THE INDIVIDUAL EFFECTS OF HEAT ACCLIMATI AND SHORT TERM PHYSICAL TRAINING ON ATTENUATING THE PHYSIOLOGICAL STRAIN RESULTING FROM EXERCISE IN THE HEAT WHILE WEARING A CHEMICAL DEFENSE ENSEMBLE

by

Neal Baumgartner, M.S.

DISSERTATION PROPOSAL

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

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THE UNIVERSITY OF TEXAS AT AUSTIN
Spring, 1993

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Memo

May 20, 1993

TO: Steve Constable
Ed Coyle
John Ivy
Gene Wissler

FROM: Jack Wilmore

SUBJECT: Neal Baumgartner's Ph.D. Proposal Changes

The purpose of this memo is to place in writing those changes to Neal's proposal that were suggested in our meeting yesterday following Neal's presentation. The suggested changes were as follows:

1. Add venous occlusion plethysmography to complement the Laser Doppler measurements, since there are problems with a variable baseline with the Laser Doppler (Coyle). We will attempt to implement this as soon as possible for inclusion in the Hot Test protocol, but not the CDE protocol since the CDE will interfere with the measurement procedure.

2. If possible, obtain a weight of the subject in the CDE at 30 minutes into the CDE test protocol, to provide an estimate of evaporation as well as to provide a possible marker of the earlier onset of sweating post-HA/STPT (Constable).

3. Delay the STPT group subjects starting their training for at least 3-4 days following all heat exposures to allow time for any possible acclimation effects to dissipate (Ivy).

4. Drop the Thermoneutral Test protocols, as this will add very little to the study, but would add considerably to the burden placed on the subject (Committee suggestion).

5. Add a CDE test 3 and Hot Test 3 where the work rate will be adjusted to bring the VO_2 post-HA/STPT up to the pre-HA/STPT values, thus matching the metabolic levels pre- and post-HA/STPT. This was a compromise agreed to by the Committee to accommodate Dr. Coyle's concern about the possible reduction in VO_2 post-HA/STPT and the effect this might have on other variables and general data interpretation (Ivy).

6. Drop the DeA and DeT part of the study. It was the decision of the Committee that this aspect of the study would have a relatively low yield of new information, and might, in fact, raise more questions than it would answer. This would reduce considerably the time commitment of the subjects.

7. Modify the STPT program. The Committee felt that the high intensity interval training proposed might be a problem with the subject population, and possibly would be a major problem if this had to be implemented in the field (Ivy/Wissler). The Committee instructed Neal to look at alternative STPT protocols, possibly increasing duration and reducing intensity, but keep energy expenditure matched to the HA group. This might be, in fact, an advantage as the subject would be exposed to increased body temperature for a longer period of time. Neal will review the literature and we will come to a decision as to the most efficacious protocol to both increase VO_2 max and to reduce possible problems with subject compliance and injury associated with high intensity interval training.

Please look this summary over very carefully and let me know if I have misinterpreted anything or have failed to include something that was discussed and agreed to include in the revised protocol.

Thanks very much for your help on getting this project moving. Neal will be keeping in contact with each of you throughout the summer informing you of his progress.

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GLOSSARY OF ABBREVIATIONS

ACTH	adrenocorticotropic hormone
ADH	antidiuretic hormone
BP	blood pressure
BSA	body surface area
C	convection
CDE	chemical defense ensemble
CV	cardiovascular
DB	dry bulb temperature
DBP	diastolic blood pressure
DeA	deacclimation
DeT	detraining
E	evaporation
FATR	fatigue rating
FR	fluid replacement
NF	no fluid
HA	heat acclimation
Hb	hemoglobin
Hct	hematocrit
HR	heart rate
HTT	heat tolerance test
K	conductance
M	metabolism
MAP	mean arterial pressure
PRA	plasma renin activity
PV	plasma volume
ΔPV	change in plasma volume
Q	cardiac output
R	radiation
RER	respiratory exchange ratio
RH	relative humidity
RPE	rating of perceived exertion
S	heat storage
SkBF	skin blood flow
SP	sweat production
SR	sweat rate
STPT	short-term physical training
SV	stroke volume
Tb	mean body temperature
Tc	core temperature
Tre	rectal temperature
TS	thermal sensation
Tsk	mean skin temperature
TWT	total walk time
VO_2 max	maximal oxygen consumption
VO2	oxygen consumption
VP	vapor pressure
W	work
WB	wet bulb temperature

SUMMARY

Extensive literature documents that heat acclimation reduces the thermal, metabolic and cardiovascular strain produced by exercise in the heat. For a given level of exercise-heat exposure, heat acclimation (HA) improves heat dissipation and reduces heat generation, thereby attenuating the level of heat storage. However, it is unknown whether HA is beneficial for attenuating the heat storage and overall physiological strain that individuals accrue when working in warm or hot conditions while wearing a chemical defense ensemble (CDE).

A series of three studies are proposed which seek to determine the independent roles of HA, defined as the adaptive changes that result from repeated or prolonged exercise in the heat, and short-term physical training (STPT) under thermoneutral conditions, in the attenuation of heat stress associated with exercise in the CDE. The purpose of the first study is to determine: a) the influence of HA and STPT on metabolic rate during submaximal exercise by comparing the physiological responses to a fixed rate, standardized, submaximal exercise bout conducted under both hot and thermoneutral conditions prior to and after separate treatments of HA and STPT; and b) the extent of day-to-day individual variability present over a well controlled course of HA by not only conducting pre and post-HA hot and thermoneutral submaximal exercise tests, but also comparing day-to-day changes in key physiological variables during nine days of HA. Tight controls during the tests and HA trials will allow the accurate assessment of daily individual variability.

The purpose of the second study is to determine the effect of both HA and STPT on physiological responses during exercise in the CDE. This will

be achieved by conducting 100 minute CDE exercise trials at 25% of maximal oxygen consumption (VO_2 max) in a warm, 30°C dry bulb temperature (DB) and 50% relative humidity (RH), environment before and after separate nine day courses of either HA or STPT.

Finally, the purpose of the third study is to determine the effect of deacclimation (DeA) and detraining (DeT) on physiological responses during exercise in a warm environment while wearing a CDE by conducting a separate 100 minute CDE exercise trial at 25% VO_2 max in a warm (30°C DB 50% RH) environment three weeks after completing HA or STPT.

INTRODUCTION

During exercise training in a hot environment one will experience greater physiological strain than that experienced during exercise of the same intensity and duration performed in a thermoneutral or cool environment. The heat load stimulates higher levels of sweating and cutaneous blood flow resulting in increased difficulty in maintaining fluid-electrolyte balance and cardiovascular stability (175). However, the body has the ability to adapt or acclimate to the combined stress of internal heat generation and external heat load (14). The adaptive changes that occur when one undergoes repeated or prolonged heat exposure and the concomitant reduction in physiological strain produced by the hot environment is considered heat acclimation. HA is produced by repeated exposure to a heat stress sufficient to raise internal body temperature to levels that provoke moderate to profuse sweating, and is most effectively accomplished by exercising in the heat (175, 183). In this proposal HA refers to exercise in the heat unless specified otherwise (*e.g.*, passive HA, sitting in the heat).

Several investigators have studied extensively the process of HA and find its traditional hallmarks are reduced thermal and cardiovascular strain manifested primarily as a reduced heart rate and core temperature and secondarily as an attenuation of the symptoms of heat strain and increased sweat production during a given level of exercise-heat stress (102, 111, 129, 133, 175, 184, 186). HA-induced physiological adaptations generally occur in two phases: cardiovascular changes including plasma volume expansion, increased stroke volume, and reduced heart rate, occur in the first six to seven days; sweat changes including increased sweat rate, earlier onset of

sweating, and decreased sweat electrolyte losses, usually occur after the fifth day (14, 67, 95, 129, 149). Complete or full HA is achieved when all responses have reached a plateau, or the point where 95% of the adaptation has occurred (14). The result of the above physiological adaptations is an improved transfer of heat from the body's core to the skin and from the skin to the environment (14, 175).

HA improves heat tolerance not only by increasing heat dissipation capacity, but also by reducing heat generation through its effect on exercise metabolic rate. However, the majority of HA investigations conducted to date have not addressed the effect HA might have on exercise metabolic rate (141). The current consensus is that HA, but not physical training in thermoneutral conditions, lowers the metabolic rate for a given rate of work, thereby, improving exercise economy (run and walk) or efficiency (cycling) (14, 92, 175). Researchers have suggested a few possible mechanisms for this reduction in exercise metabolic rate; however, there is no clear agreement as to which of these is the most effective. Potential mechanisms include the following: alteration in motor unit recruitment pattern with HA towards greater use of more efficient slow twitch fibers (141); altered thyroid activity after HA (175); and post-HA increased peripheral circulation that results in lower submaximal oxygen consumption (VO_2) because the skin has lower oxygen requirements than muscle or internal organs (12). Finally, a HA-induced reduction in the catecholamine response to exercise-heat stress has been proposed (95, 97) as a possible reason for the reduction in glycogen use post-HA, but the effect that lowered catecholamine levels might have on exercise metabolic rate has not been suggested. A reduction in exercise metabolic rate is a non-sweating means of affecting heat balance. This may

be of importance when wearing a CDE since the CDE impairs evaporative heat loss.

It is not clear from the literature whether the extent of the individual variability in physiological responses to HA is great enough to preclude forming a generalized prediction model for HA. Do the physiological responses of most individuals plateau at the same time points during the course of HA? Do all individuals achieve full HA by the last heat exposure? Only a few studies have addressed the extent of individual variability that can occur over the course of HA. Most of the studies (31, 102, 133, 150, 186) that have mentioned individual differences in HA responses reported marked differences, but did not provide reasons for these differences or fully account for factors that may have influenced the extent of the interindividual variance. Wyndham's laboratory studied the day-to-day changes in HA effector variables and reported significant individual variability in the cardiovascular and thermal responses of four subjects during a 10 day course of HA (102, 150, 186). One subject responded as if already acclimated with a heart rate (HR) 40 beats·min^{-1} less and a Tc 1°C lower than the others at the start of HA. Another subject had a insignificant reduction in Tc over the course of the HA, and a third subject had a HR 30 beats·min^{-1} greater than the others during the first five days of HA. The authors point out these interindividual differences, but they did not account for factors that likely accounted for most of the variation. The subjects exercised at different relative work rates, 37 to 52% VO_2 max, had body water deficits from 1.4 to 5.6% of body weight, and had BSA/mass ratios from 278 to 313 cm^2·kg^{-1}.

To accurately measure the extent of the individual variability, the investigator must ensure that the measured differences are actual individual differences and not the result of factors that can influence the degree of

physiological response to HA. Factors that must be controlled to elicit the true extent of individual variability include the: use of relative and not absolute rate of work, since core temperature (Tc) response is closely related to the relative work rate (44, 134); avoidance of exercise modalities that are subject to changes in task skill level (141); amount of fluid replacement since the variable levels of dehydration that can occur with *ad libitum* drinking (82) influence thermoregulatory and cardiovascular responses(105, 121); correction for non-sweat body weight changes in sweat measurements (103); avoidance of low dietary sodium intake during the HA regime (8); accounting for the body surface area (BSA)/mass ratio; and acute heat tolerance effectors such as inadequate sleep, medications, illness, alcohol abuse, substrate depletion, and sudden changes in physical activity (14).

In determination of the extent of individual variability, a study must control for the above factors and measure key thermoregulatory, cardiovascular and metabolic variables over the course of the HA regime. It must be noted that results from this work should be applied only to conditions similar to those under which the HA was conducted, as responses are specific to the type of environmental and exercise conditions used during the HA (11, 12, 175). The determination of the extent of individual variability would permit the investigator to answer the above questions, possibly form a general physiological model for responses to HA, and determine the level of caution necessary when recommending HA as means for reducing heat strain and extending work time in the CDE.

Whether or not physical training in thermoneutral or cool environments induces HA has been a controversial subject over the years. Today, investigators agree that physical training improves heat dissipation capabilities to the extent of providing a partial degree of HA (15). The

adaptations to physical training are similar to, but differ in degree and type to those induced by HA (15, 71). The primary adaptations to physical training that improve heat tolerance are an enhanced sweat response (23, 90, 98, 111) and an expanded plasma volume (37, 38), which result in lower body temperatures and heart rates for a given exercise-heat stress. Ten days of HA conducted after short-term physical training, 10 days at 70-80% VO_2 max, produced an even greater sweat response (111, 128), and similarly, HA performed after physical training further expanded plasma volume (149). Additionally, HA independently decreases both the exercise metabolic rate (175) and the salt losses in sweat and urine during exercise-heat exposure (14).

To provide any increase in heat tolerance a physical training program must exceed one week in duration (15, 111, 128, 158). Physical training in thermoneutral or cool environments will provide approximately 50% of the improvements in heat tolerance gained through HA (71) if interval or continuous training at intensities above 50% VO_2 max is employed for 8 to 12 weeks (71, 90, 111, 117, 128). In spite of the numerous investigations comparing HA and physical training, no literature exists on how the independent adaptations to HA and STPT could affect the physiological strain resulting from exercise while wearing a CDE.

The literature concerning individual protective clothing and associated equipment (*e.g.* fire fighting, industrial and military hazardous protection suits) is extensive. Studies on the CDE, just one aspect of the protective clothing literature, are numerous. These studies include documentation of the physiological strain associated with working in these highly insulative, semipermeable suits (16, 20, 25, 63, 100, 116, 170, 171); prediction of exercise-heat tolerance limits (17, 25, 100, 172); mechanical modifications

such as water or air cooled vests to enhance performance (21, 35, 107, 120, 153, 173); and mathematical modeling of heat tolerance while wearing these suits (6, 24, 180). HA and physical training are addressed in the models; however, the question remains, what are the direct and independent effects of HA and STPT on the physiological strain resulting from exercise while wearing the CDE? Do the physiological adaptations br ght about by HA and STPT increase one's work time prior to reaching excessiv thermal strain? Pilot data with HA suggest that an enhanced sweat response and a reduced exercise metabolic rate may increase total work time in the CDE.

HA is transient and decays without repeated heat exposure. There is disagreement in the literature on the rate of decay of HA. Complete HR and sweat rate (SR) adaptations and 50% of Tc reductions were lost in mine laborers after three weeks of DeA (178). However, Pandolf *et al* (118) reported only 18% of Tc reductions and 29% of HR reductions were lost after three weeks of DeA. The early adaptations to HA appear to be the first to decay (14, 39, 118, 178) and one heat exposure per week after HA does not prevent the decay of HA (122). Also, it is likely that a rapid gain - rapid loss phenomenon may occur with the increase in plasma volume (PV) and the concomitant increase in stroke volume (SV) that occur with STPT (80), since SV is reported to diminish more rapidly than other factors with detraining (41).

No investigation has examined the effects of DeA and DeT on the level of thermoregulatory, metabolic, and cardiovascular strain present while working in a CDE.

The US Air Force commander of a rapid deployment force is faced with the questions, "How best do we prepare airmen for flightline work in the CDE (possibly in warm or hot environment) in the limited pre-combat time (maybe

only 7 to 10 days) period? Also, how long will benefits of a HA or a STPT program last?" A systematic study investigating the effects of HA and STPT on exercise in the CDE will provide practical information to the commander, and also will provide valuable information on the physiological mechanisms behind HA and STPT that allow enhanced performance when working in the heat. Additionally, the commander can benefit by having the alternate choice of STPT to enhance heat tolerance since it would be more practical to have large numbers of airmen engage in STPT than could be heat acclimated in the same period of time.

STATEMENT OF PURPOSE AND SPECIFIC AIMS

The overall purpose of this dissertation is to evaluate and contrast the effects of HA and STPT on submaximal exercise metabolic rate and on physiological strain resulting from working in a CDE. Additionally, the extent of individual variability in response to HA and the effects of DeA and DeT on CDE performance will be investigated. The specific aims of this investigation are as follows:

Study 1 - Heat Acclimation and Short-Term Physical Training Effects on Exercise Economy and Individual Variability in Responses to Heat Acclimation

Specific Aims:

1. Determine the impact of a well controlled course of HA on metabolic rate during submaximal exercise in both hot and thermoneutral environments. This will be accomplished by comparing the physiological responses to submaximal treadmill exercise bouts (100 minutes at 25% VO_2 max) in both hot (43.3°C DB 50% RH) and thermoneutral (22°C DB 50% RH) conditions before and after a nine day course of HA, controlling for the confounding factors of fluid replacement, exercise habituation, and body weight changes. Key measures include exercise oxygen consumption, cutaneous blood flow, resting and exercise rectal temperature (Tre), catecholamines, plasma glucose and plasma lactate. Exercise oxygen consumption will also be measured during the first (the hot submaximal test doubles as the first HA trial), third, fifth, seventh and ninth HA trials.

2. Determine the impact of STPT on metabolic rate during submaximal exercise in both hot and thermoneutral environments. This will be accomplished by comparing the physiological responses to submaximal

treadmill exercise bouts (100 minutes at 25% VO_2 max) in both hot (43.3°C DB 50% RH) and thermoneutral (22°C DB 50% RH) conditions before and after nine days of high intensity interval run training, matched to the HA program for total energy cost and conducted in a thermoneutral environment (21-23°C DB 40-60%RH). Key measures include exercise oxygen consumption, cutaneous blood flow, resting and exercise Tre, plasma glucose and plasma lactate.

3. Investigate the extent of day-to-day individual variability that occurs over a well controlled course of HA. This will be accomplished by 1) comparing the physiological responses to submaximal treadmill exercise bouts (100 minutes at 25% VO_2 max) in both hot (43.3°C DB 50% RH) and thermoneutral (22°C DB 50% RH) conditions before and after a nine day course of HA, and 2) comparing day-to-day changes in key physiological variables during the nine days of HA. The following variables that influence heat generation, heat storage and heat dissipation will be measured during the thermoneutral and hot submaximal treadmill exercise bouts, and during the third, fifth and ninth HA trials: resting and exercise Tre, mean skin temperature (Tsk), HR, blood pressure (BP), cardiac output (Q), cutaneous blood flow, change in plasma volume (ΔPV), VO_2, sweat measurements, rating of perceived exertion (RPE), thermal sensation (TS), fatigue rating (FATR), plasma lactate, plasma glucose, and serum osmolality. SV, BSA, and heat balance equations will be calculated. Additionally, the amount of fluid replacement will be controlled. Tre, HR, BP, sweat measurements, RPE, TS, and FATR will be measured during all other HA trials. Catecholamines will be measured during the thermoneutral and hot submaximal treadmill exercise bouts.

Study 2 - Heat Acclimation and Short-Term Physical Training Effects on Physiological Strain Resulting from Work in a CDE

Specific Aims:

1. Determine the effect of HA on thermoregulatory, cardiovascular and metabolic responses during exercise in a warm environment while wearing a CDE. This will be accomplished by conducting 100 minute CDE exercise trials at 25% VO_2 max in a warm (30°C DB 50% RH) environment before and after a nine day course of HA. Measures to be obtained include: resting and exercise Tre, Tsk, HR, BP, Q, cutaneous blood flow, ΔPV, VO_2, sweat measurements, RPE, TS, FATR, plasma lactate, plasma glucose, and serum osmolality. SV, BSA, and heat balance equations will be calculated. Also, the amount of fluid replacement (FR) will be controlled.

2. Determine the effect of STPT on thermoregulatory, cardiovascular and metabolic responses during exercise in a warm environment while wearing a CDE. This will be accomplished by conducting 100 minute CDE exercise trials at 25% VO_2 max in a warm (30°C DB 50% RH) environment before and after nine days of high intensity interval run training, matched to the HA program for total energy cost and conducted in a thermoneutral environment (21-23°C DB 40-60%RH). Measures to be obtained include: resting and exercise Tre, Tsk, HR, BP, Q, cutaneous blood flow, ΔPV, VO_2, sweat measurements, RPE, TS, FATR, plasma lactate, plasma glucose, and serum osmolality. SV, BSA, and heat balance equations will be calculated. Also, the amount of fluid replacement will be controlled.

Study 3 - De-Heat Acclimation and Detraining Effects on Physiological Strain Resulting from Work in a CDE

Specific Aims:

1. Determine the effect of DeA on thermoregulatory, cardiovascular and metabolic responses during exercise in a warm environment while wearing a CDE. This will be accomplished by conducting a 100 minute CDE exercise trial at 25% VO_2 max in a warm (30°C DB 50% RH) environment three weeks after completing a nine day course of HA. Measures to be obtained include: resting and exercise Tre, Tsk, HR, BP, Q, cutaneous blood flow, ΔPV, VO_2, sweat measurements, RPE, TS, FATR, plasma lactate, plasma glucose, and serum osmolality. SV, BSA, and heat balance equations will be calculated. Also, the amount of fluid replacement will be controlled.

2. Determine the effect of DeT on thermoregulatory, cardiovascular and metabolic responses during exercise in a warm environment while wearing a CDE. This will be accomplished by conducting a 100 minute CDE exercise trial at 25% VO_2 max in a warm (30°C DB 50% RH) environment three weeks after completing nine days of high intensity interval run training. Measures to be obtained include: resting and exercise Tre, Tsk, HR, BP, Q, cutaneous blood flow, ΔPV, VO_2, sweat measurements, RPE, TS, FATR, plasma lactate, plasma glucose, and serum osmolality. SV, BSA, and heat balance equations will be calculated. Also, the amount of fluid replacement will be controlled.

HYPOTHESES

1. HA will reduce the submaximal exercise metabolic rate during exercise in both hot (43.3°C DB 50% RH) and thermoneutral (22°C DB 50% RH) environments.

2. STPT will not reduce the submaximal exercise metabolic rate during exercise in either hot (43.3°C DB 50% RH) or thermoneutral (22°C DB 50% RH) environments.

3. The HA-induced reduction in exercise metabolic rate during exercise in both hot (43.3°C DB 50% RH) and thermoneutral (22°C DB 50% RH) environments will be the result of a greater post-HA cutaneous blood flow response for a given exercise-heat stress.

4. HA will attenuate the catecholamine response to exercise in a hot (43.3°C DB 50% RH) environment.

5. HA will have greater sweat and cutaneous blood flow responses for a given core temperature than STPT during exercise in both hot (43.3°C DB 50% RH) and thermoneutral (22°C DB 50% RH) environments.

6. Substantial individual variability in thermoregulatory and cardiovascular responses to HA will occur over the nine day course of HA.

7. HA and STPT will significantly attenuate the amount of physiological strain that occurs with 100 minutes of exercise in the CDE at 25% VO_2 max in a hot environment.

8. The amount of physiological strain during the CDE test after DeA will be less than the amount during the CDE test prior to HA.

9. The amount of physiological strain during the CDE test after DeT will be the same as the amount during the CDE test prior to STPT.

SIGNIFICANCE

Because of the risk of thermal injury and the significant reduction in effective work performance when wearing the CDE, it is vital to better understand the possible benefits of HA and STPT during work when wearing a CDE. Resources have been spent on methods of altering the CDE microenvironment, such as portable cooling packs, to alleviate strain, and continued work in this area is justifiable. However, little attention has been placed on altering the physiological responses of the individual who must wear the CDE. It is well known that HA and physical training increase one's defense to the dangers of heat injury, but what are the independent effects of HA and STPT on the physiological strain resulting from exercise while wearing the CDE?

By conducting a well controlled study which follows the full course of HA it should be possible to determine: first, if the HA-induced reduction in exercise metabolic rate, a non-sweating mechanism, can provide a reduction of heat generation of a magnitude that will significantly affect the level of physiological strain experienced while wearing the CDE; and second, the extent of individual variability over the course of HA and therefore the level of caution necessary when recommending HA as a prophylactic measure. Furthermore, by conducting CDE exercise tests before, immediately after, and three weeks after nine day courses of HA and STPT it should be possible to assess the overall impact of these interventions on CDE performance and the physiological mechanisms responsible for the adaptations resulting from HA and STPT respectively.

This investigation will also lead to practical recommendations regarding the use of HA and STPT as preventive and preparatory measures

for the users of protective clothing. Finally, it is advantageous to have two potential procedures for attenuating the stress associated with wearing the CDE in unfavorable conditions since it is logistically easier to perform STPT than it is to heat acclimate.

REVIEW OF LITERATURE

The following review addresses the literature concerning the physiological alterations associated with heat acclimation and what is known about underlying mechanisms. An emphasis is placed on the effect of HA on exercise metabolic rate and the extent of individual variability that exists during a HA program. Of equal emphasis is a review of what is known concerning the possible influence of HA, STPT, and their respective decay over time on the physiological strain that results from exercise in the heat while wearing the CDE.

A. HEAT ACCLIMATION

1. Definition: HA is defined as the adaptive changes that occur when one undergoes repeated or prolonged heat exposure and the concomitant reduction in physiological strain produced by the hot environment (14, 175). HA is produced by repeated exposure to a heat stress sufficient to raise internal body temperature to levels that provoke moderate to profuse sweating. This is most effectively accomplished by exercising in the heat (175, 183). In this paper HA refers to exercise in the heat unless specified otherwise (*e.g.*, passive heat acclimation, sitting in the heat).

The terms acclimation and acclimatization are frequently used interchangeably; however, the recommendation of the International Union of Physiological Sciences states that the term acclimation refers to adaptive changes produced in the laboratory setting where as acclimatization refers to adaptations brought about by the natural environment (36).

2. Physiological Adaptations

a) List of Adaptations: Traditional hallmarks of heat acclimation are reduced thermal and cardiovascular (CV) strain manifested

primarily as a reduced HR and Tc and, secondarily, an alleviation of the symptoms of heat strain and increased sweat production during a given level of heat stress or exercise in the heat (129, 175). More specifically, the following HA-induced changes in physiological responses to a given exercise-heat stress are listed with the range of HA days required for that adaptation to plateau at approximately 95% of its maximal response:

- Decreased exercise heart rate, 2-6 days (14, 99, 102, 129, 133, 150, 165, 168)
- Increased resting plasma volume, 2-6 days (14, 102, 150)
- Improved defense of plasma volume during exercise-heat stress (14, 150)
- Increased resting and exercise stroke volume, 2-6 days (14, 102, 150)
- Increased heat loss via radiation and convection, 3-10 days (14, 128)
- Decreased rating of perceived exertion, 3-6 days (14)
- Decreased resting core temperature, 5-12 days (14, 102)
- Decreased exercise core temperature, 5-12 days (14, 99, 102, 129, 133, 165, 168)
- Decreased exercise skin temperatures, 5-12 days (14, 102)
- Decreased sodium chloride losses in sweat and urine, 5-10 days (5, 14, 49)
- Increased sweat rate, 7-14 days (14, 102, 182)
- Increased sweat sensitivity (*i.e.*, greater sweat production per change in Tc) (14, 64, 182)
- Increased exercise tolerance time (14)
- Decreased exercise metabolism (12, 14, 141)

These adaptations are for healthy well-nourished, adequately hydrated subjects. Importantly, dietary sodium and hydration status can affect these physiological adaptations to HA (8)

Interestingly, one report (176) concluded that after a course of HA subjects showed no improvement in mental adding tests conducted at three

different elevated body temperatures. The authors concluded that, for the functions tested, central nervous system adaptations did not occur in conjunction with the above physiological adaptations to HA.

b) Time Phases of Heat Acclimation: Robinson *et al* (129) reported that 80% of improvement in temperature regulation occurred within the first 7 days of HA, and the remainder by day 23. Conversely, Wyndham *et al* (184) observed that nearly the entire changes in HR, SV and PV occurred by the fifth day of HA. The rapid hemodynamic response and the latency of the sweat response are the main reasons why HA typically occurs in phases (14, 133, 175, 186). The two phases have been defined as follows:

Phase one: This phase includes primarily CV changes that progressively reduce the heart rate and CV strain associated with a given level of exercise in the heat (175). These CV changes include PV expansion and autonomic nervous system habituation which redirects cardiac output to skin capillary beds. These changes are proportional to a reduced RPE. The PV expansion and fluid regulatory hormone responses appear to be temporary and decay after eight to 14 days and are then replaced by longer lasting adaptations such as increased sweat rate (14, 175).

Phase two: In this phase, sweating begins earlier during a heat exposure, a given level of Tc elicits a higher sweat rate, and higher sweat rates can be achieved throughout the heat exposure (111, 128, 175, 182).

Wyndham *et al* (186) suggested four phases in central circulatory adaptations that could be distinguished from their data obtained over 10 days of HA. Phase one, or day 1 of heat exposure, was characterized by significant circulatory instability; a continuing fall in SV occurred throughout the heat exposure, but Q was maintained above control levels by a marked increase in HR. The second phase during days 2 and 3 of HA, was characterized by a

very rapid expansion of PV, thus attenuating the fall in SV and the increase in HR. Days 4-8 marked phase three where SV returned to near control levels and HR continued a slower decrease as PV expansion stabilized. Phase four occurred after the 6-8th day of HA and was associated with a decrease in Tre and Tsk. During this phase the decrease in HR was less than the decrease that occurred during phases two and three, SV decreased because of a reduction in PV, and therefore Q decreased toward control values. Sweat evaporation was the dominant factor for heat dissipation at this point (150, 186).

c) Resting and Exercise Temperature Changes: After nine days of passive HA, *i.e.*, 90 minute exposures in hot, dry conditions (45°C DB 24% RH), resting Tc significantly decreased by 0.2°C. The authors suggested this was due to a reduction in the thermoregulatory set point (89). Cycling at 75 watts in hot, humid conditions resulted in a decrease in resting Tc of 0.5°C by the seventh day of 10 days of HA (102). In a hot, humid environment, the difference between heat acclimated and non-acclimated subjects is delineated in part by the lower resting Tc of the heat acclimated subjects (74). A decrease in resting Tc will result in a reduced exercise Tc if the same amount of heat is produced for a given exercise-heat exposure. Thyroid alterations or a reduced resting metabolic rate have been suggested as possible mechanisms for a reduced resting Tc (175).

Mitchell *et al* (102) reported no changes, other than reductions due to lower resting Tc, in the Tc response during the first hour of four hour HA trials over a 10 day course of HA. All reductions observed in Tc occurred after the first hour of the exercise-heat exposure. Also, Tc and Tsk did not decrease during the first four days of HA, but significant drops occurred during days 7 through 10, and were attributed to simultaneous increases in

sweat responses. Apparently, decreases in resting Tc and exercise Tc and Tsk are primarily due to an enhanced sweat response, altered metabolic rate, and possible shift in temperature set point (175).

Givoni and Goldman (73, 74) have developed equations that describe the HA-induced exponential changes in Tc as a function of the number of days of exposure to work in the heat for any temperature and humidity combination. Higher metabolic heat production and environmental stress during HA will result in greater Tc differences between the acclimated and non-acclimated states. The authors predict that HA will, at a maximum, decrease initial Tc 0.5°C and working Tc 1.7°C, or 1.2°C excluding the 0.5°C difference in initial Tc. They also estimate in their equations that with each missed day of HA, an equivalent of half a day of HA benefit is lost.

d) Sweating Alterations

1) Sweating and Evaporation: After HA the combined physiological mechanisms for heat dissipation are greater at any given body temperature, so heat balance during exercise in the heat is achieved at lower Tc and Tsk. Because of the cooler skin and resulting change in sensible heat exchange, sweat rate must be greater after acclimation (175). HA increases sweating capacity to as much as 2-3 liters per hour with maximum daily rates of 10-15 liters (175); however, if the absolute rate of sweating does not exceed 400-600 $ml \cdot hr^{-1}$ during the HA exposure, increases in whole body sweat rate may not be experienced (9, 14). The rate of sweat evaporation depends upon air movement, the gradient between skin and ambient water vapor pressures, the evaporative heat transfer coefficient, and the fraction of wetted skin surface area. Physiological limits are sweating rate, regions of the total skin area involved in sweating, and state of hydration (135, 143, 175).

Sweating is a powerful means of heat dissipation because of the high latent heat of evaporation of sweat. The heat of evaporation of sweat, 2426 Joules per gram of sweat (0.58 kcal·g^{-1}), has been found to be independent of ambient temperature and humidity (162, 174) and is not appreciably affected by sweat solutes (174). Therefore, an individual exercising at a work rate of 280 W (oxygen consumption of 4 liters·min^{-1}) with an exercise efficiency of 20% requires heat dissipation of 67 kJ·min^{-1}. With the heat of evaporation of 2.43 kJ·g^{-1} this individual needs to sweat at a rate of 27.6 g·min^{-1} or an estimated 1.65 liters·hr^{-1} (143).

2) Neural Control: Sweat glands respond primarily to sympathetic cholinergic stimulation, but circulating catecholamines, epinephrine more than norepinephrine, can also stimulate eccrine sweat action. With increasing sweat rates more sweat glands are recruited first, then increased sweat production per gland occurs (143).

3) Body Temperature Relationships and Sweat Gland Changes: Sweat production depends upon the central nervous system signal and the morphological characteristics of the sweat gland, and HA induced changes in sweating are due to changes in both the sudomotor signal and the sweat glands themselves (34, 175).

Sweating is a function of Tc, Tsk and local Tsk (109, 110, 114). Changes in Tc provide the primary input to the thermoregulatory center for sweating (143), roughly ten times that of similar changes in Tsk (108). Nadel *et al* (109) independently controlled Tc, Tsk, and local Tsk with exercise, radiant heating and perfusion chamber for local temperature clamping, respectively, to measure the different influences on SR. They found that SR responded: linearly to changing Tc with Tsk and local Tsk held constant, linearly to changing Tsk with Tc and local Tsk held constant, and

exponentially to altered local Tsk with Tc and Tsk held constant. The mechanism by which local Tsk affects sweat response is unclear, but it could be a greater release of neurotransmitter substance for a given sudomotor signal, increased glandular responsiveness per amount of neurotransmitter, or a Q_{10} effect on the secretory coil (108, 109, 143).

HA results in increases in the maximal SR, as indicated by a higher plateau of the SR-Tc curve post-HA (182). Also, a shift in the threshold and an increase in the slope of the SR-Tc curve occur after HA. The threshold change is considered by some as a potentiation in sweating via a change in the central sweat drive, while the change in slope is a potentiation in sweating via a peripheral, or glandular change (111). The onset of sweating begins at a lower Tc (and lower Tsk). This is a leftward shift of the threshold and is considered by some to be a change in the thermoregulatory setpoint (43, 77, 89, 111, 128, 154, 182). The amount of threshold shift varies according to the environment used during HA and post-HA testing; generally, a greater shift has been observed when hot humid HA was employed and for tests done in the heat.

An increase in sweat sensitivity, the slope or "gain" of the SR-Tc curve, has also been reported post-HA, but the magnitude of change appears to partially depend upon study conditions. When compared over 45 different combinations of saturated air temperature, wind velocity and rate of work, heat acclimated men had a significantly greater slope of the SR-Tc curve than did unacclimated men (182). Frye and Kamon (64) reported significant increases in the slope of the SR-Tc curve after HA in hot, dry conditions and a trend towards increases in slope was shown by Henane and Bittel (89) with passive HA in hot, dry conditions, and by Roberts *et al* with post-HA tests conducted at 25°C ambient temperature (128). However, Craig *et al* using

passive HA in a hot, dry environment reported no change in slope (43), and Nadel *et al* concluded that HA does not alter the slope of the SR-Tc relationship (111), but did report greater changes in gain constants for three of their six subjects that acclimated with a warm, humid procedure versus a hot, dry one used for the others. It appears that the level of humidity during HA affects the amount of peripheral change in the sweating mechanism (sweat gland adaptation) that occurs.

The increase in sweat rate is also due to increases in both sweat gland sensitivity to sympathetic stimulation and sweat gland capacity. Increased sweat secretion during HA "trains" the sweat gland making it more sensitive to a given stimulus (175). This is supported by the work of by Chen and Elizondo (34) who suppressed sweating with local cooling during HA, thus reducing the effect of HA on the sweat glands in the local skin region by not allowing the glands to "train". Additionally, significant morphological changes and greater cholinergic sensitivity were found in sweat glands dissected from patas monkeys heat acclimated for three weeks. Pre to post-HA comparisons showed the glands hypertrophied during HA, as measured by tubular length and volume. Sweat rate increased both per gland and per unit tubular length of secretory coil, indicating an increase in sweating efficiency. The glands also produced more sweat per fixed dose of methacholine, demonstrating increased sensitivity to central nervous system stimulation (136).

4) Distribution of Sweating and Skin Wettedness:

The number of sweat glands per unit of skin surface area varies considerably between body regions; the sweat secretion for a region of skin is dependent upon both the density of sweat glands and the sweat output per gland (143). Nadel *et al* (110) found that the rates and pattern of recruitment of sweating

varied markedly over the body. During exercise at 80% VO_2 max at 26°C ambient temperature each region increased its sweat rate linearly with increased Tc, but differences in gain and onset existed. There was a tendency for the back, chest, and abdomen to begin sweating sooner and at greater rates than the arms and legs. The authors attributed these differences to local factors of gland density, and the density and distribution of nerve branches in contact with the sweat glands. HA alters these regional sweating rates and patterns by not only increasing regional sweat rates, but also by making sweating more uniform over the total body surface (175). One study found greater absolute increases in SR on the arms compared to the chest after hot, humid HA, but the chest sweating still provided more cooling due to the larger chest surface area (154). Hofler (91) reported an increase of the percentage contribution of the limbs to the total SR from initial values of 28-42% to 34-54% of total SR after 35 days of warm, humid HA. Subjects in the same study acclimated under hot, dry conditions showed no change in the relative contribution of limb SR. Higher limb sweating makes better use of the total BSA for evaporating a greater portion of the total sweat produced and evaporative coefficients are higher on the limbs for geometric reasons, thus a shift of SR distribution towards the limbs by HA increases evaporative efficiency (31, 91, 175).

By increasing SR over the entire skin surface, HA increases skin wettedness, defined as the fraction of the BSA covered by evaporative moisture and determined as the ratio between sweat evaporated from the skin to the maximum evaporative capacity of the environment (76). Candas *et al* (31) found increases in the skin wettedness ratio across 16 different environmental conditions from 0.50-0.83 before HA to 0.65-1.00 after HA. This adaptation led to a decreased sweating efficiency, *i.e.*, the ratio between

sweat evaporated to the sweat rate, as sweat drippage increased; at wettedness ratios above 0.80 more than 10% of the sweat dripped off without evaporating. However, sweat drippage should not be considered physiologically inefficient, because higher wettedness ratios are usually achieved through increased sweating on the best evaporative skin areas, the limbs. In humid conditions where 50-80% of the skin area must be wetted to maintain required evaporation, the acclimated individual can increase skin wettedness to maintain steady state body temperature even though a greater amount of sweat is lost to drippage. The nonacclimated individual can only increase evaporative rates by increasing Tsk to increase skin vapor pressure, and therefore cannot maintain thermal homeostasis (31).

The above changes are especially helpful when exercising in humid heat where greater sweat suppression occurs.

5) Hidromeiosis and Sweat Gland Fatigue: Wetting of the skin surface suppresses sweat secretion, an effect called hidromeiosis (31, 44, 57, 77, 112, 143). Mechanisms for hidromeiosis are not firmly established, but hypotheses have been proposed. Nadel and Stolwijk (112) proposed an osmotic gradient hypothesis, suggesting that sweat follows a gradient, formed by solutes remaining from evaporated sweat, to the skin surface. Hidromeiosis develops when excess water dilutes the gradient and therefore SR decreases. Brown and Sargent (27) proposed the more widely accepted hypothesis that hydration of the skin causes stratum corneum swelling and a resulting mechanical obstruction of the sweat duct.

Maximal SR is known to increase after a course of HA, but investigators propose that sweat gland "fatigue" occurs during prolonged heat exposure both before and after HA. Mitchell *et al* (102) found that the SR peaked at the end of the first hour and then declined progressively for the

remaining three hours of a four hour heat exposure. This pattern during the heat exposures did not change with HA even though HA resulted in marked increases in overall sweating capacity at any given point. Wyndham *et al* (188) had 10 men complete five hour exposures to 50 different combinations of environmental conditions and work rates and showed that the duration of heat exposure had the effect of decreasing both the maximum sweating capacity per given Tc and the slope of the SR-Tc curve. They attributed the decrease in sweat capacity and sweat sensitivity to fatigue of the sweat glands. Another study reported sweat gland fatigue as the reason for decreased SR in the latter portions of prolonged heat exposures and for a decreased responsiveness of the eccrine glands to subdermal injections of a sudorific agonist after continuous heat exposure (169).

In spite of these studies it is unlikely that sweat gland fatigue is the reason for the decline in SR after approximately two hours of heat exposure. Increasing the evaporative capacity of the environment by moving the subject from moist heat to dry heat (3), drying the skin with towels, or increasing air velocity (112), reverses the decline in SR. Skin stripped of the stratum corneum did not show sweat gland "fatigue" during a prolonged heat exposure, leading to the conclusion that hidromeiosis accounts for the reduced SR observed during a prolonged heat exposure (27). This conclusion was supported by Gonzalez *et al* (77) who exercised subjects at low intensity in 40°C with gradual increases in vapor pressure from 12 to 49 mm Hg (20 to 90% RH) during the exercise-heat trials. As vapor pressure increased, inhibiting evaporation, SR rapidly declined prior to elevations in esophageal temperature or before maximum evaporative capacity of the environment decreased to its lowest level indicating that sweat decline was closely associated with increases in ambient and skin vapor pressures. This pattern

led the authors to conclude that the cause for the decline in SR was hidromeiosis and not sweat gland fatigue or a change in central sweat drive. Interestingly, in this same study six days of HA resulted in significantly less decline of the SR with transient increases in ambient vapor pressure.

A classic study by Fox *et al* (57) also showed that the sweat suppression phenomenon, hidromeiosis, was not independent of HA. They passively acclimated two groups of subjects for 12 days, one in a hot, dry climate and the other in a hot, humid climate produced by vapor-barrier suits. Local sweat measures were accomplished by encasing the left arm of the subjects in a plastic collection bag, creating a moist microenvironment for the arm. Standard decreases in Tc and HR and increases in SR were observed during a post-HA test of intermittent exercise in 40°C DB/32°C WB environment. In a second post-HA test the subjects sat passively in a very humid environment. Both groups had the same whole body SR but the SR of both arms of the hot, humid group and the left arms of the hot, dry group increased significantly and nearly equally, whereas the right arms of the hot, dry group showed little change from pre-HA levels. Additionally the bagged arms had much less of a marked decline in SR during the two hour post-HA exposure versus the pre-HA test; the right arms of the hot, dry group had the same decline in SR during the very humid post-HA as during the pre-HA test. The authors concluded that the hot, dry and the hot, humid HA procedures increased sweat gland secretory capacity, but the hot, humid HA procedure also lessened the hidromeiotic effect. They suggest that hot, humid HA causes maceration of the skin leading to a partial shedding of the terminal keratinized portion of the sweat ducts and thus less mechanical obstruction of sweating.

In addition to HA reducing the decline in SR during humid heat exposure, HA reduces the amount of glycogen depletion in the sweat glands caused by acute heat stress (175).

6) Composition and Salt Balance: Sweat is hypotonic to extracellular fluid; sodium concentrations in sweat vary widely from 5 to 60 $meq \cdot l^{-1}$ (175), and chloride concentrations also vary widely, from less than 5 up to 100 $meq \cdot l^{-1}$ (48, 49). Sodium is reabsorbed from sweat, after secretion, during its passage down the sweat duct and the rate of sodium reabsorption has a maximum limit (5). Sodium reabsorption does not increase proportionally with increasing SR, so sodium concentration in sweat increases with SR (5, 48, 49, 175). Sweat chloride concentration also increases with increasing SR (48, 49).

Several factors can affect the sweat sodium and chloride concentrations: SR, mineralocorticoid action (175), exercise intensity (13), dietary salt intake (8), possibly hydration state (13), and HA, which increases the sweat gland's ability to reabsorb sodium and produce a more hypotonic sweat (175). HA reduces the sweat salt concentration at any given SR (4, 5, 48, 49, 60) and reduces the slope of the sweat sodium-SR curve, indicating proportionally greater reductions in sweat sodium loss at higher sweat rates (5). This salt conservation with HA is the result of a multiple hormonal response (see endocrine section below) to heat stress to prevent electrolyte imbalances. Aldosterone acts as the primary salt-sparing hormone, as shown by work with spironolactone, a competitive antagonist of aldosterone that increases sweat sodium concentration in subjects during HA (175). However it has been reported (161) that the sodium conserving response of the sweat glands during HA is dependent upon the whole body sodium deficiency and attendant water deficit; if salt intake is elevated then sweat sodium reduction

with HA will not occur. Other studies report that sweat sodium conservation occurs with HA independent of salt balance. Allan and Wilson (5) found lower sweat sodium concentration for any given SR after HA than before, even when salt deficit was prevented by ingestion of a saline solution. Additionally, Davies *et al* (45) reported that saline ingestion had no effect on the reduction in sweat sodium concentration that occurred with HA, even though it attenuated plasma aldosterone levels during HA bouts. In this study and in others (52, 60), plasma aldosterone significantly increased with acute heat stress, but was either unchanged or slightly reduced over the course of HA. Kirby and Convertino (96) did find lower plasma aldosterone levels after HA, but sweat sodium losses still decreased 59%. They proposed that HA increased the sweat gland responsiveness to aldosterone.

It is apparent that sweat sodium conservation occurs with HA regardless of sodium deficit levels. Also, plasma aldosterone concentration, although potentiated by a sodium deficit, appears to be determined primarily by the acute stress of heat and exercise (45) and may or may not decrease over the course of HA. Sweat salt conservation could be the result of morphological changes in the sweat gland or increased responsiveness of the sweat gland to aldosterone. Increased glandular responsiveness appears likely as HA-induced cardiovascular and body temperature alterations lead to increased splanchnic blood flow (125, 130, 131) and increased hepatic clearance of aldosterone (175).

In summary, HA induces changes in sweating that are essential for the body to increase heat transfer from the skin surface to the environment; HA induced cardiovascular alterations allow for improved transfer of heat from core to the surface.

e) Cutaneous Blood Flow Changes: At lower thermal loads when sweating does not occur, an increase in skin blood flow (SkBF) provides cooling by increasing sensible heat loss. When sweating is active SkBF primarily provides heat loss by transferring heat to the skin for removal by evaporation (143). Reductions in skin blood flow with HA have been suggested by some (133), and this is most likely due to the lower exercise body temperature achieved over a course of HA. However, Roberts *et al* (128) clearly showed that SkBF is higher for a given Tc following HA; the vasodilation threshold is shifted to a lower Tc by HA. Therefore, it appears important to distinguish between SkBF at a given Tc and Tsk and SkBF for a given exercise-heat stress (175).

As mentioned above, HA-induced changes in the threshold for the onset of sweating and an increase in maximal sweating levels have been reported; however, maximum SkBF after HA has not been measured (175). Gonzalez *et al* (77) reported higher chest skin conductance after six days of HA, implying an increase in maximal SkBF at a constant Tc, but SkBF levels were not actually measured.

SkBF and sweating appear to work in tandem to dump heat from the exercising body. Vasoactive intestinal polypeptide, or other vasoactive polypeptides such as histamine (66), may be released from sweat glands during exercise-heat stress and act on the local vasculature to vasodilate the cutaneous vessels (143). This agrees with the findings that the HA-induced shift in the SkBF-Tc curve parallels the similar HA-induced shift in the SR-Tc curve (175).

The increase in SkBF during the early phase of HA is important for heat transfer as sweating improvements do not occur until later in the course of HA (127). Rapid increases in blood volume and increases in venous tone

(181) permit the increases in SkBF (133). Eventually, changes in the sweating mechanism increase the Tc-Tsk gradient and SkBF demand decreases. Humid heat presents a slightly different situation as less of an increase in the Tc-Tsk gradient occurs due to limited evaporative heat transfer and demand for SkBF remains over a longer portion of the HA (102, 127).

f) Other Cardiovascular Adaptations: An early study by Taylor *et al* (168) reported that cardiovascular adjustments during HA are complete in approximately four days and the first two days are critical for successful HA. The expansion of PV is the primary driver for these critical adaptations.

1) Plasma Volume: Several studies have reported PV expansion with HA, a vital early HA adaptation (8, 39, 56, 95, 145, 146, 148-150, 184). Expansion of PV occurs rapidly, starting after the first heat exposure, but decays after seven to 14 days of HA (14). Greenleaf *et al* (83) reported increases in PV and BV of 10.6% and 6.5%, respectively, in women; and 11.9% and 7.5%, respectively, in men after six days of a 12 day HA routine of cycle exercise at 44 to 49% peak oxygen uptake in the heat, 40°C DB, 42%RH. In a nine day HA study using treadmill walking (8), PV increased 16.3% by day four, but was only 10.7% above control at day nine. Also, bench stepping in the heat for 17 days resulted in PV expansion of 10.4% after five days, but only 4.8% at the end of the study (184). Finally, comparing only pre- and post-HA values, Bass *et al* (22) reported no change in PV over three weeks of combined HA and physical conditioning. Without intermediate measures the daily changes in PV can be missed.

Some of the techniques used for measuring PV changes were questioned by Wyndham (183), who stated that labels attached to plasma

proteins may give misleading results on the fluid shifts that occur during HA. Fortney and Senay (56), using the carboxyhemoglobin method, reported lower absolute values in PV expansion than those using protein labels.

Different reasons for the disproportionately larger expansion of PV than extracellular fluid or total body water with HA (184) have been proposed. Wyndham *et al* (184) speculated that sodium and water retention were the causes of PV expansion, but this is doubtful due to findings of PV expansion and reductions in body weight occurring simultaneously with HA (8, 150). Furthermore, Wyndham later (183) countered his own hypothesis when he compared the smaller change in the extravascular space to the change in PV in his previous work (184).

Senay (145, 146, 150, 184) proposed that PV expansion during HA was due to protein and fluid translocation from the interstitial space to the vascular space. He stated that the influx of protein into the vascular space was not specific to HA, since exercise in thermoneutral conditions produced a similar response, but retention of the protein in the vascular space was dependent upon heat exposure. Ten days of HA produced a net gain of 32 grams of protein in the vascular space with 55% of the gain between the first two days of HA; whereas the exercise control group added protein to the vascular space but did not have the retention that occurred with HA (150). Senay postulated that HA, by increasing limb blood flow, helps to "flush" protein from the cutaneous interstitial space to the lymph and in turn to the vascular space, producing an increased ability to hemodilute rapidly and early in exercise-heat exposure (145, 150). Therefore, even after weeks of HA and the concomitant decrease in the amount of resting PV expansion, PV during exercise can still remain high due to this rapid hemodilution response.

Hubbard *et al* (93) compared the effects of albumin infusion on the diurnal response of PV expansion in hot and thermoneutral environments. Heat exposure, after a 25 gram albumin infusion, extended the retention time of the infused albumin and resulted in a more prolonged increase in oncotic pressure as compared to thermoneutral exposure, thus lending support to Senay's hypothesis. Harrison *et al* (88), however, questioned Senay's hemodilution hypothesis. They had subjects cycle in the heat and found a 14.7% PV increase after 11 days, and also observed a gradual increase over the 11 day period in the magnitude of hemoconcentration occurring during exercise, and for this reason concluded that hemodilution does not play a primary role in HA-induced cardiovascular adaptations. However, even though hemoconcentration occurred, the blood volume during exercise was still almost 7% greater at the end of HA than at the beginning (175).

Senay calculated that each gram of protein added to the vascular volume by HA was accompanied by 15.2 ml of fluid. Armstrong *et al* (8) found an expansion of 62.1 ml per gram of protein during HA for their high sodium diet group and only 9.4 ml per gram of protein for their low sodium diet group. Therefore, their data suggest that PV expansion during HA involved not only protein influx, but a combination of osmotic and oncotic forces, or other possible mechanisms such as cardiovascular baroreceptor control, antidiuretic hormone, cortisol, or glucocorticoids.

Convertino *et al* (39) attempted to separate the roles of exercise and thermal stress on the mechanisms of hypervolemia resulting from training and HA programs. One group of subjects trained at 60-65% VO_2 max for two hours per day for eight days in thermoneutral conditions while a second group passively acclimated to 42°C / 93% RH for the same time period. The mean Tc response over the two hours was the same for both groups, and this

was confirmed by equal areas under the Tc response curves. The exercise group increased PV 427 ml (12%), and the passive HA group increased 177 ml (5%). The results suggest that about 40% of exercise induced hypervolemia could be attributed to a thermal stimulus, body temperature increase, and the remaining 60% from nonthermal factors related to exercise. The authors propose that most of the increase in plasma protein content that occurs with classical HA is due to the exercise stimulus rather than to the thermal stimulus since the differential plasma protein increase between the two groups (31 grams for exercise group and 6 grams for passive HA group) was independent of the change in core temperature.

Several factors do influence the often extremely variable intravascular fluid response to exercise-heat stress (147) and can therefore influence results of HA studies. Studies by Senay (145, 146, 150) reporting hemodilution with HA conflict with work by Harrison *et al* (88) who find hemoconcentration with HA. Reviews by Sawka (138) and Harrison (86) systematically discuss the many influencing factors. Briefly one must consider premeasurement conditions; exercise modality, intensity and duration; ambient environment; subject acclimation and training states; and subject diet and hydration.

Posture and ambient conditions can alter PV measures. Moving from a supine to a standing position at rest can decrease PV 16% (84) and PV responses are dependent upon the skin temperature obtained immediately prior to heat stress (87). Exercise posture and modality also influence intravascular volume changes. Diaz *et al* (46) reported a 17% and a 2% PV reduction during 45 minutes of rest in the heat in an upright posture and a supine posture, respectively. A subsequent 45 minute bout of exercise in the heat while maintaining the same posture produced a further PV reduction of 3% in the upright and 11% in the supine.

Miles *et al* (101) compared arm crank exercise to cycling, and for a given submaximal VO_2 found a greater PV reduction for arm crank exercise; they attribute the greater PV efflux to the higher mean arterial pressure during arm crank exercise. Cycle, bench step, and treadmill exercise each have different PV responses (86, 88, 138, 147).

Subjects with prior heat acclimation or endurance training will have expanded resting plasma volumes and more stable responses during exercise-heat stress (37, 147). Subject diet, especially sodium intake, must also be considered as an influencing factor (8). Finally, hydration prior to and during exercise-heat stress will influence PV responses. Gaebelein and Senay (65) reported that pre-exercise fluid status affected the extent of change in osmolality and hemoglobin during exercise. After 10 days of HA, hemodilution occurred for euhydrated subjects and hemoconcentration for hypohydrated subjects during light intensity exercise in the heat (139). Similarly, Senay (145) reported that hemodilution during light exercise (35 watts) in the heat depended upon subject hydration status.

Senay *et al* (150) states that PV expansion after the first two exercise-heat exposures is the single most important mechanism responsible for HA. He concludes that the early changes in body temperature during HA are due to increased cardiovascular stability brought about by PV expansion. Others doubt that PV expansion has a direct thermoregulatory effect. Mitchell *et al* (102) concluded from the same experiment as Senay (150) that the HA-induced increase in sweat evaporation was the primary reason for the decreased body temperature and whatever events that contributed to the reduction in HR had little or no effect on the subjects' heat loss.

Sawka *et al* (140) artificially expanded PV prior to treadmill exercise in 45°C heat and found lower heart rates during the walk, but no differences in

Tc, SR, or final HR from control values. Similar responses were found by Fortney *et al* (54) when subjects cycled at 60% VO_2 max in the heat the day before and one hour after infusion of stored blood; HR decreased, Q and SV increased during exercise, but Tc and SR were not affected by the PV expansion. This same group, in a similar study, artificially expanded PV with albumin infusion prior to exercise and reported no differences in SR, but did find a small decrease in Tc of 0.11°C (55). They speculate that a greater cutaneous perfusion could account for the decrease in Tc; however Sawka (138) states that the protocol used to induce hypervolemia may affect physiological responses. Finally, Montain and Coyle (104) also showed that fluid replacement and not blood volume expansion during exercise reduced hyperthermia during two hours of cycle exercise at 62-67% VO_2 max.

After the initial phase of HA the level of PV expansion tapers and eventually returns to control values (8, 14, 22, 83, 184). How the body maintains a lower HR after PV expansion diminishes later in a course of HA is not clearly known. According to Wenger (175) it is possible that after several weeks of HA the body may use SkBF more efficiently for heat dissipation, and therefore is able to exercise at a given intensity in the heat at lower levels of PV, SV and Q. Another possibility is Senay's hemodilution hypothesis that PV during exercise can still remain high due to a greater and more rapid hemodilution response to an acute exercise-heat bout is developed over the course of HA (145, 150). Further support for this hypothesis was provided by Senay and Kok (148) who found that heat intolerant subjects failed to hemodilute to the same degree as heat tolerant subjects during exercise at the same relative intensity in the heat. One problem is that Senay assumes the hemodilution response observed early in HA when resting

PV is elevated is greater later in HA when resting PV has returned to control levels (175).

In summary, no matter the mechanism, PV expands early during HA and is the key for cardiovascular stability during the initial phase of HA. As HA progresses PV expansion gives way to improved sweating mechanisms and returns to control values. Increases in total body water and interstitial fluid that occur with HA (37, 184) provide the fluid base for the copious sweating that occurs later in the course of HA.

2) Heart Rate / Stroke Volume / Cardiac Output / Blood Pressure: HR and SV change in proportion to the PV expansion; during work in the heat HR is lower and SV is higher after HA compared to before HA (133, 184). Three explanations have been proposed for the decreased heart rate and increased stroke volume over the course of HA (175, 183). The first and strongest explanation is PV expansion. Even though the increase in PV declines after approximately 4-10 days of HA, Senay's concept of a rapid hemodilution response during an acute bout of exercise-heat stress, which develops after the initial days of HA, may explain the maintenance of lower heart rates throughout HA. At minimum, the increased PV early in HA plays an important role in ameliorating the high initial CV strain. Secondly, increased venous tone up to day four of HA was reported by Wood and Bass (181), but their measurement technique has been questioned (183). Also, Wenger (175), citing unpublished data from the Natick laboratory, states that HA lowers the Tc threshold for venodilation. Lastly, Rowell (133) hypothesized that the increased sweating with HA reduces Tsk and in turn Tc, and that a lower heart rate is secondary to these decreases. This is unlikely in that the decrease in heart rate precedes both the decrease in Tc and the increase in sweat response (183).

With the same data sets Givoni and Goldman used for predicting Tre changes with HA, they developed an equation for predicting the decrease in HR over a course of HA. They concluded that the largest difference between heat acclimated and non-acclimated individuals for peak exercise HR was approximately 40 beats·min^{-1} (74, 75).

Several studies have shown that HA improves orthostatic tolerance, demonstrated by an improved response to a 70° head-up position tilt test, in both hot (156, 160) and temperate (83, 155, 156) environments. This improvement in orthostatic tolerance is a result of the HA-induced increase in PV. In the study by Shvartz *et al* (160), the improvement in HR and Tc responses during HA paralleled the amount of improvement in heat orthostatism. For eight days subjects completed four hours of HA per day, bench stepping at a 35 watt work rate in humid heat (34°C DB 32°C WB), followed by a 70° head-up position tilt test in the same environment. The number of subjects experiencing syncope during the tilt tests decreased in the same pattern as the decrease in HR; fainting was significantly related to high HR and to a lesser extent high Tc. The largest improvement in heat orthostatism occurred on the second and third days of HA when most of the increases in PV and venous return had occurred, suggesting that improvement in heat orthostatism is related to HA-induced cardiovascular adaptations.

Cardiac output is reported to increase (113, 186) or remain unchanged (133, 184) with HA. Little is mentioned about the redistribution of cardiac output after HA, but lower Tc and HR may be associated with less vasoconstriction in splanchnic and renal beds during exercise in the heat (130).

HA does not change systolic blood pressure at rest, but diastolic blood pressure decreases, probably due to higher stroke volume and lower total peripheral resistance (133, 175).

g) VO_2 max and HA: In general, studies have reported that VO_2 max did not change (95, 97, 175) or slightly increased (144, 190) with HA. Sawka *et al* (144) conducted cycle ergometer maximal oxygen uptake tests in the hot and moderate environments before and after a nine day HA program that used walking for the exercise. VO_2 max was lower in the hot environment relative to the moderate environment both before and after HA by 8% and 7%, respectively. VO_2 max was higher by 4% after HA in both environments.

h) Metabolic Effects: HA significantly affects exercise metabolic rate, this is covered below in Section B. Plasma and muscle lactate accumulation was lower during 30 minutes of cycle exercise at 70% VO_2 max in hot (49°C) and cool (21°) environments after nine days of HA (190). The authors state that the reduced lactate levels are due to the lower exercise metabolic rate in their subjects after HA and not due to a heat-induced redistribution of Q since lactate was lower in cool conditions as well as in the heat. King *et al* (95) found lower blood lactate concentrations after HA during cycle exercise at 50% VO_2 max in the heat (40°C), but only during the first 30 minutes of a six hour intermittent exercise bout.

Muscle glycogen use during both intermittent (95) and continuous (97) exercise at 50% VO_2 max in the heat was significantly lower after HA. The 42% (95) and 47% (97) reductions in glycogen use after HA were not due to an exercise training effect as VO_2 max and citrate synthase activity did not change post-HA. Kirwan *et al* (97) ruled out a learning effect as reason for less glycogen use after 8 days of HA even though others (40) suggest less

glycogen use may be attributed to a learning effect observed in experienced cyclists. Some, but not all of the glycogen sparing probably resulted from a small but significant increase in lipid oxidation (97).

Both King *et al* (95) and Kirwan *et al* (97) suggest that less glycogen use after HA could have been due to increased muscle perfusion or reduced catecholamine levels. The increased perfusion of active muscle after HA, allowing increased delivery of blood-borne substrates (130, 133) is unlikely since recent work showed that active muscle blood flow was not reduced over control values when heat stress was imposed during exercise at a constant work rate (115, 137). Although not measured in these two HA studies (95, 97), lower catecholamine levels during exercise in the heat might have occurred after HA (99). Lower norepinephrine levels would permit increased splanchnic circulation (125, 131) and a concomitant increase in hepatic glucose delivery. However, Kirwan *et al* (97) found no differences in leg muscle glucose uptake post-HA. Finally, reduced epinephrine levels post-HA could have resulted in a decreased rate of glycogenolysis (97).

i) Hormonal Changes: Acute hormonal responses to a bout of exercise in the heat are designed to reduce urinary fluid loss, promote heat dissipation, maintain blood flow to the exercising muscles and preserve plasma volume and cardiac stability (59). The levels of response are typically altered by HA.

Circulatory and sweating responses to the initial heat exposure of a HA program initiate a hormonal cascade (59, 175) that starts with the secretion of adrenocorticotrophic hormone (ACTH), and if the plasma becomes hyperosmotic (39) antidiuretic hormone (ADH) or vasopressin. ACTH stimulates the adrenal cortex to secrete aldosterone and cortisol, both act to conserve sodium. The heat stress also increases renal sympathetic

stimulation and catecholamines, and decreases renal blood flow, all of which activate the renin-angiotensin system. Angiotensin also stimulates aldosterone secretion and maintains its blood levels as ACTH levels diminish. The renin-angiotensin-aldosterone system and cortisol act first on the kidneys and later on the sweat glands to conserve sodium. After a few days sodium balance is restored and the kidneys stop retaining sodium, but the sweat glands continue (59, 175). Conservation of salt is necessary for the body to optimally maintain plasma and extracellular fluid volumes (14).

ADH works to decrease urinary fluid loss and conserve body water and electrolytes during exercise in the heat (59) and it may play a role in expansion of resting PV or the hemodilution response to exercise-heat stress observed later in HA (150). Elevation in plasma renin activity (PRA) with heat stress enhances sodium conservation which increases plasma osmolality and thus an increase in ADH to enhance fluid retention (39). It is unknown how much effect this process has on chronic hypervolemia as the hormones decay to control levels post heat exposure. Shvartz *et al* (155) showed a 50-fold increase in ADH during orthostatic tilt tests pre-HA and a 75% reduction in this ADH response post-HA; attributing the change to plasma volume increases.

Davies *et al* (45) reported PRA significantly increased during an acute heat bout, but was unaffected by HA. However, most investigators agree that PRA effects are significantly moderated by HA (52, 53, 60, 155) and PRA activity correlates with final HR, which decreases with successive HA bouts (53). Additionally, HA-induced cardiovascular and body temperature changes allow for improved splanchnic blood flow (125, 130, 131) and hepatic clearance of renin, preventing a passive elevation of PRA (53).

Cortisol levels are considered a general indicator of the degree of body strain (14). Bonner *et al* (26) found increased cortisol levels during low intensity exercise in the heat and HA had no effect on cortisol response. However, others found increases in cortisol during exercise-heat stress only if the heat was intense or the subject was dehydrated. HA attenuated the cortisol increase, thus reflecting a decrease in total body strain (45, 61, 62).

The fluid and electrolyte regulating hormones are influenced by several factors including blood pressure, renal blood flow, plasma volume, hydration status, electrolyte status, and diurnal effects; but in general, the increased cardiovascular stability and sweat gland changes that result from HA lessen the requirement for large elevations in these hormones (14, 59).

Like cortisol, catecholamines respond to the increase in physiological strain that accompanies an exercise-heat exposure. HA generally attenuates this strain and therefore decreases the magnitude of the catecholamine response for a given environment, exercise intensity and duration, and subject fitness level (59). HA may not affect both catecholamines as Rowell *et al* (132) recently reported that circulating epinephrine did not increase when an exogenous heat stress was superimposed on to exercising subjects. Circulating norepinephrine did increase in logarithmic proportion to the increase in HR elicited by the added heat stress. It has been shown that norepinephrine excretion measured after each exercise bout in the heat decreased over eight days of HA (99). The authors speculate that lower norepinephrine levels after HA may provide the advantages of lower metabolic rate, less glycogen use, lower blood lactates and improved endurance time.

Finally, thyroid activity is depressed during heat exposure as lower circulating levels of thyroxine are observed after HA (175).

j) Hydration: according to a review by Sawka (138) little research has focused on the interactive effects of hydration levels with HA state. Hydration during exercise in the heat is important because body water deficits neutralize HA advantages. The early and rapid hemodilution response to exercise-heat stress observed during HA by Senay (145) was negated when the subject was dehydrated. Others have shown that pre-exercise hypohydration eliminated thermoregulatory improvements produced by HA (29, 142).

Most HA studies employ *ad libitum* drinking during heat bouts despite evidence that this level of drinking does not fully replace sweat loss, and impairment of exercise thermoregulation begins at dehydration levels equal to approximately 1% of body weight loss (42, 81). Early work by Pitts *et al* (121) showed that fluid replacement equal to sweat loss reduced thermoregulatory strain more than *ad libitum* drinking or no drinking during exercise in the heat by fully acclimated men. More recently, Montain and Coyle (105) reported that the magnitude of increase in both Tc and HR was related to the level of dehydration accrued by acclimated cyclists during exercise in the heat. Graded magnitudes of dehydration in this study were achieved by different levels of fluid replacement; the level that replaced the greatest amount of sweat loss resulted in the lowest level of thermoregulatory and cardiovascular strain.

Voluntary drinking during exercise in the heat not only fails to prevent some level of dehydration, but it is also quite variable. During an eight day HA program (82) *ad libitum* drinking increased from 450 ml/hour on day one to 1000 ml/hour over the last four days. Also, from day one to day eight the time to the first drink progressively shortened from 26 to 11 minutes, the number of drinks per heat exposure increased threefold, and the mean

volume per drink increased 81%. Even though the HA resulted in these improved drinking measures, the amount of sweat loss replaced increased from 40% on day one to only 70% on days 5-8. Additionally, Szlyk *et al* (167) reported that fluid intake varied widely between subjects during six hours of intermittent exercise in the heat, despite the continual availability of cool water. Twenty of 33 subjects drank enough to maintain body weight loss between 0.4 and 1.9%, whereas the other 13 subjects, classified as reluctant drinkers, accrued body weight losses up to 3.5% and concomitantly higher Tc than the other subjects.

An influencing factor during *ad libitum* drinking is fluid temperature. Subjects offered warm fluids consumed significantly smaller quantities and suffered greater dehydration and thermoregulatory strain than those who drank cool fluids (13, 166). It is the reduced quantity of fluid intake and not the temperature of the fluid per se that affects physiological performance, as Gisolfi and Copping (72) showed no difference in Tc between runners drinking 600 ml of warm water per hour and those drinking the same quantity of cold water. However, because of the high specific heat of water, consumption of large quantities of cold water during exercise in the heat may have an influence on body heat balance.

Finally, low dietary sodium intake during HA reduces total body water levels and may increase the risk of heat injury during the early days of HA , but does not affect the overall HA adaptations when compared to high dietary sodium intake (8). Additionally, the level of dietary sodium intake has no affect on whole body or intramuscular potassium balance during HA (9) and the level of hyperkalemia observed during exercise in the heat is attenuated by HA (58).

In summary, it appears greater control of fluid replacement during HA studies is warranted.

k) Body Surface Area: The rate of sweat evaporation from a fully wet surface is proportional to the area of the surface and to the difference between the water vapor pressure at the surface and the ambient vapor pressure (36). One subject in the study by Mitchell *et al* (102) had a BSA of 1.76 m^2 whereas the other subjects had areas greater than 1.92 m^2. His body temperature dropped less than the others with repeated HA exposures even though his HR and SR were similar to those of the other subjects. To achieve the same level of evaporation as the other subjects with 10% less BSA he had to increase skin vapor pressure through increased skin temperature; his measured Tsk was 1.2°C higher than the others (102).

Very often the BSA to mass ratio is considered since the more body surface area available for evaporative heat loss per unit of heat producing tissue the more efficient the thermoregulation (51). This improvement in heat loss is dependent upon the environment. Subjects with high BSA/mass ratios will gain more heat by radiation and convection than subjects with low ratios when ambient temperature is greater than skin temperature (152, 157); however, the greater cooling power of the high BSA/mass ratio tends to balance out the heat gain. In warm, humid environments where increased area is necessary to maintain the required evaporation the higher ratio has a clear advantage (152). In one study on heat intolerance (51), heat intolerant subjects had higher SR than controls, but reached a higher Tc during a controlled heat tolerance test because of their lower BSA/mass ratios.

3. Conditions to Induce HA

a) Intensity, Duration and Specificity of HA: Many have sought to determine the optimal HA exposure. In terms of length of the HA

program, four days is not enough to produce plateaus in Tc, Tsk, HR or SR (102), but, depending upon other factors, six to 23 days have been found to be sufficient to achieve plateaus (129, 158). Specific duration and intensity of the exercise-heat exposure to maximize HA adaptations are difficult to pinpoint. Robinson *et al* (129) reported that a "striking" result of HA experiments was only 1 to 1.5 hours of daily work periods in dry heat were necessary to produce HA. In another study, 1.7 hours of low intensity exercise in hot, humid conditions did produce changes in Tc and HR where one hour did not (67).

Wyndham *et al* (187) compared various combinations of exercise intensity and environmental conditions and found that an acclimation regime of moderate work (1.45 l/min VO_2) in moderate conditions (31°C WB) was better than light work (0.65 l/min VO_2) in severe conditions (36°C WB) to prepare for hard work in high wet bulb temperatures. In his review Wyndham (183) suggests that HA for four hours per day for eight to nine days is necessary to acclimate men for work in mines for six to eight hour shifts. Wyndham used low to moderate intensity exercise in his work, where as recent work shows that moderate to high intensity exercise of shorter duration can also produce full HA effects. Houmard *et al* (92) found no difference in HA benefits between nine days of running in the heat (40°C) at 75% VO_2 max for 30-35 minutes per day and nine days of running in the same environment at 50% VO_2 max for 60 minutes per day.

Specificity of HA, *i.e.*, designing acclimation bouts to closely match the expected exercise-heat stress, rather than a set protocol to meet the requirements of all environments, is most likely preferred (12, 158, 175). Additionally, heat tolerance tests conducted pre- and post-HA are usually designed to mimic the demands of a specific exercise-heat exposure. This

specificity is advantageous for predicting responses to the expected heat exposure, but the specific tests are limited to the conditions for which they are designed; a test designed for one situation will probably not be useful for other situations (11).

b) Environmental

1) Dry vs. Humid Heat: Humidity plays an important role in HA, in that SR increases markedly during humid HA (102, 158, 182), but remains unchanged in most HA studies employing hot, dry conditions (14, 89, 99, 129). As mentioned in the section above on sweating, both humid HA and dry HA shift the SR-Tc threshold and increase the SR-Tc slope, but in general, greater changes tend to occur with hot, humid conditions. Apparently more sweat gland training and a reduction in the hidromeiotic effect (57) occurs with humid HA (175). Additionally, humid HA makes more efficient use of the total BSA by increasing skin wettedness through selective increases in regional sweating (31) and greater percent contribution of the limbs (91). Gonzalez *et al* (76) conclude that HA is best stimulated by a combination of exercise and humidity levels that elicit high skin temperatures and skin wettedness values above 0.5. Air velocity must also be considered as high velocities reduce Tsk and skin wettedness levels (2).

Improved evaporative cooling in the hot, humid environment occurs not only with increased wetted skin surface area, but also with higher vapor pressure at the skin surface, the latter accomplished by increasing the skin temperature through increased skin blood flow (175). Over the course of dry HA, changes in sweating increase the Tc-Tsk gradient and SkBF demand decreases; however, as mentioned above, during humid HA less of an increase in the Tc-Tsk gradient occurs due to limited evaporative heat transfer and an increased demand for SkBF remains over a longer portion of the HA (102,

127). Therefore, humid HA may produce greater circulatory adjustments than dry HA (175).

Even though SkBF remains elevated over the course of humid HA, HR decreases as during dry HA (127). The maintenance of increased SkBF permits the continual stimulus for PV expansion by protein "flushing" from the cutaneous interstitial space as proposed by Senay (147). Thus, decreases in HR can still occur with humid HA. The fact that Senay's work was done under hot, humid conditions lends credence to this concept.

2) Seasonal: If one is involved in summer outdoor activities then a partial state of HA can be accrued and will speed the artificial HA process (175). Living and working in the hot, humid tropics and in the hot, dry desert conferred approximately 50% of the total amount of HA that was elicited artificially (189). Shapiro *et al* (151) reported that 10 days of HA in a climatic chamber did not totally eliminate seasonal differences in thermoregulation due to natural acclimatization. However, their findings are questionable since the artificial exercise-heat stress was probably too low as it did not produce significant reductions in exercise Tc for either summer or winter test periods. Moroff and Bass (106) conducted a HA program in the summer and reported that natural acclimatization did not prepare the subjects for the degree of exercise-heat stress (100 minutes of walking at 3.5 mph in 49°C DB/27°C WB) imposed during the study. Sawka *et al* (141) also reported that the season of the year had no effects on study results. Apparently the amount of outdoor heat exposure and the level of exercise-heat stress of the HA regime are factors to consider when conducting HA experiments in the summertime.

B. HA and EXERCISE METABOLIC RATE CHANGES

A significant effect resulting from HA, but apparently not from physical training in thermoneutral conditions, is the reduction of the exercise metabolic rate which results in improved exercise economy (run and walk) or efficiency (cycling) (14, 175). Robinson *et al* (129) reported a decrease of 7.6% in caloric expenditure during treadmill walking after 10 to 23 days of hot, dry HA. In a more recent study (92) the metabolic cost of running at either 50% or 75% VO_2 max decreased 4% after eight days of HA. Armstrong *et al* (12) found that after 14.5 weeks of summer outdoor training, distance runners significantly decreased their submaximal VO_2 by 8% during one hour runs at a speed of 200 meters/minute. Sawka *et al* (141) reported a decreased exercise metabolic rate of 3% and 5% during treadmill walking in a hot (49°C) and cool (20°C) environment, respectively, after 10 consecutive days of HA. Finally, Young *et al* (190) found the decrease in exercise metabolic rate was not modality specific as submaximal VO_2 during cycling decreased 2% after nine consecutive days of walking at 40-50% VO_2 max in the heat. Others report larger decreases (5 to 16%) in exercise metabolic rate, but these studies employed bench stepping exercise where reductions in metabolic rate are likely due to improvement in biomechanical skill and the concomitant reduction in power output (154, 158, 159, 165). Control groups performing the same exercise in thermoneutral conditions in three of these studies (154, 158, 159) had the same decreases in exercise metabolic rate, confirming the change was due to skill improvement.

Several physiological mechanisms have been proposed to explain the decreased exercise metabolic rate induced by HA. Sawka *et al* (141) concluded that neither a Q_{10} effect nor the thermoregulatory system were responsible for the decreased exercise metabolic rate since it was reduced in

both hot and cool environments after HA. They postulated that chronic heat exposure could increase proprioceptive afferent activity and result in greater recruitment of the more efficient slow twitch motor units, thereby reducing exercise metabolic rate. Armstrong *et al* (12) found no change in SR or Tc in the distance runners, but observed slightly higher HR and Tsk at the 50 minute point of their 90 minute post-HA test runs. From this they hypothesized there was a greater cutaneous circulation post-HA which resulted in the lower submaximal VO_2 because the skin has lower oxygen requirements than muscle or internal organs. This hypothesis is supported by others who found that submaximal VO_2 was lower in the heat (37 to 49°C) than in the cool (21°C) for the same rate of work (99, 177, 190). In the study by Young *et al* (190), the exercise metabolic rate was lower in the heat than in the cool both before HA and after HA, by 3.4% and by 4.3%, respectively.

C. STPT and EXERCISE METABOLIC RATE CHANGES

A four week physical training program on a cycle ergometer for one hour per day at 75% VO_2 max in thermoneutral conditions produced no effect on the exercise metabolic rate elicited during treadmill exercise tests in either a hot or cool environment (141). Also, three different STPT studies (78-80) showed no effect on submaximal oxygen consumption after training.

D. HA and EXTENT of INDIVIDUAL VARIABILITY

The physiological responses to HA vary according to not only the nature of the heat stress and exercise employed, but also the make-up of the individual (175). Individual variability in physiological responses to HA has been addressed in few studies. Several years ago Rowell *et al* (133) reported that the most "striking feature" of their study on the circulatory responses to dry HA was the variability in responses among different individuals. Wide interindividual variability in skin wettedness response to HA has also been

observed (31). Szlyk *et al* (167) reported a substantial variability in fluid intake and concomitant body weight loss in subjects despite continuous availability of cool water during six hours of intermittent exercise in the heat. It would have been interesting to have observed the extent of individual variability in the fluid intake response over a full course of HA.

The greatest attention to individual variability was provided in a three paper series published on an experiment conducted by the laboratory working with the South African mining industry (102, 150, 186). Marked individual variability was observed in the cardiovascular, thermoregulatory and metabolic responses of the subjects to HA and is discussed below.

Even though the presence of individual variability has been recognized by some, the extent of this individual variability has not been examined. To accurately measure the extent of individual variability, one must ensure that the differences observed are actual individual variability and not differences due to factors not measured or controlled during the investigation. Several factors can influence the level of physiological response to HA and mask the actual amount of individual variability that exists. Inadequate sleep, medications, illness, acute or chronic alcohol abuse, depletion of glycogen stores, low blood glucose, and sudden changes in training can affect responses to heat (14). Also intersubject variability is reduced if Tc is related to the relative and not the absolute exercise metabolic rate (44, 134). Maintenance of a consistent w rate over the course of HA and selection of exercise modalities that a e free from the effects of skill improvement or habituation are essentia . .).

Therm atory and cardiovascular responses depend in part upon level of dehydration (105, 121), yet most HA studies have employed voluntary drinking which fails to prevent dehydration and is quite variable (82). Some,

but not all HA studies have corrected sweat measurements for respiratory water loss, carbon weight loss, or urine production (103). Also, the amount of dietary sodium intake did not affect the final level of HA achieved, but did significantly influence HR, Tc, PV, plasma osmolality, and plasma, urine and sweat sodium levels during HA (8). Finally, BSA/mass ratio can be quite variable between subjects and affects the amount of heat dissipated during exercise in the heat.

Some of the above factors most likely account for part of the individual variability observed in the South African study (102, 150, 186). Four subjects heat acclimated for 10 days by riding a cycle ergometer at an absolute work rate of 75 watts four hours per day in a calorimetric wind tunnel at 45°C DB/32°C WB. Water consumption was voluntary. Subject C had the lowest HR and Tc throughout the HA period; the authors (102, 150, 186) reported that he responded as if he was already heat acclimated. In a review of the data one can see that subject C was probably at an advantage because he, 1) worked at a lower relative work rate (40% VO_2 max) than the two subjects who experienced difficulty acclimating; 2) maintained the best state of hydration during the HA; 3) was the only subject to meet his required evaporation the entire 10 days; and 4) had the highest BSA/mass ratio. Subject B had a limited Tc response during HA; Mitchell *et al* (102) reported that this was due in part to a BSA 10% lower than the other subjects. Also, in a review of the data, subject B was likely limited by 1) a body water deficit later in the HA period, and 2) the second highest relative work rate (46% VO_2 max). Subject D experienced a limited reduction in HR during the first five days of HA, Senay *et al* (150) found only a minor PV expansion in this subject over the first three days of HA, possibly the result a of significant body water deficit (3.4%) that developed concurrently. Also, in a review of the data,

subject D had 1) the highest relative work rate (52% VO2 max), and 2) the lowest BSA/mass ratio. Even though this was one of the few studies that addressed individual variability, some of the individual variability was probably due to the use of an absolute rate of work, lack of control over fluid consumption, and incomplete analysis of the BSA/mass ratio effect.

Once controls and measures are instituted in a study to reduce the magnitude of observed individual differences individual variability can be measured for a given set of environmental and exercise conditions. Further, the findings apply only to the conditions under which the HA was conducted since responses are specific to the conditions of HA as has been mentioned above in previous sections of this review.

E. HA and PHYSIOLOGICAL STRAIN in the CDE

The US Air Force groundcrew CDE consists of a two piece chemical protective overgarment, butyl rubber hood and mask, and rubber gloves worn over standard military fatigues. The highly insulative, semipermeable CDE, with a clo value of 2.5, impedes heat dissipation and its bulk decreases movement efficiency (163). Numerous studies have documented the physiological strain imposed by the CDE; this strain is greatly exacerbated with an increase in rate of work or environmental stress. Exercise in warm climates while wearing the CDE as compared to controls wearing a standard flight suit or shirt and shorts resulted in higher Tc, Tsk, HR (25, 100, 171), limb blood flow (20), heat storage, VO_2, sweat production (25, 100), electrolyte losses (16), plasma renin activity, plasma aldosterone concentration (63), dehydration (63, 170) and convergence of Tc and Tsk (116). Prediction of exercise heat tolerance and work tolerance times for various conditions has been determined (17, 25, 100, 172).

Researchers have also used various mechanical additions to the CDE to provide microclimate cooling to the wearer. Attenuation of heat strain and improvements in work tolerance times, but not total return to control values, are provided by the use of ice vests (21), liquid cooled vests (35, 153, 173) and air cooled assemblies (107, 120, 153, 173). Additionally, mathematical models have been developed to predict heat tolerance while exercising in the CDE (6, 24).

Despite this extensive work, investigation into the effects of HA on physiological strain while wearing CDE has been extremely limited. The only work in this area that I am aware of is currently being conducted by Dr T. M. McLellan's laboratory in Canada (personal communication). Their initial work appeared in a very recent abstract for the 1993 Aerospace Medical Association Scientific Meeting. Nine untrained and six endurance trained males wore the Canadian protective clothing ensemble while walking at 4.8 km/hr, 2% grade for a maximum of two hours in 40°C DB, 30% RH before and after six days of HA for one hour per day (conditions not reported). HA resulted in lower Tc and rating of perceived exertion in the untrained subjects, and lower Tc and Tsk in the trained subjects when wearing the protective ensemble (7).

Givoni and Goldman (74) reported that the benefits of the improved sweat response with HA can be obtained only if the sweat produced can evaporate. Differences between HA and non-acclimated subjects diminished when evaporation was restricted by high vapor pressures, low air movement, impermeable clothing. or any combination of these factors. However, as indicated by the Canadian group and pilot data from our laboratory with HA and the CDE, it is possible that HA can provide a reduction in the physiological strain associated with exercise in the CDE. Benefits could

derive from non-sweating physiological changes that result from HA and from increased sweat evaporation through the semipermeable CDE.

F. PHYSICAL TRAINING versus HA, and STPT & PHYSIOLOGICAL STRAIN in the CDE

Whether or not physical training in thermoneutral or cool environments induces heat acclimation has been a controversial subject over the years. Most agree that physical training improves heat dissipation capabilities which provide a partial degree of HA. Adaptations to physical training are similar, but differ in degree and type to those induced by HA. Also these adaptations are dependent upon the intensity, duration and modality of the training (15, 94).

1. Physical Training and HA: Agreement on the influence of physical training in thermoneutral conditions on one's state of HA did not occur quickly. Researchers in the South African gold mining industry held the position that physical training in thermoneutral environments may improve performance in the heat, but could not replace HA (164, 165, 183). Another group held that physical training, specifically distance running, brought one to a partially acclimated state or that training supplied a large portion of HA (69, 123, 124). Methodological differences between the two groups affected their conclusions: 1) conditions and duration of the heat tolerance tests were different, 2) distinctions between VO_2 max and physical training or trained state were not made, 3) cross-sectional and longitudinal studies were compared, 4) small homogeneous samples were used, 5) exercise modality, intensity and duration differed, and 6) there was a lack of matching for morphological factors and VO_2 max between control and trained subjects (15, 71).

Gisolfi (70, 71) clarified some of the earlier controversy concerning physical training and HA with a study that compared distance runners to college students, the groups matched for VO_2 max and mass-to-surface area ratios. After the college students completed eight weeks of interval training, the two groups completed a heat tolerance test. The distance runners had lower Tc, Tsk and HR than the students, but the temperature differences were eliminated when the students completed a course of HA after the eight weeks of physical training. The lower heart rates of the distance runners are indicative of higher CV stability, suggesting a more adequate cardiac output distribution and transfer of heat from the core to the periphery (15).

In a more recent study (94) distance runners, track sprinters and untrained men were compared during a cycle ergometer test at 30% VO_2 max in the heat (40°C DB/45% RH). The same relative work rate was selected so the heat dissipating capabilities of the groups could be compared under equivalent levels of heat stress; the Tc response was the same between groups as expected. Because of their high VO_2 max the distance runners worked at a higher absolute work rate and had the greater total heat load. However, due to a significantly higher sweat response the runners dissipated a greater percentage of their heat load, so the groups did not have different levels of heat storage. The trained runners displayed adaptations that provided them with certain degree of heat tolerance.

Physiological adaptations resulting from physical training are similar to those resulting from HA (15, 71). Physical training in a thermoneutral or cool environment produces an enhanced sweat response and an expansion of PV which result in higher SV and lower HR, Tc and Tsk for a given exercise-heat stress. Physical training results in a lower Tc threshold for the onset of sweating (23, 90, 98), an increased sweat sensitivity (90, 108), and an

increased sweat rate, due in part to an increase in cholinergic sensitivity of the sweat gland (28).

HA produced greater shifts in the SR-Tc curve and further increases in sweat sensitivity and rate than those changes produced by physical training alone in two longitudinal studies that acclimated subjects after they completed physical training (111, 128). Hypervolemia is a well documented response to physical training (37, 38, 79) and a 10% increase in resting PV has been shown after a single intense exercise session (68). Convertino *et al* (39) reported a 177 ml increase in resting PV with eight days of passive HA, a 427 ml increase with two hours per day of exercise at 60-65% VO_2 max for eight days in 25°C DB 60% RH, and a 552 ml increase with exercise at 50% VO_2 max for the same duration in the heat (42°C DB/50% RH). They suggest that the metabolic and other physiological responses to exercise and the thermal response to the heat are additive and are necessary stimuli for optimal PV expansion. Senay and Kok (149) found that HA after physical training further expanded PV and increased the hemodilution response during exercise in the heat. HA not only increases the sweat and PV responses further than produced by physical training, but also lowers the exercise metabolic rate (175) and has decreased sodium chloride losses in sweat and urine (14).

Generally, physical training that increases VO_2 max, or an inherently high VO_2 max, provide improved heat tolerance. In one study (118), the number of HA days necessary to reach a plateau in Tc were negatively correlated to VO_2 max. However, this correlation does not imply causation as VO_2 max, per se, may not be as important in determining heat tolerance as the physiological characteristics associated with a high VO_2 max (15, 175). Cadarette *et al* (30) found that HA eliminated the correlation that existed

between VO_2 max and Tc. Regular weekly aerobic training offered middle-aged men an advantage in exercise-heat tolerance over younger men matched for morphological factors and VO_2 max (119). In the study (94) that compared distance runners, track sprinters and untrained men during cycle exercise in the heat, both the runners and sprinters, with significantly different VO_2 max values, had sweating adaptations that allowed them to eliminate more heat than the untrained men. The authors suggest that the greater sweating response of the athletes was a consequence of increases in Tc during training rather than changes in VO_2 max. Only physical training modalities that elevate Tc during exercise and thus stimulate sweating will improve heat tolerance. Swimmers with high VO_2 max values (90) and those who increased VO_2 max through training on a cycle immersed in 20°C water (19) showed no improvements in heat tolerance.

To obtain optimal improvements in heat tolerance from physical training in thermoneutral or cool environments one should use interval or continuous training at intensities above 50% VO_2 max for 8-12 weeks that results in at least a 15% increase in VO_2 max (71, 90, 111, 117, 128). This training will provide approximately 50% of the improvements in heat tolerance gained through HA (71). Physical training at intensities less than 50% VO_2 max was not associated with improvements in heat tolerance (160). Also, Gisolfi and Cohen (71) have stated that intense physical training cannot substitute for exercise in the heat if HA is desired within two weeks.

Physical training in thermoneutral or cool environments that elevates Tc provides adaptations similar to HA. These adaptations improve heat tolerance, hasten the HA process, and are associated with a greater retention of HA when living in cool environments (14, 15, 117). However, since HA improves exercise economy, further expands PV, and raises both Tc and Tsk,

providing a higher stimulus for changes in the sweat response, the endurance trained individual must still exercise in the heat to fully HA (14, 15, 39, 71, 111, 117, 149).

2. STPT and HA: To increase heat tolerance the duration of physical training in thermoneutral or cool environments must exceed one week (15). Cycle exercise for one hour per day at 70 to 80% VO_2 max for 10 days improved heat tolerance (111, 128), but six days of bench stepping at a VO_2 of 1.9 l/min for 90 minutes provided no improvement (158). Short-term physical training, cycle exercise for two hours per day at 65% VO_2 max for three days increased PV 20%, but had no effect on thermoregulatory behavior (80). Apparently, physical training for approximately one week or less in duration is not long enough to induce adaptations in the sweat response.

3. STPT and CDE: To my knowledge no study has addressed the effect of STPT on physiological strain resulting from exercise in the heat while wearing the CDE.

G. DeA and CDE

1. Decay of Heat Acclimation: HA is transient and decays without repeated heat exposure, but the literature on the rate of decay is equivocal. Significant reductions in HA were observed in gold mine laborers after only six days on the surface working in cool conditions (185). Williams *et al* (178) measured HA decay in mine laborers at one week intervals for three weeks and saw HR and SR decline to control values by the third week. Tc declined 50% by week three. Probably because they were more physically trained, subjects in a study by Pandolf *et al* (118), lost only 18% of Tc gains and 29% of heart rate gains after 18 days of DeA. Apparently, the early adaptations to HA tend to be the first to decay (14, 15, 118, 178). Convertino *et al* (39) found that PV returned to within 60-80 ml of control values after seven days of

DeA. Also, one heat exposure per week after HA was not different from complete cessation of exposure with regard to maintenance of hypervolemia (122). Physically fit individuals have a retarded decay of HA and a more rapid reacclimation (85, 118). Factors that accelerate HA decay are: generalized fatigue and sleep loss (10), infection, alcohol abuse, salt depletion, and dehydration (175).

2. De-HA and CDE: to my knowledge no study has addressed the effect of DeA on physiological strain resulting from exercise in the heat while wearing the CDE.

H. DeT and CDE

The VO_2 max of endurance trained subjects declined 7% after 21 days of detraining. This decline was largely due to a rapid decline in maximal SV to near control levels after the first 12 days of detraining (41).

To my knowledge no study has addressed the effect of DeT on physiological strain resulting from exercise in the heat while wearing the CDE.

PRELIMINARY STUDIES

The investigator has demonstrated competence in the majority of techniques, methods and calculations necessary to measure the variables set forth in this proposal. He has worked for over two years in the environmental laboratory on a study addressing the validity of using projected work-rest cycles over the course of a duty day while exercising in the CDE. The laboratory group has conducted over 80 six hour CDE tests and over 100 HA bouts and heat tolerance tests (HTT) using a majority of the techniques listed in this proposal to measure thermoregulatory, cardiovascular and metabolic responses to exercise in the CDE. The investigator is currently practicing new techniques which include the measurement of cutaneous blood flow with a new Vasamedics BPM^2 laser Doppler velocimeter, and the measure of blood lactate and glucose with a new YSI 2300 Analyzer. These items along with a Quinton Q50 treadmill have been recently loaned to the investigator by the USAF Armstrong Laboratory. The measures of catecholamines and plasma volume (T-1824) are pending funding support.

Our laboratory conducted pilot work (n=1) to determine the possible benefits of heat acclimation on exercise while wearing the CDE. A 33 yr old male (weight-71.3 kg; VO_2 max-67 ml·kg^{-1}·min^{-1}) performed two CDE trials before and three trials after 10 consecutive days of exercise HA.

HA and HTT: The HA consisted of two hour walks in shorts and shoes at 32% VO_2 max (3.5 mph, 4.5% grade), in the heat (43.0°C DB/49.6% RH). Measurements were made during the first and tenth acclimation trials to test heat tolerance (HTTs 1 and 2). Submaximal VO_2 decreased 4.6% over the course of HA (Figure 1). This decrease in heat generation was one of the

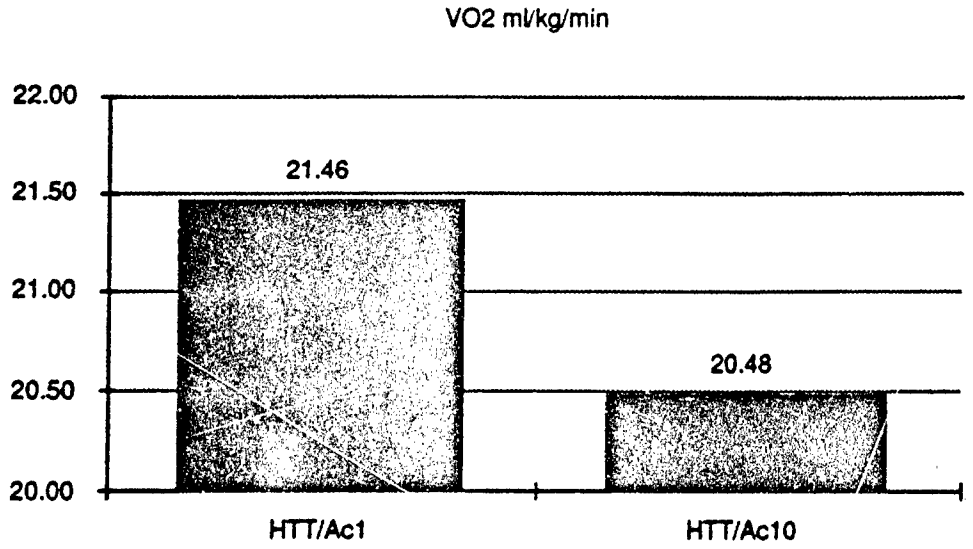

Figure 1. VO_2 for HTT 1 (Accl 1) and HTT 2 (Accl 10).

adaptations that contributed to a reduction in Tre with HA. Tre measured at the end of each trial (Tc at 120 mins) decreased from 38.7°C for HTT 1 to 37.8°C for HTT 2 and Tc at 60 minutes decreased from 38.0°C to 37.6°C. Initial Tre (Tc at 1 min) remained basically unchanged (37.0°C to 36.9°C), (see Figure 2-the jump in Tre for acclimation bout 8 is explained below). Tsk followed the same pattern as Tre. Tsk at the 120 minute mark decreased from 37.5°C for HTT 1 to 36.9°C for HTT 2 and Tsk at 60 minutes decreased from 37.2°C to 36.9°C. Initial Tsk remained unchanged. These lower mean skin temperatures are likely the result of sweating and skin blood flow changes. Other responses to HA occurred that may have led to the decrease in Tre. HR showed early decreases, likely part of the CV adaptations that occur early in HA, due primarily to PV expansion, and achieved a plateau before decreasing towards the end of the HA course (Figure 3).

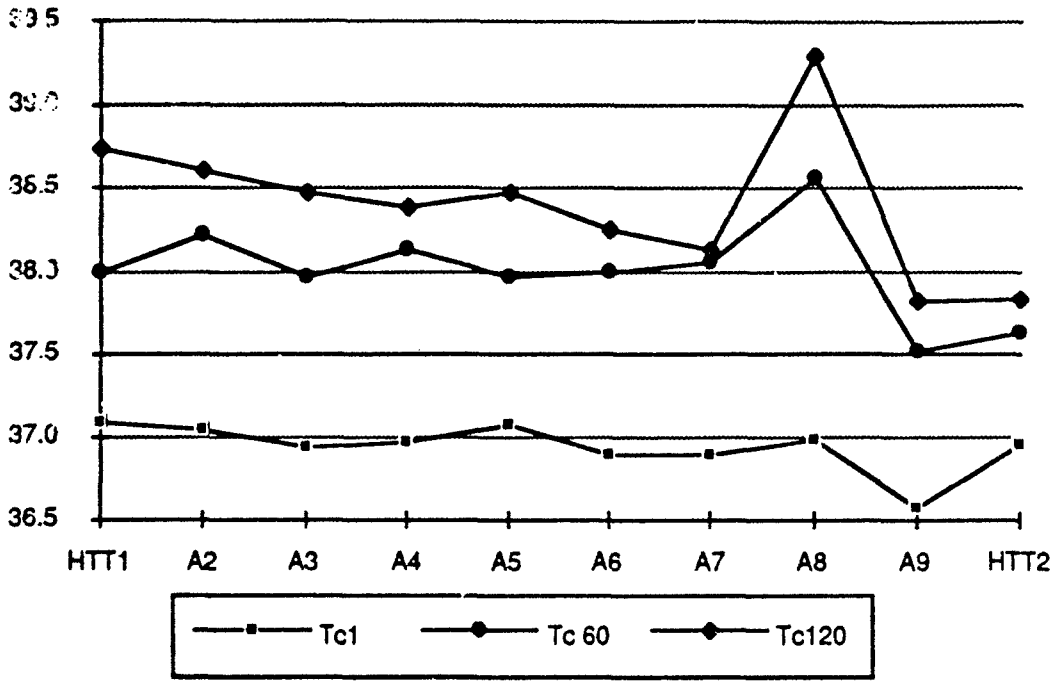

Figure 2. 1, 60, and 120 minute rectal temperatures for each acclimation bout.

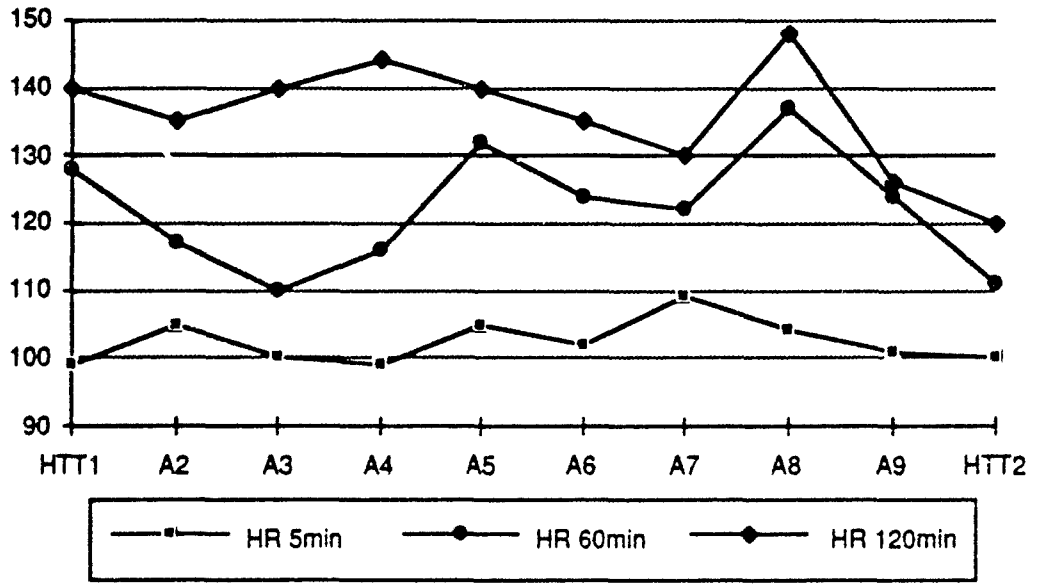

Figure 3. Heart rates (beats/min) at 1, 60, and 120 minutes for each acclimation bout.

The PV change for HTT 1 was -6.5%, but was +0.9 for HTT 2 demonstrating the defense of PV during exercise-heat stress that occurs with HA (Figure 4).

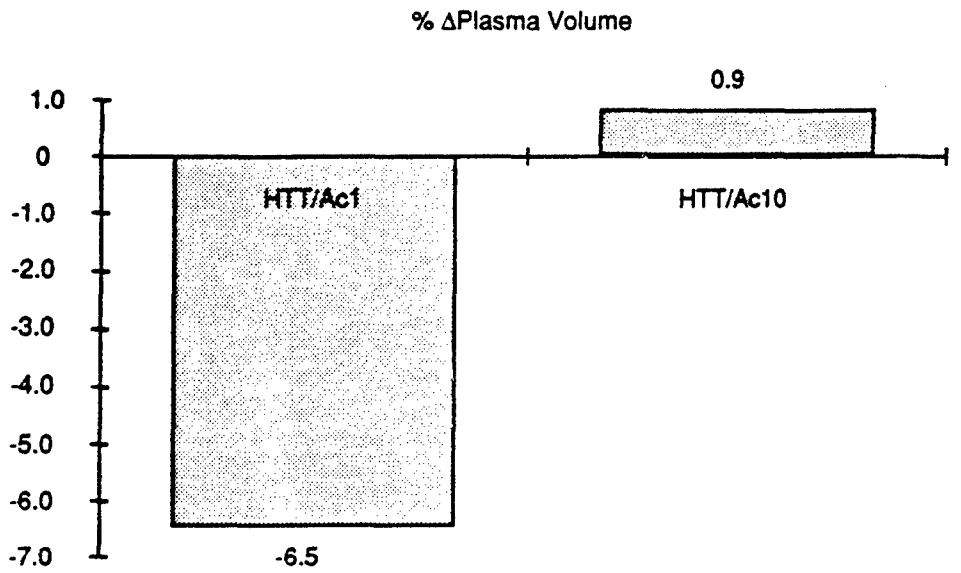

Figure 4. Percent change in plasma volume for HTT 1 and HTT 2.

SR increased steadily through acclimation bout 6 and dropped off for bouts 7, 9 and 10 (Figure 5). This is likely due to 1) an earlier onset of sweating which leads to lower Tre and thus less overall sweat drive, and 2) full FR for acclimation bouts 7 and 9 versus *ad libitum* fluid intake for bouts 1-6, and 10, and no fluid for bout 8 (Figure 7). The full FR in bouts 7 and 9 allows for greater skin blood flow levels which increase convective and evaporative heat transfer resulting in lower Tre and lower overall sweat drive. Even though the SR is the same for bouts 9 and 10 as compared to bout 1, the sweat response per change in Tre, known as sweat sensitivity (Figure 6), is greater for bouts 9 and 10.

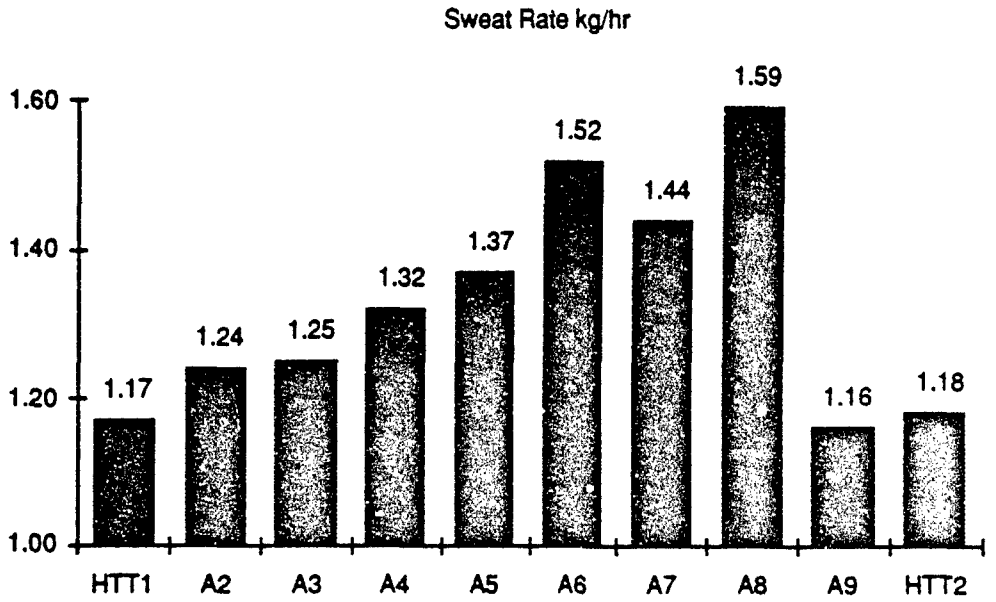

Figure 5. Sweat rate for each acclimation bout.

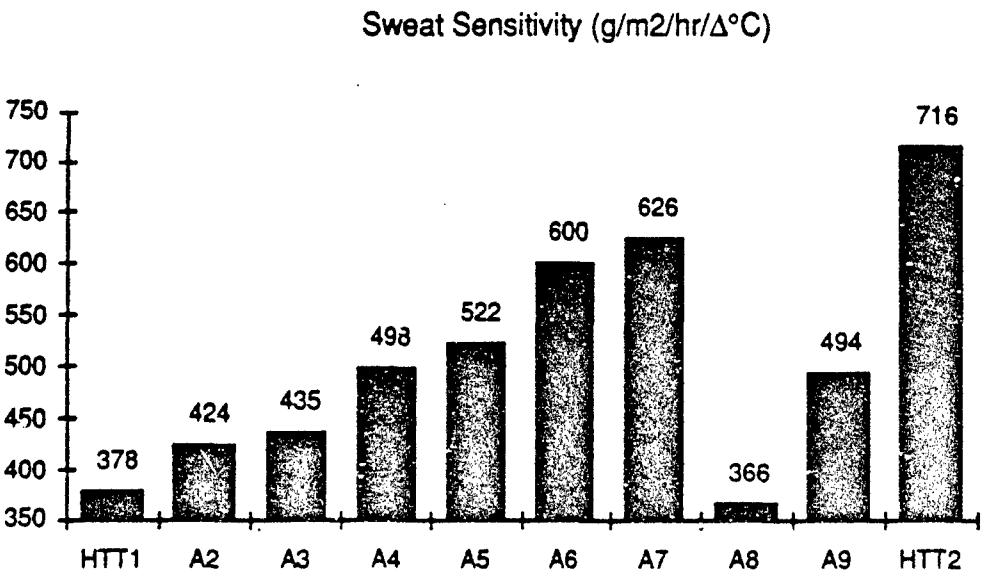

Figure 6. Sweat sensitivity for each acclimation bout.

The HR, Tre and sweat responses for acclimation bout 8 versus bouts 7 and 9 demonstrate the difference between no FR and full FR during this HA series. The proposed investigation plans to control for FR type, timing, and quantity. Percent dehydration for HTT 2 (Accl 10) was matched closely to percent dehydration for HTT 1 to avoid data bias.

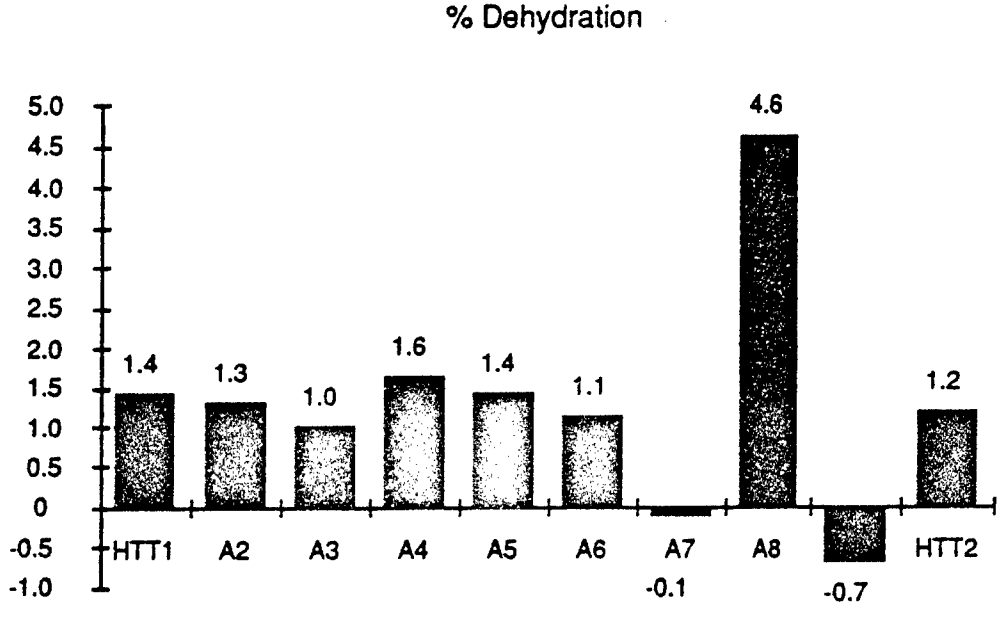

Figure 7. Percent dehydration for each acclimation bout.

CDE Tests: The subject completed two CDE tests before (Pre 1 & 2) and two after (Post 3 & 4) the 10 HA bouts. He walked at 3.0 mph-0% grade in the environmental chamber (32.4°C DB 49.2% RH) until Tre reached 39.3°C. An additional post-HA CDE test (Post 5) was conducted with the same protocol except at a higher ambient temperature (37.8°C DB 46.6%RH). For tests 1 and 3 the subject consumed no fluids (NF); for tests 2, 4 and 5 the subject attempted total FR of sweat production (SP), and replaced fluids at 95, 77, and 75% respectively. Total walk time (TWT) for test 1 was 85

minutes, we used this time as a common comparison point, indicated in Table 1 below.

Test	Pre 1 (NF)	Pre 2 (FR)	Post 3 (NF)	Post 4 (FR)	Post 5 (FR)
Temperature / RH (°C / %)	32.6 / 49	32.5 / 49	32.2 / 49	32.3 / 50	37.8 / 47
Total Walk Time (mins)	85	89	122	156	92
VO_2 at 85 min (l/min)	1.02	1.01	.93	.93	.97
VO_2 at 85 min (ml/kg/min)	14.3	14.2	13.0	13.0	13.6
Tre initial (°C)	37.4	37.3	37.1	37.0	36.9
Tre at 85 min (°C)	39.3	39.2	38.6	38.1	39.1
Tsk at 85 min (°C)	37.9	38.1	37.3	37.1	38.0
Tre at end of test (°C)	39.3	39.3	39.3	39.3	39.3
Tsk at end of test (°C)	37.9	38.1	37.8	38.2	38.1
Heat Storage at 85 min (kcal)	122	127	98	78	145
HR at 85 min (b/min)	160	151	140	138	152
MAP at 85 min (mmHg)	102	109	80	77	83
Sweat Production (kg)	1.97	2.05	2.59	3.37	3.41
Sweat Rate (kg/hr)	1.39	1.38	1.27	1.30	2.22
Sweat Evap. Rate (g/hr)	289	317	310	342	450
Swt Sens. at 85 (g/m2/hr/Δ°C)	397	396	441	603	537
% Dehydration	2.9	0.3	3.8	1.5	1.3
% Fluid Replacement	0	95	0	77	75

Table 1. CDE test results pre and post HA.

For both NF and FR 32.4°C DB test comparisons (test 1 vs 3, and 2 vs 4), the following changes occurred after HA: increased TWT, lower initial Tre, and reduced VO_2, Tre, Tsk, heat storage (S), HR, mean arterial pressure (MAP), at 85 minutes. As above for the HTTs, SR remained the same after HA, but sweat sensitivity was much higher post-HA. Sweat evaporation rate was also higher after HA, and this along with the greater sweat sensitivity point to an earlier onset of sweating.

Interestingly, the Tsk at the end of the tests, when Tre equaled 39.3°C, was slightly higher for the FR tests versus the NF tests, possibly indicating greater SkBF transferring heat to the periphery. Without the measurement of SkBF conclusions cannot be made about possible SkBF adaptations that may have occurred with HA. SkBF will be measured in the proposed investigation. Additionally, it is interesting to compare the TWTs for test 5 and test 2; roughly the same amount of exercise (92 vs. 89 minutes) was done in a higher ambient heat (37.8°C DB) after HA. For this subject HA resulted in an work environment benefit of approximately 5.4°C DB (- 10°F).

The longer TWT before reaching 39.3°C in the CDE post-HA was primarily due to the decreased submaximal VO_2 and increased sweat evaporation. The following heat balance calculations specify the areas of altered heat exchange for the CDE tests conducted at 32.4°C DB. The heat balance equation $S = M - (\pm W) \pm E \pm R \pm C \pm K$, accounts for heat production, represented by metabolism (M), and heat exchange, represented by evaporation (E), radiation (R), convection (C), and conduction (K). W represents actual work done. First, exercise metabolic rate was determined from $M\ (kJ \cdot min^{-1}) = VO_2\ (l \cdot min^{-1})$ x energy expenditure $(kJ \cdot l^{-1})$. The energy expenditure per liter of oxygen was determined from the mean respiratory exchange ratio (RER) data. The mean VO_2 values were 9% lower and mean

RER values were 1.5% higher post acclimation resulting in 7% lower M post HA.

Test	RER	VO_2 (l/min)	Metabolic Rate (kJ/min)	M (watts)
Pre 1	.82	1.02	20.59	343
Pre 2	.82	1.01	20.39	340
Post 3	.86	0.93	18.97	316
Post 4	.90	0.93	19.12	319

Table 2. CDE test mean metabolic rates in both kJ/min and watts.

The heat exchange due to evaporation was calculated (Table 3) using the value for latent heat of evaporation (liquid to vapor) of 2.43 $kJ \cdot g^{-1}$. During the CDE tests the sweat loss, calculated from clothed weight difference, equaled sweat evaporation since no drippage of sweat occurred; therefore, E ($kJ \cdot min^{-1}$) = sweat evaporation rate ($g \cdot min^{-1}$) x latent heat of evaporation for sweat ($kJ \cdot g^{-1}$). A 7% increase in evaporative cooling occurred post-acclimation.

Test	Sweat Evap. (g/hr)	Sweat Evap. (g/min)	Heat of Evap. (kJ/g)	E (kJ/min)
Pre 1	289	4.8	2.43	11.70
Pre 2	317	5.3	2.43	12.83
Post 3	310	5.2	2.43	12.54
Post 4	342	5.7	2.43	13.85

Table 3. CDE test mean heat loss rates due to evaporation.

Heat exchange due to radiation and convection was determined from the equation of Givoni and Goldman (73): R+C = (.696/clo) (Tsk - Ta). The average Tsk over 85 minutes instead of the Tsk at the 85th minute was used here. The clo value, a dimensionless clothing insulation rating, of the CDE is 2.5. The equation assumes a BSA of 1.8 so all values were adjusted for actual BSA. The calculated mean heat exchange rates due to R and C (Table 4) were a minor portion of the total both pre- and post-HA.

Test	Tsk (°C)	Ta (°C)	BSA adjust	R+C (kJ/min)
Pre 1	37.0	32.6	1.88/1.8	1.28
Pre 2	37.0	32.5	1.88/1.8	1.32
Post 3	36.7	32.2	1.89/1.8	1.30
Post 4	36.2	32.3	1.89/1.8	1.12

Table 4. CDE test mean heat exchange rates due to radiation and convection.

The mean rate of heat storage was calculated by combining the above values and assuming a 5% economy for W. The heat loss or gain through conduction was considered to be negligible. The heat balance values for each

Test	M (kJ/min)	W (kJ/min)	E (kJ/min)	(R+C) (kJ/min)	Rate of S (kJ/min)	S at 85mins (kJ)
Pre 1	20.59	1.03	11.70	1.28	6.58	559
Pre 2	20.39	1.02	12.83	1.32	5.22	444
Post 3	18.97	0.95	12.54	1.30	4.18	355
Post 4	19.12	0.96	13.85	1.12	3.19	271

Table 5. CDE test mean rate of heat storage and heat storage at 85 minutes.

test are listed in Table 5 where the rate of S in $kJ \cdot min^{-1}$ = M - W - E ± (R + C). Heat storage at 85 minutes is also listed.

The comparison of tests 1 to 3 (NF) and 2 to 4 (FR) in Table 6 specifies the avenues of increased heat loss rate and decreased heat generation rate after HA. For test 1 versus test 3 an increased heat loss rate of 0.86 $kJ \cdot min^{-1}$

Test and Δ test vs. test	M (kJ/min)	W (kJ/min)	E (kJ/min)	(R+C) (kJ/min)	Rate of S (kJ/min)	S at 85mins (kJ)
Pre 1	20.59	1.03	11.70	1.28	6.58	559
Post 3	18.97	0.95	12.54	1.30	4.18	355
Δ 1 to 3	-1.62	+0.08	-0.84	-0.02	-2.40	-204
Pre 2	20.39	1.02	12.83	1.32	5.22	444
Post 4	19.12	0.96	13.85	1.12	3.19	271
Δ 2 to 4	-1.27	+0.06	-1.02	+0.20	-2.03	-173

Table 6. CDE test heat exchange differences, pre HA versus post HA.

plus a decreased heat generation rate of 1.54 $kJ \cdot min^{-1}$ equaled a net decrease in the heat storage rate of 2.40 $kJ \cdot min^{-1}$. The reduced exercise metabolic rate and increased evaporation rate account for 65.3% and 33.9% of the change in the heat storage rate, respectively. For test 2 versus test 4 an increased heat loss rate of 0.82 $kJ \cdot min^{-1}$ plus a decreased heat generation rate of 1.21 $kJ \cdot min^{-1}$ equaled a net decrease in the heat storage rate of 2.03 $kJ \cdot min^{-1}$. The reduced exercise metabolic rate and increased evaporation rate account for 55.5% and 44.5% of the change in the heat storage rate, respectively.

These heat balance calculations indicate that the primary avenues for the decreased rate of heat storage during CDE exercise post-HA are reduced exercise metabolic rate and increased sweat evaporation rate.

In summary, these case data on HA and CDE testing suggest that 10 days of HA may 1) decrease the submaximal exercise metabolic rate and, 2) be beneficial for increasing work time and reducing metabolic, thermal, and cardiovascular strain during exercise in the heat while wearing a CDE.

Additionally, the investigator has conducted preliminary STPT trials and is presently completing a full STPT 9 day pilot (n=1) series with pre- and post-CDE tests.

METHODS

A. SUBJECTS

A total of 16 male subjects (n = 8 per treatment) will be recruited from the local community to participate in this investigation. Subjects will be 18-35 years of age, possess a maximum oxygen uptake of at least 40 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ and will not have participated in a formal physical training program during the previous three months. The subjects will be matched across two treatment groups, a HA group and a STPT group, for VO_2 max. This permits the two groups to be matched for energy expenditure during the HA and STPT treatments. All subjects will be informed verbally and in written form of the experimental procedures and potential risks, and written consent will be obtained. The subjects will be allowed to withdraw from the study at any time.

B. GENERAL APPROACH / EXPERIMENTAL SEQUENCE

The experimental sequence for the two groups differs only in the treatment (either HA or STPT) as pre- and post-treatment testing are the same for the two groups. For the seven day period prior to the first experimental test and for the three week period of DeA and DeT the physical activity and amount of natural and artificial heat exposure of the subject will be controlled. In addition to the pre-tests listed in Table 7 below, the following procedures will also be conducted during this pre-control period: baseline submaximal metabolic and cardiovascular measures, and a one hour CDE familiarization walk at 25% VO_2 max for sweat rate determination to determine fluid replacement requirements. The aims of the three studies will be met by the sequence of testing listed below in Table 7.

Test or Time Period	Procedures and Exercise	Conditions
Pre-Treatment Tests	Body Comp Test / VO_2 max - Test 1 / PV Measure 1	21-23°C DB 40-60% RH 9-11 mmHg VP
Thermoneutral Test 1	100 min walk, 25% VO_2 max	22°C DB 50% RH 10 mmHg VP
CDE Test 1	100 min walk, 25% VO_2 max	30°C DB 50% RH 16 mmHg VP
Hot Test 1	100 min walk, 25% VO_2 max	43.3°C DB 50% RH 33 mmHgVP
HA Treatment Group	9 days, 100 mins walking per day at 25% VO_2 max	43.3°C DB 50% RH 33 mmHg VP
STFT Treatment	9 days, 40 mins of intervals, work bout, 80-90% VO_2 max	21-23°C DB 40-60% RH 9-11 mmHg VP
Post-Treatment Tests	VO_2 max - Test 2 PV Measure 2	21-23°C DB 40-60% RH 9-11 mmHg VP
Thermoneutral Test 2	100 min walk, 25% VO_2 max	22°C DB 50% RH 10 mmHg VP
CDE Test 2	100 min walk, 25% VO_2 max	30°C DB 50% RH 16 mmHg VP
Hot Test 2	100 min walk, 25% VO_2 max	43.3°C DB 50% RH 33 mmHgVP
DeA and DeT Period	3 weeks of controlled activity	control heat exposure
Post-DeA / DeT Tests	VO_2 max - Test 3 PV Measure 3	21-23°C DB 40-60% RH 9-11 mmHg VP
CDE Test 3	100 min walk, 25% VO_2 max	30°C DB 50% RH 16 mmHg VP

Table 7. Experimental Sequence

C. EXPERIMENTAL PROCEDURES

1. Preliminary Testing / Pre-Control Period: The subjects will provide emergency contact and health history information (form). The subjects will be instructed to avoid physical activity and to limit passive heat exposure to no more than one hour per day in a non-air conditioned

environment. Investigators will interview subjects to encourage compliance with pre-control period procedures and to record the subjects' daily physical activity and heat exposure. Maximal oxygen consumption will be determined using an incremental protocol on a motorized treadmill (Quinton Q65). Criteria for a valid VO_2 max will be an RER greater than 1.1, no increase in oxygen consumption with increasing work rates, and a HR within five beats·min-1 of the estimated maximal HR. Body composition will be determined by hydrostatic weighing and skinfold measures. BSA and BSA/mass ratio will be calculated from height and weight data. Submaximal VO_2 and corresponding treadmill settings will be determined under thermoneutral conditions. To familiarize the subjects with the experimental procedures, the CDE, and to measure sweat rate for fluid replacement determination, the subjects will perform a one hour walk under the same conditions as the CDE test by the fourth day of the pre-control period. Initial plasma volume will be measured (Evan's blue dye, T-1824) within the last two days of the pre-control period.

2. Pre-Test Diet and Exertion: To control energy stores and hydration levels, subjects will refrain from exercise, alcohol, and medications (*e.g.* antipyretics), and consume the same food and liquid volume during the 24 hours preceding all tests. Subjects will be provided with daily salt supplements during testing and treatment periods to avoid the potentially detrimental effects of a low sodium diet during chronic heat exposure. Prior to all tests subjects will complete a pre-test questionnaire which will evaluate for sleep quantity and quality, diet, fluid intake, alcohol consumption, medications and physical activity over the previous 24 hours. Subjects will consume 5 ml of water per kg body weight 1-2 hours prior to exercise and will void bladder and bowel prior to the exercise test. Tests will be rescheduled if

the subject has a resting Tc more than 0.4°C over baseline resting Tc, a body weight deficit of more than 1.5 kilograms, or had an inadequate quality or quantity (greater than two hours under baseline) of sleep. A diurnal control of two hours within a baseline start time will be placed on the thermoneutral, hot, and CDE exercise tests.

3. Experimental Protocol: The sequence of testing will be as shown in Table 7. The CDE test will be conducted the day after the thermoneutral test and the hot test will be conducted two days after the CDE test, for the test periods pre- and post-treatment. Subjects will start their treatment trials the day after hot test 1 and complete the 9 trials within a 10 day period. Plasma volume and VO_2 max will be measured on the first day post-treatment and thermoneutral test 2 will commence the following day.

a) Thermoneutral and Hot Tests: For the pre- and post-treatment thermoneutral and hot submaximal treadmill exercise tests the subjects will walk at 25% VO_2max for 100 minutes in an environmental chamber (thermoneutral - 22°C DB, 50%RH, 9.9 mmHg vapor pressure, 1.8 $m \cdot sec^{-1}$ air velocity; hot - 43.3°C DB, 50%RH, 33.0 mmHg vapor pressure, 1.8 $m \cdot sec^{-1}$ air velocity). Test termination criteria are: Tc greater than 39.3 °C, HR greater than 95% of maximum as determined in the preliminary VO_2 max test, or volitional fatigue.

Pre-exercise: After arrival at the laboratory the subject's nude body weight will be recorded. The subject will then insert a rectal thermistor 11 cm beyond the anal sphincter and attach a heart rate monitor around the thorax. A Teflon catheter will then be inserted into an antecubital vein and secured to the forearm. Four skin thermistors, a blood pressure cuff, three electrocardiogram leads to interface with the BP unit, and a SkBF probe will be attached to the subject. At the end of the instrumentation period, with the

subject at rest in a standing position, pre-test measurements of BP, HR, SkBF, Tre, Tsk, TS, and FATR will be recorded. A 10 ml blood sample will be collected for hematocrit (Hct), hemoglobin (Hb), serum osmolality, plasma lactate, and plasma glucose concentration. The subject will then enter the chamber and start the exercise.

Exercise: Table 8 summarizes the experimental measures. VO_2 and Q will be measured between 5-15, 50-60, and 90-100 minutes. BP will be measured in conjunction with each cardiac output and at 20, 40 and 80 minutes. SkBF (laser Doppler velocimetry) will be recorded at 10 minutes and at every 20 minute interval there after. HR, Tre, Tsk, DB and WB temperatures, and RH, corrected for barometric pressure, will be measured continuously and recorded every minute. The subject's RPE, TS and FATR will be recorded at 5, 50 and 100 minutes. A 10 ml blood sample will be collected at 5 and 10 minutes and at every 20 minute interval there after for Hct, Hb, serum osmolality, plasma lactate, and plasma glucose concentration. Fluid (Gatorade) will be ingested in equal aliquots at 20, 35, 65 and 80 minutes to replace 85-100% of estimated sweat production. Gatorade is nearly isotonic and will have less of an effect on serum osmolality compared to water. The temperature of the Gatorade will be held consistent across all trials at 5°C.

Post Exercise: All instrumentation will be removed and the subject will towel dry. Nude weight and post-test urine production will be recorded for sweat and fluid loss calculations.

b) CDE Tests: For the three CDE submaximal treadmill exercise tests the subjects will walk at 25% VO_2max for 100 minutes in an environmental chamber (30°C DB, 50%RH, 15.9 mmHg vapor pressure, 1.8 $m \cdot sec^{-1}$ air velocity) while wearing the CDE, which consists of t-shirt, lycra

shorts, military fatigue shirt and trousers, a two piece outer garment, mask with canister, hood, cotton glove liners, butyl rubber gloves, socks, and shoes with plastic ankle wrap to simulate rubber overboots. The subject will insert foam nose plugs into each nostril prior to donning the mask, as an external nose clip for VO_2 measures cannot be worn with the mask in place. Test termination criteria are: Tc greater than 39.3 °C, HR greater than 95% of maximum as determined in the preliminary VO_2 max test, or volitional fatigue.

Variable	*Time, mins*													
	Pre	5	10	15	**20**	30	**40**	50	**60**	70	**80**	90	**100**	**Post**
VO_2		(5	to	15)				(50	60)			(90	100)	
Q	Pre	(5	to	15)				(50	60)			(90	100)	
BP	Pre	5		15	20		40	50	60		80		100	
Skin BF	Pre		10		20		40		60		80		100	
Blood Draw	Pre	5	10		20		40		60		80		100	
HR	Pre	*	*	*	*	*	*	*	*	*	*	*	*	
Tre	Pre	*	*	*	*	*	*	*	*	*	*	*	*	
Tsk	Pre	*	*	*	*	*	*	*	*	*	*	*	*	
DB/WB/RH		*	*	*	*	*	*	*	*	*	*	*	*	
RPE		5						50					100	
TS	Pre	5						50					100	
Fatigue Rating	Pre	5						50					100	
Fluid Replace.					20		3 5	50		6 5	80			
Body Weight	Pre													Post

Table 8. Experimental Protocol

* HR, Tre, Tsk, DB, WB, and RH are measured continuously and recorded every minute.

Pre-exercise: The same procedures as above for thermoneutral and hot tests will be completed. After instrumentation and pre-test measures are recorded the subject will put on the CDE over the instrumentation. Body weight with the CDE and instrumentation will be recorded. Additional HR, BP, and TS measures will be recorded with the subject wearing the CDE at

rest in the standing position. The subject will then enter the chamber and start the exercise.

Exercise: The same measurements as above for thermoneutral and hot tests will be completed, see also Table 8.

Post Exercise: Immediately after the test body weight with the CDE and instrumentation will be recorded. The CDE and all instrumentation will be removed and the subject will towel dry. Nude weight and post-test urine production will be recorded for sweat and fluid loss calculations.

c) HA Treatment Trials: The subjects will complete nine 100 minute, 25% VO_2 max HA bouts in an environmental chamber (43.3°C DB, 50%RH, 33.0 mmHg vapor pressure, 1.8 $m \cdot sec^{-1}$ air velocity) in a 10 day period. The first hot submaximal treadmill exercise test doubles as the first acclimation trial. The third, fifth and ninth HA trials will be conducted in exactly the same manner as the hot submaximal treadmill exercise test; the subjects will be instrumented as above for these trials. For the other HA trials only the following measures will be recorded: HR, Tre, BP, RPE, TS, FATR, and pre and post-test nude body weight and post-test urine production for sweat and fluid loss calculations. The subjects will drink water to replace 85-100% of sweat production.

d) STPT Treatment Trials: The subjects will complete nine days of interval training on a programmable treadmill in a thermoneutral environment (21-23°C DB, 40-60%RH, 9.3-10.5 mmHg vapor pressure, 1.8 $m \cdot sec^{-1}$ air velocity) over a 10 day period. Total energy cost for an interval session will be matched to the equivalent energy cost of a HA trial so energy expenditures for the two groups will be similar.

Energy cost matching: At a 0.85 RER the energy per liter of oxygen is approximately 20 $kJ \cdot liter^{-1}$ of oxygen consumed. At an oxygen consumption

rate of 1 liter·min^{-1} the energy production rate will be 20 kJ·min^{-1}. For example, a subject with a VO_2 max of 4 liters·min^{-1} exercising at 25% VO_2 max during a HA trial will consume 1 liter of oxygen per minute to produce energy at a rate of 20 kJ·min^{-1}. For 100 minutes of walking the total energy cost will be 2000 kJ. To match the equivalent energy cost over 40 minutes of interval training this subject will need to average 50 kJ·min^{-1} during the interval session.

To achieve this energy cost matching and provide a high intensity training stimulus the interval training will be conducted at a 1 minute:2 minute work:rest interval ratio where the work interval will be run at 85-90% VO_2 max and the rest interval jogged at 49-52% VO_2 max. The subjects will repeat the cycle of 90% / 49% or 85% / 52% for a total of 13 one minute work intervals, 13 two minute rest intervals and one three minute rest interval during the 40 minute session. For the example subject with a VO_2 max of 4 liters·min^{-1} the energy cost for the work intervals will equal 884-936 kJ and the cost for the rest intervals will equal 1064-1116 kJ, for a total energy cost of 2000 kJ whether run at a 90% / 49% or a 85% / 52% work:rest ratio.

These calculations of matched total energy cost will be accomplished for each subject in the STPT group so their energy cost for doing 40 minutes of interval running would be the same if they were walking at 25% VO_2max for 100 minutes. Work rates on the treadmill will be determined from the preliminary VO_2 max test. HR will be recorded during each interval training session. Tre, ΔPV, VO_2, RPE, TS, FATR, and sweat variables will be measured during the first, third, fifth, and ninth sessions. Fluid intake will be *ad libitum*.

e) DeA and DeT Period: Subjects will be instructed to avoid physical activity and to limit passive heat exposure to no more than one hour

per day in a non-air conditioned environment during this three week period. Investigators will interview subjects twice a week to encourage compliance with control period procedures. Daily physical activity or heat exposure will be recorded. Plasma volume and VO_2 max will be measured on the last day of this three week period and the final CDE submaximal treadmill exercise test will commence the following day.

D. EXPERIMENTAL MATERIALS and METHODS

1. Environmental Chamber: Thermoneutral, hot, and CDE tests and HA trials will be conducted in an Sherer environmental chamber (Gillett Co. Marshall, Michigan); that maintains temperature with a refrigerant system powered by a Copelametic 220 volt, 3 phase, 6.8 amp, 2 horsepower compressor (Copeland Refrigeration Corp., Sidney, Ohio). The chamber is equipped with a water mist humidifier (Model 707TW, Herrmidifier Co., Inc., Lancaster, Pennsylvania), and a Munters Cargocaire Model HC-150 desiccant wheel dehumidifier (Cargocaire Engineering Corp., Amesbury, Massachusetts). Chamber air velocity from a box fan (Sears Roebuck Co., Inc.) was measured with a turbine anemometer (UCS/Spirit Model 569-262).

2. Temperature Data Acquisition System: An automated temperature data acquisition system collects and records all subject and environmental temperatures with a resolution of 0.1° C over a 0-55° C range. The system consists of the following (see Fig 8): YSI 400 series thermistors (YSI, Inc., Yellow Springs, Ohio) connected through a thermistor interface box to thermistor transmitter/conditioner boards (Deban Enterprises, Inc., Yellow Springs, Ohio), which are connected through a breakout box to a 12 bit NB-MIO-16L data acquisition board (National Instruments Corp., Austin, Texas) in a Macintosh II/40 computer using LabVIEW software (National Instruments Corp., Austin, Texas). The transmitter/conditioner board is a

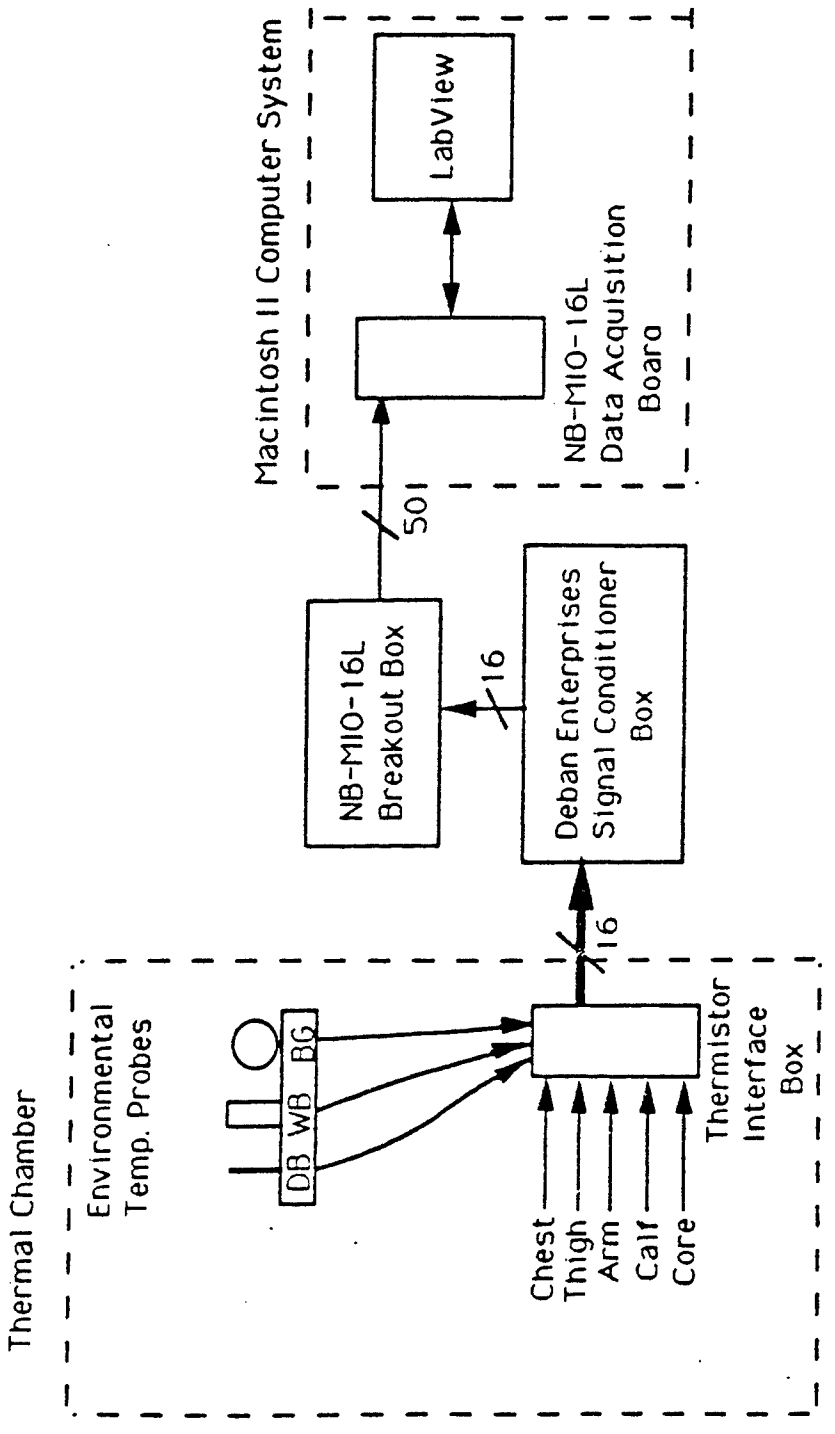

Figure 8. Temperature Data Acquisition System

single, printed-circuit card instrument that converts thermistor resistance tc a proportional voltage; a 0-10 volt signal is transmitted to the NB-MIO-16L data acquisition board which converts the analog signal to digital format. The temperature data acquisition system will be calibrated periodically with four plugs constructed with known resistance values. Two plugs are inserted into the thermistor interface box and zero and span are set for each transmitter/conditioner board. Calibration is verified in the physiological range with the other resistor plugs.

The LabVIEW software displays all temperatures through the front viewing panel of a virtual instrument, which serves as an interface between the instrument and the investigators. Temperatures are displayed and recorded continuously. A separate virtual instrument has been programmed into the system for the calculation (from dry and wet bulb temperatures corrected for barometric pressure, ASHRAE Handbook: 1989 Fundamentals, section 6.13) display, and recording of relative humidity. Dry and wet bulb and black globe temperatures are collected with a locally constructed temperature stand using YSI 410 stainless steel probes. All pre-test and STPT trial body temperature measures will be recorded with a YSI Model 2100 tele-thermometer box.

3. Oxygen Consumption: Metabolic data, including VO_2, expired ventilation (VE), CO_2 production (VCO_2), and the respiratory exchange ratio (RER) will be obtained by passing expired air through a Hans Rudolph valve (Hans Rudolph Inc., Kansas City, Missouri) co·ne·ted to a mixing chamber and volume flowmeter (impeller type) contained within a metabolic cart (SensorMedics Horizon; Anaheim, Ca·ifornia), which senses fractional expired concentrations of O_2 and CO_2 with Beckman OM-11 oxygen and LB-2 carbon dioxide analyzers, respectively. These analyzers will be calibrated

with a known gas before and after each VO_2 test. Calibration of the volume flowmeter will be performed at various flow rates using a syringe of known volume. Metabolic data are calculated on a 30 second basis by the Horizon cart. All exercise tests and trials in the environmental chamber will be conducted on a Q50 motorized treadmill (Quinton Instruments Co., Seattle, Washington). Treadmill speed will be checked throughout each test by measuring the time for 10 revolutions of the belt (length pre-measured).

During VO_2 max tests, VO_2, VCO_2, VE, and RER will be obtained by passing expired air through a two-way Hans Rudolph valve (Series 2700) connected to a mixing chamber and thermal conductivity flowmeter contained within a metabolic cart (SensorMedics 2900; Anaheim, California), which senses fractional expired concentrations of O_2 and CO_2 with zirconium oxygen and infrared absorption carbon dioxide analyzers, respectively. These analyzers will be calibrated with a known gas before and after each VO_2 test. Calibration of the flowmeter will be performed at various flow rates using a syringe of known volume. Metabolic data are calculated on a 20 second basis by the 2900 cart. All VO_2 max tests and STPT trials will be run on a Q65 motorized treadmill with a Q645 programmable controller (Quinton Instruments Co., Seattle, Washington).

4. Blood Pressure: BP will be measured using the auscultatory cuff method with a Colin Model STBP-780 semi-automatic blood pressure monitor (Colin Medical Instruments Corp., San Antonio, Texas). The BP monitor synchronizes a sound signal received from two electrocondenser microphones located in the cuff with an 'R' wave signal from three electrocardiogram electrodes. The unit uses a detection algorithm to determine BP. The monitor sends the microphone-sensed audible signal to a headphone for manual verification. The American Heart Association technique for

measuring BP will be used (18). Diastolic blood pressure (DBP) will be determined using the cessation of Korotkoff sounds (phase V); however, when a disparity exists between phase IV and V sounds, phase IV will be used. MAP will be calculated as (systolic BP + 2·DBP) / 3.

5. Heart Rate: HR will be measured with a Polar Vantage XL, Model No. 145900, heart rate transmitter and watch receiver (Polar USA, Inc., Stamford, Connecticut). HR will be measured continuously and recorded every minute for all tests and trials except for VO_2 max testing where it will be recorded every 15 seconds.

6. Cardiac Output: Q will be measured by use of the CO_2 rebreathing technique (179) in conjunction with the Horizon MMC. Steady state VCO_2 will be obtained with the Horizon as mentioned above. Steady state (± 1 mmHg) end-tidal CO_2 partial pressure will be determined from continuous breath-by-breath gas sampling at the mouthpiece. Mixed venous CO_2 partial pressure will be estimated from CO_2 partial pressure equilibrium attained during rebreathing; valid CO_2 partial pressure equilibrium will be attained if it occurs within 15 seconds. The subject will breath through a 3-way inflatable balloon-type Hans Rudolph valve, Series 8200. A rubber rebreathing bag is filled with a CO_2 - O_2 mixture from CO_2 and O_2 tanks connected to solenoids operated by an electric timing control box, which assures consistent gas concentrations and volume for each rebreathing trial.

Stroke volume will be calculated by $Q \cdot HR^{-1}$. Arterial-venous oxygen difference will be calculated by $VO_2 \cdot Q^{-1}$. Total peripheral resistance will be calculated by $80 \cdot MAP \cdot Q^{-1}$ and expressed as dynes·second·centimeter^{-1}.

7. Cutaneous Blood Flow: SkBF will be measured with a laser Doppler velocimeter (Vasamedics Inc., St. Paul, Minnesota). The probe will be secured to the medial side of the right forearm. During measurements the

arm will be supported at heart level in a sling and the CDE will be kept away from the probe by a flap cut in the sleeve of the fatigue shirt and overgarment top.

8. Plasma Volume: Will be measured by injecting a known quantity of dye T1824 (Evans blue), and the PV is calculated fro n the concentration of the dye in the plasma after 10 minutes of mixing in the circulation. With the subject resting in the supine position 5 ml of blood will be removed from a cubital vein without stasis for a Hct measure. A known quantity of dye, approximately 0.3 $mg \cdot kg^{-1}$ of body weight, will then be injected into the subject. The syringe will be filled and emptied at least five times to wash out all traces of the dye. Ten minutes after dye injection a second venous sample will be taken. PV will be calculated as [mg dye injected · (mg dye · ml $plasma^{-1})^{-1}$]. Total blood volume will be calculated from the PV and the Hct.

9. Plasma Volume Change: Venous blood will be collected without stasis and Hct and Hb concentration will be measured to assess plasma volume changes (47). Hct will be measured in triplicate with a microhematocrit centrifuge and corrected for plasma trapped with packed red cells (32) and for venous versus whole body sampling (33). Hb concentration will be measured in duplicate by the cyanmethemoglobin method. Standard Hb curves will be established with a standard supplied by Sigma Diagnostics, St. Louis, Missouri.

10. Sweat Measures: Whole body sweat production (kg) and sweat rate ($g \cdot hr^{-1}$) will be calculated from body weight loss during exercise corrected for fluid intake, urine production, blood withdrawal, and respiratory water loss and weight loss due to O_2 and CO_2 exchange (103). Body weight will be measured to the nearest 20 grams with a AND FW-150K electronic scale (A&D Inc., Acme Scale Co., San Leandro, California.). SR will also be

calculated per BSA ($g \cdot m^{-2} \cdot hr^{-1}$) and per body weight ($g \cdot kg^{-1} \cdot hr^{-1}$). BSA will be calculated according to the equation of Dubois (50). Sweat sensitivity will be calculated as sweat rate per degree change in Tre ($g \cdot m^{-2} \cdot hr^{-1} \cdot {}^{\circ}C^{-1}$). Fluid loss will be calculated from body weight loss during exercise corrected for urine production post test and weight loss due to O_2 and CO_2 exchange. Percent dehydration is calculated as the fluid loss divided by the initial nude body weight. For CDE tests sweat loss, which equals sweat evaporated if no drippage occurs, will be calculated from clothing plus instrumented weight pre to post-test difference corrected for the same factors as above for sweat production. Sweat absorbed equals sweat production minus sweat loss. Evaporative efficiency will be calculated as the ratio of sweat evaporated from the clothing to sweat produced (100).

11. Core Temperature: Tre will be measured with a thermistor (YSI 401 probe) inserted 11 cm beyond the anal sphincter. A 14 mm diameter wooden bead, attached with epoxy to the probe 11 cm from the probe tip, increases investigator and subject confidence of proper probe location throughout the test. The thermistor will be connected to the temperature data acquisition system described above.

12. Skin Temperature: Mean skin temperature will be determined from skin temperatures measured at four sites using the weighting scheme of Ramanathan (126), Tsk = 0.3 Tchest + 0.3 Tarm + 0.2 Tthigh + 0.2 Tcalf. YSI 409B surface thermistors will be connected to the temperature data acquisition system described above.

13. Mean Body Temperature: Mean body temperature (Tb) will be calculated as Tb = 0.8 Tre + 0.2 Tsk (36).

14. Heat Storage: S will be calculated as S = 3.48 $kJ \cdot kg^{-1} \cdot {}^{\circ}C^{-1}$ x body weight in kg x (0.8Tre + 0.2Tsk) (36). Heat exchange due to ingestion of fluid

will be calculated at 0.7 $kJ \cdot min^{-1}$ per °C difference between the fluid ingested and Tc (1).

15. Catecholamines: pending funding.

16. Serum Osmolality: Serum osmolality will be determined by the freezing point depression technique with a Model 3MO analyzer (Advanced Instruments, Inc., Needham Heights, Massachusetts). The analyzer will be calibrated with standard samples of known osmolality (Advanced Instruments, Inc.). The analyzer determines osmolality by measuring the temperature of an injected sample at the solid-liquid equilibrium point. The freezing point temperature of the serum sample is inversely proportional to its osmolality.

17. Plasma Glucose and Lactate: Plasma glucose and lactate concentrations will be measured by an oxidase technique with a YSI 2300 Stat Plus analyzer (YSI Inc., Yellow Springs, Ohio). For lactate measures blood samples will be deprotenized with cold perchloric acid. Ethylene diamine tetraacetic acid (EDTA) will be added to the blood samples for anticoagulation and inhibition of enzyme activity prior to cetrifugation. The analyzer operates by drawing 25 µl of plasma supernatant into a buffer-filled sample chamber where a sensor, covered with a three layer membrane, is located. The substrate diffuses through a polycarbonate membrane and contacts an immobilized oxidase enzyme and is oxidized, producing hydrogen peroxide. The hydrogen peroxide diffuses through a cellulose acetate membrane and contacts a platinum anode where it is oxidized. The resulting electron flow is linearly proportional to the steady state hydrogen peroxide concentration and, therefore, to the substrate concentration. This analyzer performs an autocalibration at preset intervals using a stock solution of known lactate concentration. By default calibration settings recalibration

will occur after every five samples or 15 minutes, whichever occurs first, after a calibration shift of 2% or greater, or after a sample chamber temperature drift of more than 1°C. Analyzer membrane integrity and linearity tests will be performed per manufacturer specifications using standards supplied by YSI.

18. Rating of Perceived Exertion: The 15-point graded RPE scale will be used during all exercise tests.

19. Thermal Sensation: Thermal sensation is a subjective scale that will be used with ratings as follows: 0-unbearably cold, 1- very cold, 2-cold, 3-cool, 4-neutral, 5-warm, 6-hot, 7-very hot, 8-unbearably hot.

20. Fatigue Rating: Fatigue rating is a subjective scale that will be used with ratings as follows: 1- extremely energetic, 2-very energetic, 3-energetic, 4-neutral, 5-slightly fatigued, 6-very fatigued, 7-extremely fatigued, 8-too fatigued to continue.

F. TIMETABLE

May 93:	1. Approval of Dissertation Committee, Graduate Studies Committee, Human Subjects Committee
	2. Complete pilot testing new techniques
	3. Recruit subjects
May-Sep 93:	Data Collection

G. DATA ANALYSIS

Data will be analyzed using a split-plot repeated measures analysis of variance. Post hoc testing will be accomplished using the Tukey HSD procedure for determining significant differences between means. An alpha value of $P < 0.05$ will be required for statistical significance.

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