THE EFFECTS OF SEX AND MENSTRUAL STATE ON THERMAL SENSATION AND AUTONOMIC THERMOREGULATION

BY

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CHAPTER I. OVERVIEW

A. ABSTRACT

This study was conducted to test the hypothesis that the sensation / integrated thermal signal (ITS) relationship is the same for males and females in the follicular and luteal phases of the menstrual cycle. The autonomic thermoregulatory system depends on afferent signals from thermal sensors located in various regions in the body such as skin, muscle, deep thoracic and abdominal structures, the spinal cord and the brain (27). These signals are integrated within the hypothatlamus as an integrated thermal signal (ITS). We also sought to confirm that thermoregulatory thresholds (sweating, vasoconstriction and shivering) are triggered at the higher core temperatures in females compared to males and in the luteal phase compared to the follicular phase.

It was hypothesized that the relationship between sensation and integrated thermal signals (ITS) is not the same for females in both phases compared to males. Instead, sensation is likely related to one's position on the thermoregulatory scale since females, in general, tend to report colder sensations when exposed to similar thermal environments and thermoregulate at higher core temperatures. Therefore, females were expected to feel colder at any given ITS or thermal environment but feel the same as males at any given thermoregulatory threshold. Likewise, females in the luteal phase were expected to feel colder at any given ITS but feel the same at any given thermoregulatory threshold compared to the follicular phase.

8 males and 8 females were seated in 33 °C water, which was gradually (4 °C · h^{-1}) warmed until sweating occurred (sweat rate increased above 50 g · m^{-2} · h^{-1}). After 10 min. of sweat data was recorded, the water was cooled at the rate mentioned above until thresholds for vasoconstriction (onset of sustained decrease

in fingertip blood flow) and shivering (sustained increase in metabolism) were determined. Thresholds were then referred to as the esophogeal temperature ($T_{es(calc)}$), adjusted to a designated skin temperature of 33 °C. Females were studied once in the follicular phase (between day 3 and day 12 post menstrual flow) and once during the luteal phase (between day 14 and day 23 post menstruation). Males were studied only once. All experiments were commenced between 8:30 a.m. and 10 a.m. Every 5 min. during immersion, subjects were asked to report their level of sensation of temperature on a visual analog scale (VAS). Subjects were also asked to report any changes in sensation since their last report and at the point at which they felt they were sweating and shivering.

Sensation of temperature is related to the ITS and not on the position one is on the thermoregulatory threshold continuum. Females in the follicular (7.0 cm) and luteal (7.1 cm) phase felt significantly warmer than males (6.0 cm) at the sweating threshold ($p < 0.05$). There were no differences in sensation of temperature at the vasoconstriction and shivering thresholds between any of the conditions. All three conditions were equally as sensitive to temperature during the warming and cooling phase of the protocol. All autonomic thermoregulatory mechanisms (sweating, vasoconstriction and shivering) were triggered at significantly higher core temperatures in the luteal phase (37.49 ± 0.25 °C) compared to both the follicular phase (37.22 ± 0.22 °C) and males (37.02 ± 0.22 °C) ($p < 0.05$). There were no significant differences between the follicular phase and males however; our results are very close to those values observed in other studies comparing thermoregulation in males and females in the follicular phase.

The sensation / ITS relationship is the same for males and females in the follicular and luteal phase of the menstrual cycle. Females in the follicular and luteal phase felt significantly warmer compared to males only at the sweating

threshold. All thermoregulatory thresholds were triggered at higher core temperatures in females in the luteal phase compared to the follicular phase and males.

B. INTRODUCTION

GENERAL THEORY OF THERMOREGULATION

Although human habitation exists in a broad range of temperatures, the body attempts to maintain core temperature (T_{co}) at 37.0 ± 0.5 °C. By balancing heat gain and heat loss, human T_{co} is regulated within this narrow range to maintain thermal homeostasis and thus, optimal functioning of metabolic processes. This is accomplished through behavioral and autonomic responses (24).

Autonomic thermoregulation operates through responses on subcortical self-governing processes such as vasomotion and sweating (physiological), and shivering and non-shivering thermogenesis responses (chemical). Behavioral temperature regulation on the other hand, operates largely through the modification of the thermal environment.

The autonomic thermoregulatory system depends on afferent signals from thermal sensors located in various regions in the body such as skin, muscle, deep thoracic and abdominal structures, the spinal cord and the brain (27). These signals are integrated within the hypothatlamus as an integrated thermal signal (ITS). This multiple integration model has been suggested by Santinoff (59) with the hypothalamus as the main coordinator for lower integrators located along the neural axis.

Behavioral responses, are based on thermal sensation and level of comfort. Depending on the state of the thermal environment, sensation and level of comfort lead to motivation to alter the characteristics of the thermal environment prior to initiation of autonomic responses. Since autonomic responses are metabolically taxing, and the body's last defense at protecting itself against dramatic changes in

T_{co}, sensation and level of comfort play an important role in human thermoregulation. Behaviors such adjusting a thermostat or voluntary selection of a suitable micro-climate (i.e. varying the amount of clothing one wears) are just some of the ways humans control their thermal environment. Whether autonomic and behavioural control of body temperature function under two independent systems which interact only in their effects, or whether they are interrelated in both function and effect, remains a point of contention (7).

Once the integrated thermal signal is increased and T_{co} exceeds 37.0 °C, heat loss mechanisms are activated. The first defense is cutaneous vasodilation which dissipates heat through convection and radiation (sensible heat loss). If, however, this does not adequately rid the body of heat, glandular excitation at the level of the skin initiates the sweating mechanism. In this manner, heat is dissipated from sweat, which is secreted onto the skin surface, and evaporated into the atmosphere.

Heat gain mechanisms are activated when the integrated thermal signal is decreased and T_{co} falls below 37.0 °C. The first defense against a decrease in core temperature is cutaneous vasoconstriction. By increasing the thermal gradient between the peripheral vasculature and the skin surface, heat loss is decreased and heat is stored centrally in the the deep body tissues. The shivering mechanism is triggered if T_{co} continues to fall, at which point additional substrates must be oxidized to provide energy to sustain a high metabolic rate (34).

Research on thermoregulation in humans is extensive (3, 23, 38, 45, 49) and has for the most part, been limited to a homogeneous population consisting mainly of young males. Few studies have attempted to delineate the differences in thermoregulation between males and females, and between females in the follicular and luteal phase of the menstrual cycle. Although review work has been done on

differences in autonomic thermoregulatory differences between these three conditions, virtually no data exists on thermal sensation, which dictates behavioral responses, between males and females, and between females in the two phases of the menstrual cycle. Data comparing thermoregulatory mechanisms between genders consistently reveal that females tend to thermoregulate at slightly higher temperatures (0.3 °C) compared to males (44). Also, females during the luteal phase of the menstrual cycle thermoregulate at slightly higher temperatures (0.3 °C) when compared to the follicular phase (54).

STATEMENT OF PURPOSE

The purpose of this study was to 1) determine whether sensation / integrated thermal signal relationship is the same for females (follicular and luteal) compared to males, and for 2) females in the luteal phase compared to the follicular phase. We also sought to confirm that autonomic thermoregulatory thresholds are 3) triggered at higher core temperatures in females (follicular and luteal) compared to males and 4) in the luteal compared to the follicular phase of the menstrual cycle.

HYPOTHESIS

It was hypothesized that the relationship between sensation and the ITS is not the same for females in both phases of the menstrual cycle compared to males. Instead, sensation is likely related to one's position on the thermoregulatory scale since females thermoregulate at higher core temperatures relative to males. Therefore, females were expected to feel colder at any given ITS but feel the same as males at any given thermoregulatory threshold. Likewise, females in the luteal phase thermoregulate at higher core temperatures compared to the follicular phase

and thus, were expected to feel colder at any given ITS but feel the same at any given thermoregulatory threshold compared to the follicular phase. Based on extensive research comparing thermoregulation between males and females and females and between the follicular and luteal phase, it was expected that the thresholds for autonomic thermoregulatory mechanisms such as sweating, vasoconstriction and shivering would be triggered at higher core temperatures (T_{co}) in females compared to males and between women in two phases of the menstrual cycle.

C. REVIEW OF RELATED LITTERATURE

AUTONOMIC THERMOREGULATION

Vasomotion

In the extremities, the arteriovenous anastomoses (AVAs) determine the local temperature, and by their action also define the thermoregulatory state of the body (62). The AVAs are a specific organ responsible for the maintenance of optimal extremity temperature. The AVAs act as 'on' and 'off' vessels meaning, they are either open when T_{∞} is higher than the setpoint or they are closed when T_{∞} is lower than the setpoint. AVAs connect the smaller arteries with the veins, thus bypassing the the nutritive vascular bed with its arterioles, capillaries and venules and are abundant in the finger tips and beneath the nail bed. As the AVAs open, they convey 90 % of the total blood supply to the hand whereas the nutritive blood conveys only about 10 %, thus dividing the vascular arrangement into a thermoregulatory and a nutritive component. The blood flow through the AVAs is responsible for the gross heat influx to the fingers and hand.

Heat transfer is a process involving two distinct alterations: 1) a reduction in the diameter of peripheral vessels, and consequently, 2) a redistribution of blood from the cutaneous and peripheral vasculature to more central locations (53). Cutaneous vessels are under neural control that is influenced by skin and core temperatures (8) as well as baroreflexes (58).

Regulation of these vessels during cold stress operates to increase vasomotor tone (53). During cooling, peripheral vasoconstriction displaces blood from the cutaneous vessels to the deeper veins (58) and in turn, increases central blood volume. In this regard, blood flow and volume to the skin is reduced. The thermal

gradient is increased which results in a lower and retarded convective heat loss and lower radiant heat loss from the skin surface. Heat flux through the cold skin must pass variable insulation barriers that are often higher than the fixed resistance typically seen at full dilation (53).

As T_{co} rises above 37.0 °C or when skin temperature (T_{sk}) is increased while T_{co} remains constant at temperatures not eliciting heat loss mechanisms, a decrease in cutaneous vasomotor-tone is observed. As a result, both blood flow and volume of blood in the peripheral veins is increased in order to dissipate heat that has accumulated in the core, causing an increase in T_{sk}. The thermal gradient between the skin surface and the ambient air/water is decreased, thus, resulting in rapid convective heat loss from the deep vessels to vessels located near the skin surface and radiant heat loss from the skin.

Rowell estimated the maximum skin blood flow obtainable by the combined effects, local and reflex, of heating. At the end of heating, core temperature was 39.1 °C and still rising at an undiminished rate, skin temperature was 40.5 °C, and computed skin blood flow was 7.8 $L \cdot min^{-1}$ and had nearly stopped rising, and near the maximum obtainable by skin and whole-body heating (58).

Sweating

As T_{co} increases, sweat glands are activated to compound the cooling effects of peripheral vasodilation (convective heat loss). Apocrine and eccrine glands secrete sweat onto the skin surface which causes evaporative cooling when it is converted from liquid to water vapor. Nadel et al. (52) conducted a study on the importance of skin temperature in the regulation of sweating. They independently varied the mean skin temperature, and core temperature, while measuring thigh-

sweating rate during rest and post-exercise. They concluded that: (a) at a constant skin temperature, sweating rate was proportional to core temperature, (b) at a constant core temperature, sweating was proportional to the mean skin temperature, and (c) at a given combination of core and mean skin temperatures, local sweating was dependent on the local skin temperature. It was proposed that the local skin temperature acted as a multiplier to the central control signal, represented by a linear additive model of core and mean skin temperatures, to determine local sweating rate. The rate of sweat evaporation depends upon air movement and the water vapor pressure gradient between the skin and the environment, so that sweat tends to collect on the skin in still or moist air. A study conducted by Mekjavic (48), determined that the onset for sweating occurred at a T_{es} of 36.9 ± 0.1 °C when subjects were heated in 40 °C water. However, the temperature at which sweating was initiated during heating from an exercise protocol was $T_{es} = 37.4 \pm 0.3$ °C. When T_{sk} is low, sweat rates are zero.

Shivering

Shivering is the main source of internal heat production when T_{co} or the integrated thermal signal falls below 37.0 °C. An increase in oxygen consumption is usually indicative of a rise in metabolic rate. Since shivering is a rapid, involuntary contraction of muscle, oxygen consumption is used as an indicator for shivhering. Wagner et al. determined that during cold exposure to room temperatures of 28, 20, 15, 10 °C, the average time to onset of shivering was 34 minutes in younger male subjects, compared to 39 minutes in younger female subjects when both were exposed to the same temperatures (63).

AUTONOMIC THERMOREGULATION THEORIES

Setpoint

It has been suggested that human T_{co} is regulated around a fixed temperature of ~37.0 °C which has been defined as the set point. As T_{co} deviates from the setpoint, heat is either gained by or lost from the core. Physiological responses such as peripheral vasodilation and sweating are triggered when T_{co} and/or the integrated thermal signal are increased. A fall in T_{co}, on the other hand initiates chemical responses such as vasoconstriction and shivering.

A change in the set point can produce a corresponding change in the threshold for each thermoregulatory response (i.e. shivering, NST, sweating, panting (in dogs) and vasomotor tone). It is important to point out that, factors such as fever, heat acclimation, phase of the menstrual cycle, and time of day (circadian cycle) can alter the core temperature thresholds for the thermoregulatory responses (53). In determining the set point, the following measurements are necessary: 1) the response (R) of the effectors and 2) the amount of the controlled variable at the condition when R = 0. In a multiple-input system the response can be zero at various combinations of temperatures. Thus, simultaneous temperature measurements in various representative sites of the body such as the hypothalamus, spinal cord, and skin should be measured for an accurate estimate of the integrated thermal signal (59).

Thresholds

The core temperature at which a thermoregulatory response is triggered at a fixed skin temperature, defines the "threshold" for that response. Active vasodilation and sweating during hyperthermia and vasoconstriction, and shivering during hypothermia are important autonomic responses in keeping core temperature constant at ~ 37.0 °C (44).

Interthreshold Range

The "interthreshold range" is defined as the range of core temperatures between the sweating and vasoconstriction thresholds that do not trigger these responses (44). Although it is small, the interthreshold range is ~ 0.2 °C in both men and women. Within the interthreshold range, core temperature varies passively without active thermoregulation (29).

Null Zone

A thermoregulatory "null-zone" of ~ 0.5 °C was demonstrated by Mekjavic et al. (48). The null-zone is defined as the range of core temperature absent of shivering and sweating. They hypothesized that the T_{co} thresholds for sweating and shivering do not coincide but instead are separated by a null zone within which neither thermoregulatory process is active.

Nine male subjects exercised on an underwater cycle ergometer at 59 % of their maximal work rate. During the 2 minutes rest period, the 20 minutes exercise protocol and the 100 minutes recovery period, subjects were immersed to the chin in water maintained at 28 °C. The results indicated that the T_{co} at which sweating ceased and shivering commenced were significantly different ($p < 0.001$) (48).

These results confirmed the existence of a thermoregulatory "null zone" between the threshold core temperatures for shivering thermogenesis and sweating. Its' magnitude was found to be 0.59 ± 0.23 °C and 0.57 ± 0.20 °C for T_{es} and T_{re} respectively.

The null zone may provide a better description of human thermoregulation since it is not restricted to a single precise temperature as described by the set point theory.

STUDIES COMPARING MALES AND FEMALES

In a study which looked at the influence of age and gender on human thermoregulatory responses to cold exposure, Wagner et al. found that the amount of fat and its' distribution were very important insulative factors in the cold. They found that both their female groups had large amounts of body fat compared to male subjects, which was distributed both centrally and in the extremities. They suggested this could have partially accounted for the greater stability in their T_{re} when they were exposed to room temperatures of 28, 20, 15, and 10 °C (63). Male subjects also had higher T_{sk}, which were related to their relatively low percentage body fat, and contributed to the consistent rates of decline in T_{re} in the cold. It was also suggested that adjustment of the rapid metabolic response (40 % within 15 minutes) in the cold helped older women to maintain T_{re} compared to men (18 % within 15 minutes).

Lopez et al. recently studied the difference in the interthreshold range between men and women (44). As stated earlier, the interthreshold range was defined as temperatures between the sweating and vasoconstriction threshold (i.e. temperatures not triggering autonomic thermoregulatory responses in non-

anesethized humans). In this study, it was found that no differences in the interthreshold range existed between men and women, but all thermoregulatory thresholds were shifted upwards by 0.3 °C in women.

Some studies agree that sweating is triggered at a slightly greater core temperature in women than men, and women tend to secrete less sweat per unit area (15, 20, 25) although Anderson (1) found no difference.

THE MENSTRUAL CYCLE

Each month the ovary comes under the influence of follicle stimulating hormone (FSH), which stimulates follicle growth and the secretion of estrogen (66). Lutenizing hormone causes the mature follicle to rupture and its remains to be transformed into a corpus luteum, which secretes progesterone and small amounts of estrogen. The cycle may be divided into 3 parts when considering the secretion of ovarian hormones. In the first part, only the ovary secretes estrogen. In the second, progesterone from the corpus luteum is produced, as are small amounts of estrogen. In the third part, the corpus luteum is breaking down. A new follicle has not yet matured so no hormones are secreted. The presence of estrogen in the blood stimulates growth of the uterine endometrium, while progesterone, working in conjunction with estrogen maintains the newly grown endometrium. In the absence of both hormones, the endometrium is unable to maintain itself and degenerates in a short time.

Day 1 of a normal 28-day cycle is the day on which menstrual flow begins. In the four days that follow, the endometrium undergoes a series of repairs. During the next 5 - 6 days, the endometrium slowly increases in thickness while estrogen is being secreted. For about ten days, the uterus is under the influence of ovarian

hormones, especially progesterone. About 24 days after the beginning of the cycle, the corpus luteum starts to degenerate and its' hormonal secretion ceases. The remaining endometrial layer is retained to become the foundation of the new endometrium, which will be built up during the next follicular phase. Menstruation usually lasts for about 3 - 6 days.

FACTORS INFLUENCING THERMOREGULATION DURING THE MENSTRUAL CYCLE

Metabolic rate

Hessemer and Bruck reported that all autonomic thermoregulatory responses of their female subjects were different between the luteal phase and the follicular phase of the menstrual cycle during rest (36). The metabolic rate was significantly increased in the luteal phase (measured between 2:45 a.m. and 3:15 a.m. at neutral temperature). This finding was further supported by a later study conducted by Hessemer and Bruck, which concluded that metabolic rate was 5.6 % higher in the luteal phase compared to the follicular phase (35).

Gonadal hormones (sex hormones):

The body temperatures of women fluctuate with hormonal status. During the follicular phase of the menstrual cycle, elevated endogenous estrogen levels lead to low body temperatures (45). Immediately following ovulation, and in tandem with the rise of endogenous progestins, body temperatures increase and continue to increase throughout the luteal phase of the menstrual cycle.

Wells et al. observed that during rest in the heat, total body electrolyte losses from sweat were significantly lower in the luteal phase compared to other menstrual phases (65). It was explained that the loss of electrolytes was a result of the progesterone stimulation of aldosterone. No menstrual phase differences were observed in total body or sweat electrolyte concentration.

In a study by Kenshalo, data revealed that greater vasodilation occurred in females during the follicular phase compared to the period of luteal phase when subjects' skin was adapted to temperatures above 36 °C (42). The change observed in cool threshold at ovulation appeared to be related to a greater release of progesterone with the rupture of the G-follicle. Hessemer and Bruck also found an increase in serum progesterone of 44.7 nmol - L^{-1} in females during the luteal phase compared to 0.7 nmol · L^{-1} in females during the follicular phase (35).

Freeman et al. studied the thermogenic action of progesterone in 254 female rats (23). It was found that the smallest daily dose of progesterone, which was capable of producing a significant elevation of rectal temperature, was 1.0mg. Daily injections of 1.0, 2.0, 5.0, and 10.0 mg of progesterone displayed consistent elevation in rectal temperature. The study confirmed that progesterone produces a thermogenic response in rats, which has been observed to be dose-related in women.

In their study on gonadal hormones and body temperature in rats, Marrone et al. (45) observed a rise in colonic temperature from all progesterone doses at proestrus (luteal phase). The mean temperature rise by the 5 mg of progesterone was 0.7 °C greater than that reported by Freeman et al. (23) for the same dose.

It was suggested that progesterone raised the colonic temperature through direct action on the pre-optic area (POA). Rothchild et al. has suggested that

progesterone may directly affect peripheral thermoregulatory mechanisms such as sweating and shivering (56).

Slow sweating responses observed in females, especially during the luteal phase of the menstrual cycle may be partially due to the involvement of hormonal mechanisms (19, 58, 65) occurring through modifications of either the central drive or the sensitivity of the peripheral receptors. Kawahata demonstrated that females treated with testosterone had a decreased onset delay of sweating, and males treated with estradiol had an increased onset delay, thus eliciting a reaction similar to females (40).

Charkoudian et al. (13) observed that exogenous estrogen-progesterone combination in oral contraceptives did not influence the vasoconstrictor response to local cooling of the skin but significantly ($p < 0.001$) augmented the vasodilator response to local warming. It was explained that, increased levels of estrogen, which are elevated during the luteal phase of the menstrual cycle, enhance nitric oxide, being a major contributor to cutaneous vasodilator responses.

Core and skin temperature

An earlier study by Haslag et al. found that oral temperatures (T_{or}) were higher during the first two hours in a climatic chamber (ambient temperature = 38 °C) in females during the follicular phase compared to females in the luteal phase (31). During the luteal phase, T_{or} was higher throughout the entire chamber exposure. Skin temperatures were slightly higher during the luteal phase relative to the follicular and pre-follicular period, however the difference was not related to T_{or}. The higher T_{or} during heat exposure in the post-ovulatory phase of the menstrual cycle did not elicit greater sweating or cutaneous vasodilation during exposure to 38 °C in a climatic chamber.

A study by Hessemer et al. looked at the influence of the menstrual cycle on thermoregulatory, metabolic, and heart rate responses to exercise at night (35). They demonstrated that at neutral temperatures, esophageal (T_{es}), rectal (T_{re}), tympanic (T_{ty}) temperatures in their female subjects were an average of 0.59 °C higher in the luteal phase than in the follicular phase. During exercise for 15 minutes on a cycle ergometer at an ambient temperature of 18 °C, T_{es}, T_{re}, T_{ty} averaged 0.5 °C higher in the luteal phase. Mean skin temperatures tended to also be higher in the luteal phase by about 0.5 °C.

During three phases of the menstrual cycle (menstrual flow, ovulatory phase, luteal phase) no significant differences were found in rectal, skin, mean body temperatures and mean skin temperatures or body heat content prior to or during the 2 h exposure to heat (48 °C dry bulb) (12). During the first 20 minutes of heat exposure, mean T_{re} dropped from the pre-heat exposure level of 37.2 °C to 36.7 °C and then steadily increased to 37.3 °C at the end of the exposure. Menstrual phase differences in T_{re} values were not significantly different and rose 0.21, 0.17, and 0.11 °C, respectively, during menstrual flow, ovulatory phase, and luteal phase heat exposure.

Gonzalez and Blanchard observed an extensive peripheral vasoconstriction in the follicular phase during early periods of ramped cold exposure, which elevated T_{es} above thermoneutral levels (30). This study looked at the effects of the menstrual cycle on heat loss and heat production (M) and core and skin temperatures to cold on 6 unacclimatized female non-smokers (18-29 yr of age). They observed that shivering thermogenesis was strongly correlated with declines in T_{sk} and finger temperature (T_{fi}) ($p < 0.0001$). It was concluded that T_{sk} and T_{es} contributed as additive inputs and T_{fing} contributed a multiplicative effect on the total control of ΔM during cold transients ($R^2 = 0.9$).

Fracscrolo et al. concluded that although T_{sk} was unchanged from the follicular to the luteal phase, T_{ty} was 0.24 ± 0.007 °C higher in the luteal phase compared to the follicular phase. The calculated skin thermal conductance (K_{sk}) was lower in the luteal phase (17.9 ± 0.6 $W \cdot m^{-2} \cdot °C^{-1}$), than in the follicular phase (20.1 ± 1.1 $W.m^{-2} \cdot °C^{-1}$). Calculated skin blood flow (F_{sk}) was lower in the luteal phase (0.101 ± 0.008 $l \cdot min^{-1} \cdot m^{-2}$) compared to the follicular phase (0.131 ± 0.015 $L \cdot min^{-1} \cdot m^{-2}$). It was concluded that during the luteal phase, a decreased thermal conductance in women exposed to a neutral environment allows the maintenance of a higher internal temperature (22).

Pivarnik et al. investigated how the menstrual cycle phase affected temperature regulation during an endurance exercise bout performed at a room temperature of 22 °C and 60 % relative humidity (54). It was observed that core temperature prior to exercise (baseline) was 0.3 °C higher during the luteal phase, compared to the follicular phase and this difference increased to 0.6 °C by the end of the exercise ($p < 0.001$).

Shivering / sweating

In one study, shivering, sweating and cutaneous vasodilation thresholds (measured at the thumb and forearm) were higher in the luteal phase of the menstrual cycle by an average of 0.47 °C compared to the follicular phase (35). It was further noted that chest sweat rate and cutaneous heat clearance at the thumb and forearm was enhanced in the luteal phase when they were related to T_{es} or time.

Bittel and Henane found that the follicular phase had a much longer sweating delay of onset than the luteal phase of the menstrual cycle during a rapid

increase in temperature (6 °C ·· min^{-1}.), which lasted 90 - 120 minutes until thermal balance was reached (5). The delay of onset refers to the time lag between the moment when thermal change is applied and the moment when sweating begins. Male subjects showed considerably shorter delays than female subjects. It was suggested that shorter delays until sweating was initiated was due to less heat being stored. Thus, it was determined that the heat content was increased to a greater extent in females than males. It was also noted that the most extensive heat storage occurred immediately after ovulation (luteal phase) and was characterized by an increase in the onset delay. The heat content was 4.0 kJ ·· kg^{-1} in males, 3.6 kJ ·· kg^{-1} in females during the follicular phase and 5.8 kJ · kg^{-1} in females during the luteal phase of the menstrual cycle. The mean onset delays were 14.2, 17.4 and 24.4 minutes respectively.

No differences were observed in the time of sweat onset between groups during different phases of the menstrual cycle (32). Havenith et al. found that the increments in sweating rate for a rise in oral temperature of 1.0 °C, was unaffected by the period of the menstrual cycle.

Sargent et al. studied the eccrine sweat gland activity during the menstrual cycle and failed to reveal any definitive evidence that its' activity was altered during the menstrual cycle (58). They found no systematic changes in sweat rate, count of active glands, and gland flow for seven females collected during the two major phases of the menstrual cycle (follicular and luteal).

A study by Wells et al. supports Sargent's findings that there are no differences in sweating rate or evaporative heat loss during exposure, which could be attributed to menstrual phase (65). Mean sweat rate and mean evaporative heat values for the luteal phase heat exposures lagged slightly behind menstrual flow

and ovulatory phase values under approximately 30 minutes of heat exposure. It was explained that the statistically insignificant results were likely due to extreme physiological individuality in eccrine sweat response.

Lower sweat production of females compared to males under equivalent heat stress is said to be the result of female sex hormones (67).

BEHAVIORAL THERMOREGULATION

In humans, behavioral thermoregulation is associated with conscious sensation of temperature and emotional feeling of thermal comfort and discomfort (33). Temperature sensation depends on the activity of cutaneous thermoreceptors whereas thermal comfort and discomfort reflect a general state of the thermoregulatory system. Temperature sensations elicited from the skin are used to judge the thermal state of objects or environments and may have a predictive value for human behaviour (33, 53). The extent to which an animal employs autonomic and behavioral means to maintain the stability of core temperature may vary greatly between species and with circumstances, but there can be little doubt that with most species including humans, the range of macro-climates which a species can tolerate depends on the use of behavioral rather than autonomic effector functions (7).

Cunningham and Cabanac used behavioral response to peripheral thermal stimuli as an index of displacement in the internal body temperature from the setpoint temperature in females during the follicular and luteal phases of the menstrual cycle (16). They concluded that the set point shifted towards higher core temperatures during the luteal phase in comparison to the follicular phase. Previous studies utilizing this method have indicated that the effective response to a

peripheral thermal stimulus (pleasantness or unpleasantness), is determined by the displacement in the body temperature above or below the setpoint temperature. Also, a positive affective response is consistently given to the thermal stimulus which would serve to correct for the displacement, i.e. hyperthermic subjects report cold stimuli to be very pleasant and warm stimuli to be unpleasant, while hypothermic subjects report warm stimuli as very pleasant and cold stimuli as unpleasant (11).

Technological advancements offer humans the unique ability to artificially control the thermal environment through the adjustment of thermostats, which function very much like our own physiological thermoregulatory system. Using the process of negative feedback loops, thermostats turn heat on when ambient temperatures fall below a set temperature and turn heat off when they rise above the set temperature. This can be considered as a part of the humans' ability to behaviorally thermoregulate.

Human beings have a wide range of options for controlling their body temperatures. Adjustment of the microclimate can alter thermal insulation by the use of clothing. The macroclimate, however, entails the use of advanced technology to regulate electronic systems such as ventilation, air conditioning and heating, all of which are controlled by a central thermostat functions much like the hypothalamus in humans. Technology has given humans the ability to control, to an extent, the climate within which he / she lives and thus, allows humans to live in the most extreme temperatures on earth (53). Thermal sensation and level of comfort / discomfort is, in a sense, the anticipation of changes in the body's thermal state by using nervous signals related to rate of change in skin temperatures and / or core temperature.

Pandolf suggests that the drive in human beings for behavioral thermoregulation are overridden by other factors such as concerns for personal appearance which may cause people to dress inappropriately for their activity and thermal environment. Well-motivated individuals, such as athletes and military recruits, sometimes exercise in hot environments to the point of endangering themselves (53).

The mechanization and industrialization of society has led to more people spending time in artificial climates. As a result, increased interest in indoor environmental conditions and the temperature at which they should be set have developed (18). This is essential in order to satisfy and accommodate the highest percentage of people (both males and females) so that they may function optimally (i.e. achieve thermal comfort).

THERMAL COMFORT

Thermal comfort is defined by Fanger as "that condition of mind which expresses satisfaction with the thermal environment". He goes on to define thermal neutrality as "that condition in which the subject would prefer neither warmer nor cooler surroundings". A person exposed to an extremely asymmetric radiant field can be in thermal neutrality without being comfortable. However in most cases, says Fanger, thermal neutrality will be the same as thermal comfort and the two concepts can be treated synonymously.

Thermal comfort plays an essential role in a wide variety ways. For example, thermal comfort in humans is the primary purpose for the heating and air conditioning industry which has had a radical influence on the construction of buildings, the choice of materials used to build and thus, on the whole building

industry itself. In a broader perspective, human desire to be thermally comfortable has led to one of the main reasons for building houses at all, at least in the form we know them today (18).

BEHAVIORAL THERMOREGULATORY THEORIES

Thermoneutrality

The physiological definition of thermoneutrality is 'the range of ambient temperatures in which reflexive heat loss and heat production mechanisms are minimally active'. The behavioral definition of thermoneutrality, on the other hand, is the preferred or most thermally comfortable ambient temperature (33) .

Thermoneutral Zone

The thermoneutral zone is the range of temperatures at which the basal rate of heat production equals the rate of heat lost to the environment, and a minimal amount of thermoregulatory effort is required to maintain a constant body temperature (33). The thermoneutral zone is not to be confused with thermoneutrality whereby the term 'thermoneutral zone' is strictly from a physiological stand point. The "lower critical temperature", lies below the low end of the thermoneutral zone where the metabolic rate rises in response to low ambient temperatures and body temperature is held constant.

According to Fanger, the most important variables which influence the condition of thermal comfort are: activity level (heat production in the body), thermal resistance of the clothing (clo-value), air temperature, mean radiant temperature, relative air velocity, and water vapor pressure in ambient air.

Investigations involving college - aged subjects have shown that mean skin temperature and sweat secretion at a given activity level are closely related with the sensation of thermal comfort (18).

Overshoot Phenomenon

Both Gagge et al. (26) and Hardy et al. (30) have described the overshoot phenomenon as a sensory reaction to physiological vasoconstriction, but based on the evidence of skin temperature, which decreases and is accompanied by bradycardia. This suggests that perceptual overshoot may be a characteristic physiological response to rapid cooling whereby perception/sensation of temperature is skewed towards greater levels of discomfort (from rapid cooling) resulting from physiological responses such as low skin temperatures (vasonstriction) and bradycardia.

BEHAVIORAL THERMOREGULATION STUDIES

In addition to measuring various physiological responses in men and women during rest and heat exposure, subjects in a study conducted by Cunningham et al. (15), gave oral reports on thermal sensation and the degree of thermal comfort/discomfort according to two numerical category scales which were extended from those used by Gagge et al. (26). Discomfort/comfort and sensation shifted towards lower core temperatures (T_{ty} + T_{sk}) in men compared to women during cold exposure. In other words, men tended to feel more uncomfortable and felt colder than women at the same given temperature.

Fox et al. explained that one reason why females are better equipped to rely on vasomotor adjustments and thus, avoid sweating might be due to behavioral

gender differences (20). She explained that for social reasons, women may have always preferred to avoid sweating more than men and as a result, have worn lighter clothing in general. Bittel et al. also pointed out that social and behavioral factors may have led to women being less acclimatized than men in a hot environment which is indicated by their higher sweating thresholds and lower sweat rates (5).

Hoffman et al. found that subjects were unable to reliably assess how cold they were (37). The highest correlation observed between perceived temperature and actual temperature was $r = 0.51$. 12 male volunteers between the ages of 21-26 years wore a Stearns IFS-571 floatation suit and placed recumbent in a cold water tank at 10 °C. Subjects remained immersed for 180 minutes unless their core temperature reached either 35.0 °C or an observed rate of fall greater than 1 °C · h^{-1}. Using a visual analog display which was converted and transformed to an equal-interval 100 cm scale to generate scores from 100-0 for perceived cold from "start of the immersion sensation" to "extreme cold". The correlations of their reports of perceived cold and actual temperatures when their core temperature went below 36.1 °C showed no statistically significant differences compared to their reports of perceived cold and actual temperature when their core temperature was above 36.1 °C. Neither the core nor surface temperatures measured correlated highly with cold sensation. In those five subjects who were cooled to a core temperature below 36.1 °C, no clear contribution of core temperature to cold sensation was observed. It was suggested that surface temperatures from multiple body sites caused an inability to formulate a perceptual response. Also, rapid cooling in this study caused an "overshoot", which is a phenomenon earlier described by Gagge et al. (26) and by Hardy et al. (30).

A recent study by Frank et al. determined the relative influence of core and cutaneous temperatures to thermal comfort and autonomic responses in humans (21). By independently controlling skin and core temperature, it was determined that both contribute equally to the perception of temperature. Eight men aged 22 - 28 years, were studied on three separate days. On each day, a different skin temperature was chosen (cold, neutral and warm). The specific skin temperature was achieved by using two circulating-water mattresses, which were placed over and beneath the subject. Intravenous fluid was administered through a 30cm, 16-guage catheter into the right antecubital vein. The mattress temperatures were set at the desired temperature either of 14, 34, or 42 °C on the days of cold, neutral, and warm skin study respectively. Core cooling followed and was accomplished over a 45 min. period by infusion of a cold intravenous fluid (40 ml · kg^{-1} at 4 °C) at 70 ml · min^{-1}. The T_{co}/T_{sk} ratios for thermal comfort was 1:1 but for thermoregulatory responses, the T_{co}/T_{sk} ratio was ~ 2:1 to 4:1. For subjective thermal comfort, the slopes (comfort vs. T_{co} or T_{sk}) were similar for T_{co} and T_{sk} however, the slope was much greater for all other thermoregulatory responses (blood flow, metabolic heat, epinephrine and norepinephrine) for T_{co}. It was concluded that for every 1 °C of core hypothermia, 1 °C of cutaneous warming would be required to achieve thermal comfort, whereas 3 - 4 °C of cutaneous warming would be required to reverse the adrenergic and metabolic responses.

PHYSIOLOGICAL PARAMETERS EFFECTING THERMOREGULATION

Metabolic rate

The metabolic rate is the energy required to maintain all body functions at rest and under active conditions. The metabolic rate is the measure of the quantity of heat required to raise 1g (1ml) of water 1 °C, from 14.5 °C to 15.5 °C. Changes in oxygen consumption (VO_2) normally observed during thermal stress or exercise are associated with changes in the metabolic rate therefore, VO_2 serves to reflect changes in the metabolic rate (53).

Kollias et al. (43) found that the metabolic rate in their lean subjects increased to 2 - 3 times normal values and remained at that level or higher throughout the 15 minutes of immersion in 20 °C water. After 60 minutes of immersion, rectal temperatures decreased 1.4 °C in the lean group compared to only a 0.4 °C decrease in the obese group. The obese group also showed little increase in metabolic activity compared to the lean group.

According to Fox et al., one reason why females are better equipped to rely on vasomotor adjustments and avoid sweating is the lower basal metabolic rate which allows them to maintain thermal equilibrium by convective and radiant exchanges at higher environmental temperature than men (20).

Blood Flow

Changes in blood flow are determined by factors such as nutrient and metabolic requirements of tissues (i.e. transport of nutrients), and the thermal state of the body. Blood flow regulation, for the purpose of maintaining thermal homeostasis, is controlled at the level of the arterioles and venules as opposed to

the capillaries as is the case with nutrient and hormonal transport / delivery and removal of waste products.

In an experiment, a naked person in a climatic chamber was exposed to air temperature of 18 °C. A decrease in blood flow indicated that the AVA closed as the individual cooled down. Both T_{co} and hand temperature decreased. Once finger temperature (T_{fi}) fell below 25 °C, the subject performed moderate work on a cycle ergometer for 10 minutes. As T_{co} increased, T_{fi} also increased however, as work ceased, T_{fi} decreased (the AVA closed). At the end of the experiment, a tourniquet was placed around the forearm, arresting the blood flow to the hand. T_{fi} fell at the same rate with arterial occlusion as that seen with exposure to 18 °C. The experiment demonstrated that when AVAs close, there is virtually no blood flow to the limb (just as in the tourniquet condition) (62). It is known that females have a lower skin perfusion than males and that there are differences in blood flow at different reproductive stages (3). Bartelink et al. determined that peripheral skin circulation (determined by mean skin temperature) was 25.9 ± 3.0 °C in the luteal phase compared with 28.4 ± 3.7 °C in the follicular phase.

Cutaneous contribution to thermoregulatory control varies considerably even among relatively similar persons (14). Cheng et al. found that cutaneous contributions to the control of vasoconstriction and shivering differed among their volunteers. In men, skin temperature contributed 15 - 32 % to vasoconstriction and 14 - 29 % to shivering compared to 18 ± 4 % to vasoconstriction and 18 ± 7 % to shivering in women.

Rennie et al. has stated that the body can regulate heat loss over a wide range through the control of blood flow at the level of the skin. Differences in the perfusion response between genders have been suggested, with lower skin

temperatures (T_{sk}) being documented in women exposed to standardized cold stress compared to men. Differences in T_{sk} are often reported to be a result of increased adipose tissue however, only after peripheral vasoconstriction has occurred is subcutaneous adipose tissue of any value (55).

Shivering and sweating (rates & thresholds)

Most studies comparing thermoregulatory mechanisms between males and females generally agree that females thermoregulate at higher core temperatures than males (5, 44). It is widely accepted that humans tend to thermoregulate at ~37.0 °C (12, 53) and deviations from the regulated value will elicit certain physiological reactions to compensate for heat gain or heat loss, from or towards the core. Exposure to hot temperatures triggers the sweating mechanism and as a result, heat is lost via evaporation and convection as the body attempts to return core temperatures to the setpoint. On the other hand, exposure to cold temperatures results in vasoconstriction and shivering heat production to maintain T_{co} at the set point.

Women have normally demonstrated an earlier response to cold temperatures by earlier vasoconstrictive action and a greater shivering threshold than men at a given temperature (44, 64). With respect to women, men tend to show a delayed response to the cold and approach steady state in the cold more slowly (15).

In a study of rate and gender dependence of the sweating, vasoconstriction, and shivering thresholds in humans, Lopez et al. found that the vasoconstriction and shivering thresholds were significantly higher in women than men (44). Eight men and eight women were cutaneously warmed until sweating was initiated and then were cooled by a central venous infusion of cold fluid. The sweating / shivering thresholds were 37.0 ± 0.3 °C / 35.6 ± 0.5 °C in men compared to 37.3 ± 0.2 °C / 36.1 ± 0.6 °C in women respectively. Since the increases in each response were comparable, the interthreshold range remained around 0.2 °C in each sex.

Women consistently began shivering at higher values of core temperatures than did men (15). It was found that the difference between men and women for shivering was larger than for sweating thresholds. It was also noted that women came closer to thermal steady state at the end of 1 hour cooling, which was indicated by a higher metabolic rate and skin temperature.

Some studies have concluded that sweating is triggered at slightly higher core temperatures in women compared to men and women secrete less sweat per unit area than men (2, 5, 20, 36). Sweat rate in women exposed to hot temperatures are also greater than those normally seen in men under similar conditions (17, 25, 35, 44, 51).

It has been suggested by Frye et al. that exposure to a dry bulb temperature of 37 °C increases sweating in men which is necessary for adequate evaporative cooling (25). Men only require the recruitment of ~ 75 % of the available sweat glands compared to women who recruited ~ 90 %. Thus, men generally have a larger reserve capacity to increase sweating via the recruitment of additional sweat glands. Women, on the other hand, maintain lower sweat rates and skin wetness (w) than the men in humid heat (wet bulb temperature = 30 °C). Despite this, women maintain sufficient evaporative heat loss for the maintenance of thermal equilibrium due to greater sweating efficiency. The study concluded that women reduce sweat output in the humid heat and improve sweating efficiency via a reduction in the number of actively secreting sweat glands, whereas men reduce sweat gland flow without improving sweating efficiency. When evaporation is not restricted, (i.e. in a dry environment, dry bulb temperature = 37 °C), both sexes maintain the necessary sweat rates for adequate evaporative cooling. However, it was determined that men have a greater reserve capacity for further increasing sweating.

A study by Bittel and Henane supports the above finding by observing that the temperature threshold for the onset of sweating in all 5 of their female subjects was shifted towards higher T_{co} (i.e. began sweating at higher a T_{co}). This indicated a decreased sensitivity of the sweating control system to increase in core temperature. The women had lower heat dissipation in the hot environment (T_{db} = 30 °C, wind speed = 0.4 m · sec^{-1}), and it was suggested that the lower heat dissipation was related to later and less extensive sweating in women than men under the same climatic conditions. This led to an increase of the body heat content with a rise in body temperatures (5).

Previous studies have suggested that much of the difference, and perhaps all of it, could be attributed to the normal morphological differences between sexes (36).

Subcutaneous fat

Subcutaneous fat forms a layer immediately below the skin surface. The variation in distribution of subcutaneous fat between individuals may account for differences in thermoregulatory responses. Subcutaneous fat serves as an effective insulator against exposure to cold air (60). The insulative capacity is even more evident during cold-water immersion where heat conduction is approximately 25 times greater than air (6, 47, 55).

Subcutaneous fat greatly enhances the effectiveness of vasomotor adjustments and enables fat individuals to retain a large percentage of metabolic heat and to thermoregulate at higher temperatures despite considerable environmental cold stress (10, 43). This conclusion is based on reports of lower skin temperature in obese subjects as compared with leaner subjects.

Studies have also explained that the difference in skin temperature between obese and lean subjects may be due to a greater tolerance to cold temperatures by obese subjects as they shiver less at a given T_{sk}.

A study of metabolic response in men and women in relation to total body fat (10) looked at subjective sensations of subjects during cold air exposure (10 °C). There did not appear to be any close relationship between sensation and body fatness. The most obese subject (40 % fat), complained and shivered frequently during every experiment. On a scale of 1 to 5 (1 = warm, 2 = cool, 3 = cold, 4 = very cold, 5 = painful), the subject selected "painful" as her rating at the end of the 2h period, compared to two male subjects with 20.3 % and 13.1 % fat respectively, who indicated cold for the same temperature.

McArdle et al. found that relatively greater limb fat for similar trunk fat thickness of females compared with males provided them with extra protection from heat loss due to increased blood flow in the exercising limbs. The limb-to-trunk skin-fold ratio was 34 % higher compared with men of similar percent fat and total skin-fold thickness. Although thermoregulatory benefits were provided through exercise, it was explained that females had the added benefit of a more favorable distribution of subcutaneous fat (47).

Kollias et al. reported that lean subjects increased their metabolism by up to three times compared to obese subjects within 15 minutes of immersion in cold water (20 °C) (43). A rapid decrease in rectal temperature (T_{re}) and a greater rate of change was also observed in the lean group. Obese subjects maintained significantly lower tissue conductance (one determinant of heat loss) from the core to the skin surface, which provided evidence for an inverse relationship between conductance and subcutaneous fat thickness, perfusion and heat loss from the core.

According to Fox et al. a rise in core temperature to the sweat threshold for sweating onset would be postponed in women via vasomotor mechanisms which increases the flow of cool blood returning from the periphery to the core following a large increase in metabolic heat production (20). In general, women have the added benefit of a thicker subcutaneous fat layer which helps insulate the core from heat gain during a transient exposure to hot conditions.

Bernstein et al. found no evidence that a thicker subcutaneous fat layer provides an insulating effect by diminishing heat loss (4). Subjects were seated for 3h in environments of 25 °C and 18 °C (30 % RH). It was explained that since the obese subjects did not have lower skin temperatures than non-obese subjects, the greater mass per unit of heat-losing surface area in the obese subjects would slow the decrease in mean skin temperature. Thus, it was the greater heat content of a large body, which resulted in slower cooling.

A study by Wagner et al. looked at the influence of age and gender on human thermoregulatory response to exposure to 10 °C air (63). Older women maintained their rectal temperature better than young males, young females and older males. It was found that older women did well in cold exposure to 10 °C air by virtue of their body fat insulation and rapid rise in metabolic rate.

These studies clearly indicate that subcutaneous fat serves as an excellent insulator against cold temperatures and protects the core from any heat gain during increases in temperature.

In general, women have a greater amount of subcutaneous fat which partly explains why they may be better protected against thermal stressors, demonstrated by a greater temperature gradient between T_{co} and T_{sk} (25). However, other studies have found that a greater amount of subcutaneous fat does not necessarily

contribute to a smaller heat loss or better protection against low temperatures. Also, considering that thermal receptors are located ~1mm below the surface of the skin, it does not hold that individuals with greater subcutaneous fat would be less "thermally sensitive" than less obese individuals since the physiological significance of thermal receptors would be lost.

Surface-area: mass ratio

Since the rate of heat transfer is a function of surface area, subjects with a larger surface area are able to lose heat at a faster rate than subjects with a smaller surface area, provided the metabolically active tissue mass is the same (2).

Kollias et al. found that heat production was greater after 45 - 60 minutes of immersion in 20 °C water in women who had less than 27 % body fat. Their surface-area: mass ratio (2.9) was also greater than for men (2.3) of comparable body fatness. It was also observed that males and females with greater than 30 % body fat and comparably low surface area: mass, produced low values for heat production. Therefore, under identical conditions of cold exposure, lean women, who had a relatively larger surface area: mass than men of comparable fatness, would cool at a faster rate (43).

Bernstein et al. showed in their study that during exposure to air temperature of 25 °C, obese subjects were shown not to have lower T_{sk} than leaner subjects (4). They believed that the greater mass per unit of heat losing surface area in obese subjects was believed to slow the decrease in mean skin temperature. In other words, cooling would result from the greater heat content of a large body thus, as was expected, higher skin temperatures in the obese subjects was found.

According to Avellini et al., the generally smaller surface area to mass ratio in men is advantageous in environments where ambient temperature exceeds skin temperatures, since less heat is gained from the environment via radiation and convection (2).

This study is supported, in part, by a study conducted by Shapiro et al. (61), who suggested that under dry conditions, a high surface area: mass ratio can be an advantage because it allows rapid forced heat gain by convection and radiation, in which case, the high surface-area: mass ratio would work in two different directions. More evaporative cooling power on one hand and more heat gain form the environment on the other hand.

Most researchers who have included body surface area to mass ratio in their studies to explain (in part) the differences in thermoregulation between individuals with different body types and composition, agree that a greater body surface - area: mass ratio leads to increased heat dissipation when ambient temperatures exceed skin temperatures (2, 4, 49, 63). This is quite often the case with women who generally have a greater surface - area: mass ratio compared to men. Consequently, when skin temperatures are below ambient temperature, people with low surface area: mass ratios tend to gain less heat from the environment.

Fitness level

Brouha et al. reported that non-acclimated men and women responded similarly to exercise in moderate humid environments when the exercise work-load was adjusted relative to maximum aerobic capacity (9). This study was supported in part by Wyndham et al. who found that the reaction of five out of ten acclimatized men who played active sports was no different than those subjects

who were sedentary (67). It was also found that the physiological responses of one athletic woman (gymnast), who did not complete the acclimatization procedure, were no better than the other subjects. However, it was found that non-acclimated men who exercised at the same absolute work rate as non-acclimated women in a hot humid environment reported fewer incidents of distress and had lower rectal temperatures and heart rates, and higher mean sweat rates.

Fox et al. found that athletic pursuits contribute to acclimatization to heat exposure (20). Even though the men in this study had higher average maximum oxygen uptake values (45.6 ml · min^{-1} · kg^{-1}) than women (35.0 ml · min^{-1} · kg^{-1}), no correlation between oxygen uptake and sweating capacity was found. Women had significantly lower oxygen uptakes and initial sweating onset than men, but it was found that the interdependence of these two factors was weak.

In 1990, Havenith et al. looked at the influence of individual parameters on the reaction to heat stress (32). It was found that gender lost its influence once VO_2 and other anthropometric measurements were included into the prediction equations for skin blood flow, heat storage, skin temperature, core temperature, heart rate, blood pressure and sweat evaporation rate.

Avellini et al. concluded that sex related differences of their subjects may have been explained by the initial physical fitness levels of his subjects who were all exposed to 36 °C dry bulb heat (2).

Women with a greater aerobic capacity and who had similar surface-area: mass ratios as males and lower heart rates, maintained similar core temperatures values and less loss of body fluids through sweat. It was concluded that aerobic capacity is an important factor to consider when men and women are compared in the heat. Sex related differences in response to acute heat exposure disappear, with the exception of the higher sweat rates for men (15, 25).

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CHAPTER II.

THE EFFECTS OF SEX AND MENSTRUAL STATE ON THERMAL SENSATION AND AUTONOMIC THERMOREGULATION

A. INTRODUCTION

In humans, resting core temperature is regulated through autonomic thermoregulatory mechanisms (physiological) and behavioural (psychological) processes. Although core temperature is maintained at ~37.0 °C, resting core temperatures and thermoregulatory thresholds for sweating, vasoconstriction, and shivering are shifted towards warmer temperatures (~0.3 °C) in females compared to males (27). Females in the luteal phase of the menstrual cycle have also been shown to have higher resting core temperatures by about 0.3 °C (20, 22, 28, 33) and increased thermoregulatory thresholds (22) compared to the follicular phase.

Behavioural thermoregulation encompasses a series of actions that are dependant on conscious sensation of temperature and with perception of thermal comfort and discomfort (13). The extent to which an animal employs autonomic and behavioural means to maintain the stability of core temperature may vary greatly between species and with circumstances, but with most species including humans, the range of macro-climates which a species can tolerate depends more on the use of behavioural rather than autonomic effector functions (5). There are a limited number of studies comparing sensation of temperature between males and females (11, 12, 17, 24), and no information on the sensation of temperature of females in the two phases of the menstrual cycle.

Cunningham et al. exposed 3 men and 3 women to transients of air temperature (range, 16 – 48 °C). At the onset of shivering, men reported that they felt warmer than females, however, there were no differences in sensation of temperatures between men and women at the sweating threshold (2). Gagge et al. observed an increase in the threshold for sweating in females. At a given thermal input, women felt colder than men and thus, air temperatures had to be increased

for women in order to achieve similar levels of sensation as men (5).

The purpose of this study was 1) to determine whether the relationship between thermal sensation and the ITS is the same for a) males and females (follicular and luteal), and b) females in the luteal phase compared to the follicular phase. The purpose was also 2) to confirm that autonomic thermoregulatory mechanisms are triggered at higher core temperatures in females compared to males and in the luteal phase compared to the follicular phase. The relationship between sensation and ITS was not expected to be the same for females in both phases of the mestrual cycle compared to males. Instead, sensation is likely related to one's position on the thermoregulatory scale since females, in general, tend to report colder sensations when exposed to similar thermal environments. Therefore, females were expected to feel colder at any given ITS but feel the same as males at any given thermoregulatory threshold. Likewise, females in the luteal phase were expected to feel colder at any given ITS but feel the same at any given thermoregulatory threshold compared to the follicular phase.

B. METHODS

SUBJECTS

With approval from the Committee On Research Involving Human Subjects (Faculty of Physical Education and Recreation Studies), 8 males and 8 females were tested in a water bath. All subjects were tested at the same time of day in order to control for circadian rhythms. Females were tested during the follicular and lutealphase of the menstrual cycle. Each female was asked if she had normal menstruation for the 2-month period prior to the study. They were asked to keep a record of the length (in days) of menstruation and menstrual cycle. All females were informed that the follicular phase included days 1-8 (menstrual

flow/menstruation) and the luteal phase included days 11-23 (post-menstruation). Men were studied only once.

INSTRUMENTATION

Esophogeal temperature (T_{es}) was monitored with a Mon-a-therm esophogeal thermocouple (Mallinckrodtt, St. Louis, MO) inserted through a nostril to the level of the heart. Probe insertion depth was determined from sitting height according to the formula where probe length (m) = 0.479 • sitting height (m) -0.044 (31).

Cutaneous heat flux ($W \cdot m^{-2}$) and $T_{sk(avg)}$ was measured from twelve sites by thermal flux transducers (Concept Engineering, Old Saybrook, CT). The transducers were calibrated using a Rapid-k instrument (Dynatech, Cambridge, MA). Body surface area (BSA) was calculated by [area (m^2) = $weight^{0.425}$ (kg) · $height^{0.725}$ (cm) - 0.007184]. The following regional percentages were assigned based on Hardy and Dubois (19): forehead 7 %, upper chest 8.7 %, abdomen 8.8 %, scapula 8.7 % and lower back 8.8 %, anterior thigh 9.5 %, posterior thigh 9.5 %, shin 6.5 %, calf 6.5 %, dorsum of the foot 7 %, dorsum of the hand 5 %, and upper arm 14 %. Flux values for each transducer ($W \cdot m^{-2}$) were converted into $W \cdot region^{-1}$ [flux at region (Watts) = transducer flux ($W \cdot m^{-2}$) • body surface area (m^2) · regional percentage - 0.01].

Fingertip blood flow (peripheral vessel tone) and heart rate was assessed using an Ohmeda Biox 3900 pulse oximeter (Ohmeda, Louisville, CO) with a clamp-type oximeter probe placed on the middle digit. Ohmeda Pulse Oximeter computes the perfusion index. Infrared light of two wavelengths is emitted from one side of the probe, passes through the finger tissues, and is absorbed by the detector. The intensity of transmitted signals is proportional to the amount of blood between the emitter and detector. The difference between the maximum (systole)

and minimum (diastole) signals gave fingertip blood flow during each cardiac cycle.

Oxygen consumption was determined by analysis of O_2 and CO_2 content of the expired air. Expired air was collected through a rubber face mask with one-way valves and directed to a 2.6 L mixing chamber via corrugated tubing. Mixed expired air was continuously sampled from the mixing box at a rate of 500 $ml \cdot min^{-1}$ and analyzed by a Vmax 229D series Pulmonary Function Analysis/ Cardiopulmonary Exercise Testing Instrument (Sensor Medics, Yorba Linda, California).

Analog data from the thermocouples was collected using an electrically isolated Mackintosh computer equipped with a MIO-16L 16 channel analog-digital converter (National Instruments, Austin TX). Data was digitized asynchronously at 2 Hz, averaged over 5 seconds, and scaled using appropriate corrections. The process was controlled by a "virtual instrument" LabView graphical signal processing software (National Instruments, Austin TX).

Sweat rate was measured using a ventilated capsule (~5.0 x 3.5cm) placed on the forehead. Anhydrous compressed air was passed through the capsule over the skin surface at a rate of 1 l/min (Brooks 5850 mass flow controller, Emerson Electric, Hatfield, PA). Vapour density of the effluent air was determined based on the relative humidity and temperature of the air measured by an Omega HX93 humidity and temperature sensor (Omega Engineering, Stanford, CT). It was calibrated by placing it above saturated salt solutions. Sweat rate was the product of the difference in water content between effluent and influent air, and the flow rate. The value was adjusted for the skin surface area under the capsule and expressed in $g \cdot m^{-2} \cdot hr^{-1}$. Flow meters in the inlet and outlet tubing of the capsule allowed the detection and correction of any leaks in the system. Sweat rate was

monitored for 5 minutes following initiation of sweating.

A visual analog scale was used to determine thermal sensation during the experiments. On one side, the scale was divided into 10 cm (1 cm = the coldest the subject had ever felt and 10 cm = the hottest the subject had ever felt) with 1 mm subdivisions. The subjects were presented with the side of the scale labelled cold and hot. The reverse side of the scale (cm / mm divisions) was used to quantify the level of sensation

PROTOCOL

All subjects reported to the laboratory at the same time of day (8:30 a.m.) to ensure that time of day did not influence any changes in thermoregulatory mechanisms. Subjects were instructed to abstain from alcohol and other diuretics including caffeine for 24 h prior to testing to ensure normal hydration. They were asked to rest for what they considered an average nightly rest for them in order to eliminate any influences on the results from fluctuations in the circadian cycle (sleep-wake cycle). Subjects were also asked to abstain from any heavy exercise for 8 h prior to the study.

Once instrumented, subjects were placed into a tub of stirred water to the level of the clavicles. The temperature of the water upon entry was approximately ~ 33 °C (thermoneutral). The water was warmed at a rate of 4 °C · h^{-1} until sweating was detected (Tw ≅ 41 °C). Water entered at a rate of 1 L · 33 sec^{-1} at ~ 40 °C. At this rate, it was determined that water temperature would increase at the desired rate of 4 °C · h^{-1}. Esophogeal temperature was not expected to rise above 38.5 °C.

After at least 5 minutes of sweating data was collected, the water was cooled at 4 °C · h^{-1} until vasoconstriction and shivering were detected. The rate and

temperature at which cold water entered the tank was 1 L · 46 sec^{-1} at ~ 13 °C. Again, it was determined that at this rate, water temperature would decrease at the desired rate of 4 °C · h^{-1}. Esophogeal temperature was not expected to drop below 35.5 °C. The experiment was terminated after at least 5 minutes of sustained shivering data was collected. The subject was re-warmed in a water bath at 38 – 40 °C until core temperature returned to pre-study (baseline) values (~37.0 °C).

Every 5 minutes throughout the study, subjects were asked to report their level of thermal sensation on the VAS measuring. They were also asked to report their sensation of temperature at sweating and shivering. Subjects were also asked to report any changes in sensation since the last report. The slide bar was returned to 5 cm (thermoneutral) after each report so that the subject would not be influenced by their previous report. The ramp rate of change in temperatures for all experiments was small and gradual (4 °C · h^{-1}) so that thresholds could be accurately detected, and to alleviate the overshoot phenomenon. Both Gagge et al. (4) and Hardy et al. (6) have described the overshoot phenomenon as a sensory reaction. It has been suggested that sensation of temperature is skewed towards greater levels of discomfort from rapid cooling resulting from physiological responses such as low skin temperatures (vasoconstriction) and bradycardia. The slow ramp change in water temperature also allowed us to evaluate changes in perception over a wide range of water and skin temperatures.

DATA ANALYSIS

Skin and core temperature contribute to thermoregulatory responses (18, 26, 27). Most protocols for changing thermal stress in humans result in changes in both core and skin temperatures. Thus, it is difficult to compare thermoregulatory thresholds for various conditions. One method to deal with this problem is to take

actual core temperatures at different skin temperatures and adjust or correct them to a similar "designated" skin temperature.

Core temperature contributes more to thermoregulatory responses such as sweating, blood flow, and metabolic heat production than skin temperature (18). A ß-value is the proportional contribution (%) of skin temperature to a thermoregulatory response; the ß-value for skin being 0.1 for sweating (32) and 0.2 for vasoconstriction and shivering (10). Skin and core temperatures also contribute to thermal sensation. Frank et al. recently demonstrated the proportional contribution of skin to thermal perception by independently controlling skin and core temperature in eight men (ages 22 - 28 years) (13). It was determined that skin and core temperature contributed equally (1:1) to thermal perception. Based on this data, we have assigned the ß-value for thermal perception to be 0.5.

The following formula was used in our analysis to correct core temperature for a common designated skin temperature for sweating, vasoconstriction, shivering and sensation to compare the adjusted core temperature at which these autonomic responses and sensations occur. Since T_{es} is not entirely responsible in eliciting autonomic responses and nor does it contribute 100 % to thermal sensation, the proportional contribution (β-value) of skin to these responses must be considered. The following formula will be used to correct T_{es} values [$T_{es(calculated)}$] to a designated T_{sk} (29)

$$T_{es\,(calculated)} = T_{es} + (ß/1\text{-}ß)\,[T_{skavg} - T_{sk\,(designated)}]$$

where T_{es} is the actual esophogeal temperature, T_{skavg} is the actual average skin temperature, $T_{sk(designated)}$ will be set at 33 °C, and $T_{es(calculated)}$ is the T_{es} equivalent at a T_{skavg} of 33 °C. $T_{sk(designated)}$ will be set at 33 °C because this is the mid-range of skin temperatures we expect throughout the experiments (i.e. 25 - 41 °C). $T_{sk(designated)}$ will

be subject to change depending on the mid-range values we receive for skin temperatures in the study.

All variables including T_{es}, $T_{es(calc)}$ and T_{sk} were plotted vs. time (min) for all experiments.

Thresholds for sweating, vasoconstriction, and shivering were compared between males and females in the follicular and the luteal phase using unpaired t-tests. Females in the follicular and luteal phase were compared using a paired t-test. A sweat rate of 50 $g \cdot m^{-2} \cdot h^{-1}$ was determined as the threshold for sweating. The threshold for vasoconstriction was determined once a sustained decrease in fingertip blood flow was observed, and the threshold for shivering was determined when sustained elevation in metabolism (VO_2) was observed. Thresholds were referred to as the core temperatures ($T_{es(calc)}$) adjusted to the designated mean skin temperature of 33 °C for that threshold. $T_{es(calc)}$, T_{es}, T_{sk} and sensation / perception was determined at the thresholds for all autonomic responses. $T_{es(calc)}$, T_{es}, T_{sk}, and thermal sensation at thresholds were also compared.

Thermal sensation was plotted with respect to changes in $T_{es(calc)}$ for all groups. A linear regression analysis was calculated for thermal sensation and $T_{es(calc)}$ during the warming and cooling phase. We compared the position of the linear regression line during warming and cooling to determine whether thermal sensation in humans was related to the ITS or the position one is on the thermoregulatory threshold continuum. We chose to compare the position of the linear regression lines by comparing the highest (during warming) and lowest (during cooling) values for $T_{es(calc)}$ for which a thermal sensation was recorded for all our subjects. These values were $T_{es(calc)} = 40$ °C (for warming) and at $T_{es(calc)} = 37$ °C (for cooling). Thermal sensitivity was also determined by calculating the slopes of the linear regression line. All data was reported as means, ± standard deviations

and $p < 0.05$ was used to define significance.

C. RESULTS

PHYSICAL CHARACTERISTICS

The physical characteristics of our male and female subjects are presented in Table 1. Upon immersion, baseline temperatures of the water were slightly lower in the follicular phase compared to males. Mean resting core temperatures were 0.21 ± 0.19 °C higher in the follicular phase and 0.3 ± 0.12 °C higher in the luteal phase when both were compared to males at $p < 0.05$.

Table 1. Morphometric data. Values are mean ± SD for the age, height, weight, body-mass index (BMI).

	Age (yrs)	Height (cm)	Weight (kg)	BMI	Tes baseline (°C)	Tw baseline (°C)
Males	24.6	182.1	79.2	23.9	36.6	34.1
	(2.5)	(3.7)	(7.2)	(2.1)	(0.1)	(0.5)
Females - F	22.6	168.9*	68.6*	24.1	36.8*	33.6*
	(2.4)	(5.0)	(10.8)	(3.8)	(0.2)	(0.3)
Females - L	22.6	168.93*	68.61*	24.1	36.9*	33.9
	(2.4)	(5.0)	(10.8)	(3.9)	(0.1)	(0.7)

* Significantly different from males at $p < 0.05$.

WARMING AND COOLING RATES OF ESOPHOGEAL AND SKIN TEMPERATURE

During the warming phase, all subjects showed similar rates of increase in core temperature, however; faster skin-warming rates were observed in females in the luteal phase compared to the follicular phase (Table 2). Core temperatures for females in the luteal phase cooled more rapidly than for males at $p < 0.05$. The time difference between the first decrease in Tsk and the first decrease in Tes was calculated to determine the delay in core cooling (lag time) between skin and core

temperatures. The core temperatures in both female groups took significantly less time to begin cooling compare to males ($p < 0.05$).

Table 2. Core (T_{es}) and skin (T_{sk}) warming and cooling rates for males and females in the follicular and luteal phase.

	Males	Females - F	Females - L
Skin warming rate ($°C \cdot h^{-1}$)	3.6	3.3	3.5†
	(1.0)	(0.3)	(0.3)
Core warming rate ($°C \cdot h^{-1}$)	1.1	1.3	1.2
	(0.3)	(0.4)	(0.5)
Warming time (min)	38.0	56.6*	54.7*
	(13.9)	(9.2)	(7.5)
Skin cooling rate ($°C \cdot h^{-1}$)	3.6	3.8	3.8
	(0.51)	(0.2)	(0.6)
Delay in core cooling (min)	14.2	7.8*	7.7*
	(7.8)	(2.1)	(2.6)
Core cooling rate ($°C \cdot h^{-1}$)	0.8	1.1	1.1*
	(0.2)	(0.3)	(0.4)
Cooling time (min)	129.1	130.4	134.2
	(39.2)	(27.3)	(32.5)

Values are mean ± SD for males, and follicular, and luteal phase.

* Significantly different from males at $p < 0.05$

† Significantly different from follicular phase at $p < 0.05$

THERMAL SENSATION AND SENSATION / ITS RELATIONSHIP

For comparative purposes of sensation, values of $T_{es(calc)}$ are presented with a $\beta = 0.5$. At the sweating threshold, females in the luteal (7.0 cm) and follicular (7.1 cm) phase felt warmer than males (6.0 cm) at $p < 0.05$ (Table 3 and Fig. 1). These results are consistent with $T_{es(calc)}$ at the sweating threshold (Table 4). Values for $T_{es(calc)}$ were higher for females in the luteal phase compared to the follicular phase and males at $p < 0.05$. $T_{es(calc)}$ was also significantly higher for females in the

follicular phase compared to males ($p < 0.05$) (Table 4). Thermal sensation and $T_{es(calc)}$ at the vasoconstriction (Table 3 and Fig. 2) and shivering thresholds (Table 3 and Fig. 3) were similar between males and both female conditions.

Table 3. Thermal sensation and sensitivity at the sweating, vasoconstriction, and shivering thresholds for warming and cooling.

	Males	Females - F	Females - L
Sensation at sweating (cm)	6.0	7.1*	7.0*
	(0.7)	(1.4)	(1.3)
Sensation at vasoconstriction (cm)	5.1	5.4	5.1
	(1.0)	(1.0)	(0.9)
Sensation at shivering (cm)	3.1	2.7	1.1
	(0.7)	(1.4)	(0.4)
Sensation at 37 °C	4.1	4.0	3.6
	(0.8)	(0.6)	(0.8)
Sensation at 40 °C	6.1	6.4	6.8
	(0.6)	(1.0)	(1.2)
Sensitivity to warming ($cm \cdot °C^{-1}$)	0.5	0.8	0.6
	(0.3)	(0.5)	(0.3)
R^2 of sensation and T_{es} during warming	0.5	0.4	0.4
Sensitivity to cooling ($cm \cdot °C^{-1}$)	0.5	0.6	0.6
	(0.1)	(0.3)	(0.2)
R^2 of sensation and T_{es} during cooling	0.7	0.7	0.8

* Significantly higher than males at $p < 0.05$.

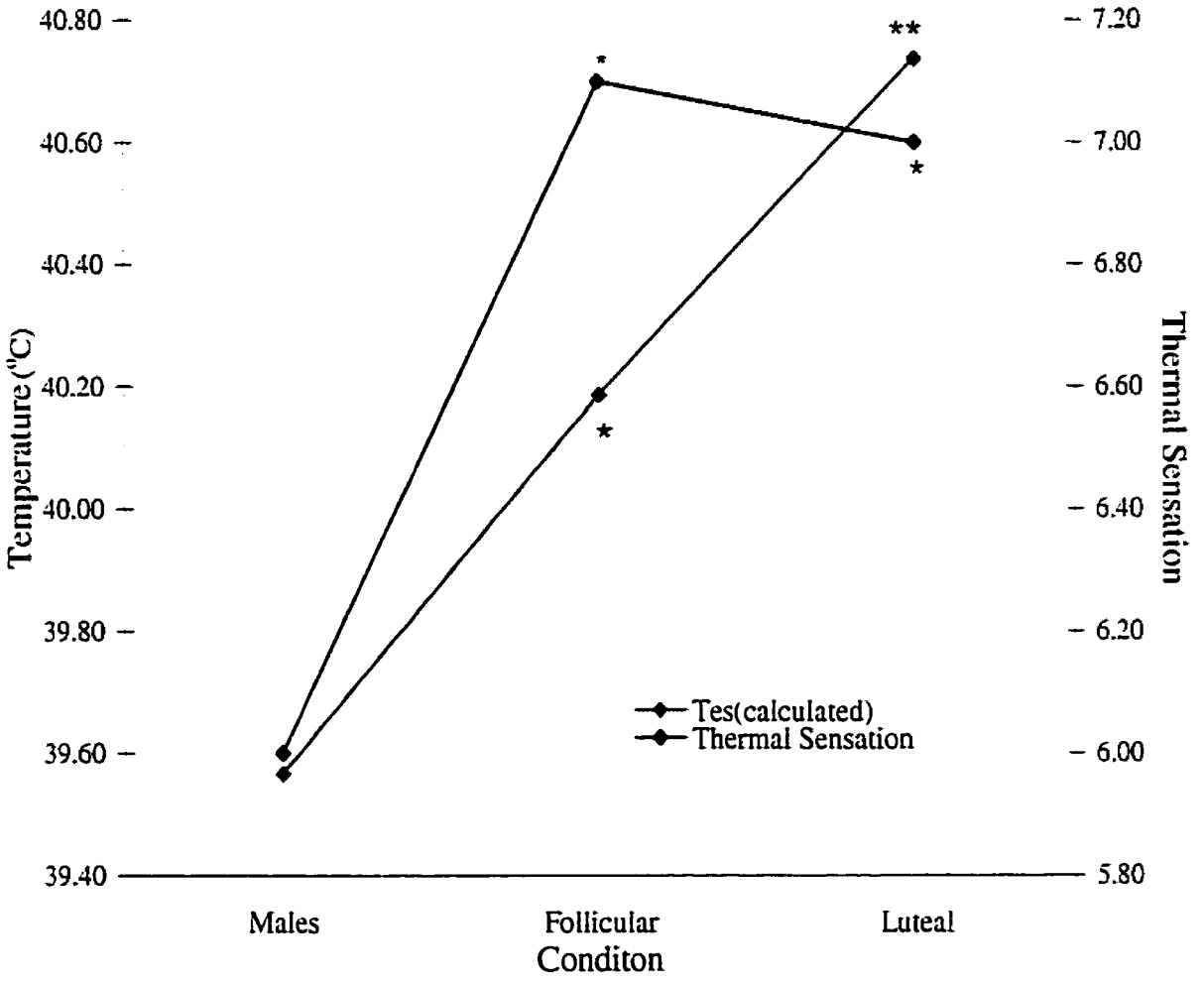

Fig. 1. $T_{es(calc)}$ ($\beta = 0.5$) and thermal sensation at the sweating threshold for males and females in the follicular and luteal phase.

* Significantly different from males at $p < 0.05$

** Significantly different from males and follicular phase at $p < 0.05$

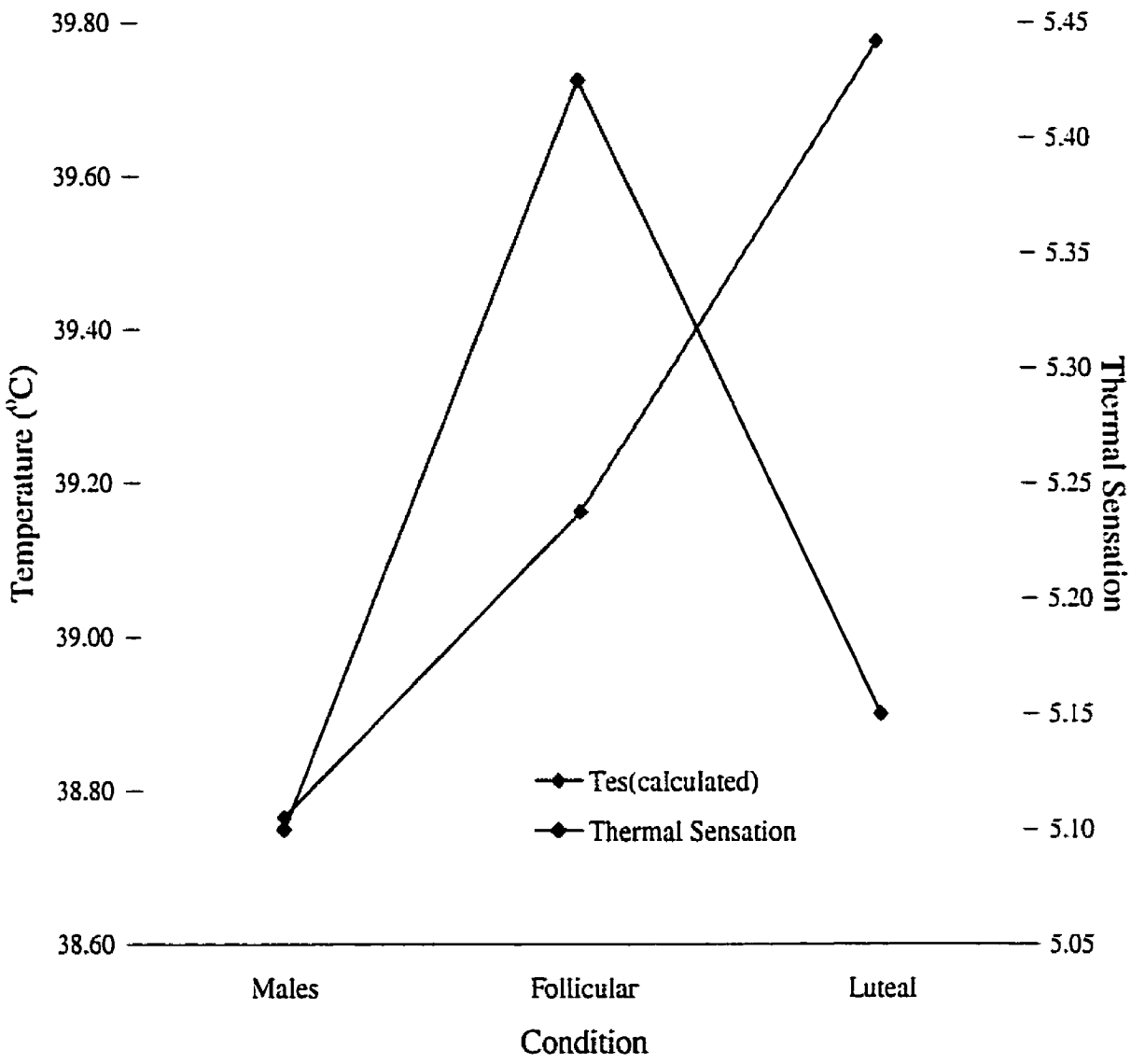

Fig. 2. $T_{es(calc)}$ ($\beta = 0.5$) and thermal sensation at the vasoconstriction threshold for males and females in the follicular and luteal phase.

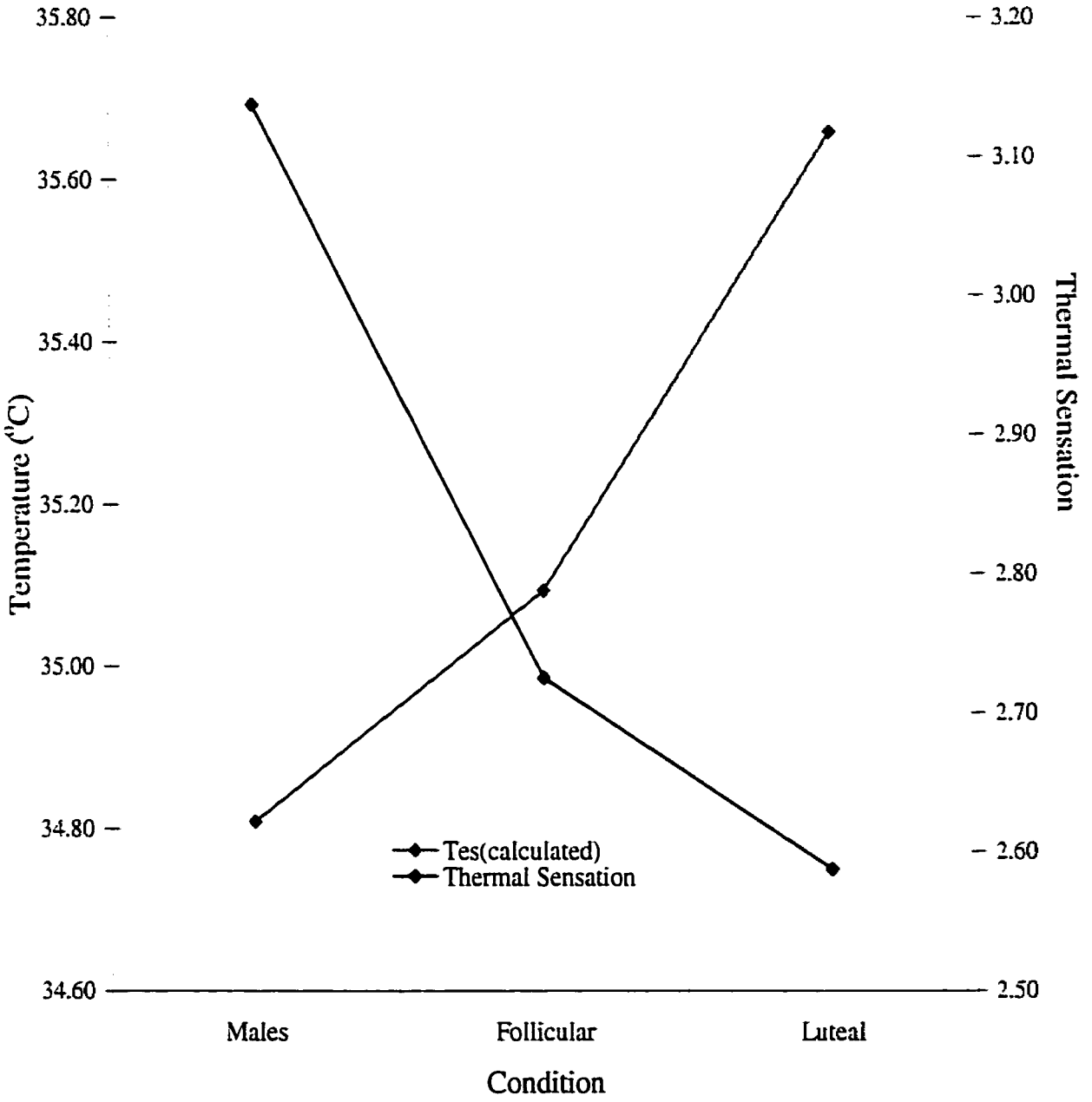

Fig. 3. $T_{es(calc)}$ ($\beta = 0.5$) and thermal sensation at the shivering threshold for males and females in the follicular and luteal phase.

We compared sensation of temperature during warming at $T_{es(calc)}$ = 40 °C and during cooling at $T_{es(calc)}$ = 37 °C to determine whether the position of the linear regression lines (sensation / ITS relationship) during warming (Table 3 and Fig. 4) and cooling (Table 3 and Fig. 5) were the same for all three groups. Thermal sensation at at both esophogeal temperatures (37 °C and 40 °C) were the same for males and females in the follicular phase and luteal phase.

Thermal sensitivity was determined by calculating the slope of the linear regression lines, which were plotted with respect to thermal sensation and $T_{es(calc)}$. β = 0.5. All subjects had similar levels of sensitivity to changes in water temperature during warming (Table 3 and Fig. 4) and during cooling (Table 3 and Fig. 5).

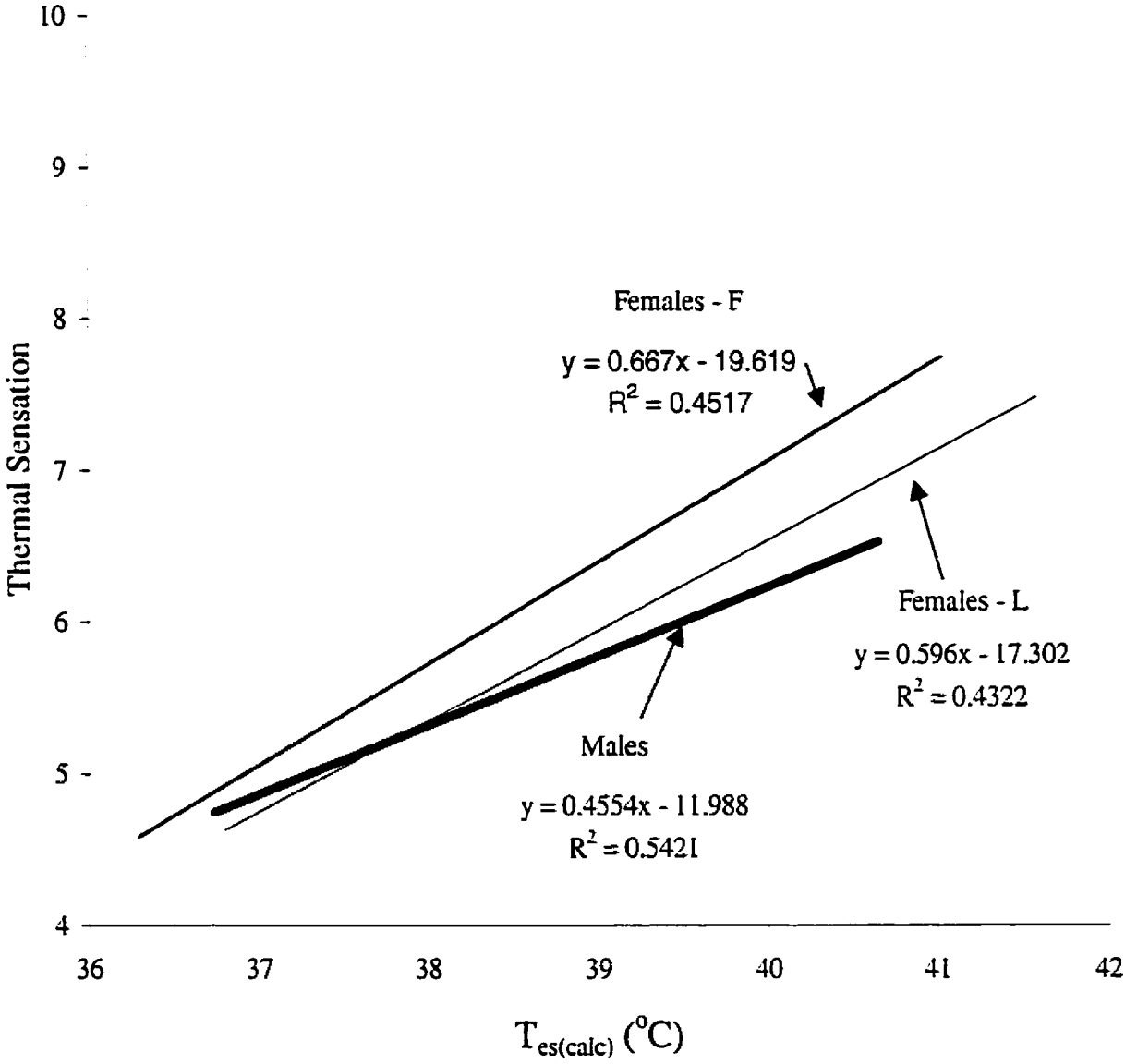

Fig. 4. Thermal sensation and $T_{es(calc)}$ (ITS) relationship for males, and females in the follicular and luteal phase during the warming phase.

No significant differences in the position or slope of the linear regression lines.

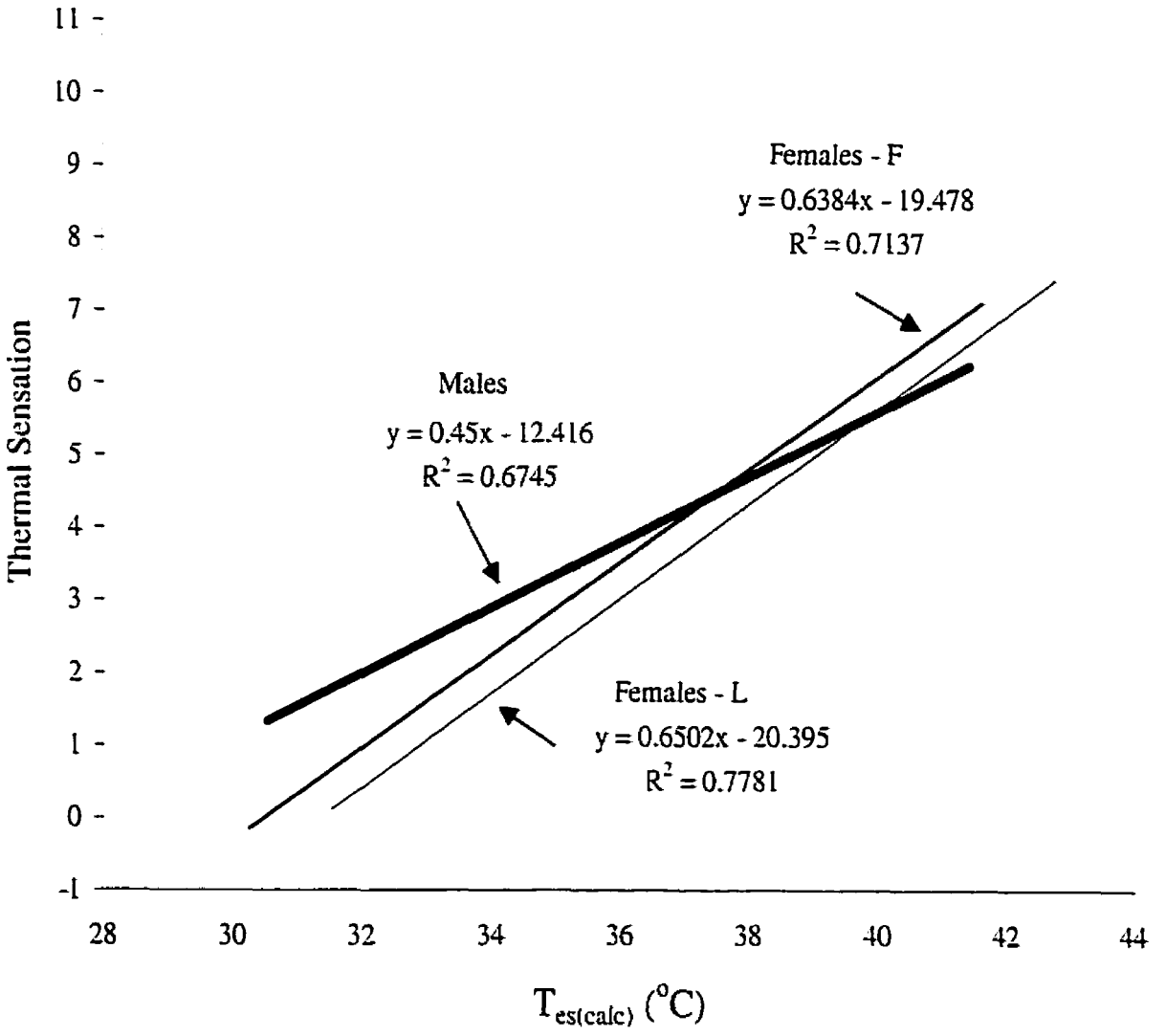

Fig. 5. Thermal sensation and $T_{es(calc)}$ (ITS) relationship for males and females in the follicular and luteal phase during cooling.

No significant differences in the position or slope of the linear regression lines.

THRESHOLDS

Sweating

Females in the luteal phase had higher sweating thresholds [T_{es} with $\beta = 0.1$] compared to males and the follicular phase and warmer skin temperatures compared to males. Females in both phases began sweating later and at warmer water temperatures than males (Table 4).

Table 4. Mean values for time to sweating, water, skin, and actual esophogeal temperatures for the sweating threshold. Core temperatures at threshold were corrected for skin temperature using the β-value = 0.1.

		Males	Females (follicular)	Females (luteal)
	Time (min)	35.3	51.5*	49.1*
		(18.4)	(8.3)	(6.3)
	Twater (°C)	36.4	37.0*	37.2*
		(0.8)	(0.5)	(0.6)
	Tskavg (°C)	35.9	36.3	36.6*
		(0.7)	(0.5)	(0.6)
SW	Tes(actual) (°C)	36.7	36.8	37.1*
		(0.2)	(0.2)	(0.2)
	Tes(calc) β=0.1 (°C)	37.0	37.2	37.5*†
		(0.2)	(0.2)	(0.2)
	Tes(calc) β=0.5 (°C)	39.6	40.2*	40.7*†
		(0.8)	(0.5)	(0.7)

Values are mean ± SD for males, follicular and luteal phase.

* Significantly different than males at $p < 0.05$

† Significantly different than follicular at $p < 0.05$

Vasoconstriction

Females in the luteal phase had higher thresholds [T_{es} with $\beta = 0.2$] for vasoconstriction than males and the follicular phase at $p < 0.05$. The time (min) to sweating onset, water temperature and average skin temperature at the vasoconstriction threshold were similar for all three conditions (Table 5).

Table 5. Mean values for time to vasoconstriction, water, skin, and actual esophogeal temperature at the vasoconstriction threshold. Core temperatures at threshold were corrected for skin temperature using β-value = 0.2.

		Males	Females - F	Females - L
	Time (min)	77.9	95.2	91.7
		(36.1)	(16.9)	(27.1)
	T_{water} (°C)	35.4	35.3	35.7
		(1.3)	(1.1)	(1.0)
	T_{skavg} (°C)	34.9	35.2	35.6
		(2.1)	(1.0)	(0.8)
VC	$T_{es(actual)}$ (°C)	36.8	37.0*	37.2*†
		(0.2)	(0.2)	(0.2)
	$T_{es(calc)}$ β=0.2 (°C)	37.3	37.5	37.8*†
		(0.6)	(0.4)	(0.2)
	$T_{es(calc)}$ β=0.5 (°C)	38.8	39.2	39.8
		(2.1)	(1.2)	(0.8)

Values are mean ± SD for males, and follicular and luteal phase.

* Significantly different than males at $p < 0.05$

† Significantly different than follicular phase at $p < 0.05$

Shivering

Females in the luteal phase had higher thresholds for shivering [T_{es} with β = 0.2] than males and the follicular phase. The time (min) to shivering, water temperature and average skin temperature at the threshold were similar for all three conditions (Table 6).

Table 6. Mean values for time to shivering, water, skin, and actual esophogeal temperature at the shivering threshold. Core temperatures at threshold were corrected for skin temperature using β-value = 0.2.

		Males	Females - F	Females - L
	Time (min)	143.7	157.9	153.1
		(41.1)	(30.1)	(29.2)
	T_{water} (°C)	30.9	30.8	31.2
		(1.3)	(2.5)	(2.2)
	T_{skavg} (°C)	31.0	31.1	31.5
		(1.6)	(2.0)	(1.7)
SH	$T_{es(actual)}$ (°C)	36.8	36.9*	37.1*†
		(0.2)	(0.2)	(0.2)
	$T_{es(calc)}$ β=0.2 (°C)	36.3	36.5	36.8*†
		(0.5)	(0.5)	(0.5)
	$T_{es(calc)}$ β=0.5 (°C)	34.8	35.1	35.6
		(1.6)	(2.0)	(1.8)

Values are mean ± SD for males, follicular and luteal phase.

* Significantly different from males at $p < 0.05$

† Significantly different from follicular at $p < 0.05$

D. DISCUSSION

The present study is the first to examine and compare the differences in sensation of temperature between young males and young females in the follicular and luteal phase of the menstrual cycle while exposed to ramp changes in water temperature (4 °C · h^{-1}). Differences in thresholds for sweating, vasoconstriction, and shivering were also examined.

We hypothesized that the thermal sensation / ITS relationship is not the same for males, and females in the follicular and luteal phase of the menstrual cycle. Rather, sensation of temperature is related more to the position one is on the thermoregulatory threshold continuum. Our hypothesis was based on the fact that females thermoregulate at slightly higher core temperatures (11, 12, 16, 27) and in general, report feeling colder when exposed to similar thermal environments as males. Thus, we expected females to feel colder at any given ITS and feel the same at any thermoregulatory threshold as males. Similarily, since females in the luteal phase thermoregulate at higher core temperatures (15, 22, 23, 28), we expected them to feel colder at any given ITS and feel the same at any thermoregulatory threshold as the follicular phase.

During the warming phase, females in both phases felt the same as males at similar ITS however, they felt warmer than males at the sweating threshold. Females in the follicular and luteal phase also felt the same at similar ITS as well as at the sweating threshold. Therefore, thermal sensation during warming was related more to the ITS rather than to the position on the thermoregulatory threshold scale.

Thermal sensation was also related to the ITS and not to the position one is on the thermoregulatory threshold continuum during cooling for all three conditions. All subjects felt the same at similar ITS however, unlike the sweating

threshold, all subjects felt the same at the thresholds for vasoconstriction and shivering.

Subjects in a study conducted by Cunningham et al. (11), gave oral reports on thermal sensation and the degree of thermal comfort / discomfort according to two numerical category scales which were extended from those used by Gagge et al. (17). She exposed her subjects (3 men and 3 women) to transients of air temperatures (range = 16 – 48 °C). Air velocity was 55cm · sec^{-1} during heating and 65cm · sec^{-1} during cooling. Discomfort / comfort and sensation shifted towards lower core temperatures (T_{ty} + T_{sk}) in men compared to women during cold exposure. In other words, males tended to feel more uncomfortable and felt colder than females at the same given temperature (ITS), suggesting that sensation is related to the position on the thermoregulatory threshold continuum. No differences in sensation were found at the sweating threshold in her study. I the present study, water as opposed to air to manipulate core and skin temperatures and compare sensation and autonomic thermoregulatory thresholds, our results indicated that females in both phases felt significantly warmer at the sweating threhold compared to males. Also in contrast to Cunningham's findings, no differences were detected between males and females at the vasoconstriction and shivering thresholds. The high air velocity used during the warming phase of Cunningham's study could have affected sensation of temperature. It is possible that her subjects felt cooler as a result of a disruption of the boundary layer directly in contact with the skin. This effect is similar to a person standing outside on a hot summer day where the sensation of heat is shifted towards cooler sensations as a result of rapid air movement over the skin. Although water was stirred in our study to disrupt the boundary layer of water and maintain uniform temperature throughout all regions of the skin, the high conductivity of water and its' greater

skin coverage may have caused subjects to remain closer to sensations of warmer temperatures. Even greater air velocities during cooling in Cunningham's study could be the reason why females felt significantly cooler than males. As with warming, the high air velocity over the skin may have caused female subjects to feel cooler where as the movement of water in the present study remained the same. Therefore, femlales in Cunningham's study may have sensed temperatures towards cooler sensations throughout her protocol since air velocities were high during warming and even higher during cooling.

Cunningham's results regarding sensation at thresholds must be interpreted carefully since she did not take into account the relative contribution of skin temperatures to sensation. Since core temperatures were not corrected for changes in skin temperatures, thermal sensation at thresholds could not be accurately compared between subjects. This fact was acknowledged in the latter study by the investigator.

Significantly warmer sensations of temperature at the sweating threshold and no differences in sensation at the vasoconstriction threshold, shivering threshold or at any given ITS could be explained by the additive effects of several factors. Hot and cold receptors responsible for sending afferent signals to the hypothatlamus for initiation of autonmic thermoregulatory mechanisms are also responsible for sensation of temperature which initiate behavioural thermoregulation. Hot receptors in females may be more sensitive than cold receptors, explaining why sensation of temperatures at the sweating threshold were higher compared to males while sensation at the vasoconstriction and shivering thresholds were the same between these two conditions. Due to the nature of neural activity of thermal receptors in the skin, sensation of temperature may be less sensitive during transient changes in skin temperatures (especially colder temperatures) caused by

transient bursts of activity (afferent signaling to central integrator). The initiation of the sweating mechanism may increase the activity of a different type of receptor causing a contiuous discharge of afferent signals.

Because water is 25 times more conductive relative to air (used in Cunninham's protocol), thermal sensation in females in the present study may have been heightened at the sweating threshold. Water immersion may have increased the number and activity of hot receptors directly exposed (receptors at the level of the skin) to the water medium. Assuming that these receptors function both as part of the autonmic thermoregulatory mechanism circuit and sensation of temperature, water may have caused a "heightened" sensation of warmth at the sweating threshold in females.

The combined increase in both skin and core temeperatures in the luteal phase could have further heightened sensation of temperature at the sweating threshold. There were no significant differences in skin temeratures or rates of change in skin temperature between males and females at the vasoconstriction and shivering threshold and consequently, sensation at these thresholds were the same for all three conditions. Again this suggests that hot receptors, especially in the skin, may be more sensitive than cold receptors.

Progesterone has consistantly been shown as the main factor responsible for higher thermoregulatory thresholds in females in the luteal phase. Progesterone is a thermogenically active hormone which is in its' highest concentration during the luteal phase of the menstrual cycle. The effects of progesterone may extend into the realm of thermal sensation, stimulating the neural activity of those hot receptors imbeded in the deep body tissues and further heightening sensation at the sweating threshold.

According to Frank et al. (13), sensation depends equally on skin temperature as it does on core temeperature however, the study he conducted only included males. The relative contribution of skin to thermal perception could be more or less for females. If this is the case, $T_{es(calc)}$ would shift towards either higher or lower values which in turn could shift sensation of temperature at a given ITS towards warmer or colder temperatures. Thus, a greater or lesser contribution of skin temperature to thermal sensation in females would suggest that sensation is dependent more on the position one is on the thermoregulatory threshold continuum rather than on the ITS.

If skin temperature of females contributes less than 50% to sensation, our findings that females felt warmer at the sweating threshold compared to males would be justified however, it could not account for the absence of difference in sensation at the vasoconstriction and shivering thrshold since females would feel warmer at these thresholds also. Females would also feel warmer at any given ITS. However, if skin temperatures actually contribute more than 50 % to sensation in females, then females would feel the same as males at all thresholds including sweating, and colder at any given ITS compared to males. This would support our finding that males and females felt the same at the vasoconstriction and shivering thresholds.

The possibility that thermal sensation is influenced by thermal experience should be considered. Individuals who regularily expose themselves to moderate to extreme thermal environments, especially to a water medium, would not be representative of a normal population. For exmple, the receptors responsible for sensation of temperature in competitive or avid recreational swimmers compared to individuals with little or no exposure to thermal stress, could be desensitized when both groups are exposed to a given thermal environment. Thus, in order to

elicit similar levels of sensation, the magnitude of change in environmental temperature would have to be greater for these individuals

Sensation of temperature could also be affected by body composition and fitness levels. Females who exercise regularily and who's sweating mechanism is well trained, may also show adaptive qualities to sensation when exposed to thermal stress.

Behavioral sex roles causing females to feel significantly warmer at the onset of sweating compared to vasoconstriction and shivering has also been considered. Socially, females may have always preferred to avoid sweating more than men and as a result, have worn lighter clothing in general (4, 12). This aversion to sweating could possibly manifest itself as an accentuated sensation at the sweating threshold. Research has shown that the rates and volume of sweating are much less in females compared to males (1, 4, 12, 16). Fox explained that the sex differences in the functioning of the thermoregulatory system can be explained on their hypothesis that women always tend to be less heat-acclimatized than men, even when the two sexes live in the same climate and appparently follow a similar pattern of living. Because heat acclimatization is essentially a training response, differences between the sexes which are not primarily thermoregulatory in nature make it easier for women to maintain thermal equilibrium without recourse to sweating. She explained that one reason why females are better equipped to rely on vasomotor adjustments and thus, avoid sweating might be due to behavioral gender differences (12). Bittel et al. also pointed out that social and behavioral factors may have led to women being less acclimatized than men in a hot environment which is indicated by their higher sweating thresholds and lower sweat rates (4). Although sweat rates were not calculated in our study, females in both phases had higher sweating thresholds. This phenomenon may be responsible for the hypersensitivity

of hot receptors in females mentioned above. Since the sweating mechanism is less trained in females, thermal sensation at the onset of sweating may be greatly enhanced or hypersensitive. This is similar to individuals who are regularily exposed to cold water such as competitive swimmers who may be desensitized to colder temperatures.

Our male subjects showed a wider range of core temperatures over which they reported neutral or near neutral sensations compared to females, which is in accordance with Cunningham's study. The fact that our male subjects deviated less from thermoneutral sensations throughout the entire protocol and reported levels of sensations closer to neutral at all thresholds may also be rooted in the realm of gender roles in society. Due to gender expectation and other male oriented stereotypes, it is conceivable that our male subjects were less inclined to indicate their true psychological state within the thermal environment they were placed.

This latter phenomenon could stem from societal expectation causing males to feel that overtly expressing emotions such as pain, would be interpreted as a form of weakness. In fact, one male subject reported a neutral sensation throughout the entire warming phase including at the sweating threshold and most of the cooling phase of the protocol. Cunningham also observed such a phenomenon among her male subjects. Females, on the other hand, may have been more comfortable with indicating their true level of sensation. Throughout the warming and cooling phase of the protocol, females, on average, indicated warmer and colder sensations of temperature according to the VAS and thus, deviated more from thermoneutral (5 cm) compared to males. Also, factors such as sex and culture could possibly play a major role when considering motivation to indicate sensation / pain. For example, cultures which impress upon its' people, especially males, to restrain from expressing feelings of pain, may alter the motivation to

report true sensations of temperature.

At a similar thermal environment or ITS, there are no differences in thermal sensation between young males and females (follicular and luteal). Heightened sensations at the sweating threshold for females could be explained by the additive effects of 1) a hyper sensitivity of hot receptors in females only at the sweating threshold and not during transient changes in temperature 2) the high conductive nature of water and its ability to cover a greater skin surface area thereby increasing the number and activity of hot receptors in the skin at the sweating threshold 3) higher skin temperatures and warming rates in the luteal phase 4) thermogenic effect of progesterone 5) thermal experience and amount of exposure to thermal stress 6) body composition 7) fitness levels 8) behavioural sex roles and cultural influences on motivation to express feelings such as pain and sensation.

Autonomic thermoregulatory thresholds are triggered at warmer core temperatures in females in the follicular phase by ~0.3 °C compared to males (1, 2). In 1994, Lopez et al. conducted a study examining the dependence of rate and gender on thresholds (27). They concluded that all thresholds were ~0.3 °C higher in females compared to males. In the present study, although the differences in thresholds were not significantly higher in the follicular phase compared to males, the trends in thresholds between these two conditions are consistent with other studies including that of Lopez et al. The mean core temperature at which all three thermoregulatory mechanisms were activated was ~0.27 °C higher in the follicular phase compared to males. A difference of ~0.03 °C compared to those values observed by Lopez et al. Higher core temperatures in the follicular phase have been shown to be the result of circulating hormones such as estrogen and

progesterone, although the latter is present in reduced concentration compared to the luteal phase.

Since the rate of heat transfer is a function of surface area, subjects with a larger surface area are able to lose heat at a faster rate than subjects with a smaller surface area, provided the metabolically active tissue mass is the same (1). Kollias et al. (26) found that heat production was greater after 45 - 60 minutes of immersion in 20 °C water in women who had less than 27 % body fat. Their surface-area: mass ratio (2.9) was also greater than for men (2.3) of comparable body fatness. It was also observed that males and females with greater than 30 % body fat and comparably low surface area: mass, produced low values for heat production. Therefore, under identical conditions of exposure to cold temperatures, lean women, who had a relatively larger surface area: mass than men of comparable fatness, would cool at a faster rate. Individuals with larger surface areas : mass ratios would also affect the amount of heat gained. Females in our study had comparable BMI to men thus, it could be possible that the faster core cooling rates in our femals may be explained by a larger body surface areas. Higher skin warming rates and skin temperatures observed in females in the luteal phase may have resulted from larger surface areas compared to males, which may also have contributed to warmer sensations at the sweating threshold. Also, the shorter lag time between core and skin cooling in females, suggesting that females in the present study may have had larger heat losing surface areas relative to body weight. Most researchers who have included body surface area to mass ratio in their studies to explain (in part) the differences in thermoregulation between individuals with different body types and composition, agree that a greater body surface - area: mass ratio leads to increased heat dissipation when ambient temperatures exceed skin temperatures (1, 3, 30, 35). This is quite often the case

with women who generally have a greater surface - area: mass ratio compared to men. Consequently, when skin temperatures are below ambient temperature, people with low surface area: mass ratios tend to gain less heat from the environment

All thermoregulatory thresholds were triggered at significantly higher core temperatures in the luteal phase (~ 0.27 °C) compared to the follicular phase, which was very close to values (~ 0.3 °C) observed in other studies (8, 11, 14). Higher thresholds in the luteal phase have been explained by changes in the hormonal status during ovulation. It's believed that lower core temperatures during the follicular phase are a result of increased estrogen levels (28), and higher core temperatures during the luteal phase are caused by the thermogenic properties of progesterone. Progesterone is at its highest concentration during the luteal phase (15, 22, 25, 34). It has also been suggested that lower thermal conductance in the luteal phase may contribute to higher internal temperatures compare to the follicular phase. Fracscrolo et al. concluded that although T_{sk} was unchanged from the follicular to the luteal phase, T_{ty} was 0.24 ± 0.007 °C higher in the luteal phase compared to the follicular phase. The calculated skin thermal conductance (K_{sk}) was lower in the luteal phase (17.9 ± 0.6 W · m^{-2} · $°C^{-1}$), than in the follicular phase (20.1 ± 1.1 W · m^{-2} · $°C^{-1}$). Calculated skin blood flow (F_{sk}) was lower in the luteal phase (0.101 ± 0.008 L · min^{-1} · m^{-2}) compared to the follicular phase (0.131 ± 0.015 L · min^{-1} · m^{-2}). It was concluded that during the luteal phase, a decreased thermal conductance in women exposed to a neutral environment allows the maintenance of a higher internal temperature (14).

LIMITATIONS OF PROTOCOL

All our subjects reported neutral sensation during the first 10 min. of baseline. After each report, the slide bar on the VAS was returned to the neutral position by the investigators. The purpose of doing this was so that subjects would not be influenced by their previous report. In hindsight, our subjects may have given a more accurate report had they been given the opportunity to compare sensory stimulus from one temperature to the other. A visual history of previous reports may have offered more precise transfer of sensation to the visual analog scale.

Frank et al. (13) determined that skin and core temperatures contribute equally to thermal sensation. A β value of 0.5 was used in the present study to correct core temperature to compare thermal sensations at thresholds. Frank only included males in his study to determine the relative contribution of skin to thermal sensation therefore, it is conceiveable that skin temperature may contribute more or less to sensation of temperature in females. Comparisons of sensation at thresholds between males and females are difficult to justify with no evidence that skin temperatures of females contribute a similar amount to sensation as has been observed for males.

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CHAPTER III. SUMMARY

The focus of this thesis was to determine whether the relationship between sensation and the integrated thermal signal is the same for males and females in the follicular and luteal phase of the menstrual cycle. Our results are applicable only to young adults and therefore, should be interpreted carefully. Sensation of temperature may be different for older adults especially for post-menopausal women. We also sought to confirm that autonomic thermoregulatory thresholds such as sweating, vasoconstriction and shivering are shifted towards warmer core temperatures in females compared to males and in the luteal phase compared to the follicular phase of the menstrual cycle.

This study demonstrates that females in both phases sense temperature the same as males when they are exposed to similar thermal environments (integrated thermal signal). At the sweating threshold, females feel warmer than males and feel the same at the vasoconstriction and shivering thresholds. Warmer sensations only at the sweating threshold in females could be the result of the additive effects of several factors such as 1) a hyper sensitivity of hot receptors in females only at the sweating threshold and not during transient changes in temperature 2) the high conductive nature of water and its ability to cover a greater skin surface area thereby increasing the number and activity of hot receptors in the skin at the sweating threshold 3) higher skin temperatures and warming rates in the luteal phase 4) thermogenic effect of progesterone 5) thermal experience and amount of exposure to thermal stress 6) body composition 7) fitness levels 8) behavioural sex roles such as a less trained sweating mechanism in females (sweat less and at a lower rate compare to males) caused by consistantly dressing towards cooler

temperatures to avoid triggering the sweating mechanism for social reasons – increasing the hypersensitivity of hot receptors at the sweating threshold.

All autonomic thermoregulatory mechanisms were increased towards higher core temperatures in females in the luteal phase compared to both males and females in the folicular phase. Although results were not significant, the differences in thermoregulation between the follicular and luteal phase are comparable to other studies. The thermogenic activitiy of progesterone which is increased in concentration during the luteal phase has been demonstrated as the reason for which core temperatures are increased in this phase. Lower thermal conductance in the luteal phase may also contribute to higher internal temperatures compare to the follicular phase as has been suggested by Fracscrolo et al. (14).

APPENDIX I.

A. ETHICS APPROVAL FORM

FACULTY OF PHYSICAL EDUCATION AND RECREATION STUDIES

COMMITTEE ON RESEARCH INVOLVING HUMAN SUBJECTS

TITLE OF PROPOSAL:

The Effects of Gender and Menstrual State on Behavioral and Autonomic Thermoregulation

PRINCIPAL INVESTIGATOR:

Dr. Gordon Giesbrecht
Mr. Prithpal S. Pachu

SPONSORING AGENCY: NSERC

The Committee on Research Involving Human Subjects (Faculty of Physical Education and Recreation Studies) has evaluated the above proposal according to the criteria of the University of Manitoba Committee on Research Involving Human Subjects and finds it to be:

X
_____ acceptable

_____ not acceptable

under the approval category: _____ Approved; __X__ Approved with Modifications;
_____ Renewal Approved; _____ Approved in Principle; _____ Tabled; ____ Withdrawn;
_____ Denied

May 9, 2000

Dr. Michael Mahon, Chair

Notes:

the experiment. They will also be asked to report any changes in sensation or discomfort that they feel since the last report.

B. INFORMED CONSENT

The Effects Of Gender And Menstrual State on Behavioral And Autonomic Thermoregulation

Introduction

The following narrative will provide you, as a subject, insight into the purpose, methodology, risks and discomforts to be encountered in the following series of studies.

Protocol

We will gradually (4°C/h) warm the water until subjects sweat. We will then gradually (4°C/h) cool the water until the subjects vasoconstrict and then shiver. This protocol will be conducted twice on women, once in the follicular phase of the menstrual cycle and again in the luteal phase of the menstrual cycle in a water bath. Men will only be studied once. We will determine whether any differences in perception and sensation in temperature exist between men and women (follicular phase) and women in the follicular and luteal phase of the menstrual cycle. We will also determine the differences in the thresholds for sweating, vasoconstriction and shivering between these groups.

All subjects will be studied at the same time of day (8:30a.m.) to ensure that time of day does not influence any changes in thermoregulatory mechanisms. Subjects will be instrumented and asked to sit outside of the water bath to collect baseline values. They will then be placed into a tub of stirred water to the level of the collar bones. The temperature of the water upon entry will be approximately 33°C. This is a comfortable thermoneutral temperature. Once baseline values are collected in the tub for 10min., the water will be warmed at a rate of 4°C/h until the subjects sweat. Warming will take ~1.5 hours and core temperature is not expected to rise above 38.5°C. There are no expected complications from having a transient (5min.) peak core temperature of 38.5°C. After 5 minutes of sweating, the water will be cooled at 4°C/h until subjects shiver. Cooling will take 2-3 hours and core temperature is not expected to drop below 35.5°C. The experiment will be terminated after 5 minutes of shivering is recorded, after which the subject will be re-warmed in a water bath at 38 - 40°C until core temperature has returned to pre-study (baseline) values (~37.0°C).

Throughout the study, subjects will be asked to indicate their level of thermal sensation/comfort using a visual analog scale (VAS) every 5 minutes for the duration of

Methods

Subject selection: Healthy, non-pregnant subjects between 18 and 40 years old will be studied. We will exclude those taking any medication and females who are on oral contraceptives.

Although we request permission to study 10 volunteers in each group, our previous studies demonstrate that in many cases, results are highly statistically significant after only six subjects. We will thus make a practice of analyzing our data once after completing studies in six volunteers; the remaining four are completed only if necessary. We feel that this arrangement provides a reasonable balance between "statistical purity" and minimizing volunteer exposure. As the study described here may require different treatments or procedures, the consent is formatted to allow us to identify required procedures for each volunteer.

Subjects will wear a swimming suit during the study and sit in the Laboratory for Exercise and Environmental Medicine (room 211 Max Bell Center). This is a well-equipped laboratory and is outfitted with emergency supplies and monitor defibrillator. The room has been checked and approved for volunteer use by Health Science Center Biomedical Engineering. For female subjects, only those with normal menstrual cycles (28 - 30 days) and not on oral contraceptives will be chosen for the study. Subjects will be instructed to abstain from alcohol and other diurrhetics including caffeine for 24h prior to testing to ensure normal hydration. They will also be asked to rest for what they consider an average nightly rest for them in order to eliminate any influences on the results from fluctuations in the circadian cycle (sleep-wake cycle). Subjects will also be asked to abstain from any heavy exercise 8h prior to the study.

Experimental procedure: Female subjects will be studied on two different days, once during the follicular phase and once during the luteal phase of the menstrual cycle. Men will only be studied once. The warming and cooling procedure will be similar for each study for both men and women in both phases of the menstrual cycle.

Instrumentation.

1. Esophageal temperature monitor: In order to monitor the core or central body temperature, esophageal temperature will be monitored. This will be accomplished with an esophageal temperature probe, approximately 2 mm in diameter, inserted through a nostril, while the subject swallows sips of water through a straw so that the tip of this probe lies in the esophagus or food tube at the level of the heart. There usually is mild discomfort and a mild gagging reflex from swallowing this probe. This sensation soon passes however. The only untoward effect of this small device is occasionally a minor nose bleed which can be easily controlled by pressure on the nose. This probe is much smaller than the probe usually used in hospital to record esophageal temperature in conscious and unconscious patients.

2. Tympanic temperature monitor. An alternative indicator of changes in core temperature is the tympanic membrane. A flexible, thermocouple probe will be placed into one ear and left in place during the study. Placement of the thermometer in one ear is not painful but it will decrease hearing while in place.

3. Fingertip blood flow (peripheral vessel tone), will be assessed using a modified Ohmeda Biox 3700 pulse oximeter (Ohmeda, Louisville, CO) with a clamp-type oximeter probe placed on the middle digit.

4. Cardiac monitoring. Heart rate will be monitored continuously during the cooling process with a DC battery operated monitor attached to the skin with adhesive pads. This monitoring is for safety purposes only and was used in our previous studies where no abnormalities were expected or found.

5. Skin temperature and heat flux measurement. Up to 12 disks (~2.5 cm in diameter) will be taped to the skin at various positions on the body. These disks give an indication of skin temperature as well as flow of heat to or from the skin at that point. Some hair may need to be shaved in order to tape disks on, and some discomfort may be experienced upon removing the tape.

7. Ventilation and metabolism measurement. Subjects will be asked to wear a snugly fitting face mask so that ventilation and metabolism can be measured. This will not cause any discomfort. Subjects may remove the mask if they wish to speak to the investigators.

8. Sweat rate. Sweat rate will be measured by using a ventilated capsule (~5.0 x 3.5cm) placed on the forehead or shoulder and held by an elastic strap.

The rise and fall of body temperature will be monitored by the esophageal temperature probe. Cardiac activity will be monitored continuously with the portable monitor. Core body warming and cooling will continue until sweating and shivering is detected respectively. This should take approximately 3-4 hours. It should be reemphasized that the study will be terminated after 5 minutes of shivering is recorded, or if the subject so desire for any reason, or if the investigators deem it necessary.

Following the study subjects will be asked to enter a warm water bath (38-40°C). After body core temperature reaches pre-study levels the monitoring equipment will be removed and subjects will be asked to dry off, dress and after about 30 minutes of further observation with instructions, leave. If subjects have any untoward symptoms such as dizziness, signs of infection, excessive soreness of the joints or skin application sites etc. they may call either Dr. G. Bristow (bus: 788-6321 or res: 889-0416) or Dr. G. Giesbrecht (bus: 474-8646 or res: 895-8671) . If the situation warrants it, subjects will be seen by Dr. Bristow in follow-up. We would like to restate that your participation is voluntary and may be terminated at any time. Furthermore, you will be remunerated $50.00 for each study involving instrumentation and whole body cooling.

SUBJECT'S COPY

Name: _____ Date: _____

Study: _____

UNIVERSITY OF MANITOBA

LABORATORY FOR EXERCISE AND ENVIRONMENTAL MEDICINE

The Effect Of Gender And Menstrual State On Behavioral And Autonomic Thermoregulation.

CONSENT TO BE A RESEARCH SUBJECT

The study in which I have been asked to participate involves increasing body temperature until sweating is initiated and then lowering body core temperature until shivering is initiated. The investigators have previously conducted many cooling studies and have informed me that no complications were experienced as a result of a similar decrease in core temperature (**see below**).

A. Purpose and Background: Dr. Gordon Giesbrecht and his colleagues are studying temperature regulation, behavioral and physiological responses to warm and cold exposure. I am being asked to participate because I am healthy, not pregnant, not on oral contraceptives and between 18 and 40 years of age.

B. Procedures: The study will require 1 day (males) or 2 separate days (females), each trial lasting up to 4-5 hours (including setup and recovery). During the study, my body temperature may decrease by as much as 1.5°C.

The study will include the following specific procedures:

- In each trial the subject will be warmed then cooled gradually (see below). My heart rate and electrocardiogram will be monitored continuously throughout this period. I will be asked several times throughout the water immersion if I would like to exit. Immersion will end when either I wish to get out, the investigator advises exit for safety or other reasons, or when I shiver for 5 minutes. This portion of the trial may be slightly uncomfortable due to the cool sensation, shivering, and possibly, muscle cramps. Serious complications including death due to heart rhythm abnormalities do not occur at this core temperature. A core temperature of less than 25°C is necessary to produce this complication, although preceeding non life threatening minor heart rhythm abnormalities

occur at higher core temperatures. Therefore, the heart monitoring mentioned above will provide added assurance against serious complications by providing early warning of any such abnormalities.

- A thin, flexible tube will be inserted through my nose to midway down my oesophagus (feeding tube),(i.e. at the level of the heart) to measure core body temperature. This may cause a sore throat or minor nose bleed.

- I will have 20+ skin probes taped to the surface of my skin to measure temperature, blood flow, heat loss, blood oxygen, sweating, and electrical signals from my heart, muscles, and brain. Removal of adhesive and tape may cause mild discomfort.

I will wear a snugly fitting face mask so that my ventilation and metabolism can be measured. This will not cause any discomfort. I may remove the mask if I wish to speak to the investigators.

This procedure may be mildly uncomfortable but is not harmful.

I will be asked to place a flexible, cotton-covered thermometer into one of my ears and leave it in place during the study. Placement of the thermometer in one ear is not painful but it will decrease my hearing while in place.

Warming Method.

I will sit in a tub of stirred water to the level of the collar bones. The temperature of the water upon entry will be approximately 33°C and warmed at a rate of 4°C / hour to ~41°C or until I sweat.

Warming will take ~1.5 hours and core temperature is not expected to rise above 38.5°C.

Cooling Method.

I will still be in a tub of stirred water to the level of the collar bones. The temperature of the water will be cooled at a rate of 4°C / hour to ~22°C or until I shiver.

Cooling will take ~2-3 hours and core temperature is not expected to drop below 35.5°C.

C. Confidentiality: Any information obtained in connection with this study that can be identified with me will remain confidential and will be disclosed only with my permission. In any written reports or publications, I will not be identified.

D. Benefits: There will be no direct benefit to me from these procedures other than an honorarium. However the investigators may learn about temperature regulation and thermal sensation, and will share these results at the end of the study, upon my request.

E. Questions: I have talked with Prithpal & Dr. Giesbrecht and/or Bristow about this study and my questions have been answered. If I have any other questions I may call (204) 474-6864 or 789-3321.

F. Consent: I have been given a copy of this consent form to keep. Participation in this research is voluntary. I may decline to participate in the study or may withdraw from it at any time. I just have to say so.

G. Payment: Because this study involves my time and some discomfort, will be reimbursed $50.00 for each study involving instrumentation and cold water immersion. Payment will be in the form of a check mailed after a delay of about three to six weeks.

SIGNATURE: _____

DATE: _____

WITNESS: _____

INVESTIGATOR:_____

INVESTIGATOR'S COPY

Name: _____ Date: _____

Study: _____

UNIVERSITY OF MANITOBA

LABORATORY FOR EXERCISE AND ENVIRONMENTAL MEDICINE

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