the subject was brought back to supine and the negative pressure chamber activated. The pressure in the chamber was reduced -8 mm Hg for approximately 30 seconds, then -16 mm Hg for approximately 30 seconds, and finally reduced -30 mm Hg for a maximum of two minutes. The air pressure in the chamber was then returned to normal atmospheric pressure. At no time during any orientation was the pressure reduced further than -30 mm Hg.

Underwater weighing. The underwater weighing was accomplished in a tank especially designed for the purpose (Doerr and Reed, KSC NASA Biomedical Engineering, Appendix F). The subject entered the tank and submerged himself to the neck. He then removed any remaining air bubbles attached to him or his clothing. The subject was seated in the underwater weighing chair and was submerged to his upper lip. The subject got out of the chair and after the tare weight of the chair was determined, the subject returned to the chair and put on the seatbelt. On command, the subject exhaled as deeply as possible and submerged his entire head. The subject was asked to exhale any additional air, and a weight was determined using a calibrated electrical load cell connected to a vertical eight-channel Brush, Incorporated,

Mark 200 recorder. The subject then raised his head. This procedure was repeated five times to acquaint the subject with the procedure.

The subject was then asked to get out of the chair and the chair was retared with the mouthpiece and tubing used in determining residual volume. The subject returned to the chair, put on the seatbelt and a noseclip, and inserted the mouthpiece. The mouthpiece was connected to a spirometer by a weighted tube. The mouthpiece had a two-way valve which allowed the subject to breathe room air until the procedure started. While the subject breathed room air, the spirometer was purged with oxygen until the nitrogen sensor (Model 505 Nitroalyzer, Med-Science, Co.) indicated a nitrogen concentration of less than 0.5%. Then the spirometer was filled with 3-4 liters of oxygen (depending upon the size of the subject), and this amount was recorded. The subject was asked to exhale as much air as possible and submerge his head. After exhaling the remaining air in his lungs, the subject turned the mouthpiece valve and held his breath. The weight was taken and the subject raised his head. The subject then breathed deeply for a maximum of ten breaths from the spirometer. When the nitrogen concentration stabilized, the subject removed the mouthpiece. The nitrogen concentrations were read directly off the sensor and were recorded on the Brush vertical recorder. This procedure was repeated five times. These data were used to derive the subject's density, percent of body fat, fat mass, and lean body mass. The first five weighings used an estimate of residual volume (RV) derived from the following formula:

RV (males) = 0.048 X Height (inches) + 0.0115 X Age (years) - 2.24.

For the final five weighings, residual volume was directly calculated using the nitrogen wash-out method described above and in Appendix F.

After the residual volume was either estimated or calculated, body density (Db) was calculated from the following formula:

$$Db = Ma/\{[(Ma-Mw)/Dw]-(RV+Vgi)\}$$

(Ma = Mass in air, Mw = Mass in water, Dw = Density of water at test temperature, Vgi = Volume of air in gastrointestinal tract, assumed to be 100 ml)

Using the body density derived above, percentage of body fat was then obtained using the formula of Siri (113):

Percentage of body fat = 100 X [(4.950/Db) - 4.500].

Experimental Procedure

Initial Instrumentation. For the head-down tilt and lower body negative pressure protocol, the subject arrived at the laboratory at 0800 hours after having fasted for at least six hours. This eliminated the effect of digestive mechanisms on catecholamine response. The subject dressed in shorts and socks and was then weighed. After the weighing, the subject was instrumented with the Frank ECG system, electromyogram (EMG) electrodes on the right calf, and the left calf was measured and marked for maximum girth.

The Frank system was used to monitor the subject's electrocardiographic patterns and heart rate during the procedure. The same electrode placement pattern was used as had been previously utilized during the treadmill test.

Electromyogram (EMG) activity was monitored using three skin electrodes and an EMG signal conditioner (Duvoisin and Reed, NASA Biomedical Engineering, KSC, FL) which amplified the EMG signal. The site used for the EMG electrode placement was the interior lateral portion of the soleus muscle. An area of approximately five inches by seven inches was shaved and cleared of hair. This area was thoroughly scrubbed using isopropyl alchohol. The electrodes were applied using adhesive disks and electrode

cream paste. After connection to the EMG amplifier, the EMG signal was branched to two outputs. One branch patched the EMG signal to the Brush vertical recorder where electrical activity of the muscle was recorded and used as an indication of muscular contraction levels. In addition to branching the EMG activity to the recorder, the signal was routed to a Hewlitt-Packard Model 3400A Voltmeter which was used as a biofeedback apparatus for the subject. Readings were taken from the voltmeter during the testing to compare with the levels traced on the vertical recorder to provide a calibration for the bio-feedback. Since it was desired to monitor resting responses during the head-down tilt and lower body negative pressure, the subjects were asked to keep the signal activity as low as possible using the voltmeter gauge as a reference.

To determine fluid shifts in the left calf, the percent change of the circumference of the calf was monitored during the protocol. During the initial instrumentation, the subject was put in a supine position for five minutes. This allowed for fluid stabilization, especially in the lower body. The left calf was measured and marked at its point of greatest circumference. This measurement was recorded and used for determining the length of the mercury-in-silastic strain gauge used to monitor calf changes during the procedure.

Final Instrumentation. After initial instrumentation, the subject entered the lower body negative pressure chamber on the tilt table. The subject was instructed to move as far into the chamber as the restraining saddle would permit. Because the chamber would be sealed slightly superior to the iliac crest, the subject's positioning in the chamber was critical. The restraining saddle was adjustable so the subject could move up or down if the iliac crest was not in the

proper position. After positioning, the subject's lower body was sealed in the negative pressure chamber.

At this time, the strain gauge was fit around the subject's left calf using the measurement marks made during initial instrumentation. The mercury-in-silastic strain gauge was connected to a Strain Gauge Amplifier, (Technology, Incorporated, Houston, TX). The strain gauge signal after passing through the amplifier was patched to the Brush vertical recorder. During the protocol, readings were available directly from the amplifier or on the Brush recorder.

At the same time the strain gauge was being connected, the EMG signal conditioner was connected to the EMG electrodes on the right calf. After functional check-outs with the strain gauge and EMG systems, the cuff of the automatic sphygmomanometer was positioned on the left arm so that the Korotkoff microphone contained in the cuff was directly over the brachial artery. Blood pressure was monitored on the Brush horizontal recorder by a technician. Systolic and diastolic blood pressures were recorded directly. Mean arterial pressure (MAP) was calculated using the formula:

$$MAP = (1/3*Systolic)+(2/3*Diastolic).$$

Pulse pressure (PP) was also calculated using the formula:

$$PP = (Systolic - Diastolic).$$

The last step in subject instrumentation (Figure 3) involved the insertion of a 21-gauge catheter for blood sampling. The catheter was inserted into an antecubital vein in the right arm and then secured with tape to the subject's arm. The catheter was attached to a three-way stopcock. A drip of isotonic saline was attached to one port of the stopcock. The saline drip kept the catheter patent for the duration of the procedure. During prescribed intervals, blood samples of three ml were drawn. Immediately after sampling, the catheter was flushed with

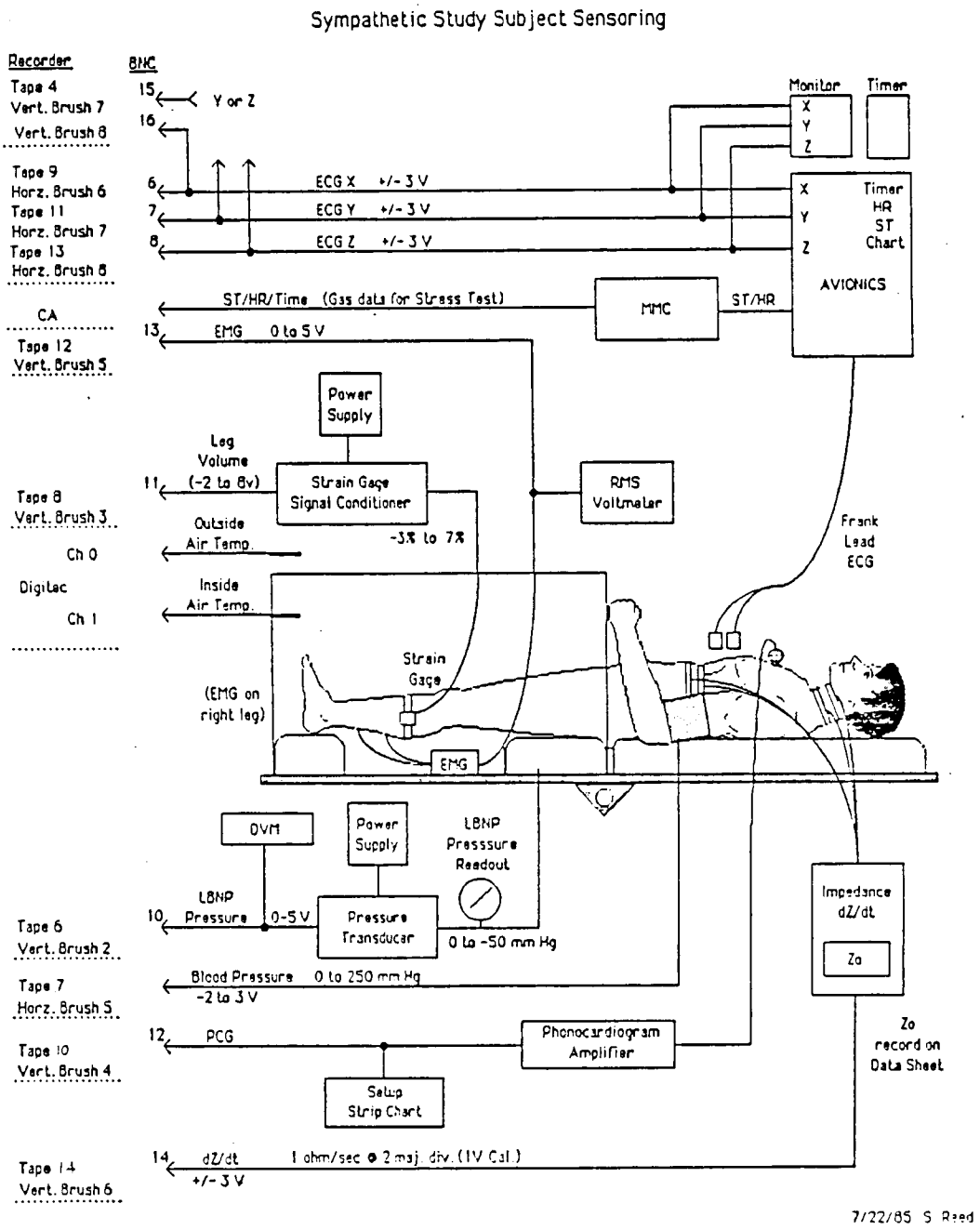

Figure 3. Subject Instrumentation

one ml of heparin and then flushed with saline. This method was a further safeguard against blood clotting in the catheter and stopcock. After successful insertion of the catheter, a drape was suspended across the subject's arm, eliminating any view of the blood sampling procedure by the subject. This was done to reduce any stressful reactions by the subject to the blood sampling.

Protocol. After catheterization, the data acquisition and recording equipment were given a final operational check and lights in the laboratory were dimmed. The procedure then began (Appendix G).

During recording intervals, the vertical recorder was run at 100 mm of paper per second; otherwise, the recording speed was one mm per second.

From minute zero to minute 19, the subject was in a supine resting state. The rest period served to reduce all physiological variables to their resting baseline after the period of instrumentation. This rest period also allowed time for the laboratory staff to solve any measurement and equipment problems that may have occurred with the start of the procedure.

At minute 20 of the protocol, the table was tilted head-down six degrees. This position was maintained for 90 minutes (from minutes 20 to 110 of the protocol). During this period and the rest of the protocol, subject interaction was kept to a minimum to reduce any possible effects on the sympathetic nervous system or the instrumentation.

After the head-down tilt period, the tilt table was returned to supine for one minute, (protocol minute 110-111). This provided for a smooth transition into lower body negative pressure.

At protocol minute 111, the negative pressure chamber was activated. From protocol minutes 111-112, the air pressure in the chamber was reduced -8 mm Hg. At minute 112, the chamber air pressure was reduced -16 mm Hg.

These first two minutes at -8 mm Hg and -16 mm Hg provided an opportunity to check for air bleeds in the waist seal and were a transition to lower chamber pressures.

After protocol minute 112, the chamber's air pressure was reduced -30 mm Hg. This pressure was maintained for three minutes. Then, at protocol minute 116, the air pressure in the chamber was reduced -40 mm Hg for five minutes. After this stage (minute 121) the air pressure was reduced -50 mm Hg for five minutes. At the end of minute five at -50 mm Hg (protocol minute 126) the chamber's air pressure was returned to normal atmospheric pressure. After the return to normal pressure, a five minute recovery period ensued (from protocol minutes 126-131).

Negative Pressure Termination. Because lower body negative pressure is an orthostatic stressor, subject syncope was a possibility. If one or more of the following presyncopal symptoms was evident, the lower body negative pressure test was immediately terminated and the recovery period automatically begun.

1) Completion of five minutes at -50 mm Hg.
2) A sudden bradycardia of greater than 15 beats per minute.
3) A reduction of systolic blood pressure greater than 25 mm Hg between adjacent one minute blood pressure readings.
4) Clammy skin, profuse sweating, or extreme pallor of the skin.
5) Subject nausea or dizziness.
6) Subject request.

Data Reduction and Analysis

Data Collection. Data collection took place at several different points during the protocol. The heart rate, leg strain gauge level, EMG level, and

blood pressure were collected at the end of the baseline resting phase (protocol minute 19-20). During the head-down tilt period, the same cardiovascular variables were recorded for 30 seconds at the following protocol minutes: 25, 35, 50, 80, and 110. These collection periods coincided with minutes 5, 15, 30, 60, and 90 of the head-down tilt. The cardiovascular data were collected during lower body negative pressure at protocol minutes 116, 121, and 126. These measurements were made at lower body negative pressure stages -30 mm Hg, -40 mm Hg, and -50 mm Hg, respectively.

Blood samples were taken at nine different times during the protocol to determine the plasma levels of norepinephrine and epinephrine. Three ml blood samples were drawn at protocol minutes 20, 25, 35, 50, 80, 110, 116, 121, and 126. These blood samples were used to determine norepinephrine and epinephrine at the intervals corresponding to 0, 5, 15, 30, 60, and 90 minutes of head-down tilt, and 5, 10, and 15 minutes of lower body negative pressure, respectively.

Catecholamine Assay. The three ml blood sample was used to determine plasma catecholamine levels. This sample was put into a polystyrene tube containing 60µl of EGTA-glutathione solution. After the sample was added to this solution, a final concentration of 1.8 mg of EGTA and 1.2 mg of glutathione per ml of blood existed. This solution was immediately centrifuged in a refrigerated centrifuge (Beckman Incorporated, Model TJ-6) at 7,000 rpm for 10 minutes. The plasma was then put into polyethelene tubes and frozen at -20° Centigrade for later analysis.

The catecholamine assay used was a modification of the method of Cryer, et al. (29). A complete copy of the assay procedure is found in Appendix H. Catecol-O-methyl transferase was extracted using a procedure developed by

Axelrod and Tomchick (4). A 100 picogram (pg) Epinephrine and Norepinephrine standard was run internally with every third plasma sample. The interassay coefficent of variation was derived by dividing the standard deviation of the standards by the standards' mean. The interassay coefficent of variation for norepinephrine and epinephrine was nine percent. Baseline sensitivity of the assay was derived by the following method. After determining the counts per minute per tube for the internal standards in each run, (averaging the internal standards for each run and dividing by 100), the standard deviation of the of the blanks in the same run was calculated. This value was multiplied by two and this product was divided by the counts per minute per tube figured above. This product was multiplied by 20 to correct the value to give a baseline sensitivity in picograms per milliliter. The baseline sensitivity for the assay for plasma norepinephrine and epinephrine was 15 pg/ml. While all norepinephrine values were anticipated to be well above the baseline sensitivity, some resting epinephrine values were close to the baseline sensitivity. However, these data points were left in the data set because the values were reproducible and could indicate trends in the data.

Statistics. All statistical analyses were accomplished on an IBM 3081 mainframe equipped with version 82.3 of the Statistical Analysis System (SAS). Several different statistical procedures were needed to completely analyze the data.

Differences between the descriptive data of VO_2max, strength levels, age, height, weight, fat free mass, body density and body fat percentage for the groups were determined using one-way analysis of variance procedures. A type of multiple stage testing, the REGWQ test, was used to determine differences between specific group means *post hoc.* This procedure is similar to Duncan's

test and the Student Newman-Keuls test, but is more conservative and less prone to inflated Type I error rates.

Testing the experimentally derived data called for a univariate repeated measures analysis. The statistical analysis used a 2X2X9 repeated measures design analyzed with split plot methods in SAS. Inflation of Type I error rates and violation of sphericity have been reported using the split plot repeated measures method (96). It was suggested by O'Brien and Kaiser (96) that repeated measure designs be tested using a derivation of multivariate methods. However, using O'Brien and Kaiser's method, missing data points and small subject numbers combined with large number of observations resulted in incomplete analysis. Recently, it was reported that the inherent problems of the split plot method could be overcome using a correction factor know as the "Geisser-Greenhouse" correction (87). However, the use of this correction factor has not been validated by other studies in the statistical literature. Therefore, the split plot repeated measures method was determined appropriate for the data.

Because specific hypotheses were put forward in Chapter I, *a priori* comparisons were planned to test these hypotheses. This method is thought to add more power to the data analysis (56). If any of the preplanned comparisons yielded significant results, *post hoc* testing using the Duncan multiple stage test, would be employed.

Because the preplanned comparisons were not orthogonal or independent, the alpha level ($p<.05$) was corrected using the Bonferroni correction (56). The alpha level (.05) was divided by the number of preplanned comparisons to be made within each analysis (2). The resulting Bonferroni alpha level of significance was $p<.025$.

When non-significant results are reported, one question to be considered is that of the power of the design (95). Pilot data collected before the start of this

study suggested that six subjects per group would provide sufficent power for significance.

CHAPTER IV

RESULTS

The results report the data pertaining to the following hypotheses that were set forward in Chapter I:

1) There will be no difference between the groups' catecholamine levels during head-down tilt.

2) There will be a decrease in catecholamine levels and heart rate within the first 15 minutes of head-down tilt in all groups.

3) Individuals with high levels of aerobic fitness will exhibit diminished catecholamine levels and blood pressure during lower body negative pressure as compared to individuals with low levels of aerobic fitness.

4) Individuals with high levels of leg strength will not exhibit diminished catecholamine or blood pressure responses during lower body negative pressure as compared to individuals with low leg strength levels.

The results are organized in three sections. The first section describes the physical characteristics of the subjects by group. Results of the head-down tilt phase are described in the second section. The third section reports the lower body negative pressure responses. Individual subject data are reported in Appendix I.

Descriptive Data

The physical descriptive variables are noted for each group in Table 1. There were no differences among the group heights ($p<.57$), weights ($p<.63$), or ages ($p<.29$). No significant difference in VO_2max was exhibited between the high aerobically fit, high strength (HFHS) group (56±5 ml O_2/(kg·min)) and the high aerobically fit, low strength (HFLS) group (52±2 ml O_2/(kg·min), $p<.12$). Also, no significant difference was observed between the low aerobically fit, high

TABLE 1

PHYSICAL CHARACTERISTICS BY GROUP

	Groups			
Data	HFHS	HFLS	LFHS	LFLS
Age (yrs)	29±5A	30±4A	31±4A	33±3A
Height (cm)	178.2±5.1A	180.8±6.1A	176.8±4.8A	179.6±3.9A
Weight (kg)	79.2±5.5A	78.2±8.7A	80.9±15.1A	85.6±10.4A
VO_{2max} (ml O_2/(kg·min))	56±5A	52±2A	41±5B	41±2B
Leg Strength (ft·lbs.)	106±3A	80±8B	118±15A	83±8B
Body Fat (%)	14.3±2.4A	15.7±5.2A	16.5±5.0A	22.8±5.0B
Body Density	1.067±0A	1.062±.01A	1.063±.01A	1.047±.01B
Fat Free Mass (kg)	67.8±5.4A	65.6±5.9A	67.0±10.1A	65.9±6.8A

Observations with different letters are significantly different, $p<.05$.

strength (LFHS) group (41±5 ml O_2/(kg·min)) and the low aerobically fit, low strength (LFLS) group (41±2 ml O_2/(kg·min), $p<.77$). VO_{2max} differed significantly between the high aerobically fit (HF) groups (i.e. HFHS and HFLS groups) and the low aerobically fit (LF) groups, (i.e. LFLS and LFHS groups), (54±4 versus 41±3 ml O_2/(kg·min) respectively, $p<.01$). This result was expected due to the study design.

No differences in leg strength were noted between the HFHS (106±3 ft·lbs.) and LFHS groups (118±15 ft·lbs., $p<.13$) or the HFLS (80±8 ft·lbs.) and LFLS groups (83±8 ft·lbs., $p<.56$). A significant difference ($p<.01$) was observed

in leg strength between the high strength groups (HFHS and LFHS) and the low strength groups (HFLS and LFLS). This difference was also expected because of the design of the study.

The LFLS groups had a significantly greater ($p<.05$) percentage of body fat than did the other three groups. The LFLS group also had a lower body density than the other three groups. Even though significant differences between the groups in body fat percentage and body density were noted, no differences were found between the fat free mass of the groups.

Head-Down Tilt

In all groups, calf circumference decreased during head-down tilt (Figure 4). This is representative of the central fluid shift that occurs during exposure to weightlessness or to a simulation of microgravity. This decrease was expected due to prior observations in the literature (93,127).

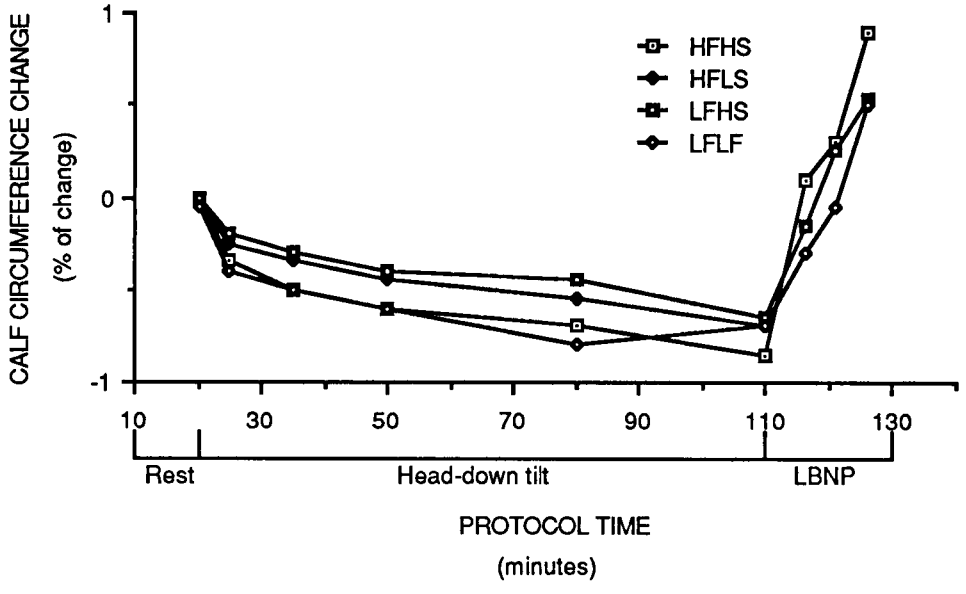

Figure 4. Calf circumference changes during the experimental protocol by group.

The variables used in this study as an indication of the sympathetic nervous system's response to head-down tilt were plasma catecholamine levels. The catecholamines measured in the plasma samples were epinephrine and norepinephrine. The resting epinephrine and norepinephrine values seen in this study are similar to values reported by other studies (23, 24, 42, 101).

Because epinephrine values were so low, much variation was noted in the observations. The epinephrine values noted in Table 2 often exhibited standard deviations as large as the mean value. While these values can be used as general indicators of trends, one must be careful in using these data because of the high standard deviations and the proximity of some of the values to the baseline sensitivity of the assay.

When comparing the plasma epinephrine values during head-down tilt, no difference was seen between the groups (Table 2). However, at minute 90 of head-down tilt, the LFHS groups exhibited a high epinephrine level (Table 2). Upon closer inspection it must be noted that the standard deviation was larger than the mean value at this point (58±63 pg/ml). The large standard deviation

TABLE 2

PLASMA EPINEPHRINE DURING HEAD-DOWN TILT

	Groups			
Time	HFHS	HFLS	LFHS	LFLS
0	14±17	24±17	22±18	29±35
5	16±17	18±22	23±22	15±15
15	16±12	18±25	30±31	15±16
30	17±12	26±16	34±30	18±12
60	19±15	19±17	28±22	25±21
90	32±29	24±22	58±63	30±22

was caused by a large increase in one subject's plasma epinephrine value at 90 minutes of head-down tilt (Subject 680, Appendix I). Reasons for the increase in epinephrine in this subject at the 90 minute point are not known. No record of abnormal proceedings or occurrences during experimentation were noted. Removing this data point reduces the mean and standard deviation of this group at 90 minutes of head-down tilt to a value similar to the other groups' observations at this point (35±28 pg/ml).

It was noted in Chapters I and II that no data are available on plasma catecholamine levels during the first 15 minutes of head-down tilt. Heart rate changes during this time are also controversial. In this study, plasma epinephrine did not change during the first 15 minutes of head-down tilt (Table 2). This was also true of plasma norepinephrine levels (Table 3). Heart rates of the groups did not change from baseline to 15 minutes of head-down tilt (Table 4).

TABLE 3

PLASMA NOREPINEPHRINE DURING HEAD-DOWN TILT

	Groups			
Time	HFHS	HFLS	LFHS	LFLS
0	223±55	184±64	184±51	243±104
5	214±65	188±50	199±72	251±125
15	244±41	201±74	208±79	277±151
30	245±46	197±79	232±78	233±75
60	272±86	201±109	214±99	271±156
90	245±96	239±121	225±86	232±72

While blood pressures (systolic and diastolic) were recorded during this study, we did not evaluate blood pressure changes during head-down tilt since the majority of the literature reports that blood pressure is stable throughout spaceflight and microgravity simulation (3, 42, 80, 82, 83, 93, 104). Therefore, blood pressure means for each group are contained in Appendix J.

TABLE 4

HEART RATE DURING THE FIRST 15 MINUTES OF HEAD-DOWN TILT

	Head-Down Tilt (min)		
Group	0	5	15
HFHS	50±5	50±6	49±5
HFLS	49±5	49±6	49±6
LFHS	59±8	61±8	59±8
LFLS	63±2	65±7	61±3

Lower Body Negative Pressure

Classical lower body negative pressure responses were noted in this study. There was an increase in calf circumference during lower body negative pressure (Figure 4). This was due to an increase in fluid volume in the lower extremities due to an increase in transmural pressure as a result of decreased external pressure (89). Also noted was an increase in heart rate in all groups during lower body negative pressure (Figure 5). This has been reported by several authors (11, 43, 46, 58, 79, 81, 88, 97, 98, 115, 119, 136).

As a consequence of high aerobic fitness, resting heart rate is reduced (101). This effect was noted in the high fit (HF) groups. Generally, heart rate was lower in the HF groups than in the low fit (LF) groups during rest, head-down tilt, and lower body negative pressure (Figure 5). It was felt that this

difference was the result of the higher aerobic fitness levels of the HF groups and not due to any experimental manipulation.

The difference in heart rate (ΔHR) from baseline (90 min head-down tilt) to the -50 mm Hg stage of lower body negative pressure was similar in all groups (Table 5). Therefore, no group showed different heart rate gain responses to lower body negative pressure.

Since lower body negative pressure is an orthostatic challenge, it was anticipated that some subjects might not complete the lower body negative pressure protocol. Four subjects out of the twenty-four were not able to

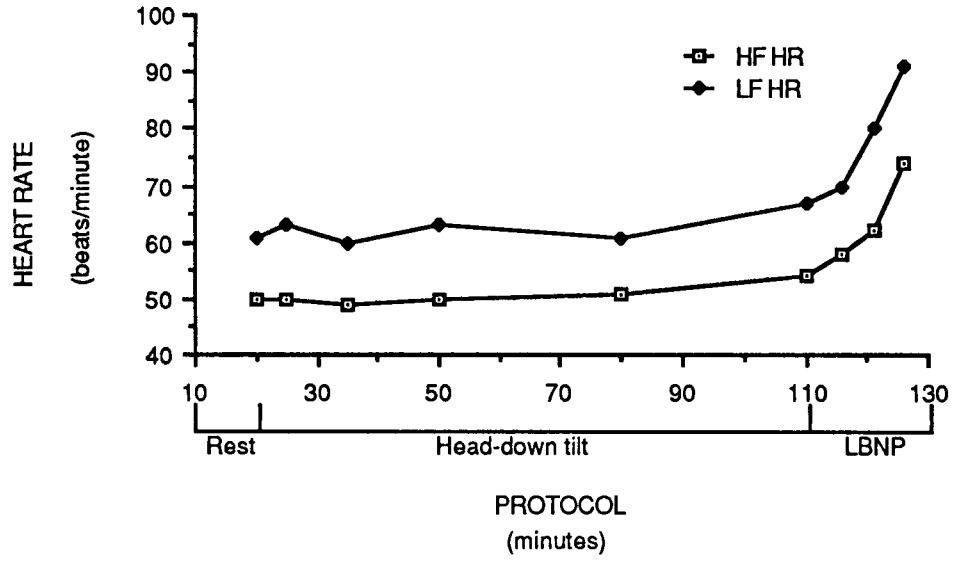

Figure 5. Heart rate (HR) during experimental protocol in high aerobic fit (HF) and low aerobic fit (LF) groups.

TABLE 5

HEART RATE DIFFERENCES BETWEEN 90 MINUTES HEAD-DOWN TILT AND -50 MM HG LOWER BODY NEGATIVE PRESSURE

	Groups			
	HFHS	HFLS	LFHS	LFLS
Δ Heart rate	22±8	20±8	27±10	21±4

No significant difference between groups ($p<.51$).

complete the lower body negative pressure protocol. Coincidentally, these four subjects were equally distributed among the groups.

During lower body negative pressure, intense forearm venoconstriction was exhibited in the majority of the subjects. This venoconstriction made blood sampling during lower body negative pressure difficult. As a result, there were a reduced number of samples obtained at some sampling periods during lower body negative pressure. The number of samples obtained at each stage of lower body negative pressure is noted in Table 6. The split-plot repeated measures analysis corrected for the unbalanced sample size in the model by adjusting the means. It is these adjusted means which were compared in the analysis and are reported in this chapter.

Plasma epinephrine levels observed during lower body negative pressure suffer the same constraints as those noted during head-down tilt: low values and high standard deviations. Nevertheless, it was observed that the HF groups exhibited a significantly lower ($p<.0014$) plasma epinephrine level than the LF groups, (36±33 pg/ml vs. 59±47 pg/ml, respectively), from 90 minutes of head-down tilt to -50 mm Hg negative pressure . No significant differences were observed in plasma norepinephrine levels between the HF (347±141 pg/ml) and LF (369±150 pg/ml) groups during lower body negative pressure. The mean

arterial pressure of the HF groups (83±9 mm Hg) was found to be significantly lower ($p<.0004$) than that exhibited by the LF groups (89±10 mm Hg) during lower body negative pressure.

TABLE 6

NUMBER OF PLASMA EPINEPHRINE AND NOREPINEPHRINE SAMPLES AT EACH STAGE OF LOWER BODY NEGATIVE PRESSURE

	Stage							
	0		-30		-40		-50	
	E	NE	E	NE	E	NE	E	NE
Group	n	n	n	n	n	n	n	n
HFHS	5	5	3	3	5	5	5	5
HFLS	6	6	4	4	4	4	5	5
LFHS	6	6	6	6	5	5	5	5
LFLS	6	6	5	5	5	5	5	5

E = Epinephrine, NE = Norepinephrine, n = number of samples.

Plasma epinephrine levels were significantly higher ($p<.0066$) in the HS groups (57±50 pg/ml) than in the LS groups (38±22 pg/ml) during lower body negative pressure. There was no difference in plasma norepinephrine levels between HS and LS groups during lower body negative pressure (367±87 pg/ml vs. 350±95 pg/ml, respectively). Mean arterial pressure was also not significantly different between the strength groups during lower body negative pressure (HS=87±9 mm Hg vs. LS=86±4 mm Hg).

The significant differences in plasma epinephrine in both the strength and aerobic fitness comparisons led to *post hoc* investigation. Upon further analysis, it was found that the LFHS group exhibited a higher plasma

epinephrine level than the HFLS group during lower body negative pressure (Table 7). While the LFHS group epinephrine level was higher than the HFLS group's value, the LFHS group's level was not different from the other two groups (HFHS and LFLS group). Closer inspection revealed that the HFLS group's epinephrine levels during lower body negative pressure did not change from minute 90 of head-down tilt (24±22 pg/ml) to -50 mm Hg negative pressure (43±38 pg/ml, Appendix J). Also during this further analysis, it was noted that the LFHS group had a significantly higher mean arterial pressure than the other three groups during lower body negative pressure (Table 7).

TABLE 7

PLASMA EPINEPHRINE AND MEAN ARTERIAL PRESSURE DURING LOWER BODY NEGATIVE PRESSURE

	Groups			
Variable	HFHS	HFLS	LFHS	LFLS
EPI	53±36^{AB}	29±24^{B}	67±48^{A}	47±45^{AB}
MAP	83±5^{A}	85±12^{A}	94±10^{B}	87±10^{A}

Means with different letters are significantly different ($p<.01$).

CHAPTER V

DISCUSSION

Descriptive Data

The study design called for classification of each subject by aerobic fitness level and leg strength level. The design proved adequate as shown by the significant differences between the aerobic fitness and strength classifications reported in Chapter IV (Table 1, pg. 53). The number of subjects used in each group (6) was derived from a power analysis of pilot data collected before this study. The experimental interventions, head-down tilt and lower body negative pressure, both elicited the effects which had been predicted by the literature. In all groups, head-down tilt caused a significant decrease in calf circumference. This decrease in calf circumference has been interpreted to represent the headward shift of fluids during microgravity and simulated microgravity (93). During lower body negative pressure, calf circumferences increased due to an increased transmural pressure and leg fluid volume (89). Therefore, the experimental treatments produced the physiological responses necessary to test the hypotheses (Figure 5, pg. 58).

It was endeavored to keep the ages, weights, and heights of the subjects in all groups the same since it has been suggested in the literature that subject age, weight, and height might influence the physiological response to lower body negative pressure (68, 75, 109, 110). There were no differences between the groups in age, weight, or height in this study. There was however, a significantly higher percentage of body fat in the LFLS group than in the other three groups. The effect of increased body fat on either microgravity adaptation or physiological response to orthostatic stress has not been reported in the literature.

The remainder of this discussion will focus on the hypotheses put forward in Chapter I and the results reported in Chapter IV. Other information not directly relating to these hypotheses is presented in Appendixes I and J.

Head-Down Tilt

Initial changes in catecholamines and heart rate. This study showed that there was no change in the plasma catecholamines, norepinephrine or epinephrine, in any group from baseline rest to 15 minutes of head-down tilt. There was also no change in heart rate in any group during the first 15 minutes of head-down tilt.

The only other study to consider plasma catecholamines at 15 minutes of head-down tilt is one by Goldsmith, et al. (42). Goldsmith, et al. also noted no change in plasma norepinephrine levels at 15 minutes of head-down tilt. The value reported by Goldsmith, et al. for plasma norepinephrine at 15 minutes (185±85 pg/ml) was similar to the figures seen for norepinephrine in our groups. Goldsmith, et al. however, did not report plasma epinephrine levels during head-down tilt. To the author's knowledge, this is the first study to measure plasma epinephrine levels during the first 30 minutes of head-down tilt.

Goldsmith, et al. (42) noted that plasma norepinephrine may not be an accurate indication of the activity of the sympathetic nervous system during the early phases of head-down tilt (42). They suggested that during this period sympathetic discharge to the vascular beds may be selectively decreased and not reflected in the plasma samples from the forearm. However, Goldsmith, et al. (42) based this argument on the assumption that the headward shift of fluids during head-down tilt resulted in an activation of the Frank-Starling mechanism. They stated that since the Frank-Starling mechanism should have occurred during the head-down tilt due to a presumed increased preload, the maintenance of blood pressure could be due to a selective decrease in sympathetic discharge to some vascular beds leading to a decreased peripheral

resistance. Thus, selective decreased sympathetic discharge would not have been indicated by samples taken in the forearm (42). The statement that the plasma norepinephrine level may be a selective sample and not representative of the activity of the sympathetic activity in all of the vascular beds is a logical one. However, the complex reasoning used by Goldsmith, et al. (42) to suggest the selective decrease in sympathetic discharge during head-down tilt may be inappropriate. The assumption that the Frank-Starling mechanism is activated during early exposure to head-down tilt needs to be reevaluated. Several authors have reported no increase in stroke volume or cardiac output with head-down tilt (65, 80, 93, 127). Therefore, the complex reaction suggested by Goldsmith, et al. (42) to justify their speculations, may not occur.

Tomaselli, et al. (127) suggested that the central fluid shift during the early minutes of head-down tilt may be sequestered in the compliant great veins or the pulmonary vasculature. Lollgen, et al. (80) noted that the right heart was more compliant than the left heart and that a slight increase in venous pressure did not necessarily mean that there would be an activation of the Frank-Starling mechanism. Sequestering of the central fluid overload may have prevented the activation of the baroreceptors in the carotid sinus and aortic arch. If this logic holds for head-down tilt, there would seem to be no stimulus for any change in the activity of the sympathetic nervous system. Therefore, during head-down tilt, plasma norepinephrine and epinephrine would stay stable, as they did during our study.

This study showed no changes in heart rate within the first 15 minutes of head-down tilt in any group. If the central fluid overload caused by head-down tilt is sequestered in the great veins and pulmonary vasculature, no pressure load would activate the baroreceptors to lead to a decreased heart rate. Our data would seem to support this theory.

The stability of heart rate in the first 15 minutes of our study confirms the results of some studies (3, 42, 53, 65, 80, 82, 83, 130) while disagreeing with

others (27, 58, 93, 126). As noted in Chapter II, it is tempting to infer that the difference in the heart rate responses noted may be related to the tilt angle used in the studies. The studies that noted no change in heart rate with head-down tilt (3, 42, 53, 65, 80, 82, 83, 130) used tilt angles from -5° to -30° whereas the studies that observed a decrease in heart rate with head-down tilt used angles from -6° to -30°. Therefore, it does not seem that tilt angle is a determining factor in heart rate response to head-down tilt.

There does not seem to be a clear answer as to why heart rate is reduced in some studies during head-down tilt and not in others. Some researchers have implied that head-down tilt induces an increase in stroke volume and cardiac output (58, 64, 83). To keep blood pressure at normal levels, as has been observed during head-down tilt and spaceflight (3, 42, 80, 82, 83, 93, 104), a decrease in heart rate leading to a decrease in cardiac output or a decrease in peripheral resistance would have to occur. The studies that have reported a decrease in heart rate with head-down tilt (27, 58, 93) have not necessarily reported an increase in stroke volume or cardiac output. It is possible that peripheral resistance decreased in these cases to keep blood pressure stable. However, with our data showing no change in plasma catecholamine levels or heart rate and a stable blood pressure (Appendix J) within the first 15 minutes of head-down tilt, it does not seem possible that peripheral resistance changed. Our data suggest that sympathetic nervous system activity and heart rate were stable during the initial period of head-down tilt because of a sequestering of shifted fluid in the pulmonary vasculature and the great veins with no resulting load on the carotid and aortic baroreceptors.

Differences between group catecholamine levels. It was clearly shown in our study that there were no differences between the groups' catecholamine levels during head-down tilt. This result applied to measurements of both plasma epinephrine and norepinephrine. Winder, et al. (134) originally implied that training did not change resting catecholamine levels. This was confirmed

by Claytor (23). As far as the author knows, literature on the effect of strength training on resting plasma catecholamine levels does not exist. Raven and Smith (99) postulated that weightlifiters' autonomic nervous systems were dominated by the sympathetic nervous system. If this is true, this augmentation may only occur during exercise. Our results do not indicate that high leg strength influenced plasma catecholamine levels during head-down tilt. Because there was no difference in sympathetic nervous system activity between the groups during head-down tilt, it can be assumed that any differences in adaptation to microgravity among the groups would not be due to the sympathetic nervous system.

Lower Body Negative Pressure

It was shown in this study that individuals with low aerobic fitness and high leg strength levels exhibited significantly greater mean arterial pressures and generally higher plasma epinephrine levels during lower body negative pressure than individuals with other combinations of aerobic fitness and strength. Plasma norepinephrine levels did not differ among the groups during lower body negative pressure.

Lower body negative pressure causes an unloading of the cardiac baroreceptors resulting in a sympathetic activation. Increases in plasma norepinephrine levels as a response to lower body negative pressure testing are well documented in the literature (43, 47, 81, 91, 105). Plasma epinephrine levels have also been reported to increase by Lollgen, et al. (81) during lower body negative pressure.

The plasma norepinephrine levels observed in our study were similar to those seen in other studies using lower body negative pressure (43, 47, 91). However, plasma norepinephrine and epinephrine values reported recently by Lollgen, et al. (81) during lower body negative pressure were considerably higher than values from other studies (43, 47, 91) and those values reported in this study. The only description of the catecholamine assay used by Lollgen, et

al. (81) in their study was a brief statement as follows: "Plasma catecholamines were analyzed using a commercially available radioimmunoassay." Without description of the procedure used to derive their catecholamine values, further quantitative discussion of Lollgen, et al.'s data would be difficult.

Sather, et al. (86) reported no difference in plasma norepinephrine values between high fit and low fit subjects during lower body negative pressure. Our observations seem to validate this. Further information in the literature on differences in catecholamine response to lower body negative pressure between differently trained groups is not available. However, Claytor (23) showed that plasma norepinephrine and epinephrine levels were the same in sedentary and high fit individuals subjected to standing and several other low-level psychological and physiological stressors. He concluded that the decrease in circulating plasma catecholamines during submaximal work after training would not transfer to other stressors. In other words, a trained person would not respond with an attenuated plasma catecholamine level during stressors that did not recruit the same physiological systems as did the training stress. The highly trained individuals responded to the psychological and physiological stressors with the same plasma catecholamine levels as did the untrained individuals (23). The stress employed in this study, lower body negative pressure, while not the same as standing, may have produced a similar physiological effect. The lower body negative pressure may have circumvented the trained systems in each individual to produce its effects. In other words, the stress imposed by lower body negative pressure did not envoke the same physiological reflexes as does aerobic training or strength training in each subject. Therefore, equal plasma norepinephrine responses were observed among the groups since the trained systems were not recruited.

Plasma epinephrine showed similar responses in the LFHS, LFLS, and HFHS groups. A significant difference was exhibited between the LFHS and HFLS groups' plasma epinephrine levels during lower body negative pressure.

These two groups are opposed; each having no aerobic or strength characteristics in common (Table 7, pg. 61). The HFLS group had the smallest mean and the LFHS group had the largest. Inspection of the individual data for the HFLS groups (Appendix I) did not show an abnormal number of epinephrine values that were zero. Rechecking and repeating the statistical procedure confirmed the result reported. Robertson, et al. (100) noted that with standing, plasma epinephrine levels did not change while plasma norepinephrine levels increased. Robertson, et al. (100) offered no explanation of the stability of plasma epinephrine during orthostasis. Ross (101) noted that while norepinephrine levels generally increased with increasing stress, epinephrine levels usually do not increase until stress on the body is intense. While admittedly infringing upon speculation, a lower body negative pressure protocol to -50 mm Hg may not have been of sufficient magnitude to elicit an increase in plasma epinephrine levels in individuals with high aerobic fitness and low strength levels.

During the lower body negative pressure, the LFHS group exhibited a higher mean arterial pressure than did any of the other groups. This result is interesting. The effect of physical training on blood pressure is not well understood. Two cross-sectional studies reported that competitive weightlifters exhibited higher resting blood pressures than did runners and controls (84, 116). However, recent abstracts on longitudinal strength training programs have failed to find an increase in resting blood pressure after strength training (26, 54). The source of discrepancies between these studies may be the length of time that the weightlifters had been involved in training. Both longitudinal studies used novice weightlifters and subjected them to 12 week strength training programs. The cross-sectional studies used weightlifters that had been intensively strength training for several years. These individuals were highly motivated during training because of competitive reasons. Perhaps blood pressure does change after intense and extremely long term training.

Physiological arguments for an increase in blood pressure after strength training have not been validated. Longhurst, et al. (84) suggested that the differences that they saw in blood pressure in strength-trained athletes was because of an abnormally increased left ventricular mass-to-volume ratio. One other speculation centered on resetting of the baroreceptors with intense training (124). Neither of these speculations has been confirmed nor has a satisfactory theory for an increase in blood pressure after chronic strength training been put forward.

The effect of endurance exercise upon blood pressure has been researched more thoroughly. In an extensive review, Tipton (124) concluded that aerobic training may reduce blood pressure in hypertensive populations. Tipton doubted the applicability of this result to normal populations (124). Tipton emphasized that the mechanisms for any reduction in blood pressure in any population after aerobic training are not known (124). However, current speculation implies that any reduction in blood pressure after aerobic training may be due to a decrease in resting cardiac output.

The increased mean arterial pressure exhibited in the LFHS group during lower body negative pressure could be explained by a strength training augmentation in blood pressure. The reason that the other HS group, (the HFHS group), may not have shown an augmented blood pressure during lower body negative pressure was a canceling effect of the aerobic training on blood pressure. If high aerobic fitness were to lead to a reduced blood pressure and high strength led to an increased blood pressure, then the two effects may offset each other and result in a normal blood pressure.

Reasons for the LFHS group's higher mean arterial pressure during lower body negative pressure are not apparent. Increases in muscular mass and tone with weightlifting may be responsible for a mechanically induced increased venous tone, even during rest. While this is appealing speculation,

there is no literature or data to confirm it.

The higher mean arterial pressure of the LFHS group during lower body negative pressure would keep cerebral perfusion stable during the venous pooling in the lower extremities (89). Thus, this group may exhibit more stable cardiovascular responses and more resistance to lower body negative pressure syncope.

Conclusions

In conclusion, this study showed that:

1) In the first 15 minutes of head-down tilt, there is no change in sympathetic nervous system activity or heart rate.
2) Varying levels and combinations of aerobic fitness and strength do not result in differences in sympathetic nervous system activity during 90 minutes of head-down tilt.
3) Aerobic fitness levels or leg strength levels do not influence plasma norepinephrine responses during lower body negative pressure.
4) Individuals with high leg strength and low aerobic fitness may be predisposed to higher mean arterial blood pressure during lower body negative pressure.

Recommendations

After completion of this study, the following recommendations are suggested:

1) Further investigate the immediate effects of head-down tilt and clarify the mechanisms which compensate for the cephalid fluid shift.
2) Further investigate the specificity of training in weightlifters, concentrating on sympathetic nervous system activity.

3) Investigate possible reasons for plasma epinephrine stability during lower body negative pressure in individuals with high aerobic fitness and low leg strength.
4) Limit data collected during each experiment to guarantee accurate, reliable, and worthwhile observations.
5) Unless specifically indicated or called for, separate head-down tilt and lower body negative pressure treatments in future experiments.

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APPENDIXES

APPENDIX A

RECRUITMENT LETTER

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RECRUITMENT LETTER

Biomedical Laboratory
O & C, Room 3214
867-4132

You are invited to participate in an upcoming study at the KSC Biomedical Laboratory related to the space environment and human physiology. The study is designed to investigate the effects of different fitness and strength levels during simulated weightlessness and reentry.

We are currently looking for 24 male subjects for the study. Subjects will be asked to come to the laboratory for three visits for 1-4 hours each visit. The visits will be spaced approximately one week apart. If you are interested in participating in this study, you may come to the laboratory to view the apparatus and further discuss the experimental procedure.

Please feel free to call me at 867-4962 if you have any questions, would like to see the lab, or are interested in being a participant.

Sincerely yours,

Tim Lightfoot

APPENDIX B

APPOINTMENT LETTERS

APPENDIX B

APPOINTMENT LETTERS

Dear _____,

This is a short reminder that your physical exmaination has been scheduled for _____ at _____ a.m. in Room 3214 of the O&C Building. We request that you not consume any food or drink (except for water) at least 12 hours prior to the physical examination. This will prevent your blood test from giving erroneous results. Orange juice, coffee, and a granola bar will be provided after your fasting blood sample is obtained.

During this visit you will also be asked to take a Cybex leg strength test. Please bring gym shorts and a comfortable shirt to take this test.

Included with this letter is a packet containing medical history and health questionnaires, and a privacy information sheet. Please fill out the forms to the best of your knowledge and sign them. Please bring these forms with you on the appointment date.

Thank you again for participating in the study, and we look forward to seeing you.

Sincerely,

Tim Lightfoot

Dear _____ ,

You have been scheduled to come to the Biomedical Laboratory on _____ at _____for a treadmill stress test. Enclosed is a meal bar for you to eat at least two hours prior to the test. You may also have up to six ounces of citrus juice with the meal bar.

Please remember to bring comfortable running shoes, shorts, and a loose fitting shirt when you come for the test. When you arrive at the laboratory, you will change into these clothes.

After you have changed clothes, your height and weight will be measured and a pulmonary function study will be done. This test evaluates the amount of air you can hold in your lungs and how fast you can breathe in or out. It takes approximately ten minutes and requires you to breathe through a tube into a machine, with a noseclip on your nose. This is done prior to the stress test to insure that you have no major airway obstruction which might be a risk to you during the stress test.

Following the pulmonary function study, eight physiological sensors will be placed on your chest and back to monitor heart rate and rhythm during the stress test.

You will then be ready to walk/run on the treadmill. Your breathing will be monitored constantly during this test, thus you must breathe through a mouthpiece. This is how your maximum oxygen capacity is measured. Blood pressure will also be measured during the stress test. Your test will be monitored by an engineer, an exercise physiologist, and a registered nurse. A physician will also be on hand. The treadmill walk will get progressively steeper and faster until you reach your physiological limit or "max". Your legs or lungs will tell you when this point is reached. A slow walk cool-down period will follow. You may then shower in our facility. The results of your test will be discussed with you after the test. The entire procedure will require approximately one and one half hours of your time.

If you have any questions about the test, please feel free to contact us. If you are unable to keep the scheduled appointment, please notify our office by phone. Our phone number is 867-4132 or 867-2962. Your interest and cooperation in our program is appreciated, and we look forward to including you in our subject pool.

Sincerely,

Tim Lightfoot

Dear _____ ,

_____ at _____ will be your second visit to our laboratory for the study in which you are participating. At this visit, a plasma volume measurement, underwater weighing, and an orientation to the equipment you will encounter on your next visit will take place. Please bring a swimsuit for the underwater weighing. Towels and shower facilities will be provided.

Please refrain from drinking alcoholic beverages the night before your visit and refrain from exercise at least ten hours before the test session. Both of these requests will insure that the plasma volume data will be correct.

Thanks again for participating.

Sincerely,

Tim Lightfoot

Dear _____ ,

Your last visit to our lab is scheduled for _____ at _____ . This visit will consist of the head-down tilt and lower body negative pressure protocol. This session will last approximately three hours. Please refrain from drinking any substances that contain alcohol or caffeine (tea, beer, coffee, etc.) for at least six hours prior to the test. Also, please try not to eat anything eight hours before the test.

Please bring shorts and socks for the test. After the test your participation in the study will be ended. Thanks again for your participation.

Sincerely,

Tim Lightfoot

APPENDIX C

PHYSICAL EXAMINATION PACKET

APPENDIX C

PHYSICAL EXAMINATION PACKET

Dear Subject,

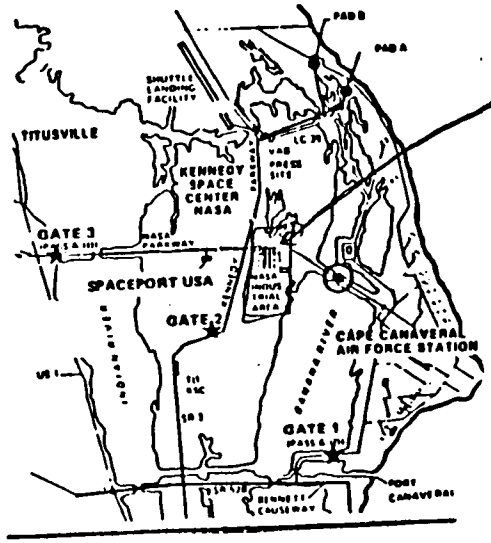
This letter concerns your participation in our study. As you probably know, KSC is a restricted area. Only if you have a clearance badge are you allowed in the industrial area where our laboratory is located. We have arranged for you to receive a temporary clearance badge which you can pick up when you come for your appointment. This badge must be picked up at either Gate 1 or Gate 3, (see map 1 attached). Enter either badging station and give them your name and that you are visiting the Bionetics Corporation to participate in a research project. Be sure to allow at least 45 minutes for picking up your badge since the badging stations are often crowded.

After receiving your badge, proceed to the Operations and Checkout building (see map 2). You will have to show your badge at one guard station to be admitted into the industrial area. Proceed to the O&C building and park in the east parking lot. Enter the door marked C-1 (map 2). After you enter door C-1, on your right, approximately 3 doors down, will be a staircase. Go up to the third floor and turn left. Go through a set of double doors and look for Room 3214. It will be the second door on the left after the double doors. You are there!

If there are any problems at any time during your entry to KSC, feel free to call 867-2962 or 867-2980 and I will help. Thanks again for your participation.

Tim Lightfoot

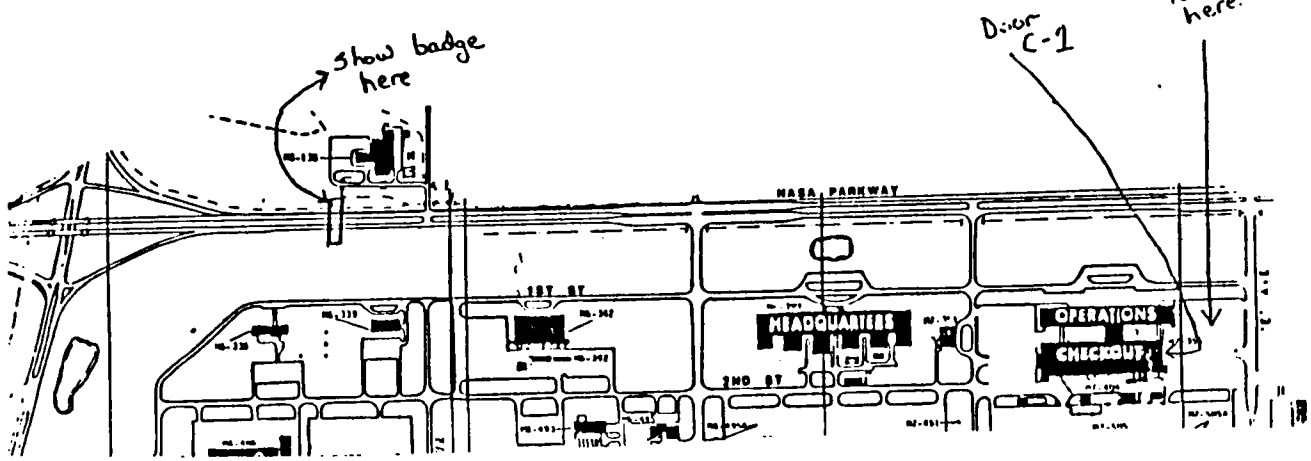
MAP 1



You are coming here.

Pick up badge at Gate 3 or 1.

MAP 2
Industrial Area



REPORT OF MEDICAL HISTORY

(THIS INFORMATION IS FOR OFFICIAL AND MEDICALLY-CONFIDENTIAL USE ONLY AND WILL NOT BE RELEASED TO UNAUTHORIZED PERSONS)

1. LAST NAME—FIRST NAME—MIDDLE NAME		2. SOCIAL SECURITY OR IDENTIFICATION NO.
3. HOME ADDRESS *(No. street or RFD, city or town, State, and ZIP CODE)*		4. POSITION *(title, grade, component)*
5. PURPOSE OF EXAMINATION	6. DATE OF EXAMINATION	7. EXAMINING FACILITY OR EXAMINER, AND ADDRESS *(Include ZIP Code)*

8. STATEMENT OF EXAMINEE'S PRESENT HEALTH AND MEDICATIONS CURRENTLY USED *(Follow by description of past history, if complaint exists)*

9. HAVE YOU EVER *(Please check each item)*

YES	NO	(Check each item)
		Lived with anyone who had tuberculosis
		Coughed up blood
		Bled excessively after injury or tooth extraction
		Attempted suicide
		Been a sleepwalker

10. DO YOU *(Please check each item)*

YES	NO	(Check each item)
		Wear glasses or contact lenses
		Have vision in both eyes
		Wear a hearing aid
		Stutter or stammer habitually
		Wear a brace or back support

11. HAVE YOU EVER HAD OR HAVE YOU NOW *(Please check at left of each item)*

YES	NO	DON'T KNOW	(Check each item)	YES	NO	DON'T KNOW	(Check each item)	YES	NO	DON'T KNOW	(Check each item)
			Scarlet fever, erysipelas				Cramps in your legs				"Trick" or locked knee
			Rheumatic fever				Frequent indigestion				Foot trouble
			Swollen or painful joints				Stomach, liver or intestinal trouble				Neuritis
			Frequent or severe headache				Gall bladder trouble or gallstones				Paralysis (include infantile)
			Dizziness or fainting spells				Jaundice or hepatitis				Epilepsy or fits
			Eye trouble				Adverse reaction to serum, drug or medicine				Car, train, sea or air sickness
			Ear, nose, or throat trouble								Frequent trouble sleeping
			Hearing loss				Broken bones				Depression or excessive worry
			Chronic or frequent colds				Tumor, growth, cyst, cancer				Loss of memory or amnesia
			Severe tooth or gum trouble				Rupture/hernia				Nervous trouble of any sort
			Sinusitis				Piles or rectal disease				Periods of unconsciousness
			Hay Fever				Frequent or painful urination				
			Head injury				Bed wetting since age 12				
			Skin diseases				Kidney stone or blood in urine				
			Thyroid trouble				Sugar or albumin in urine				
			Tuberculosis				VD—Syphilis, gonorrhea, etc.				
			Asthma				Recent gain or loss of weight				
			Shortness of breath				Arthritis, Rheumatism, or Bursitis				
			Pain or pressure in chest				Bone, joint or other deformity				
			Chronic cough				Lameness				
			Palpitation or pounding heart				Loss of finger or toe				
			Heart trouble				Painful or "trick" shoulder or elbow				
			High or low blood pressure				Recurrent back pain				

12. FEMALES ONLY: HAVE YOU EVER

			Been treated for a female disorder
			Had a change in menstrual pattern

13. WHAT IS YOUR USUAL OCCUPATION?

14. ARE YOU (Check one)

☐ Right handed ☐ Left handed

93-102

YES	NO	CHECK EACH ITEM YES OR NO. EVERY ITEM CHECKED YES MUST BE FULLY EXPLAINED IN BLANK SPACE ON RIGHT	
		15. Have you been refused employment or been unable to hold a job or stay in school because of: A. Sensitivity to chemicals, dust, sunlight, etc.	
		B. Inability to perform certain motions.	
		C. Inability to assume certain positions.	
		D. Other medical reasons (*If yes, give reasons.*)	
		16. Have you ever been treated for a mental condition? (*If yes, specify when, where, and give details*).	
		17. Have you ever been denied life insurance? (*If yes, state reason and give details.*)	
		18. Have you had, or have you been advised to have, any operations? (*If yes, describe and give age at which occurred.*)	
		19. Have you ever been a patient in any type of hospitals? (*If yes, specify when, where, why, and name of doctor and complete address of hospital.*)	
		20. Have you ever had any illness or injury other than those already noted? (*If yes, specify when, where, and give details.*)	
		21. Have you consulted or been treated by clinics, physicians, healers, or other practitioners within the past 5 years for other than minor illnesses? (*If yes, give complete address of doctor, hospital, clinic, and details.*)	
		22. Have you ever been rejected for military service because of physical, mental, or other reasons? (*If yes, give date and reason for rejection.*)	
		23. Have you ever been discharged from military service because of physical, mental, or other reasons? (*If yes, give date, reason, and type of discharge: whether honorable, other than honorable, for unfitness or unsuitability.*)	
		24. Have you ever received, is there pending, or have you applied for pension or compensation for existing disability? (*If yes, specify what kind, granted by whom, and what amount, when, why.*)	

I certify that I have reviewed the foregoing information supplied by me and that it is true and complete to the best of my knowledge.
I authorize any of the doctors, hospitals, or clinics mentioned above to furnish the Government a complete transcript of my medical record for purposes of processing my application for this employment or service.

TYPED OR PRINTED NAME OF EXAMINEE	SIGNATURE

NOTE: HAND TO THE DOCTOR OR NURSE, OR IF MAILED MARK ENVELOPE "TO BE OPENED BY MEDICAL OFFICER ONLY."
25. Physician's summary and elaboration of all pertinent data (*Physician shall comment on all positive answers in items 9 through 24. Physician may develop by interview any additional medical history he deems important, and record any significant findings here.*)

TYPED OR PRINTED NAME OF PHYSICIAN OR EXAMINER	DATE	SIGNATURE	NUMBER OF ATTACHED SHEETS

1. The information to be provided on this form is authorized to be collected by NASA pursuant to the Space Act, 42 USC 2473, 44 USC 3101, Public Law 79-658, Public Law 91-66, Public Law 92-255, and BOB Circular A-72. Providing this information is voluntary under these authorities.

2. The principal purpose within NASA for which the information is intended to be used is to render a comprehensive health maintenance physical program.

3. This information will be incorporated into the KSC medical system of records. In addition to the internal NASA uses of this information the routine uses of this information outside of NASA will be for referral of medical information to private physicians designated by the employee in writing and patient referrals. Other routine uses of this information outside of NASA are disclosures:

a. Upon request to a federal, state, local, or foreign law enforcement agency for law enforcement purposes.

b. To a federal, state, or local agency when necessary to obtain information relevant to a NASA decision concerning the hiring or retention of an employee, the issuance of a security clearance, the letting of a contract, or the issuance of a license, grant, or other benefit.

c. To a federal agency in response to its request in connection with the hiring or retention of an employee, the issuance of a security clearance, the reporting of an investigation of an employee, the letting of a contract, or the issuance or a license, grant, or other benefit by the requesting agency.

d. Upon request to the Department of Justice in connection with pending court or administrative proceedings for the purpose of representing the Government or in the course of presenting evidence or to parties or counsel involved in the proceeding for pretrial discovery.

e. Upon request to Congress, other federal agencies, and other organizations having legal and administrative responsibilities related to programs and individuals in the records.

4. The implications of not providing all, or any part, of the information requested are that the results and findings of the medical examination wil be incomplete, and statistical summaries will be less factual.

1. Disclosure of your social security number on this form is voluntary.

2. NASA is authorized under Public Law 79-658 and Office of Management and Budget BOB Circular A-72, to obtain an individual's social security number where necessary to identify both civil service and contractor employee's medical records.

3. The social security number is needed to assure accuracy in identifying the individual and medical information pertaining to the individual.

HUMAN RESEARCH CONSENT

I, _____, do hereby consent to participate as a test subject in
Name of Subject
_____, a description of which is attached herto,
Title of Research/Tests(s)
which research/test(s) will be conducted at the John F. Kennedy Space Center under the direction of _____.
Principal Investigator

The research identified herein has been explained to me and I am aware of the possible foreseeable consequences that may result from my participation and that such participation may otherwise cause me inconvenience and discomfort.

It is my understanding that I am considered medically qualified to participate in this research/test(s).

My consent is freely given and I understand that I may withdraw this consent at any time unless such withdrawal is unwise, dangerous, or impossible.

The foregoing shall not be construed as a release of the United States from any future liability which may arise from or in connection with the tests or experiments in which I am to participate as a subject.

_____ _____
Signature of Subject Date

Approved:

_____ _____
Signature & Title of Supervisor of Test Subject Date

_____ _____
Signature of Principal Investigator Date

CONSENT FOR TREADMILL STRESS TESTING

In order to evaluate my cardiovascular functional capacity as a means of clearing me for the research subject pool, I voluntarily agree to undergo an exercise stress test in the Physiological Stress Laboratory.

I understand that this test, like all medical procedures, may involve a cardiovascular risk, and in very rare cases cause abnormal heart rhythms, fainting, or chest pain.

I understand that there will be continuous electrocardiogram monitoring, beginning before and continuing until after testing is completed. The test will be conducted by trained experts in a careful manner and will be discontinued if any abnormality is observed. I realize that the laboratory is equipped to respond to an emergency situation and a physicain is available during all tests.

I understand the results of this test may be used for research but that my identity will not be revealed.

I have read the above and give my consent to proceed with the test.

TIME _____ SIGNED _____

DATE _____

WITNESS _____

APPENDIX D

MAIN STUDY CONSENT FORM

APPENDIX D

MAIN STUDY CONSENT FORM

SYMPATHETIC NERVOUS SYSTEM RESPONSE TO ORTHOSTATIC STRESSES
CONSENT FORM

I understand that my medical history and the results of a treadmill stress test of maximal aerobic capacity have been reviewed by a NASA physician and I am judged to be medically fit to participate in this study.

I have discussed my participation in this study with personnel of the Biomedical Laboratory. I understand that my participation in this study requires me to visit the Biomedical Stress Laboratory three (3) times.

During the first visit, I will complete a questionnaire and then have a maximal treadmill stress test. This test will be the same as the treadmill test I took before entering the subject pool. This first session will be approximately 2 hours in duration. The risks of exercise include fatigue and possible muscle soreness and a slight risk of cardiac problems.

The second visit will be of approximately 3 hours duration. It will include Cybex leg strength testing of the knee joints and underwater weighing. Also, resting plasma volume will be determined at this visit. The Cybex may cause some muscle strain and/or fatigue as well as slightly increased blood pressure with exertion. The resting plasma volume will be measured by inserting a safe dye into a vein in my arm. Then, a blood sample from my other arm will be taken. The procedure may cause some discomfort or a possible hematoma. At this visit the study protocol and monitoring equipment will be reviewed with me again, and I will briefly experience the LBNP device with negative pressure applied.

The third visit will be approximately 3 hours in duration and include the entire test protocol of head-down tilt and lower body negative pressure. For this I will be required to lie on the test table with my lower body (from the waist down) inside a negative pressure box. Physiological sensors will be applied for data collection and monitoring purposes.

I realize that the head-down tilt test is of minimal risk but has been associated with facial puffiness, sinus filling, and sinus headache. The lower body negative pressure test consists of consecutive stages of increasing negative pressure

about my body. It may feel like air moving past the waist and over my legs, or I may have a reversal of these sensations. There is a slight chance that I may feel faint with LBNP, and if so, the test will be stopped.

I understand that, if necessary, I will be shaved in the areas where electrocardiographic sensors are to be positioned. Two strips of tape electrodes will be put around my neck and two around my lower chest to measure the stroke volume of my heart. The circumference of my left leg will be measured at mid-calf, and a mercury strain gauge will be applied at this area. A blood pressure cuff will be applied to my arm, and blood pressure will be monitored every minute during the LBNP portion of the protocol.

A catheter for blood sample collection will be placed in a vein of my arm by trained and competent personnel. This will be stabilized with tape and left in place throughout the protocol. It is from this catheter that the blood samples will be drawn during the head-down tilt/LBNP test. This will occur during the third visit to the lab. Minor local discomfort, dizziness, fainting, or possible hematoma may be associated with this procedure.

I understand that the test procedure will be conducted and monitored by trained/experienced personnel and is not considered hazardous. The investigation is designed to minimize all possible risks. I have discussed the protocol with the laboratory personnel, and the benefits, risks, and hazards of the study have been explained to my satisfaction. I realize that I may withdraw from the study at any time. I understand that my test results may become part of a published scientific paper, but my privacy will be maintained and identity not disclosed.

Signature _____ Date _____

APPENDIX E

BRUCE TREADMILL PROTOCOL

APPENDIX E

BRUCE TREADMILL PROTOCOL

BRUCE TREADMILL STRESS TEST PROTOCOL
(MODIFIED)

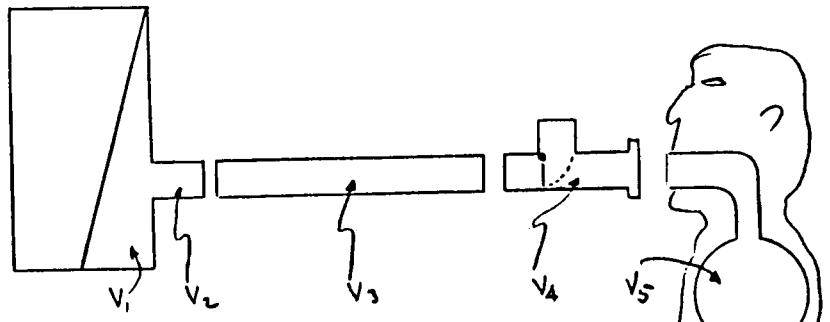
Minutes	Event	MPH	Grade
1-4	Standing rest	--	--
4-5	Warm-up walk	1.7	0%
5-8	Stage I	1.7	10%
8-11	Stage II	2.5	12%
11-14	Stage III	3.4	14%
14-17	Stage IV	4.2	16%
17-20	Stage V	5.0	18%
20-23	Stage VI	5.5	20%
23-26	Stage VII	6.0	22%
	-RECOVERY-		
1	Cool-down	2.5	10%
1-5	Cool-down	1.7	0%
5-10	Standing Recovery	---	----

APPENDIX F

UNDERWATER WEIGHING APPARATUS

HYDROSTATIC WEIGHING

DOERR
12-7-83



A. INIATIALLY- ASSUME ① V_1, V_2, V_3 - 100% O_2
② V_4, V_5 : 79.6 % N_2

B. FORCED EXPIRATION - V_5 MINIMUM

C. TOTAL N_2 IN SYSTEM : 79.6%$(V_4 + V_5)$

D. CLOSE VALVE TO ROOM, OPEN TO SPIROMETER

E ASSUME UNIFORM MIXING OF N_2 THROUGHOUT $V_1 \rightarrow V_5$

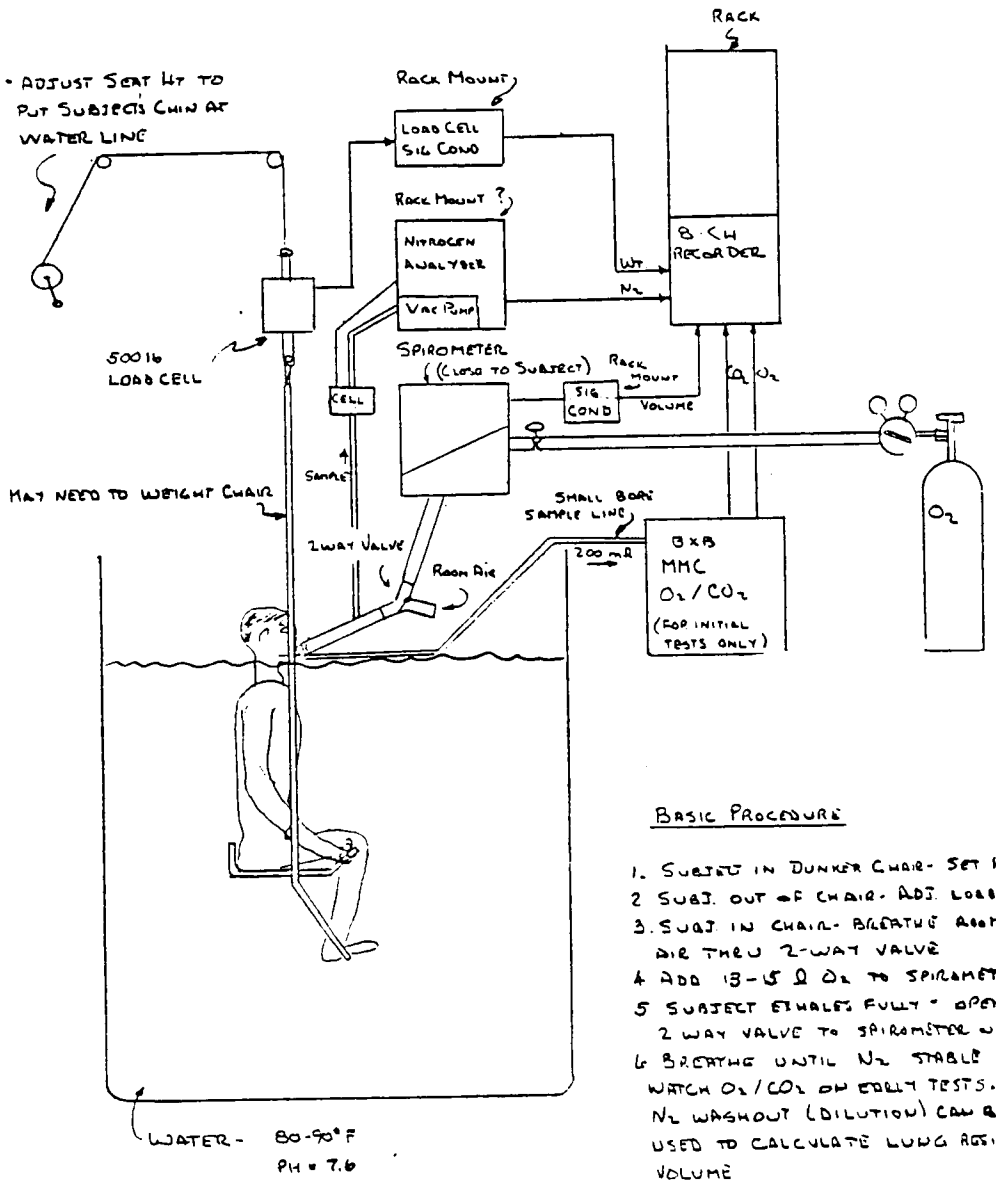
F. ACTUAL VOLUME OF N_2 (C) DOES NOT CHANGE

G. THEN (FINAL %N_2) $\sum_1^5 V$: .796 $(V_4 + V_5)$

H. SOLVING FOR

$$V_5 = \frac{(F\%N_2)(V_1+V_2+V_3+V_4) - .796\,V_4}{.796 - F\%N_2} = \underline{\text{RESIDUAL VOLUME}}$$

Body Fat Measurement System
(Fat Tub)



Basic Procedure

1. Subject in Dunker Chair - Set Ht.
2. Subj. out of chair - Adj. Load Cell "0"
3. Subj. in chair - Breathe Room Air thru 2-way valve
4. Add 13-15 ℓ O_2 to Spirometer.
5. Subject exhales fully - open 2 way valve to Spirometer w/ O_2
6. Breathe until N_2 stable - watch O_2/CO_2 on early tests. N_2 washout (dilution) can be used to calculate lung residual volume
7. Subj exhales fully - Discard mouthpiece - put head underwater
8. Read wt. from load cell.

APPENDIX G

STUDY PROTOCOL

APPENDIX G

TEST PROTOCOL
SYMPATHETIC STUDY
TIM LIGHTFOOT

Recording Times	Condition	Record on Data Sheet
0	Assume supine position, Equipment check-out, Start test	
19:25 - 19:50	Rest	Leg, BP, EMG, Blood
19:50 - 20:00	Tilt Transition	
20:00 - 110:00	-6° tilt	
24:40 - 25:05	HDT	Leg, BP, EMG, Blood
34:40 - 35:05	HDT	Leg, BP, EMG, Blood
49:40 - 50:05	HDT	Leg, BP, EMG, Blood
79:40 - 80:05	HDT	Leg, BP, EMG, Blood
109:25 - 109:50	HDT	Leg, BP, EMG, Blood
110 - 111	LBNP Transition	
111 - 112	-8 mm Hg	
112 - 113	-16 mm Hg	
113 - 116	-30 mm Hg	
115:25 - 115:50	-30 mm Hg	Leg, BP, EMG, Blood
116 - 121	-40 mm Hg	
120:25 - 120:50	-40 mm Hg	Leg, BP, EMG, Blood
121-126	-50 mm Hg	
125:25 - 125:50	-50 mm Hg	Leg, BP, EMG, Blood

HDT = Head-down tilt, LBNP = Lower body negative pressure, Leg = Calf Circumference, BP = Blood pressure, EMG = Electromyogram, Blood = 3ml blood sample.

APPENDIX H

CATECHOLAMINE ASSAY

APPENDIX H

CATECHOLAMINE ANALYSIS

I. Catecholamines + ^{3}H S-adenosyl methionine COMT ^{3}H methoxyderivatives
Epinephrine and norepinephrine are converted to ^{3}H metanaphine and ^{3}Hnormetanephrine, respectively, during incubation with catechol-0-methyl-transferase (COMT) and ^{3}H S-adenosyl methionine (^{3}H-SAM). The corresponding metanephrines are extracted into acetic acid and washed with a series of tolune isoamyl washes. The metanephrine and normetanephrine are seperated by thin layer chromatography (TLC). They are eluted from the TLC silica gel and oxidized to vanillin with sodium periodate. The vanillins corresponding to epinephrine and norepinephrine are extracted into a tolune-liquifluor solvent and counted in a scintillation counter. The output is proportional to the levels to catecholamines.

II. Reagents

1. THAM--Fisher T395
2. EGTA·Na2--Sigma E3251
3. MgCl2·6H2O--Fisher M33
4. Glutathione--Sigma G4251
5. Boric Acid--Matheson Coleman & Bell (MCB) BX865, CB225
6. EDTA·Na2--Mallinckrodt 49931
7. Metanephrine HCl--Sigma M8625
8. Normetanephrine HCl--Sigma 7127
9. Toluene--Fisher T-324
10. Isooamyl Alcohol--Fisher A-393
11. Glacial Acetic Acid--Fisher A-38
12. Sodium Periodate--Fisher S-398
13. Glycerin--Fisher G33
14. Ammonium Hydroxide--Fisher A669
15. HCl--Fisher A144
16. Epinephrine--(100µg/ml) BIORAD
17. Norepinephrine--(100µg/ml) BIORAD
18. ^{3}H SAM--New England Nuclear or ICN Radio chemicals (5-15 uCi)
19. Ethanol--Chem Stores
20. Methanol--Chen Stores

21. Silica Gel Plates (10 * 20 cm 25 μ) ANALTECH
22. Benzene--Fisher B-245
23. Tert Amyl Alcohol--Fisher A-730
24. Methyl Amine (40%)--Fisher M223
25. Liquifluor--New England Nuclear NEF903
26. H_2SO_4 (pH 2):ethanol (9:1)

III. Daily Working Solutions

A. Assay Buffer: Tris - Add 6.05 gm of THAM, 1.9 gm EGTA-Na_2, and 3.05 gm $MgCL_2.6H_2O$ to approximately 20 ml of water.* Adjust pH to 8.3 with concentrated HCl or NaOH. The initial pH is close to this value. Bring volume to 25.0 ml with water.

B. Glutathione Solution: .1 Molar - Add 30.7 mg of reduced glutathione to a small test tube and all 1 ml of water. Vortex lightly and keep on ice.

C. Stopping Solution: 1.0 m Boric Acid + .2 m EDTA·Na_2
   1. Add: 1.55 gm boric acid + .93 gm EDTA·$2H_2O$·Na to 20 ml H_2O.
   2. Adjust pH to 11.1.
   3. Bring to 25 ml with water.

   This solution can be prepared in advance and aliquots can be stored frozen.

D. Metanephrine & Normetanephrine: .2 μmoles/50 μ1 of borate buffer, which is .935 mg/ml of Met and .88 mg/ml of NorMet. For every 5 ml of the stopping solution add 4.67 mg of metanephrine and 4.4 mg of normetanephrine. Prepare prior to use.

E. Tolune-isoamyl alcohol (3:2)
   Combine 300 ml of toluene and 200 ml of isoamyl alcohol.

F. Acetic Acid: .1 N
   Bring 2.95 ml of glacial acetic acid up to 500 ml with water.

G. Sodium Periodate Solution: 4% w/v NaIO4
   1 gm of NaIO4 up to 25 ml with water. Prepare fresh.

*It is understood that distilled water is always used.

H. Ammonium Hydroxide Solution: .05 M NH4OH
1 ml of NH4OH up to 300 ml with water.

I. HCl: 1.0 N
1. 8.3 ml of concentrated HCl up to 100 ml.
2. .01 HCl: 1.0 ml of 1.0 N HCl to 100 ml.
3. .001 HCl: 1.0 ml of 1.0 N HCl to 1000ml.

J. Epinephrine & Norepinephrine Standards: 100 pg/10µl
1. 100 µl of BioRad Epinephrine (100 µg/ml) and 100 µl of BioRad Norepinephrine (100 µg/ml) are brought to 50 ml with .01 N HCl in a volumetric.
2. Bring 5 ml of the above (1) to 100 ml with .001 N HCl in a volumetric.
3. 10 µl of (2) will give 100 pg of E & NE.

K. Enzyme: COMT
Prepared according to the procedure of Axelrod and Tomchick (1958).

L. H_2SO_4·Ethanol Solution: (9:1)
Prepare a H_2SO_4 solution of pH = 2. Simply add concentrated H2SO4 to water (ca 250 ml) until pH = 2. This will require only a drop or two.
Use 9 ml of this for every 1 ml of Ethanol (95%).

M. Toluene--Liquifluor (1000:50 v/v)
Add 50 ml of Liquifluor to 1000 ml of toluene.

IV. Reaction

A. Turn on water bath and set to 37°C.

B. Prepare two sets of test tubes (13 x 100 mm). Each sample should be done in duplicate. The number of internal standardds will depend on the type of experiment but a duplicate should be considered a minumum. Label tubes with a magic marker (not water based).

C. Remove enzyme, samples, buffer, and standard plasma from freezer. Thaw and keep on ice. Thaw ^3H SAM only before use.

D. Prepare the enzyme cocktail in a round bottom 13 x 100 mm tube. Add in the following order in amounts sufficient for the assay plus 3 (see below):
Buffer solution, glutathione and ^3H SAM and H_2SO_4:Ethanol (9:1); vortex lightly and add COMT enzyme.

Assay	x1	x20	x50	x100
Buffer	5 µl	100 µl	250 µl	500 µl
Glutathione	1 µl	20 µl	50 µl	100 µl
^3H SAM	5 µl	100 µl	250 µl	500 µl
H_2SO_4-Ethanol (9:1)*	5 µl	100 µl	250 µl	500 µl
Enzyme	25 ul	500 ul	1.25 ul	2.5 ul

*This solution is used to dilute the isotope. It is the solvent vehicle for the ^3H SAM. If higher counts are required for the assay, this should be omitted and the quantity of ^3H SAM indicated on the chart should be doubled (i.e., 10 µl/tube).

E. Incubation mixture
The first set of tubes will receive the following:
1. Blanks
   a. 50 µl of sample vehicle (i.e., water that is mixed with EGTA-glutathione in the same concentration as that of blood samples).
   b. 40 µl of enzyme cocktail (#4).
   c. 10 µl of .001 N HCl.
2. Standards (internal)
   a. 50 µl of plasma.
   b. 40 µl of enzyme cocktail.
   c. 10 µl of 100 pg standard.
3. Plasma samples
   a. 50 µl of plasma.
   b. 40 µl of enzyme cocktail.
   c. 10 µl of .001 N HCl.

4. The plasma samples and blanks can be pipetted with the fixed volume 50 µl positive displacement pipette. The tip does not have to be replaced after each sample.
5. The enzyme cocktail, .001 N HCl and standards can be pipetted with the Eppendorf repeater pipette. Please note correct setting and adaptor size for volume desired.
6. Vortex (lightly) samples.

F. Stopping the Reaction

Place reaction tubes in ice bath and add 50 µl of the Borate stopping solution that contains the metanephrine and normetanephrine carriers (see section III-C and III-D).

Vortexing is not necessary. Gently shake tube rack.

V. Extraction

The second set of tubes will be used here. They will each receive 100 µl of .1 N acetic acid (see section III-F).

A. Add 2 ml of tiluene-isoamyl alcohol (3:2) to incubation tubes. Vortex well and centrifuge.

B. Quick freeze:

Prepare an ice bath of methanol and dry ice. Methanol level should only be deep enough to cover the bottom of test tubes (i.e., ca 1/2-1 inch).

1. Submerge tube to level of aqueous phase.
2. Blot outside of tube. Decant the organic phase into its corresponding tube containing the .1 N acetic acid (see section V above).
3. Rhythm: decant one tube while the next tube is in ice bath.

C. Vortex and centrifuge the acetic acid, organic solution (see section V-B-2).

D. Quick freeze and aspirate offf organic phase without touching suction pipette to pellet.

E. Add 1 ml of toluene-isoamyl alcohol to thawed aqueous phase.

F. Vortex and centrifuge.

G. Quick freeze, aspiration, and discard organic phase as in D above. The assay may be stopped at this point. Cap tubes and keep at -20°C.

--The centrifuging is done on setting 4 (centrifuge #1) and 7 (centrifuge #2) for ca. 1-2 min. Not critical.

VI. Thin Layer Chromatography

A. Add 100-150 µl of ethanol to be thawed acetic acid from section V-G above (for the number of tubes in one spotting run, i.e., 14).

B. Slowly pull acetic acid-ethanol solution into syringe. Do not pull excess air into syringe. Should have small bubble on the end of plunger.

C. Turn on dryer and spotter.

D. Place dryer approximately 3 cm from plates and set temperature control between 100-200 (60°C).

E. Position syringes so that tips touch TLC plates. Set plunger speed to slowest possible speed.

F. Prepare 44 ml of developing solution (6:2:3) in a 50 ml graduate.
1. 24 ml tertiary amyl alcohol.
2. 8 ml benzene.
3. 12 ml methylamine
4. mix gently (solution should be clear).

G. Put developing solution in developing tank immediately before use. Carefully place plates in tank. Develop until solvent runs the entire plate (ca. 40-50 minutes).

H. Dry plates and visualize spotes under UV. Utilizing a scapel, carefully outline the spots. (Hint: best seperation is obtained while plates are still somewhat damp.)

I. Scrape spots into acid washed scintillation vials (use a scapel). The metanephrines are the top zone and normetanephrines are the bottom zone.

VII. Oxidation

A. Add 1 ml of .05 M NH_4OH to vials. Vortex vigorously.

B. Line up vials and add 50 ul or 4% periodate solution at time intervals. Vortex vigorously for 5 minutes.

C. Stop reaction by adding 50 µl of 10% glycerol solution, 5 minutes after step B. Maintain order and timing of step B.

D. Add 1 ml of .1 N acetic acid to each vial and vortex.

E. Add 10 ml of toluene-liquifluor (1000:50 v/v) to each scintillation vial. Shake by hand vigorously (for about 10 sec.).

F. Count each vial for 2-10 minutes.

APPENDIX I

INDIVIDUAL DATA

APPENDIX I

INDIVIDUAL DATA

The individual data are arranged by subject number (SUB) and time of data collection (TIME). Data collected at protocol minutes 20, 25, 35, 50, 80, 110, 116, 121, and 126 are coded as TIME = 1, 2, 3, 4, 5, 6, 7, 8, and 9 respectively. Each subject was classified according to aerobic fitness and strength with high aerobic fitness = 1, low aerobic fitness = 2, high strength = 1, and low strength = 2. The following data were collected and abbreviated as follows: Systolic blood pressure (SBP); Diastolic blood pressure (DBP); Calf circumference (LEG); Plasma epinephrine (EPI); Plasma norepinephrine (NOREPI); Heart rate (HR); Mean arterial pressure (MAP); and Pulse pressure (PP).

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
248	2	2	1	109	70	0.0	18	226	67	83	39
			2	120	75	-0.35	15	255	77	90	45
			3	110	78	-0.4	31	210	64	88	32
			4	114	71	-.5	29	195	92	85	43
			5	120	72	-.7	61	216	77	88	48
			6	122	75	.9	72	224	102	90	47
			7	118	80	0.1	41	379	82	92	38
			8	115	78	.5	43	518	104	90	37
			9	110	74	.8	105	573	118	86	36
249	1	2	1	116	67	0.0	45	149	49	83	49
			2	116	68	-0.25	62	147	45	84	48
			3	125	75	-0.35	67	160	47	92	50
			4	119	71	-0.4	46	133	44	87	48
			5	122	69	-.5	50	136	43	86	53
			6	128	67	-.6	62	253	48	87	61
			7	112	62	.6	.	.	52	78	50
			8	117	74	0.4	.	.	53	88	43
			9	95	62	.8	106	274	61	73	33
294	2	2	1	105	78	-0.3	18	401	62	87	27
			2	104	79	-.6	7	470	65	87	25
			3	110	72	-.6	0	564	62	84	38
			4	105	74	-.6	13	369	62	84	31
			5	115	79	-1.1	34	559	68	91	36

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
294	2	2	6	110	80	-1.5	33	338	68	90	30
			7	109	90	-1.4	28	422	74	96	19
			8	89	76	-1.5	16	523	80	80	13
			9	.	.	.	.	.	.	.	.
369	1	2	1	110	80	0.0	17	181	51	90	30
			2	117	75	-0.25	11	206	48	89	42
			3	108	76	-0.4	10	254	47	86	32
			4	109	75	-.5	22	215	47	86	34
			5	120	72	-.55	28	192	50	88	48
			6	120	77	-.6	37	197	52	91	43
			7	112	80	0.2	16	327	63	90	32
			8	120	80	0.4	16	481	63	93	40
			9	115	85	.8	44	513	67	95	30
478	1	2	1	95	65	0.0	13	136	51	75	30
			2	103	72	-0.4	10	155	51	82	31
			3	96	70	-0.4	0	125	49	78	26
			4	107	72	-.55	26	166	45	84	35
			5	102	70	-.6	13	162	50	80	32
			6	103	75	-.8	0	188	58	84	28
			7	110	73	0.2	.	.	56	85	37
			8	100	70	.55	.	.	63	80	30
			9	95	70	.9	16	336	82	78	25
516	1	1	1	105	74	0.0	18	174	51	84	31
			2	108	75	-0.45	37	172	52	86	33
			3	101	74	-.6	28	189	54	83	27
			4	106	77	-.7	32	210	52	86	29
			5	105	77	-1.0	17	216	57	86	28
			6	105	70	-1.1	7	209	54	82	35
			7	101	70	0.0	.	.	64	80	31
			8	90	70	-.5	79	300	62	76	20
			9	.	.	.	.	.	.	.	.
527	1	2	1	122	67	0.0	46	125	47	85	55
			2	113	71	-0..3	11	135	48	85	42
			3	110	71	-.5	21	135	49	84	39
			4	108	75	-.65	41	131	57	86	33
			5	117	75	-.8	14	116	58	89	42
			6	129	73	-1.0	14	111	51	92	56
			7	127	77	-0.1	33	155	50	94	50

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
527	1	2	8	123	85	0.25	29	170	56	98	38
			9	118	87	.65	35	216	67	97	31
553	2	2	1	115	79	0.0	96	336	63	91	36
			2	112	85	-.6	39	292	66	94	27
			3	115	77	-.8	31	313	62	90	38
			4	117	72	-.9	30	254	60	87	45
			5	115	76	-1.05	21	208	62	89	39
			6	111	70	-1.15	22	201	64	84	41
			7	106	70	0.05	42	291	66	82	36
			8	97	71	0.3	49	401	68	80	26
			9	68	40	0.15	208	472	83	49	28
570	2	1	1	115	82	0.0	6	105	50	93	33
			2	114	75	-0.2	0	90	51	88	39
			3	115	83	-0.4	0	96	50	94	32
			4	113	86	-.5	0	143	49	95	27
			5	129	85	-0.4	0	93	53	100	44
			6	124	90	-.7	0	113	56	101	34
			7	120	90	-0.2	27	199	69	100	30
			8	127	85	.5	30	290	72	99	42
			9	124	94	.5	68	454	86	104	30
629	1	1	1	110	68	0.0	47	177	52	82	42
			2	100	64	-0.3	38	159	46	76	36
			3	110	60	-.5	30	209	45	76	50
			4	113	60	-.6	30	202	50	78	53
			5	110	65	-.75	42	159	47	80	45
			6	105	66	-.8	60	189	53	79	39
			7	105	70	0.15	56	325	64	82	35
			8	105	69	.5	82	330	73	81	36
			9	100	65	.95	102	458	81	76	35
630	1	2	1	108	62	0.0	13	213	40	77	46
			2	111	58	-0.3	11	218	42	76	53
			3	111	68	-0.3	10	219	41	82	43
			4	115	72	-0.4	22	194	43	86	43
			5	115	75	-.6	11	182	46	88	40
			6	114	72	-0.35	22	221	46	86	42
			7	107	65	0.15	30	282	54	79	42
			8	107	77	0.4	11	368	69	87	30
			9	101	82	.7	12	486	77	88	19

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
634	1	1	1	115	77	0.0	6	308	48	90	38
			2	112	60	-.55	9	291	51	77	52
			3	117	64	-.7	20	271	51	82	53
			4	122	63	-.8	15	261	51	82	59
			5	113	64	-.9	8	285	51	80	49
			6	118	64	-1.05	18	259	62	82	54
			7	113	65	0.3	11	296	63	81	48
			8	122	74	.6	24	406	68	90	48
			9	123	77	.9	95	466	76	92	46
635	2	2	1	112	77	0.0	7	130	60	88	35
			2	117	85	-0.35	3	108	58	96	32
			3	119	79	-.6	1	137	58	92	40
			4	114	70	-.7	10	151	56	84	44
			5	111	75	-.85	21	157	53	87	36
			6	118	80	-1.05	7	120	56	92	38
			7	115	80	-0.1	.	.	58	92	35
			8	112	86	0.3	.	.	66	94	26
			9	95	80	.65	71	359	80	85	15
637	2	2	1	115	69	0.0	36	196	63	84	46
			2	114	74	-0.4	25	205	61	87	40
			3	120	64	-0.4	29	226	57	82	56
			4	112	68	-.6	25	206	57	82	44
			5	110	75	-.75	14	273	55	86	35
			6	118	70	-1.0	25	251	55	86	48
			7	110	78	-0.45	23	245	59	88	32
			8	110	75	-0.1	32	406	66	86	35
			9	100	70	0.3	68	518	73	80	30
643	1	1	1	110	80	0.0	0	226	54	90	30
			2	115	83	-0.2	3	304	55	94	32
			3	118	76	-0.2	3	297	54	90	42
			4	120	77	-0.3	17	324	52	91	43
			5	126	74	-0.3	25	382	56	91	52
			6	115	85	-0.4	8	161	58	95	30
			7	110	70	0.2	.	.	59	83	40
			8	110	78	0.4	38	501	72	88	32
			9	98	83	.6	129	649	90	88	15

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
644	1	1	1	112	72	0.0	11	267	41	85	40
			2	112	65	-0.3	10	188	40	80	47
			3	114	73	-0.45	13	268	41	86	41
			4	117	68	-.6	9	260	38	84	49
			5	115	65	-.8	24	359	43	82	50
			6	123	62	-.9	67	405	46	82	61
			7	120	63	0.0	43	364	52	82	57
			8	117	64	0.3	57	411	55	82	53
			9	108	53	1.3	74	487	67	71	55
645	1	2	1	110	64	0.0	8	297	57	79	46
			2	105	70	-0.1	2	265	59	82	35
			3	104	70	-0.2	3	311	60	81	34
			4	118	67	-0.1	0	344	58	84	51
			5	110	66	-0.1	0	416	57	80	44
			6	117	68	-1.0	9	466	60	84	49
			7	100	80	-0.4	16	634	65	86	20
			8	55	32	-.65	43	572	53	40	23
			9	.	.	.	.	.	.	.	.
650	1	1	1	116	67	0.0	3	188	54	83	49
			2	108	69	-0.3	0	173	58	82	39
			3	113	71	-0.4	0	233	51	85	42
			4	109	68	-.6	0	215	58	82	41
			5	107	66	-.6	0	234	51	80	41
			6	110	69	-.7	.	.	57	82	41
			7	109	72	0.0	.	.	58	84	37
			8	106	67	0.4	.	.	62	80	39
			9	102	70	.8	12	472	73	80	32
663	2	2	1	108	76	0.0	0	167	66	86	32
			2	108	72	-0.1	0	175	64	84	36
			3	116	71	-0.2	0	211	62	86	45
			4	113	70	-0.35	1	221	61	84	43
			5	117	82	-0.4	0	214	61	94	35
			6	115	88	-0.35	22	256	68	97	27
			7	118	86	0.0	9	382	75	96	32
			8	120	84	0.3	7	380	88	96	36
			9	98	84	.6	58	429	94	88	14

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
671	2	1	1	115	72	0.0	53	221	60	86	43
			2	110	85	-0.2	39	210	73	93	25
			3	135	77	-0.2	37	202	65	96	58
			4	120	72	-0.35	33	227	75	88	48
			5	125	73	-.5	27	210	68	90	52
			6	130	86	-.65	34	208	77	100	44
			7	120	85	0.0	31	258	91	96	35
			8	110	84	0.2	59	452	97	92	26
			9	117	83	.6	91	709	111	94	34
677	2	1	1	135	79	0.0	29	164	54	98	56
			2	134	79	-0.3	33	278	58	97	55
			3	144	74	-0.35	39	210	58	97	70
			4	136	70	-0.45	53	259	54	92	66
			5	130	86	-.6	35	244	52	100	44
			6	145	75	-.7	26	252	65	98	70
			7	144	78	0.0	42	362	57	100	66
			8	140	88	0.4	44	473	73	105	52
			9	97	78	.9	71	799	74	84	19
679	2	1	1	118	58	0.0	10	180	57	78	60
			2	111	57	-0.25	0	137	55	75	54
			3	105	55	-0.3	0	152	52	72	50
			4	108	62	-0.3	0	145	53	77	46
			5	112	62	-.5	3	128	56	78	50
			6	112	65	-.5	77	169	68	80	47
			7	98	42	-0.2	152	220	58	60	56
			8	.	.	.	.	.	.	.	.
			9	.	.	.	.	.	.	.	.
680	2	1	1	126	86	0.0	9	256	62	99	40
			2	126	85	0.0	13	260	61	98	41
			3	118	77	-0.1	22	317	60	90	41
			4	119	77	-0.2	40	343	61	91	42
			5	123	82	-0.4	44	375	61	96	41
			6	123	89	-.5	176	365	62	100	34
			7	117	88	-0.1	65	514	73	98	29
			8	117	86	0.15	55	417	82	96	31
			9	113	93	0.45	181	636	93	100	20

SUB	FIT	STR	TIME	SBP	DBP	LEG	EPI	NOREPI	HR	MAP	PP
683	2	1	1	118	66	0.0	24	177	72	83	52
			2	119	66	-0.3	52	220	67	86	49
			3	126	70	-0.4	83	271	70	88	56
			4	126	75	-.5	75	276	73	92	51
			5	122	65	-.75	56	234	68	84	57
			6	130	67	-.9	37	241	68	88	63
			7	120	70	-0.4	62	303	78	86	50
			8	119	70	-0.5	50	366	86	86	49
			9	118	70	0.2	106	333	97	86	48

APPENDIX J

GROUP MEANS

APPENDIX J

GROUP MEANS

Presented below are the actual group means and standard deviations for each variable at each data collection point during the protocol. The adjusted means used in data analysis were generated by the statistical analysis and used the reported means and standard deviations below as base means. The groups (GROUP) were classified as high fit, high strength (HFHS); high fit, low strength (HFLS); low fit, high strength (LFHS); and low fit, low strength (LFLS). The protocol collection periods (TIME) are coded as 1, 2, 3, 4, 5, 6, 7, 8, and 9, and correspond to the following protocol minutes, respectively: 20 (end of rest), 25, 35, 50, 80, 110 (head-down tilt measurements), 116, 121, 126 (LBNP measurements). The following variables are reported by abbreviation: Heart rate (HR); Systolic blood pressure (SBP); Diastolic blood pressure (DBP); Mean arterial pressure (MAP); Pulse pressure (PP); Calf circumference change (LEG); Plasma Epinephrine (EPI); and Plasma Norepinephrine (NOREPI).

GROUP	TIME	HR	SBP	DBP	MAP	PP	LEG	EPI	NOREPI
HFHS	1	50±5	111±4	73±5	86±3	38±7	0±0	14±17	223±55
	2	50±6	109±5	69±8	83±6	40±8	-.35±.13	16±17	214±65
	3	49±5	112±6	70±6	84±4	42±9	-.48±.17	16±12	244±42
	4	50±6	114±6	69±7	84±5	46±10	-.60±.17	17±12	245±46
	5	50±5	113±8	68±6	83±5	44±9	-.73±.25	19±15	272±86
	6	55±5	113±7	69±8	84±6	43±12	-.82±.26	32±29	245±97
	7	60±5	110±6	68±4	82±1	41±10	.11±.13	37±23	328±34
	8	65±7	108±11	70±5	83±5	38±12	.28±.40	56±25	390±79
	9	77±9	106±10	70±12	82±8	37±15	.91±.26	82±44	506±80
HFLS	1	49±5	110±9	68±6	82±6	43±10	0±0	24±17	184±64
	2	49±6	111±6	69±6	83±4	42±8	-.27±.10	18±22	188±50
	3	49±6	109±10	72±3	84±4	37±8	-.36±.10	18±25	201±74
	4	49±7	113±5	72±3	86±1	41±8	-.43±.19	26±16	197±79
	5	51±6	114±7	71±4	86±4	43±7	-.52±.23	19±17	201±109
	6	52±5	118±10	72±4	88±3	47±12	-.72±.26	24±22	239±121
	7	57±6	111±9	73±8	86±6	38±12	.11±.34	24±9	350±203
	8	60±6	104±25	70±19	81±21	34±8	.22±.44	25±14	398±173
	9	71±9	105±11	77±11	86±10	28±6	.77±.10	43±38	365±130

GROUP	TIME	HR	SBP	DBP	MAP	PP	LEG	EPI	NOREPI
LFHS	1	59±8	121±8	74±10	90±8	47±10	0±0	22±18	184±51
	2	61±8	119±9	74±11	90±9	44±11	-.21±.11	23±22	199±72
	3	59±8	124±14	73±10	90±9	51±13	-.29±.12	30±31	208±79
	4	61±11	120±10	74±8	89±6	47±13	-.40±.11	34±30	232±78
	5	60±7	124±6	76±10	92±9	48±6	-.46±.24	28±22	214±99
	6	66±7	127±11	79±11	95±9	49±15	-.66±.15	58±63	225±86
	7	71±13	120±15	76±18	90±15	44±15	-.15±.15	63±46	309±116
	8	82±10	123±11	83±7	96±7	40±11	.24±.22	48±11	400±73
	9	92±14	114±10	84±10	94±8	30±12	.53±.25	103±46	586±190
LFLS	1	63±2	111±4	75±4	87±3	36±6	-.05±.12	29±35	243±104
	2	65±6	112±6	78±6	90±4	34±8	-.40±.19	15±15	251±125
	3	61±3	115±4	74±6	87±4	42±8	-.50±.21	15±16	277±151
	4	65±13	112±4	71±2	85±1	42±5	-.61±.18	18±12	233±75
	5	62±9	115±4	76±4	89±3	38±5	-.82±.26	25±21	271±146
	6	69±17	116±4	77±7	90±5	38±9	-.69±.86	30±22	232±72
	7	69±9	113±5	81±7	91±5	32±7	-.30±.57	29±14	344±73
	8	78±15	107±12	78±6	90±7	29±9	-.04±.74	29±18	446±69
	9	90±17	94±16	70±17	78±16	25±10	.48±.29	102±62	470±82

VITA

John Timothy Lightfoot was born in Cisco, Texas on May 18, 1960. He was raised in Rocky Mount, Louisiana, where he attended school and graduated from Rocky Mount High School in May 1978. He entered Northeast Louisiana University in September 1978 and graduated with a B.S. in Physical Education in December 1981. He then accepted a graduate teaching assistantship at Northeast Louisiana University and entered the graduate program in Exercise Physiology. He completed his M.Ed. in Exercise Physiology in August 1982.

After one year of public school teaching, he accepted a teaching assistantship at The University of Tennessee, Knoxville, in the School of HPER. After completing his dissertation collection on a pre-doctoral grant from Bionetics, Inc., at Kennedy Space Center, Florida, he graduated with a Doctor of Philosophy degree in Education in August 1986. He accepted a position as a post-doctoral research fellow in the Division of Environmental Physiology at Johns-Hopkins University in Baltimore, Maryland.

The author is a member of the American College of Sports Medicine and the Aerospace Medical Association. He is married to the former Kellye Watkins. They have no children, but have two childish dogs.