INFLUENCE OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE DURING COMPENSABLE AND UNCOMPENSABLE HEAT STRAIN

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science
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Influence of menstrual cycle phase and oral contraceptive use during compensable and uncompensable heat strain.

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Abstract

The purpose of this study was to determine the influence of menstrual cycle phase and oral contraceptive use during compensable and uncompensable heat strain. Eighteen women (18-35 yr), who differed only with respect to oral contraceptive use (n=9) or non-use (n=9), performed light intermittent exercise at 40°C, 30% relative humidity while wearing either Canadian Forces combat clothing or NBC protective clothing. Thermoregulatory responses in each clothing configuration were compared during the early follicular (EF, days 2-5), late follicular (LF, days 9-12), and mid luteal (ML, days 19-22) phases of the menstrual cycle. Rectal temperature was elevated in ML compared with EF among the non-users, but not the users in both clothing configurations. There were no phase-related or group-related differences in any of the other indices of heat strain. Tolerance times were similar between the two groups in all three phases during the compensable heat strain trials. During uncompensable heat strain, tolerance times were significantly longer during EF (128.1 ± 13.4 min) compared with ML (107.4 ± 8.6 min) for the non-users, indicating that these women are at a thermoregulatory advantage during the EF phase of their menstrual cycle. For the users, tolerance times were similar in all three phases and did not differ from those of the non-users during uncompensable heat strain. Our results demonstrate that oral contraceptive use appears to make the thermoregulatory responses to heat strain more uniform over the course of the menstrual cycle.
I feel that choosing to do a Masters degree has been one of the best decisions I have made thus far. It was a truly enriching experience and, as a result, I have much to be thankful for. To begin, I would like to sincerely thank Dr. Tom McLellan for his supervision and guidance over the last two years. I am extremely grateful to Tom for the opportunity that he provided me with and for his advice, flexibility, criticism, and support. I feel I have been fortunate to work with such a great supervisor. Next, I would like to express my sincere appreciation for the excellent technical assistance of Debbie Kerrigan-Brown, Ingrid Smith, Nota Klentrou, Robert Limmer and Jan Pope throughout the study. I couldn't have done it without you. I would like to thank the subjects who participated in this study, for I know that walking in the heat with an NBC suit on was not the most pleasant experience. Finally, I would like to thank all of my friends and family for their encouragement and support. You have been a big part of helping me become the person I am today.
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Chapter 1

INTRODUCTION

There are a number of industrial and operational settings in which protective clothing must be worn in order to protect individuals from harmful exposure to hazardous materials. Firefighters, emergency service personnel, industrial maintenance workers and military personnel are some examples of occupations where protective clothing may be required due to the increased risk of exposure to hazardous materials such as nuclear, biological or chemical (NBC) agents. Although the protective clothing is effective in offering protection to the individual from this hazardous environment, the clothing impairs heat dissipation from the body. Heat must be transported from the core to the skin, from the skin through each clothing layer, and then from the clothing to the environment. Present protective clothing designs consist of either impermeable suits that effectively eliminate evaporative heat loss to the environment or thick semi-permeable suits that severely reduce (but do not eliminate) both evaporative and non-evaporative heat exchange. For semi-permeable clothing, the nature of the fabric used and the various treatments of the fabrics determine the clothing’s permeability to water vapour. Furthermore, the air layers that are created between the skin, underwear, work clothing and the protective overgarment contribute to the thermal insulation and water vapour resistance of the protective system. Depending on its insulation and permeability characteristics, protective clothing has the potential to change an environment of compensable heat strain into one of uncompensable heat strain.

Clothing has been designed to protect military personnel who must continue operations in a wide range of environments. Aside from the climatic extremes that Canadian Forces (CF) personnel must be prepared to work in, there is also the threat that the enemy may use NBC agents. The CF NBC protective system consists of a semi-permeable overgarment and
impermeable rubber boots, gloves, mask and respirator. This ensemble is normally worn over combat clothing and boots, which in turn are layered over a T-shirt, undergarments and socks. The protective clothing ensemble has an insulative value equivalent to 1.88 clo (0.29 m²·°C⁻¹·W⁻¹) and a permeability index of 0.33. Due to the thickness and insulative nature of the NBC ensemble, in combination with its semi-permeable and impermeable components, both non-evaporative and evaporative heat loss from the skin surface are impaired (McLellan, 1991). Since the evaporation of sweat is the major avenue by which humans dissipate heat in a hot environment (Gagge and Gonzalez, 1996), the wearing of NBC clothing can result in severe thermoregulatory strain and a significant reduction in work tolerance. Research has shown that wearing NBC protective clothing causes performance decrements, increases the time to complete a task, induces heat casualties at a higher than normal rate, and decreases work tolerance times in healthy, young men (Armstrong et al., 1991; Cortilli et al., 1996; McLellan, 1994; Montain et al., 1994; White et al., 1991).

McLellan (1993) and McLellan et al. (1993a&b; 1996) have performed a number of studies to establish the heat strain and work tolerance times associated with varying ambient conditions and metabolic rates for healthy, young men wearing different levels of the CF NBC protective clothing. From the results of these studies, a decreasing curvilinear relationship, described by a hyperbolic function, was found to exist between work tolerance time and average metabolic rate (McLellan, 1993 and McLellan et al., 1996). Using this relationship, the CF have been able to establish safe work/rest guidelines for operational use in the field while wearing NBC protective clothing. The current guidelines for NBC operations are based on the physiological responses of healthy, young males to uncompensable heat strain. Although women comprise 10 - 20% of the CF personnel, the extent of thermoregulatory strain and impairment in heat tolerance for women under similar conditions of uncompensable heat strain while wearing the NBC protective clothing is not known.
It has been well established that the menstrual cycle affects temperature regulation under conditions that do not restrict evaporative heat loss. Basal body temperature exhibits a biphasic rhythm in which core temperature is approximately 0.4°C higher in the luteal phase compared with the follicular phase (Frascarolo et al., 1990; Hessemer and Bruck, 1985; Horvath and Drinkwater, 1982; Kolka and Stephenson, 1989). Likewise, the core temperature thresholds for the onset of thermoregulatory sweating, cutaneous vasodilation and skin blood flow are also higher in the luteal phase compared with the follicular phase (Avellini et al., 1980; Hessemer and Bruck, 1985; Kolka and Stephenson, 1989). The rise in basal body temperature during the luteal phase is generally attributed to the thermogenic effect of the increase in progesterone levels following ovulation (Lebrun, 1994).

Tolerance time while wearing NBC clothing in an uncompensable heat stress environment is governed by three factors; initial core temperature, final core temperature and the rate of heat storage. If the latter factor is unchanged following a given treatment because the characteristics of the clothing determine the rate of heat exchange between the body and the environment, and if the same final core temperature is reached under all conditions, then any change in tolerance time is influenced primarily by a change in the initial core temperature. Indeed, such was the case following endurance training or heat acclimation programmes (Aoyagi et al., 1995; McLellan and Aoyagi, 1996) where changes in tolerance time were attributed to differences in the initial rectal temperature. In theory, therefore, the elevated core temperature following ovulation should place women at a disadvantage during the luteal phase of their menstrual cycle while wearing the NBC clothing.

Preliminary results for the United States NBC protective clothing have demonstrated that the separation in core temperature between the luteal and follicular phases is maintained through 45 min of uncompensable heat exposure (Kolka and Stephenson, 1995). However, it is not known what
influence menstrual cycle phase may have on other physiological indices of heat strain or how menstrual cycle phase affects exercise tolerance time during uncompensable heat strain. Also, it is not known how oral contraceptive use may affect the thermoregulatory responses during uncompensable heat strain. Since oral contraceptives negate the surge in progesterone, it is conceivable that women using this method of birth control may be at a thermoregulatory advantage while performing exercise in the NBC protective clothing.

The purpose of the present investigation, therefore, was to determine the influence of menstrual cycle phase and oral contraceptive use on the thermoregulatory strain and physical work tolerance times experienced by healthy young women while wearing normal combat clothing or the full CF NBC protective clothing ensemble. The combat clothing configuration represents an environment of compensable heat strain, whereas the NBC clothing configuration represents an environment of uncompensable heat strain. The work intensity and the ambient environment chosen in the present investigation were similar to the conditions used by McLellan et al. (1992) to evaluate the heat strain and physical work tolerance times for healthy young men under equivalent conditions of compensable and uncompensable heat strain.
Chapter 2

REVIEW OF LITERATURE

2.1 TEMPERATURE REGULATION

2.1.1 Normal Body Temperature

Human beings are homeotherms and regulate their internal body temperature within a narrow range near 37°C. The human body is able to maintain its core temperature within a ± 2°C range, in spite of up to 10-15 fold increases in the rate of heat production compared with rest and exposure to a wide range of environmental conditions. This entails frequent modification to the avenues of heat loss from the body, which are regulated to match the variation in heat production.

Heat production is one of the principle byproducts of metabolism (Cooper, 1991). In resting humans, approximately 70% of the metabolic heat is produced by the 'core' organs, in particular, the liver, the brain and the heart (Sawka and Wenger, 1988). During muscular exercise, up to 90% of the metabolic heat can be produced by the skeletal muscles (Nadel, 1977). Heat is transferred by the blood flowing from the body core to the periphery where heat exchange with the environment occurs.

Considerable temperature gradients exist between and within different body cavities and blood vessels (Sawka and Wenger, 1988). Therefore, when discussing human temperature regulation, it is common to divide the body theoretically into a warm internal core and a cooler outer shell. The warm internal core consists of the vital or 'core' organs inside the head, thorax and abdomen. The muscles, skin and other subcutaneous tissues of the limbs comprise the cooler outer shell. The shell serves as a locus for heat storage and buffers the effects of changing environmental temperature on the body core (Cooper, 1991). The temperature of the shell is influenced by a number
of factors, including: (1) environmental elements such as air temperature, air movement and thermal radiation, (2) thermoregulatory responses such as skin blood flow and sweat secretion, and (3) the temperature of underlying tissues (Wenger, 1996). As a result, its temperature can vary widely, whereas the temperature of the warm internal core remains fairly constant, fluctuating only slightly from one site to another, depending on the metabolic rate of the surrounding tissues, the source and magnitude of blood flow and the temperature gradients between neighbouring body regions (Wenger, 1996).

2.1.2 Measurement of Core Temperature and Skin Temperature

The assessment of body core temperature and skin temperature is an essential aspect to the understanding of temperature regulation in humans. Core temperature is measured either to estimate average internal temperature to determine changes in heat storage in the core or to allow an estimation of the core temperature input to thermoregulatory control (Sawka et al., 1996). Core temperature should be measured at a site whose temperature is not biased by environmental temperature. Rectal temperature ($T_r$), measured by introducing a thermistor 5 to 20 cm past the anal sphincter, is recognised as a good indicator of core temperature. The rectum is well insulated from the environment, so that its temperature is independent of environmental temperature. Although rectal temperature is typically higher than other estimates of core temperature (i.e. esophageal and tympanic temperature) (Saltin and Hermansen, 1966; Sawka and Wenger, 1988) and is slower to respond to rapid changes in arterial blood temperature (Saltin et al., 1970), steady-state rectal temperature is recognised as a reliable index to assess body core heat storage (Nielsen and Nielsen, 1962).

The temperature of the shell is determined by placing thermistors on the skin at various sites. Skin temperature is usually not uniform over the body surface because it varies with the surrounding conditions, the state of
vasodilation at each thermistor site and with different clothing configurations. Thus, mean skin temperature ($\bar{T}_{sk}$) is used to express the temperature of the shell (Wenger, 1996). $\bar{T}_{sk}$ is calculated by weighting the temperature measured at each skin thermistor site according to the fraction of body surface area that it represents. Skin temperature is one of the major factors determining heat exchange with the environment. It provides the thermoregulatory system with important information about the need to conserve or dissipate heat (Wenger, 1996).

2.1.3 Heat Exchanges

There are four principal avenues by which the body can gain or dissipate heat: conduction, convection, radiation and evaporation. Conduction is the direct exchange of heat from surfaces that are touching. Since a small fraction of the body area is in contact with solid surfaces, this mode of heat transfer plays a relatively minor role in overall body heat exchange, generally accounting for not more than 1-2% of the total heat loss (Clark and Edholm, 1985; Mitchell, 1974). Convection is the mechanism of heat exchange whereby the warm skin or clothing exchange heat with the adjacent air layer (Clark and Edholm, 1985). The characteristics of the temperature gradient and thickness of the air layer determine the amount of heat exchange with the surroundings. Radiative heat exchange is the transfer of heat by the exchange of electromagnetic energy (Mitchell, 1974). Evaporative heat exchange involves the loss of latent heat through the evaporation of sweat from the skin surface (Sawka et al., 1996).

These methods of heat transfer can be classified into two categories - non-evaporative and evaporative heat exchange. Non-evaporative heat exchange between the skin and the environment usually involves the conduction of heat through the skin and clothing layers, followed by heat loss via convection and radiation from the outer clothing, skin surface or respiratory tract to the surrounding environment (Gagge and Gonzalez, 1996).
Heat loss via evaporative heat exchange depends upon the combined effects of skin and internal body temperature on the sweating drive, and the ability of sweat to evaporate from the skin surface (Gonzalez, 1988). The extent of heat exchange by this process is governed by environmental factors such as ambient temperature, air movement, relative humidity, barometric pressure and clothing, and by the physical properties of the skin surface, such as its temperature and wettedness due to sweating (Gagge and Gonzalez, 1996).

Sawka and Wenger (1988) and Sawka et al. (1996) reviewed the effect of environmental temperature (5°C to 35°C) on the mechanism of heat exchange in subjects cycling at a constant metabolic rate (approximately 650 W). Total heat loss, heat storage and elevation of core temperature were approximately the same in all environments; however, the relative contributions of non-evaporative and evaporative heat exchange to total heat loss varied with ambient temperature. In low ambient temperatures approximately 70% of the total heat loss was accomplished through non-evaporative heat exchange (Sawka and Wenger, 1988; Sawka et al., 1996). As the ambient temperature increased, non-evaporative heat exchange diminished, and there was a greater reliance upon evaporative heat exchange. When the ambient temperature was equal to skin temperature, evaporative heat exchange accounted for essentially all of the heat loss (Sawka and Wenger, 1988; Sawka et al., 1996). Furthermore, when the ambient temperature exceeded the skin temperature, there was heat gain to the body by conduction, convection and radiation (Sawka and Wenger, 1988).

Air movement and the water vapour pressure gradient between the skin and the environment, multiplied by the evaporative heat-transfer coefficient and the wetted area of the skin also influence the rate of evaporative heat loss (Sawka et al., 1996). The relationship between these variables is summarised in the following equation:

\[ E = h_e \cdot A_s \cdot w \cdot (P_{sk} - P_A) \]

Eq. 1
where $P_{sk}$ is the water vapour pressure at the skin surface, $P_A$ is the ambient vapour pressure, $w$ is the skin wettedness, $A_d$ is the body surface area, $h_e$ is the evaporative heat-transfer coefficient, and $E$ is the evaporative heat loss from the skin to the environment (Wenger, 1996). The wider the water-vapour pressure gradient between the skin and the environment for a given evaporative heat-transfer coefficient, the greater the rate of evaporation (Sawka et al., 1996). For example, when the relative humidity is high, the ambient vapour pressure approaches that of the skin. As a result, the water-vapour pressure gradient between the skin and the environment is diminished and the rate of evaporation is greatly reduced (McArdle, Katch and Katch, 1996). As well, the rate of sweat evaporation depends upon air movement, so that in still or moist air, sweat tends to collect on the skin (Sawka and Wenger, 1988). When this occurs, the skin becomes wetted and there is a reduction in sweat secretion, an effect known as hidromeiosis (Wenger, 1996).

The rate at which heat is lost is determined almost entirely by two factors: (1) how quickly heat can be transferred from the core to the skin, and (2) how quickly heat can then be lost from the skin to the surrounding environment. Heat conduction to the skin by the blood is controlled by the degree of cutaneous vasodilation. This vasodilation is controlled almost entirely by the sympathetic nervous system in response to changes in the body core temperature and changes in the environmental temperature. Non-evaporative heat exchange is influenced primarily by the environment whereas evaporative heat exchange is affected by sweat rate and the limits imposed by the external environment (Gagge and Gonzalez, 1996).

2.1.4 Heat Balance

When the rate of heat production in the body is greater than the rate at which heat is being lost, heat accumulates in the body and the core temperature rises. Conversely, when heat loss exceeds heat production, both
body heat content and body temperature decrease. The continual variation in heat loss from the body is regulated to match the variation in heat production so as to maintain internal core temperature within a narrow range around 37°C.

The basis for determining the effects of the environment on an individual is derived from the First Law of Thermodynamics, used in the heat balance equation (Cooper, 1991):

\[ \dot{S} = M \pm W - E \pm R \pm C \pm K \ [W \cdot m^2] \]  \hspace{1cm} \text{Eq. 2}

where \( \dot{S} \) = rate of heat storage in the body; \( M \) = rate of metabolic heat production; \( W \) = rate of positive or negative power accomplished or absorbed by the body; \( E \) = rate of evaporative heat loss; \( R \) = rate of radiant heat exchange from or to the body; \( C \) = rate of convective heat transfer from or to the body; \( K \) = rate of conductive heat transfer from or to the body.

The term \( '\dot{S}' \) in the heat balance equation represents whether an individual is able to maintain a thermal steady-state with the environment. It is the net result of the interaction of environmental conditions, physical parameters (such as clothing, insulation or absorptivity), and physiological responses (Santee and Gonzalez, 1988). At thermal steady-state, \( \dot{S} = 0 \). When \( \dot{S} > 0 \), the body gains heat. When \( \dot{S} < 0 \), the body loses heat. Normally, the loss or gain of heat from the body occurs on a short-term basis and lasts only until the thermoregulatory system is able to reestablish heat balance. However, if the thermal stress is too great for the thermoregulatory system, the body will continue to gain or lose heat until either the stress diminishes so that the thermoregulatory system can again reestablish the balance, or dangerous hyper- or hypo-thermia occurs (Wenger, 1996).
2.2 THERMOREGULATORY RESPONSES TO HEAT

2.2.1 Introduction

Our thermoregulatory system is so effective that through both physiological and behavioural responses, humans are able to tolerate most naturally occurring ambient conditions (Fortney and Vroman, 1985). Behavioural temperature regulation is accomplished primarily through conscious behaviours and includes changes in clothing, level of activity and shelter (Gagge and Gonzalez, 1996). The motivation for behavioural temperature regulation is most likely a direct result of thermal sensation and thermal discomfort (Gonzalez, 1988). Physiological temperature regulation operates through the autonomic nervous system, and includes control of the rate of metabolic heat production, the transfer of heat from the core to the skin, and sweating. Unless the heat stress exceeds the capability of the thermoregulatory system's effectors, these responses will continue to increase until the body is able to regain heat balance, thus preventing any further rise in core temperature (Sawka and Wenger, 1988).

2.2.2 Thermal Receptors and the Thermoregulatory Centre

Temperature sensitive free nerve endings have been found in abundance near the skin surface and in the preoptic area of the hypothalamus (Nadel, 1977). The thermal receptors near the skin surface transmit information about their temperatures through afferent nerves to the thermoregulatory centre in the hypothalamus where much of the integration of temperature information occurs (Fortney and Vroman, 1985). The thermoregulatory centre acts like a central integrator and generates a "thermal command signal" that participates in the control of sweating, vasodilation and vasoconstriction (Sawka and Wenger, 1988).

Changes in mean skin temperature allow the thermoregulatory system to respond appropriately to mild heat or cold exposure with little change in
core temperature. On the other hand, changes in core temperature of only a few tenths of a degree elicit about nine times as great a thermoregulatory response as a 1°C change in mean skin temperature (Wenger, 1996). The sensitivity of the thermoregulatory response to small changes in core temperature allows the thermoregulatory system to keep internal temperature relatively constant. The sensitivity of response to changes in mean skin temperature allows the system to respond appropriately to changes in environmental temperature over a wide range with little change in internal temperature (Sawka and Wenger, 1988).

If thermal balance is upset as a result of an increase in metabolic heat production or ambient temperature, causing excess heat to be stored in the body, the temperature in the core and/or skin will increase. The changes in these temperatures will be detected by thermal receptors. In response to information from these receptors, the thermoregulatory controller will call for responses that increase heat loss, i.e., increased skin blood flow and sweat production.

The regulation of both sweating and skin blood flow is based on the feedback the thermoregulatory centre receives from the thermal receptors about core and skin temperatures in relation to the thermoregulatory set-point. The thermoregulatory set-point is the target core temperature and is the reference point which determines the thresholds of all the thermoregulatory responses (Wenger, 1996). Both sweating and skin blood flow depend on core and skin temperatures in the same way. That is, a change in the threshold for sweating is accompanied by a similar change in the threshold for cutaneous vasodilation.

2.2.3 Cutaneous Vascular Response to Heat Stress

One of the most significant thermoregulatory responses to heat stress is the increase in cutaneous blood flow. Skin blood flow (SkBF) carries heat by
convection from the core tissues to the skin. Heat is dissipated, at a rate proportional to the difference between skin and ambient temperature, to the surrounding environment through radiation and convection, or by the evaporation of sweat (Fortney and Vroman, 1985). This increase in skin blood flow occurs by dilation of cutaneous veins and relaxation of the resistance vessels, resulting in the opening of new skin capillary beds (Fortney and Vroman, 1985). Skin blood flow can increase from approximately 0.2-0.5 L·min⁻¹ in normothermia to values exceeding 7-8 L·min⁻¹ in hyperthermia (Rowell, 1977).

Increased skin blood flow is distributed between the capillaries and arteriovenous anastomoses (Johnson and Proppe, 1996). Capillaries provide the sites for nutrient exchange in tissues. Arteriovenous anastomoses (AVAs) are thick-walled connections that provide convenient shunts between the arterioles and venules (Johnson et al., 1986). Blood passing through the AVAs detours the exchange vessels, allowing heat to be dumped from the blood as it flows through the cutaneous venous system (Gagge and Gonzalez, 1996). All areas of skin have capillaries, but not all areas have arteriovenous anastomoses. Those areas of the skin which contain AVAs are termed acral sites and include regions with high surface area compared to volume ratios, such as the digits, lips, ears, cheeks and palmar surface of the hands and feet (Kenney and Johnson, 1992). AVAs are uncommon in the skin of the torso, arms and legs. The areas that do not contain arteriovenous anastomoses are termed the nonacral sites. The differentiation between these two regions is important when discussing neural control of skin blood flow (Kenney and Johnson, 1992).

2.2.4 Neural Control of Skin Blood Flow

The mechanisms that produce cutaneous vasodilation, and thus increased skin blood flow, include the withdrawal of sympathetic vasoconstrictor tone, an increase in active sympathetic vasodilator activity,
and the direct effect of heat on the blood vessels. The small increases in SkBF observed with mild heating are accomplished by vasoconstrictor withdrawal, whereas more intense heat stress causes an active cutaneous vasodilation (Rowell, 1978).

2.2.4.1 Active Vasodilation

Active vasodilation accounts for 90%-100% of the increase in SkBF that is observed with a rise in internal temperature during heat stress (Rowell, 1977). This type of vasodilation is termed 'active' because an increase in SkBF occurs, either directly or indirectly, from increased sympathetic nerve activity (Johnson and Proppe, 1996). This is in contrast to 'passive' vasodilation, in which the increase in blood flow is due to the withdrawal of vasoconstrictor nerve activity (Rowell, 1978). Active vasodilation occurs in almost all areas of the skin, except the acral regions (i.e., hands, feet, lips, ears and nose) (Wenger, 1996). Since the vascular beds are very compliant, vasodilation increases the amount of blood pooled in them, allowing a longer interval for heat transfer from the warm blood to the cooler skin (Fortney and Vroman, 1985). The mechanism by which active cutaneous vasodilation is effected is unresolved.

2.2.4.2 Withdrawal of Sympathetic Vasoconstrictor Activity

Reflex vasoconstriction is an important mechanism in the control of cutaneous circulation. Mediated primarily through adrenergic sympathetic fibres (Wenger, 1996), this system is found in both the acral and nonacral skin regions. However, its role appears to be of greater significance within the acral sites, as heat flow within these areas is thought to be solely a function of reflex vasoconstrictor activity (Johnson and Proppe, 1996). Elevations in skin blood flow in a given acral site generally occur by reflex withdrawal of sympathetic adrenergic drives (Gagge and Gonzalez, 1996). Reducing the flow
of nerve impulses in these fibres allows the blood vessels in these areas to dilate, hence increasing blood flow.

Although much of the reflex increase in SkBF observed during heat stress is brought about by active cutaneous vasodilation, the withdrawal of vasoconstrictor tone can cause almost a doubling of skin blood flow when $T_{re}$ and/or $\bar{T}_{sk}$ are low (Rowell, 1978). As well, reflex vasoconstriction plays a major role in controlling skin blood flow in our daily lives. Neither sweating nor active cutaneous vasodilation are called upon except when the rate of metabolic heat production and/or ambient temperature is fairly high (Johnson and Proppe, 1996). Through increases and decreases in vasoconstrictor nerve activity, the body is able to regulate its temperature within narrow limits on an ongoing basis.

2.2.4.3 Local Thermal Control of Cutaneous Blood Vessels

Local skin temperature can also affect skin blood flow through direct actions on the blood vessels themselves. A local change in thermal load brings about an adequate change of local skin temperature and local sweat rate (Werner and Heising, 1989). Directly heating the skin can maximally vasodilate that area, whereas directly cooling the skin can cause almost complete vasoconstriction, even in the absence of nervous signals (Johnson and Proppe, 1996). Consequently, the overall cutaneous vascular response to environmental heat stress includes any local effects of temperature.

2.2.5 Evaporative Heat Loss

The evaporation of sweat is an important avenue of heat exchange for humans. As ambient temperature increases, the effectiveness of heat loss by conduction, convection and radiation decreases and there is a greater reliance upon evaporative heat loss to maintain core temperature (McArdle, Katch and Katch, 1996). The increasing demand for evaporative heat loss results,
initially, in an increased recruitment of sweat glands, and then in an increase in sweat secretion per gland (Sawka and Wenger, 1988). At 30°C, for every gram of sweat that evaporates from the skin surface, 2.43 kilojoules (kJ) of heat (known as the latent heat of evaporation) is absorbed in the process (Sawka et al., 1996).

Sweat glands respond to thermal stress predominantly through sympathetic cholinergic stimulation from the anterior hypothalamus; however, circulating catecholamines (in particular epinephrine) may also contribute to thermoregulatory sweating (Fortney and Vroman, 1985; Sawka et al., 1996). The increase in thermoregulatory sweating closely parallels the increase in body temperature (Saltin et al., 1972). Above a threshold core temperature, a linear relationship exists between sweat production and the rise in core temperature (Fortney and Vroman, 1985). Core temperature is the dominant factor in the control of SkBF and sweat rate during thermal stress (Wyss et al., 1974); however, for a given sudomotor signal to the sweat gland, local skin temperature and skin wettedness also influence the amount of sweat secreted (Sawka and Wenger, 1988).

When core temperature and skin temperature are low enough that sweating does not occur, the body can control non-evaporative (i.e., via convection and radiation) heat loss by varying skin blood flow alone (Sawka and Wenger, 1988). Under conditions in which sweating does occur, the tendency of skin blood flow to warm the skin is roughly offset by the tendency of sweating to cool the skin. Once sweating has begun, skin blood flow serves chiefly to deliver to the skin the heat that is to be removed by evaporation. Skin blood flow and sweating work in partnership to dissipate heat under such conditions.
2.3 CARDIOVASCULAR RESPONSES TO HEAT STRESS

2.3.1 Introduction

The degree to which skin vasodilates during heat stress has the potential to produce a great demand for increased skin blood flow. There are only two ways the cardiovascular system can provide the blood flow needed to meet the enhanced cutaneous vascular demand. These are an elevated cardiac output and redistribution of blood flow from other tissues to the skin (Johnson, 1986). Humans depend on a combination of both mechanisms to provide the required blood flow.

2.3.2 Increased Cardiac Output

During mild heat stress, the cardiovascular system is able to meet the need for increased skin blood flow without a substantial change in cardiac output (CO). However, when heat stress becomes significant, cardiac output must increase in order to maintain skin blood flow. A number of investigators have examined the adjustment in CO during acute heat stress. Koroxenidis et al. (1961) observed that directly heating subjects for a period of 50-60 min caused CO to increase 60% from the resting value. Heart rate (HR) increased by 49% and stroke volume (SV) rose by 9%. As well, central blood volume between the superior vena cava and radial artery decreased from 1,650 mL before heating to 1,250 mL after 50 min of heating, as a result of venous pooling. When the subjects were heated for 105 min, there was no further progressive increase in SV (Koroxenidis et al., 1961). Sherif et al. (1970) found that subjects who were exposed to an ambient environment at 40°C for 2 hrs experienced a 95% increase in CO. CO rose from its initial mean value of 5.28 L·min⁻¹ to 10.29 L·min⁻¹. HR increased 67% (from 74 b·min⁻¹ to 124 b·min⁻¹) and SV slightly increased from 74 mL·b⁻¹ to 84 mL·b⁻¹ (+ 14%). Sherif et al. (1970) also observed that total peripheral resistance (TPR) decreased 55%, from an initial mean value of 18.7 (units) to 8.4 (units).
Faithfull et al. (1984) observed similar changes in CO, HR and SV in subjects heated to a core temperature of 41.8°C for a period of 2 hrs.

Cardiac output is determined by the stroke volume and heart rate. The increase in cardiac output during heat stress is essentially a product of an increased heart rate (HR), as stroke volume (SV) changes very little during heat stress (Faithfull et al., 1984; Koroxenidis et al., 1961; Rowell, 1974; Sherif et al., 1970). The intrinsic heart rate increases by about 10 beats per minute for each 1°C rise in body temperature (Clark and Edholm, 1985; Faithfull et al., 1984; Gorman et al., 1984). The increase in HR is achieved in three ways: (1) the direct effect of temperature on the sinoatrial node; (2) parasympathetic withdrawal; and (3) elevated sympathetic activity (Johnson and Proppe, 1996). Gorman et al. (1984) demonstrated that 40% of the HR response to environmental heat stress can be attributed to the influence of local temperature on the sinoatrial node, and the other 60% is the result of autonomic control. Their data suggest that approximately 75% of the autonomic effect is due to a reduction in parasympathetic outflow to the heart (Gorman et al., 1984). The lack of significant change in SV observed during heat stress is most likely because reduced cardiac filling is balanced by an elevated inotropic state (Johnson and Proppe, 1996; Rowell, 1974).

2.3.3 Redistribution of Blood Flow

A reduction in blood flow in the noncutaneous regions of the body is an important component of the cardiovascular response to heat stress. In resting humans, 40% to 50% of cardiac output is distributed to the splanchnic and renal circulation, and their redistribution could be a major source of skin blood flow during heat stress. The redistribution of blood flow during heat stress is achieved through vasoconstriction in both the splanchnic and renal areas via the sympathetic nervous system (Johnson and Proppe, 1996). Splanchnic and renal blood flow diminish in proportion to the intensity of heat strain and this reduction has two effects. The first is that it allows a
corresponding diversion of cardiac output to the skin. Second, since the vascular beds are very compliant, a decrease in their blood flow reduces the amount of blood pooled in them, helping to compensate for decreases in central blood volume caused by reduced plasma volume and blood pooling in the skin (Wenger, 1996).

Rowell (1974) presents an excellent summary of the average circulatory changes in subjects directly heated for 30 - 53 min with a skin temperature of 40 - 41°C. Acute heat stress resulted in an increase in cardiac output of 6.6 L·min⁻¹, a decrease in splanchnic blood flow (SBF) of 0.6 L·min⁻¹, a decrease in renal blood flow (RBF) of 0.4 L·min⁻¹, and a reduction in muscle blood flow (MBF) of 0.2 L·min⁻¹. SV increased only slightly during the heat exposure from 100 mL to 108 mL. The changes in CO, SBF, RBF, and MBF contributed to the increase in skin blood flow of 7.8 L·min⁻¹.

2.4 THERMOREGULATORY RESPONSES TO EXERCISE IN THE HEAT
2.4.1 Increased Metabolic Heat Production

The efficiency of muscular contraction for activities such as walking, running or cycling is reported to vary between 20 - 25% for humans (McArdle, Katch and Katch, 1996). Thus, during exercise 75 - 80% of the increased energy demand of muscular contraction is converted to heat. Blood perfusing the active skeletal muscles is warmed and the warmer blood carries heat to other body regions. As a result, core temperature is elevated (Sawka and Wenger, 1988). This increase in thermal load represents a significant physiological threat to the thermoregulatory system (Gagge and Gonzalez, 1996). Increases in internal body temperature of more than 3.0°C can be accompanied by central nervous system dysfunction, circulatory failure, and eventually, irreversible tissue damage and death (Nadel, 1977). Without the activation of thermoregulatory mechanisms, moderate exercise would be limited to fifteen minutes or less (Nadel, 1977).
To illustrate the effect of metabolic heat production on the thermoregulatory system, let us compare the energy expenditure of an average healthy individual during different activities. Sleeping results in the expenditure of 80 W (J·s⁻¹), walking slowly costs 230 W, jogging costs 660 W and sprinting results in the expenditure of approximately 1750 W (Clark and Edholm, 1985). For a 60 kg female with a specific heat of the body tissues of 3.47 kJ·kg⁻¹·°C⁻¹, heat production of approximately 210 kJ would raise core temperature 1.0°C if there were no mechanisms for heat loss. Thus, an energy expenditure of 700 W would increase core temperature 1.0°C in 5 min \[\frac{(210 \times 10^3)}{(700 \text{ J·s}^{-1})(60 \text{ s·min}^{-1})}\]. Since an increase in core temperature of more than 3.0°C can result in central nervous system dysfunction, circulatory failure and eventually tissue damage and death, moderate exercise represents a significant threat to thermoregulatory homeostasis.

The increase in heat production occurs almost immediately at the onset of exercise. During the early stages of exercise the rate of heat production exceeds the rate of heat dissipation. Thus, body heat storage is increased and core temperature rises (Sawka et al., 1996). Input proportional to the rise in core temperature is integrated with input from peripheral receptors by the thermoregulatory centre in the hypothalamus, eliciting the appropriate heat dissipating reflexes (Fortney and Vroman, 1985). Rising body temperatures during exercise in the heat educe from the thermoregulatory centre two effector output signals. These are: (1) elevated skin blood flow, and (2) increased sweat output (Fortney and Vroman, 1985). Core temperature continues to rise until heat loss has increased enough to balance heat production and steady-state values are achieved (Wenger, 1996). Steady-state rectal temperature is largely independent of ambient temperature (between 5°C to 30°C) and is proportional to the metabolic rate (Saltin et al., 1970). However, when the combined metabolic and environmental heat stress is great enough, the thermoregulatory load-error results in the further elevation of the steady-state core temperature (Sawka and Wenger, 1988).
During exercise in the heat, the primary cardiovascular challenge is to provide, simultaneously, enough blood flow to the exercising skeletal muscle to support metabolism and enough blood flow to the skin to dissipate heat (Sawka et al., 1996). In conditions where cardiac output is limited, such as during heavy exercise in the heat, competition occurs between the muscle and skin vascular beds (Fortney and Vroman, 1985). On the one hand, if skin blood flow is inadequate, body temperature will rise at a faster rate, and thus limit exercise endurance. Alternatively, if muscle blood flow is insufficient, muscle fatigue and discomfort will limit exercise performance (Fortney and Vroman, 1985).

The question of priority is raised because two major vascular beds are competing for CO. Research has demonstrated that the relative intensity of exercise (% maximal oxygen consumption) affects the ability of the cardiovascular system to meet the combined thermal and metabolic demands (Rowell, 1974). The cardiovascular system is able to provide a small increase in cardiac output (approximately 2 to 3 L·min⁻¹) and skin blood flow in response to prolonged mild exercise in the heat, whereas during prolonged moderate-to-heavy exercise in the heat, HR rises maximally with no further increase in CO or SkBF (Rowell, 1974). MBF does not appear to be affected by exercise heat-stress. Nielson et al. (1990) demonstrated that there is no reduction in leg blood flow in subjects exercising at 60 - 70% of their VO₂max (maximal oxygen consumption) in the heat compared to leg blood flow during exercise at the same relative intensity in a cool environment.

The competition for blood flow between the cutaneous and muscular vascular beds results in the peripheral displacement of blood volume and the subsequent reduction in cardiac filling pressure (Rowell, 1974). When exercise in the heat is prolonged, the competing demands for blood flow result in a continuous and time-dependent gradual decline in central venous
or right arterial mean pressure, central blood volume, stroke volume and blood pressure, accompanied by a progressive rise in heart rate to near maximal values (Rowell, 1974). This effect, known as “cardiovascular drift”, occurs for two reasons. First, the dilated vascular bed of the skin accommodates a large volume of blood, thereby reducing central blood volume (Wenger, 1996). Second, the strong reliance on heat loss via increased sweat secretion can result in a net loss of body water, further reducing blood volume (Sawka et al., 1996). Therefore, heat stress can reduce cardiac filling and stroke volume through both pooling of blood in the skin and reduced blood volume. To compensate for the reduced cardiac filling and stroke volume, a higher heart rate is required to maintain cardiac output (Sawka et al., 1996).

2.4.3 Compensatory Responses During Exercise-Heat Stress

Several reflex adjustments compensate for peripheral pooling of blood and for possible decreases in plasma volume, in order to maintain cardiac output during exercise-heat stress (Wenger, 1996). A redistribution of blood flow occurs in several vascular beds. Blood is diverted towards exercising muscles and the skin from the non-exercising muscles and the splanchnic and renal regions (Fortney and Vroman, 1985). The effects of temperature and exercise on reflex vasoconstriction seem to be additive, so that at any exercise intensity the reduction in splanchnic blood flow is greater at a higher skin temperature (Sawka et al., 1996). Also, cardiac contractility may increase to help preserve stroke volume in the face of impaired cardiac filling (Sawka et al., 1996).

The final distribution of blood flow within the body depends upon a number of factors. Exercise intensity and duration, the ambient conditions, hydration level and posture can influence the blood flow distribution (Fortney and Vroman, 1985). For example, during exercise at ambient temperatures below 30°C, mean skin temperature is primarily a function of
the ambient temperature and is, to a large extent, independent of the work rate (Gagge and Gonzalez, 1996). However, when ambient temperature increases above 30°C, there is a greater dependence upon evaporative heat loss to defend core temperature during exercise and therefore there is an increased demand for skin blood flow. Generally, only when the combined metabolic and external heat loads exceed the body's ability to meet the competing demands for skin and muscle blood flow, do skin and internal body temperatures rise appreciably (Gagge and Gonzalez, 1996).

### 2.5 Compensable and Uncompensable Heat Stress

When an individual is capable of maintaining thermal equilibrium in the face of thermoregulatory challenge, that individual is said to be experiencing compensable heat stress. In this situation, the required evaporative cooling ($E_{\text{req}}$) for the body is less than the maximum evaporative capacity ($E_{\text{max}}$) of the environment. From the heat balance equation, $E_{\text{req}}$ can be calculated as (Givoni and Goldman, 1972):

$$E_{\text{req}} = M \pm W \pm (R + C + K)$$  \hspace{1cm} \text{Eq. 3}

$E_{\text{max}}$ is determined as (Berglund, 1988):

$$E_{\text{max}} = h_e (P_{sk} - P_A)$$  \hspace{1cm} \text{Eq. 4}

where $h_e$ is the evaporative heat transfer coefficient, $P_{sk}$ is the skin vapour pressure assuming 100% saturation at $T_{sk}$ and $P_A$ is the ambient vapour pressure.

A thermal environment of compensable heat stress can become one of uncompensable heat stress by wearing clothing that restricts evaporative heat loss, which decreases $h_e$, and/or by increasing $P_A$ (Kraning and Gonzalez, 1991). During uncompensable heat stress the body's evaporative cooling
requirement \( (E_{\text{req}}) \) exceeds the maximum evaporative capacity \( (E_{\text{max}}) \) of the environment. Individuals are unable to achieve thermal balance and will continue to store heat until exhaustion occurs (Montain et al., 1994). As a result, uncompensable heat stress is, by definition, time limited (Kraning and Gonzalez, 1991). Because uncompensable heat stress hinders job performance and can lead to exhaustion, it is important to understand the magnitude of physiological strain humans can tolerate and what factors modify tolerance to heat strain. Knowledge of such information will assist in improving occupational safety guidelines for human heat exposure (Montain et al., 1994).

2.6 FACTORS THAT MODIFY THE THERMOREGULATORY RESPONSE TO EXERCISE AND/OR HEAT STRESS

2.6.1 Circadian Rhythm

The time of day can influence body temperature. Temperature is lowest early in the morning and gradually rises throughout the day, peaking in the evening. The amplitude of this daily variation ranges from 0.7°C to 1.5°C among individuals and has been shown to persist in both fasting and bedridden subjects (Clark and Edholm, 1985). The threshold temperatures for the onset of cutaneous vasodilation and the onset of sweating also follow this pattern, as increases in their threshold temperatures closely parallel the circadian increase in resting core temperature (Stephenson et al., 1984). The similar daily variations in core temperature and in the thresholds for all the thermoregulatory responses indicates that the thermoregulatory set-point itself follows a circadian rhythm (Sawka et al., 1996). The thermoregulatory set-point varies with time of day in a sinusoidal fashion, with the minimum in the early morning and the maximum in the late afternoon or evening.
2.6.2 Age

Considerable debate has focused on the effect of age on the thermoregulatory response to heat stress. Much of this discussion is the result of the methodological difficulties associated with comparing the heat loss responses of younger and older subjects. The reason for this is because it is difficult to control for both $\dot{V}O_{2\text{max}}$ and level of physical activity between the two groups. When younger and older individuals are matched on the basis of $\dot{V}O_{2\text{max}}$ per kilogram of body mass, there is often a 10% to 15% difference in absolute $\dot{V}O_{2\text{max}}$ between groups (Havenith et al., 1995). Also, to match younger and older subjects for similar $\dot{V}O_{2\text{max}}$ implies that the older individuals are more physically active compared with the younger group (Tankersley et al., 1991). Thus, it is difficult to distinguish the relative importance of age, since cardiovascular fitness also impacts the physiological responses to heat stress.

There are two recent studies that have considered the relative importance of the age and fitness status during thermoregulatory heat stress. Tankersley et al. (1991) compared the heat loss responses of normally active young males to normally active older males and highly active older males. Their results demonstrate that heat loss is impaired in normally active older men compared with normally active younger men. However, when younger and older subjects were matched for similar $\dot{V}O_{2\text{max}}$ (i.e., normally active younger men and highly active older men), heat loss responses were similar between the two groups (Tankersley et al., 1991). The results of Havenith et al. (1995) suggest that, while age contributes to the cardiovascular responses to heat stress (HR and SkBF are both lower with increasing age), the thermoregulatory (heat storage and core temperature) and sweating responses are more closely related to $\dot{V}O_{2\text{max}}$ and physical activity level. Both studies suggest that once these variables are accounted for, there is no significant effect of age.
The thermoregulatory response to exercise in the heat is influenced by hydration status. Body hydration affects the ability to regulate internal body temperature and the ability to maintain circulatory stability during exercise-heat stress (Nadel et al., 1980). Hydration level is of particular importance during exercise in the heat because a body water deficit will counteract the thermoregulatory advantages induced by heat acclimation or high aerobic fitness (Sawka, 1988). Hypohydration (reduced body water) results in increased core temperature during exercise in the heat, reduced heat tolerance and reduced aerobic exercise performance (Latzka et al., 1996). The core temperature response during exercise-heat stress is linearly increased for each percent decrease in body weight (Sawka et al., 1985). A water deficit of as little as 1% of body weight increases core temperature during exercise, and the greater the water deficit, the greater the subsequent elevation of core temperature (Sawka et al., 1996). During submaximal exercise with moderate heat strain, hypohydration has been shown to reduce maximal aerobic power by 6% and exercise tolerance time by 12% from euhydration levels (Sawka, 1988).

When blood volume is decreased, such as during hypohydration, cutaneous blood flow is decreased for a given core temperature, reducing the convective transfer of heat from the body core to the skin (Nadel et al., 1980). As well, the ability to transfer heat to the environment by the evaporation of sweat is affected by a decrease in blood volume (Fortney et al., 1981). Sweating rate is lower for a given core temperature and the potential for heat dissipation through sweat evaporation is reduced compared with euhydration levels (Sawka, 1988). Therefore, both non-evaporative and evaporative heat exchange are affected by hypohydration.

Hydration status during exercise in the heat is an important consideration because the cardiovascular system’s ability to provide enough
blood flow to the working muscles and to the skin for the dissipation of heat is challenged by any reduction in blood volume. During submaximal exercise in the heat, hypohydration (i.e., a decrease in body weight of 3-4%) causes an increased heart rate and a decreased stroke volume and cardiac output relative to euhydration (Sawka et al., 1996). The lower cardiac output is most likely due to the reduction in stroke volume and lower circulating blood volume (Nadel et al., 1980).

Latzka et al. (1996) recently conducted an in-depth study on the potential benefits of hyperhydration during exercise-heat stress. The results of their study clearly demonstrate that hyperhydration (i.e., an increase in body weight of 2%), when compared with euhydration, does not impart any physiological advantage during exercise in the heat. Rectal temperature, esophageal temperature, skin temperature, local sweating, whole body sweating and heart rate did not differ between the euhydrated and hyperhydrated states (Latzka et al., 1996).

2.6.4 Heat Acclimation

Acclimation to a given level of exercise-heat stress can be acquired by 7 to 10 days of daily exercise in the heat and involves both thermoregulatory and cardiovascular improvements (Wenger, 1988). The three classical signs of heat acclimation are lower heart rate, lower core temperature and higher sweat rate during exercise-heat stress (Sawka et al., 1996). Sweating begins earlier and at a lower core temperature following acclimation, signifying that the core temperature threshold for the onset of sweating is decreased (Wenger, 1996). Accompanying the decrease in the threshold for the onset of sweating is a reduction in the threshold for cutaneous vasodilation, so that heat transfer from the core to the skin is maintained (Wenger, 1996).

The cardiovascular improvements that reduce heart rate during exercise-heat stress arise within the first week of heat acclimation, whereas
the changes in sweating develop more slowly (Wenger, 1996). It is most likely that since total body water and plasma volume are elevated during the first week of acclimation, these changes contribute to the rapid adaptation of the cardiovascular system (Wenger, 1996). However, the alteration in plasma volume seems to be a temporary adjustment to exercise-heat stress and disappears by the time full acclimation is achieved (Wenger, 1996).

Following acclimation, the increased sensitivity of the sweat glands to stimulation, their increased ability to reabsorb salt and thus preserve electrolytes in the extra-cellular fluid, and their improved ability to sustain high sweat rates reduce the levels of core and skin temperatures reached during a given exercise-heat stress and prolong tolerance time (Sawka et al., 1996; Wenger, 1996). The enhanced sweating capacity of the sweat glands is most likely due to their resistance to hidromeiosis and fatigue (Sawka et al., 1996; Wenger, 1988). The lower threshold for the start of sweating signifies that evaporative cooling begins earlier in exercise and the increased sweat output maximises evaporative cooling (McArdle, Katch and Katch, 1996). Hence, for a given amount of metabolic heat production, the heat acclimated individual is able to dissipate more heat through evaporative heat transfer and has reduced dependence on non-evaporative heat transfer.

Heat acclimation is not a permanent state and gradually disappears if not maintained by regular heat exposure (Sawka et al., 1996). The cardiovascular and thermoregulatory improvements gained from heat acclimation are lost in the order in which they were attained. Thus, the cardiovascular adaptations decline more quickly than the change in sweating capacity and the reduction in exercise core temperature (Wenger, 1996).

2.6.5 Fitness Status

Improvements in exercise-heat tolerance can be acquired through physical training in a cool environment. Aerobically fit individuals
experience less physiological strain and greater tolerance to exercise at high ambient temperatures (Sawka et al., 1996). As well, physical training facilitates the process of heat acclimation (Pandolf, 1979). Aerobic exercise in a cool environment increases the sensitivity and potential of the sweating response. Sweating begins at a lower internal temperature and a larger volume of more dilute sweat is produced compared with the sweating response of an unfit individual (McArdle, Katch and Katch, 1996; Nadel et al., 1974). The ability of an aerobically fit person to achieve a steady-state sweating rate at a lower body temperature reduces the strain imposed on the cardiovascular system during exercise-heat stress (Nadel et al., 1974).

The best improvements in exercise-heat tolerance occur after 8 to 12 weeks of strenuous interval training or continuous exercise at an intensity greater than 50% VO$_{2\text{max}}$ (Armstrong and Pandolf, 1988; Gisolfi, 1973). In addition, it appears as though the improvements in exercise-heat tolerance are maximised when physical training results in an increase in VO$_{2\text{max}}$ of at least 15% (Armstrong and Pandolf, 1988). Furthermore, it seems that the exercise-induced increase in body temperature is an important component of enhanced tolerance (Armstrong and Pandolf, 1988). The exercise-induced increase in core temperature causes adjustments in the peripheral circulation and evaporative cooling similar to those observed during heat stress (McArdle, Katch and Katch, 1996). While aerobic training in a cool environment can produce 50% of the total adjustment resulting from heat acclimation (Gisolfi, 1973), it is much less effective than acclimation achieved through exercise in the heat. Full heat acclimation is usually not achieved without actual exposure to heat stress (McArdle, Katch and Katch, 1996).

**Gender**

Women, as a population, are generally smaller in size, have a larger surface area-to-mass ratio, and have a higher relative fat content than men (Stephenson and Kolka, 1993). As well, women tend to have a lower
maximal aerobic capacity than men (Kenney, 1985). The cardiorespiratory fitness of women is, on average, only 70% of men's and therefore women must work relatively harder than men at any absolute workload (Kolka and Stephenson, 1995). Since it is the relative workload, and not the absolute workload, that determines core temperature and heart rate during exercise (Rowell, 1974), work performed at the same absolute intensity will result in higher levels of core temperature and heart rate in women compared with men. Studies by Hertig and Sargent II (1963), Shapiro et al. (1980) and Wyndham et al. (1965) have all demonstrated that females maintained higher heart rates and core temperatures than males during exercise-heat stress at similar absolute intensities.

Another difference between males and females, in terms of their physiological responses to exercise-heat stress, is that sweating occurs later, and at a higher body temperature in women than in men (Bittel and Henane, 1975; Cunningham et al., 1978). When compared to males, females exhibit a longer absolute delay before sweat onset (Avellini et al., 1980) and lower sweat rates (Avellini et al., 1980, Hertig and Sargent II, 1963; Wyndham et al., 1965). Due to the delayed onset of sweating and lower sweating sensitivity, the evaporative rate is lower in women than in men, leading to greater heat storage (Bittel and Henane, 1975; Frye and Kamon, 1981). As a result of these physiological differences, women, in general, are less tolerant to a given imposed heat stress than men (Kenney, 1985; Senay, 1973).

When comparing the physiological differences between the male and female responses to heat stress, important consideration must be given to the environmental conditions. Heat production is related to weight, whereas heat loss is a function of surface area (Shapiro et al., 1980). Since men are usually heavier than women, they tend to have a smaller surface area-to-weight ratio (Avellini et al., 1980). In a hot-dry environment, men tend to be at a thermoregulatory advantage. Their small surface area-to-weight ratio reduces the amount of heat gained from the environment via radiation and
convection (Avellini et al., 1980), and their higher sweat output allows for greater evaporative cooling (Hertig and Sargent II, 1963). In hot-wet environments, where the evaporative capacity of the environment is a limiting factor, women appear to be at an advantage. The higher surface area-to-mass ratio of women provides more surface area for evaporative heat loss and facilitates greater non-evaporative (radiative and convective) heat transfer (Shapiro et al., 1980). Furthermore, the lower sweat rate of women is advantageous in such an environment since excessive sweating will not enhance evaporative cooling, but rather it will result in greater dehydration (Avellini et al., 1980).

To illustrate the influence of ambient conditions on the gender differences in heat tolerance, Shapiro et al. (1980) compared the physiological responses of men and women to both dry and humid heat stress, in both a mild and hot environment. Following a period of heat acclimation, Shapiro et al. (1980) observed that men and women experienced similar physiological responses when exposed to a comfortable ambient environment (20°C, 40% relative humidity; 0.93 kPa). Under mild-wet and hot-wet conditions, females tolerated heat better than males. They exhibited lower core and skin temperatures, lower rates of heat storage, lower sweat rates and less dehydration than males (Shapiro et al., 1980). In contrast, males appeared to tolerate hot-dry heat better than females. Under these conditions the men experienced lower core and skin temperatures, lower heart rates and less heat storage (Shapiro et al., 1980).

Recent studies have emphasised the importance of controlling for fitness status, body size, and acclimation state when comparing gender differences in thermoregulation (Avellini et al., 1980; Kenney, 1985; Kolka and Stephenson, 1995). When men and women are matched for these characteristics, thermoregulatory function does not appear to differ between the two genders. For example, Havenith and van Middendorp (1990) demonstrated that both the percentage of body fat and the surface area-to-
mass ratio have a significant influence on the rate of heat storage, and that the effect of gender disappears when males and females are matched for these variables. Kolka and Stephenson (1995) related that when men and women are paired for aerobic capacity, the previously observed differences between men and women during heat exposure are minimised. Finally, the results of Frye and Kamon (1981) and Frye et al. (1982) illustrate that after acclimation, gender differences in thermoregulatory function are no longer evident.

Avellini et al. (1980) conducted a comprehensive study to resolve the effect of the interaction of all of these variables, as well as the impact of menstrual cycle phase, on gender differences in heat tolerance. A group of male and female subjects were chosen by the investigators, controlling for similar body surface area, surface area-to-weight ratio, maximal aerobic capacity and menstrual cycle phase. Subjects were tested both before and after a ten-day acclimation to humid heat, with the females tested during both the pre- and post-ovulatory phases. The results from their study demonstrated that prior to acclimation women in the pre-ovulatory phase experience less physiological strain to humid heat stress compared with both women in the post-ovulatory phase and men. During the pre-ovulatory phase, women had longer tolerance times, lower rectal temperatures and lower heart rates (Avellini et al., 1980). The responses of the men and the women during the post-ovulatory phase were similar, except the men exhibited higher sweat rates and heart rates throughout the heat-stress test (Avellini et al., 1980). Following the acclimation period, the rectal temperature and heart rate responses of all three groups were similar during exercise-heat stress (Avellini et al., 1980). The difference in sweat rate between men and the women was amplified after heat acclimation, with the men producing relatively greater amounts of sweat. However, the greater level of sweat secretion did not impart any physiological advantage to the males. Avellini et al. (1980) concluded that aerobic capacity is an important factor to consider when men and women are compared in the heat. It appears as though once subjects with similar anthropometric characteristics and aerobic capacities are
acclimated to humid heat, there are no gender-related difference in heat tolerance and thermoregulatory responses between men and women (Lebrun, 1994). While sweat rate may differ between men and women, aerobic capacity, acclimation state and surface area-to-mass ratio are more important than this gender difference in determining the thermoregulatory responses to heat stress.

2.6.7 Clothing

2.6.7.1 Effect of Clothing on Heat Exchange

Clothing influences the rate of heat exchange between the skin and the environment in a number of ways (Holmer, 1995). Clothing layers reduce the effectiveness of non-evaporative (radiative and convective) heat exchange. When humans are clothed, they do not exchange heat directly with the environment, except at exposed skin sites (Gagge and Gonzalez, 1996). Heat must be transported from the core to the skin, from the skin through each clothing layer, and then from the clothing to the environment. Clothing also interferes with air motion across the skin and as a result there is less transfer of heat by convection and less heat loss by evaporation (Gagge and Gonzalez, 1996). Evaporation from the clothing surface limits the effectiveness of evaporative cooling because the site of the phase change is remote from the skin. The cooling efficiency of sweating depends on the transmission of water vapour from the skin surface to the environment through clothing (Holmer and Elnas, 1981). Accordingly, the water vapour permeability of the clothing is a crucial and limiting factor for the magnitude of evaporative heat loss that is possible in a clothing system (Holmer and Elnas, 1981).

The insulative nature of a particular clothing ensemble is described by 'clo', the unit for thermal insulation. One clo is defined as the insulation necessary to maintain, in comfort, a resting subject in a normally ventilated room at a temperature of 21°C and a humidity of less than 50% (Gagge and Gonzalez, 1996). One clo unit is the thermal resistance equivalent to 0.155
m^2\cdot{}^\circ{}C\cdot{}W^{-1} \text{ (Gonzalez, 1988). With 1 clo unit of insulation, a man with a surface area of 1.8 m^2 will lose 10 kcal\cdot{}h^{-1} or 42 kJ of heat by radiation and convection for every degree Celsius difference between his average skin temperature and the air temperature (Berglund, 1988). Half of this value, 5 kcal\cdot{}h^{-1} or 21 kJ, will be lost with 2 clo units of insulation (Berglund, 1988).}

The ability of sweat to be evaporated through clothing is described by the Woodcock permeability index (i_m) with values ranging from 0 for impermeable fabrics to 1 for evaporation of sweat in air. A permeability index of 1 signifies that an individual has the same capacity for evaporative heat loss as a psychrometric wet bulb thermometer (a thermometer with a fully wetted surface, ventilated by a fan or slung at the end of a chain to produce maximum evaporative cooling) (Berglund, 1988). A 100% sweat soaked, naked man has an i_m of approximately 0.5 (Berglund, 1988). The i_m for most conventional clothing (i.e., long sleeves and pants) is approximately 0.45 (Berglund, 1988).

### 2.6.7.2 Protective Clothing Systems

In many industrial settings, protective clothing must be worn to prevent harmful exposure to physical and chemical stress factors. Often, adequate protection in these environments is provided through the use of impermeable or semi-permeable clothing systems. The nature of the fabric used in these clothing ensembles and the various treatments of the fabric render them highly impermeable to water vapour. Thus, the ability to evaporate sweat from the skin surface is severely impaired. As well, the air layers that are created between the skin, underwear, work clothing and the protective garment contribute to the thermal insulation and vapour resistance of the protective system (Nunneley, 1989). Depending on the permeability and insulation characteristics of the fabric, protective clothing has the potential to change an environment of compensable heat stress into one of uncompensable heat stress.
The low moisture permeability that is typical of most protective clothing systems, in combination with the trapped air layers and the high insulative nature of the clothing fabric, hinders the dissipation of metabolic heat from the body. The characteristics of the protective clothing can result in higher skin temperatures, more wetted skin, and a greater subjective discomfort compared with conditions when workers do not have to don the protective gear (Montain et al., 1994). Furthermore, the addition of impermeable clothing while working in a comfortable and warm environment causes body temperature and heart rate to rise at a faster rate (White et al., 1991). Thus, the wearing of protective clothing while performing work in a warm environment can create significant strain on the thermoregulatory system.

2.6.7.3 Nuclear, Biological and Chemical (NBC) Protective Clothing

Canadian Forces (CF) personnel are required to sustain military operations in a wide range of environments. More recent areas of deployment include the Middle East, Croatia, Rwanda and Somalia. Aside from the climatic extremes that CF personnel must be prepared to work in, there is also the threat that the enemy may use nuclear, biological and chemical agents. Clothing has been designed, therefore, to protect military personnel who must continue operations in the face of such hostile conditions.

The Canadian Forces NBC protective system consists of a semipermeable overgarment and impermeable rubber boots, gloves, mask and respirator. This ensemble is normally worn over combat clothing and boots, which in turn are layered over a T-shirt, undergarments, and socks. The normal operational clothing (i.e., combat clothing, boots, undergarments, T-shirt and socks) has an insulative value equivalent to 1.09 clo (0.169 m²·°C·W⁻¹) and a permeability index (iₘ) of 0.58. The addition of the
protective clothing increases the total insulation of the ensemble to 1.88 clo (0.29 m²·°C·W⁻¹) and reduces the $i_m$ to 0.33.

When the current NBC ensemble was introduced, it had been designed for operations in central Europe where climatic conditions are similar to those observed in Southern Ontario. The fall and winter are typically cold, and the spring and summer are much warmer. Temperatures rarely exceed 30°C on an average summer day. In 1990/1991, with the development of conflict in the Middle East, CF personnel were faced with providing military service in a much hotter, more hostile operational environment. The CF base at that time was located in the coastal region of Qatar, and temperatures there were above 40°C daily. These hot environmental temperatures prompted the need for further research that established work and rest guidelines that commanders could use when personnel were required to don the NBC protective ensemble.

2.6.7.4 Constraints Imposed By NBC Clothing

Protective clothing, like the NBC ensemble, has been shown to cause significant thermoregulatory and cardiorespiratory strain (Cortilli et al., 1996). First, the bulk and weight of the protective clothing increase the energy cost of work (Holmer, 1995). Metabolism was 13% higher in subjects wearing the NBC clothing compared with subjects wearing normal operational clothing walking at the same speed and grade of elevation (Aoyagi et al., 1994). Second, the thermal stress, the weight bulk and pressure on the face and head, the increased external dead space, and the additional inspiratory and expiratory breathing resistance imposed by the mask and respirator contribute to the physiological and psychological strain while performing work in NBC clothing (Muza, 1986). As well, the thickness and insulative nature of the NBC ensemble severely reduce the dissipation of metabolic heat compared with wearing normal operational or combat clothing (McLellan et al., 1990; McLellan, 1991). Finally, because the components of the NBC protective...
system are either semi-permeable or impermeable to water vapour penetration, evaporative heat loss from the body is impaired (McLellan, 1991).

Since the evaporation of sweat from the skin surface is the major avenue by which humans dissipate heat in a hot environment, work associated with wearing protective clothing can result in heat strain and reduction in work performance (Carter and Cammermeyer, 1985). Research has shown that wearing protective clothing against a nuclear, biological, or chemical threat in warm ambient environments causes performance decrements and decreases work tolerance times (Kraning and Gonzalez, 1991; McLellan et al. 1990; McLellan, 1991; McLellan et al., 1993a; Montain et al., 1994).

2.6.7.5 Heat Strain in NBC Clothing

A number of studies have characterised the magnitude of the heat strain during activity while wearing NBC protective ensembles. White et al. (1991) found that the wearing of chemical protective clothing in a hot environment (34°C, 55% relative humidity; 2.9 kPa) while walking on a level treadmill at a pace of 4 km·h⁻¹ resulted in non-steady state responses for heart rate, skin and rectal temperatures, indicating significant progressive thermoregulatory strain. Also, the subjects in their study reported that the use of chemical protective clothing increased the perception of thermal stress, the perceived ratings of work and the difficulty of inspiration and expiration. Armstrong et al. (1991) established that exercise in the U.S. military NBC clothing severely challenged the thermoregulatory and circulatory homeostatic mechanisms. The work of Aoyagi et al. (1994) demonstrated that neither endurance training nor heat acclimation improved exercise tolerance for moderate work rates when wearing the protective ensemble. Furthermore, Aoyagi et al. (1994) determined that the higher rates of sweat secretion following endurance training and heat acclimation did not increase evaporative cooling, but rather served only to decrease blood volume and
increase discomfort while performing work in the NBC gear. Montain et al. (1994) concluded that NBC protective clothing reduced the physiological strain a person can tolerate during uncompensable heat stress. They attributed the lower physiological tolerance to both the cardiovascular instability that results from the significant cutaneous vasodilation and increased venous compliance, and the discomfort of encapsulating the head with the face mask and hood (Montain et al., 1994). Finally, Tilley et al. (1981) concluded that in hot/humid conditions (i.e., 30°C and 60-65% relative humidity; 2.6 kPa) soldiers would be able to do little work in daylight hours while wearing full NBC ensembles without incurring severe heat casualties. They suggested that in hot/dry conditions (i.e. 35°C and 30-35% relative humidity; 1.4 kPa) soldiers would be able to sustain light activity while dressed in full NBC protection provided commanding officers were aware of the necessity of sufficient rest and water replenishment.

2.6.7.6 Influence of Ambient Environment and Metabolic Rate on Work Tolerance Time In Canadian Forces NBC Protective Clothing

McLellan (1991, 1993, 1994) and McLellan et al. (1990, 1992, 1993a&b, 1996) performed a number of studies to establish the heat strain and work tolerance times associated with varying ambient temperatures, ambient vapour pressures and metabolic rates for healthy, young men wearing different levels of the Canadian Forces NBC protective clothing. They analysed the influence of metabolic rate and level of NBC protection (i.e., combat clothing alone, combat clothing and NBC overgarment, or combat clothing, NBC overgarment, respirator, mask, gloves and boots) on work tolerance time at 40°C and 50% relative humidity (3.7 kPa) (McLellan, 1993), 18°C and 50% relative humidity (1.0 kPa) (McLellan et al., 1993a), and 30°C and 50% relative humidity (2.1 kPa) (McLellan et al., 1993a). They also compared different physical work intensities and work/rest schedules, such as light intermittent work, light continuous work, moderate continuous work and heavy continuous work, to determine the impact of metabolic rate on
work tolerance time in a warm ambient environment (McLellan et al., 1992; McLellan et al., 1993b; McLellan et al., 1996). As well, they investigated the effect of metabolic rate and ambient vapour pressure on heat strain in the CF protective clothing (McLellan et al., 1992; McLellan et al., 1996). In addition to the ambient environments cited above, work tolerance was examined at 40°C and 30% relative humidity (2.2 kPa) (McLellan et al., 1992), 40°C and 15% relative humidity (1.1 kPa) (McLellan et al., 1996) and 40°C and 65% relative humidity (4.8 kPa) (McLellan et al., 1996).

From the results of these studies, a decreasing curvilinear relationship was found to exist between work tolerance time and average metabolic rate (McLellan, 1993; McLellan et al., 1996). For all of the different ambient environments examined, this relationship could be described by a hyperbolic function. The influence of varying ambient environments on the relationship between work tolerance time and metabolic rate is summarised in Figure 1 (reproduced from McLellan et al., 1996). The vertical asymptote of the hyperbolic function, which defines infinite tolerance time, occurs at an average metabolic rate below zero (McLellan, 1993). This implies that body heat storage will continue to increase even under resting conditions for the environmental conditions studied.

It is apparent, from Figure 1, that differences in ambient temperature and humidity have more influence on tolerance times at low metabolic rates. McLellan (1993) originally reported that at metabolic rates above 15 to 20 mL·kg⁻¹·min⁻¹, the characteristics of the clothing minimise the influence of ambient conditions on body heat storage. It was also reported that at metabolic rates below 15 mL·kg⁻¹·min⁻¹, the ambient conditions begin to have a greater influence on sweat evaporation and tolerance time (McLellan, 1993). McLellan (1993) concluded from these results that a decrease in the ambient vapour pressure, due to either a decrease in temperature or humidity, will increase the vapour pressure gradient between the clothing surface and the environment, which in turn, will increase the evaporation of sweat from the
clothing. This increased evaporation from the clothing should eventually be reflected in increased evaporation of sweat from the skin, which should decrease body heat storage and prolong tolerance time (McLellan, 1993).

Figure 1: The relationship between tolerance time and metabolic rate (expressed in units of oxygen uptake) while wearing NBC protective clothing at a series of different ambient vapour pressures. Reproduced from McLellan et al. (1996) with permission.

The results from a more recent study demonstrate that differences in ambient vapour pressure influence tolerance times during both light (approximately 350 W) and heavy (approximately 500 W) exercise (McLellan et al., 1996). In the previous studies, $P_A$ was varied from 40°C, 30% relative humidity (2.2 kPa) (McLellan et al., 1992) to 40°C, 50% relative humidity (3.7
kPa) (McLellan, 1993) and 30°C, 50% relative humidity (2.1 kPa) (McLellan et al., 1993a), whereas in McLellan et al. (1996) the Pa was set at 40°C, 15% relative humidity (1.1 kPa) and 40°C, 65% relative humidity (4.8 kPa). The greater variation in ambient vapour pressure in the latter study had a significant impact on all indices of heat strain, regardless of metabolic work rate (McLellan et al., 1996). The data from this study oppose the author's previous hypothesis that variations in ambient vapour pressure have little or no impact on tolerance time and other indices of heat strain at heavier metabolic rates while wearing the CF protective clothing.

### 2.6.7.7 Intermittent vs. Continuous Work Schedules

A number of investigators have suggested the potential benefit of introducing work/rest schedules while wearing NBC protective clothing to reduce the metabolic rate and thus increase tolerance time (Cortilli et al., 1996; McLellan, 1993; McLellan et al., 1993b; Tilley et al., 1981). Kraning and Gonzalez (1991) on the other hand, found that intermittent work induced more physiological strain than continuous work when heat stress was uncompensable because the rest periods represented an interruption in the usual rate of heat transport via the cutaneous circulation. It is important to note, however, that Kraning and Gonzalez (1991) chose a protocol in which both intermittent and continuous work resulted in the same average rate of heat production.

The proposed benefit from implementing an intermittent work schedule while performing operations in NBC protective clothing stems from the reduction in the rate of heat production. A proper schedule of work and rest decreases the average metabolic rate, thus reducing the amount of metabolic heat produced. The total amount of time required to complete the task will increase if rest schedules are implemented, but there will be less physical stress to the soldier (McLellan et al., 1993b).
Using the known relationship between work tolerance time and average metabolic rate, work/rest schedules can be determined that may prolong work time while wearing the NBC protective clothing. McLellan (1994) provides a summary of estimated work tolerance times for different tasks performed while wearing full NBC protection in several different operating ambient environments. Work and rest schedules for work tolerance times of 1.0 to 5.0 hours for different tasks performed in full NBC gear are also suggested. The benefits of rest periods to increase the total work performed are only evident when ambient conditions allow body cooling to occur (McLellan and Frim, 1994). If the ambient temperature exceeds body temperature, there will be no increase in total work time since heat storage will continue to increase during the rest periods (McLellan, 1994).

2.6.8 Menstrual Cycle

2.6.8.1 The Menstrual Cycle

Before discussing how the menstrual cycle influences thermoregulation, it is important to first understand the basic physiology of the menstrual cycle. The menstrual cycle is conventionally divided into distinct phases that are named either for the changes that occur in the ovary (i.e., the follicular and luteal phases) or for the changes that occur in the lining of the uterus (i.e., the menstrual, proliferative and secretory phases). In the majority of women of reproductive age, the menstrual cycle lasts between 25-30 days, with a median length of a cycle being 28 days (Carr, 1993). Most studies comparing the relative length of the follicular and luteal phases have found that the length of the luteal phase is remarkably constant and lasts 13 to 14 days, whereas the length of the follicular phase can last anywhere from 10 to 16 days (Carr, 1993). The variable length of the follicular phase explains the range in the duration of normal menstrual cycles.

The changes that occur over the course of a menstrual cycle are regulated by the interactions of the hypothalamus, the pituitary gland, and
the ovaries. Regulation of the menstrual cycle begins in the hypothalamus, which releases gonadotropin-releasing hormone (GnRH). GnRH is released in a pulsatile pattern and travels directly to the anterior pituitary through the hypothalamic pituitary portal vessels. The secretion of GnRH pulses by the hypothalamus results in increased pituitary release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH promotes ovarian follicle growth, whereas LH stimulates final oocyte maturation and ovulation. The predominant ovarian hormones involved in the regulation of the menstrual cycle are estrogen and progesterone. The synchronous action of these hormones prepares the endometrium for fertilization. As well, feedback from these hormones regulates the activity of the hypothalamus and pituitary gland.

A normal menstrual cycle starts with the follicular phase, and the first day of menstrual flow is labeled as day 1 of the cycle. The shedding of the endometrial lining occurs because of declining estrogen and progesterone levels during the last few days of the preceding cycle (Hatcher et al., 1988). During the early follicular phase (days 1-4), the low levels of estrogen and progesterone stimulates the secretion of gonadotropin-releasing hormone (GnRH) and follicle-stimulating hormone (FSH), resulting in follicular growth in the ovary. Within the first half of the follicular phase, a cohort of follicles begin to develop in response to FSH (Hodgen, 1989). During the mid follicular phase, follicle development continues but FSH levels begin to decline due to the negative feedback of estrogens and inhibin secreted by the developing follicle (Carr, 1993). By approximately day 7, a dominant follicle is evident, and the rest of the cohort become atretic. The dominant follicle continues to produce increasing amounts of estrogen during the late follicular phase (days 8-12). Peak estrogen levels are achieved 24-36 hours before ovulation (Hamm, 1991). When estradiol levels rise to 200 pg·mL⁻¹ and are sustained for 48-50 hours, estrogen stimulates luteinizing hormone (LH) release (Hamm, 1991). FSH is inhibited by estrogen and LH begins to
peak. About 9 hours after the LH surge, ovulation occurs (Hodgen, 1989). This corresponds to approximately day 14-15 of the menstrual cycle.

During the luteal phase, the follicle involutes to become the corpus luteum and progesterone levels rise rapidly, reaching a peak on about the 20th day of the cycle (Hamm, 1991). A serum progesterone level of more than 3 ng·mL⁻¹ is good evidence that ovulation has occurred and peak levels should reach 8 to 10 ng·mL⁻¹ (Hatcher et al., 1988). Estrogen levels rise at the same time as progesterone, but to a lesser degree. The presence of high levels of estrogen and progesterone inhibits the secretion of GnRH and FSH, thus blocking new follicular growth. If conception does not occur the destruction of the corpus luteum causes a drop in estrogen and progesterone levels. When these hormone levels drop significantly, the secretion of GnRH and FSH is no longer suppressed and the cycle begins again.

2.6.8.2 Influence of Menstrual Cycle During Compensable Heat Stress

It has been well established that the menstrual cycle affects temperature regulation. Basal body temperature exhibits a biphasic rhythm during the menstrual cycle in which core temperature is approximately 0.4°C higher in the luteal phase than in the follicular phase (Bemben et al., 1995; Stephenson and Kolka, 1993). This observation has been reported by several investigators, including Frascarolo et al. (1990), Hessemer and Bruck (1985a, 1985b), Hirata et al. (1986), Horvath and Drinkwater (1982), Kolka and Stephenson (1989), and Pivarnik et al. (1992). The rise in basal body temperature during the luteal phase of the menstrual cycle is generally attributed to the thermogenic effect of the increase in progesterone levels following ovulation (Lebrun, 1994).

There have been some reports that resting core temperature does not differ between the two phases of the menstrual cycle. Frye et al. (1982) compared the thermoregulatory responses of four eumenorrheic, four ammenorrheic and four young men to exercise-heat stress. They reported no
differences in core temperature, skin temperature or sweating rate between the pre- and post-ovulatory phases of the menstrual cycle or between the menstrual and amenorrheal women (Frye et al., 1982). Likewise, Wells and Horvath (1973) reported no significant differences in rectal temperature, skin temperature, oxygen consumption or total body sweating rates between the phases of the menstrual cycle. In looking at these observations, it is important to note that neither Frye et al. (1982) nor Wells and Horvath (1973) included hormonal verification of cycle phase.

The elevation in core temperature during the luteal phase represents an increase in body heat content. A number of studies have tried to determine whether this heat storage results from an increase in metabolic heat production, a decrease in heat loss, or a combination of both. Two investigations that have supported the concept that the increase in body heat content during the luteal phase is associated with an increase in heat production are Hessemer and Bruck (1985a) and Horvath and Drinkwater (1982). Hessemer and Bruck (1985a) studied the influence of the menstrual cycle on shivering, skin blood flow and sweating responses in ten healthy women. They found that resting basal metabolic rate was higher during the luteal phase compared with the follicular phase. Horvath and Drinkwater (1982) also reported a higher rate of metabolic heat production during the luteal phase compared with the follicular phase. In contrast to these findings, Bittel and Henane (1975), Carpenter and Nunneley (1988), Frascarolo et al., (1990) and Stephenson and Kolka (1985) all observed that menstrual cycle phase has no effect on metabolic rate. In the study by Frascarolo et al. (1990), the values for metabolic heat production and total heat loss obtained during the luteal phase were not significantly different from those observed in the follicular phase. The results of this study indicate that a small difference in internal temperature can be maintained without a significant change in heat production or heat loss.
The concept that a small difference in internal temperature can be maintained without a significant change in heat production or heat loss implies that the thermoregulatory setpoint is reset to a higher level during the luteal phase. If the thermoregulatory setpoint is increased in the luteal phase, then there must also be a parallel change in the threshold for the onset of all the thermoregulatory effectors. Stephenson and Kolka (1993) established that the core temperature thresholds for the onset of sweating, cutaneous vasodilation, and vasoconstrictor activity were higher in the luteal phase compared with the follicular phase. Several other investigators have supported the observation that the onset of thermoregulatory sweating and cutaneous vasodilation occur at an elevated internal temperature (Avellini et al., 1980; Bittel and Henane, 1975; Hessemer and Bruck, 1985a&b; and Kolka and Stephenson, 1989). Hessemer and Bruck (1985a) also found that the core temperature threshold for shivering increased in the luteal phase compared with the follicular phase. It appears as though the thresholds for the onset of the thermoregulatory effectors are shifted upward during the luteal phase, fulfilling the criterion that a change in the thermoregulatory setpoint must be observed by parallel changes in all involved thermoregulatory effectors (Stephenson and Kolka, 1993).

A number of investigators have questioned whether the slope of the relationship of sweat rate-to-core temperature is altered during the luteal phase. Hessemer and Bruck (1985a&b) observed that the slope of the relationship between sweat rate and core temperature, and between thumb and forearm heat clearance and core temperature increased in the luteal phase, indicating an increase in the sensitivity of the heat loss responses. They concluded that the greater sensitivity of heat loss responses to changes in body temperature during the luteal phase may partly counteract the elevated threshold onset temperatures for the thermoregulatory effectors. Similarly, Grucza et al. (1993) found that the gains for sweating for women not using oral contraceptives were greater in the luteal phase compared with the follicular phase. In comparison, Bittel and Henane (1975) found that the
absolute delay in time before the onset of sweating was longer in the post-ovulatory phase than in the pre-ovulatory phase. Although there was no clear change in the slope of the relationship between sweat rate and core temperature, the higher temperature for the onset of sweating indicated a decreased sensitivity of the sweating control system to an increase in core temperature during the luteal phase (Bittel and Henane, 1975). Similarly, the results of Pivarnik et al. (1992) indicated a decrease in sweat sensitivity during exercise in the luteal phase compared with the follicular phase. Finally, investigations by Avellini et al. (1980), Hirata et al. (1986) and Kolka and Stephenson (1989) demonstrated that there was no change in the slope of the relationship between forearm blood flow to core temperature, and sweat rate to core temperature, during the luteal phase compared with the follicular phase. Their results suggest that once sweating began, it followed a similar progression in both the follicular and luteal phases, implying a parallel shift in the sweat rate to core temperature relationship.

One further observation from the work of Hessemer and Bruck (1985a&b) was that both sweat rate and cutaneous blood flow were higher in the luteal phase compared with the follicular phase. The finding that cutaneous blood flow is greater in the luteal phase has been supported by Hirata et al. (1986), who found a tendency for higher forearm blood flow in the luteal phase (although the difference was not statistically significant), and Stephenson and Kolka (1993) who reported that limb blood flow is higher in the luteal phase compared with the follicular phase.

A number of investigators have observed the opposite effect. Bittel and Henane (1975) and Frascarolo et al. (1990) found that skin blood flow and thermal conductance were lower in the luteal phase. Frascarolo et al. (1990) suggested that the decrease in these parameters corresponds to an increase in cutaneous thermal insulation and that this may be the mechanism responsible for the rise in internal temperature during the luteal phase. Horvath and Drinkwater (1982) observed a decrease in forearm blood flow in
the luteal phase, with no significant difference in evaporative heat loss or total sweat rate between the two phases of the menstrual cycle. The finding that there is no significant difference in evaporative heat loss and sweat rate between the two phases of the menstrual cycle has been substantiated in a number of studies (Carpenter and Nunneley, 1988; Frye et al., 1982; Pivarnik et al., 1992; Senay, 1973; Wells and Horvath, 1973).

One possible reason for the discrepancies in the results reported by these authors is that the combined influence of exercise and heat stress tends to mask the differences observed in resting core temperature during the follicular and luteal phases of the menstrual cycle (Horvath and Drinkwater, 1982; Stephenson and Kolka, 1993). This may be one of the reasons for the lack of significant findings in some studies. Another possible reason is that differences in thermoregulation may be attributable more to inter- and intra-individual variation than to differences in menstrual phase (Frye et al., 1982). Finally, since the alterations in sweat rate and metabolic rate are subtle, they could be easily missed if hormonal status is not carefully monitored (Carpenter and Nunneley, 1988).

2.6.8.3 Influence of Menstrual Cycle During Uncompensable Heat Stress

While a number of investigators have attempted to quantify the thermoregulatory strain during uncompensable heat stress in young, healthy men (Aoyagi et al., 1994; Cortilli et al., 1996; Holmer and Elnas, 1981; Kraning and Gonzalez, 1991; McLellan et al., 1996; Montain et al., 1994; White et al., 1991), there has been comparatively little research done to represent the physiological strain experienced by women under similar conditions of uncompensable heat stress. Kolka et al. (1994) looked at heat exchange in women wearing chemical protective clothing while performing continuous exercise in the heat during the early follicular phase of the menstrual cycle. Subjects performed treadmill exercise (1.34 m·s⁻¹, 2% grade), while wearing NBC protective clothing, in an ambient environment of 30°C and 30%
relative humidity (1.3 kPa). The combination of the clothing system, the ambient environment and the exercise intensity created a situation of uncompensable heat stress.

The results from their study demonstrated that, in young, healthy women, the wearing of NBC protective clothing while performing continuous exercise in the heat leads to significant physiological strain. Core temperature increased at a rate of 0.03 °C·min⁻¹ during the experiments, and resulted in an increase in internal temperature of greater than 1.5°C (Kolka et al., 1994). The investigators concluded that, when tightly controlled for the early follicular phase of the menstrual cycle, women wearing chemical protective clothing ensembles experience similar thermoregulatory strain as predicted for men. These results cannot, however, be generalised to all phases of the menstrual cycle.

Subsequent to this investigation, Kolka and Stephenson (1995) examined the physiological responses of young, healthy women to uncompensable heat stress during the early follicular, late follicular and mid luteal phases of the menstrual cycle. The investigators compared two different environments that resulted in uncompensable heat stress. In the first series of experiments, four women performed exercise at an intensity of approximately 40% \(\dot{V}O_2_{\text{max}}\) in an ambient environment of 30°C and 35% relative humidity (1.5 kPa) while wearing NBC protective clothing. In the second series of experiments, three women performed exercise at a similar intensity in an ambient environment of 38°C and 60% relative humidity (4.0 kPa) while wearing shorts and a T-shirt. The ambient conditions in the second study simulated the conditions inside the protective clothing (Kolka and Stephenson, 1995). Tolerance times in these conditions approximated only 45 min.

The results from both studies demonstrated that even under conditions that limit evaporative heat loss, whether it be due to the wearing
of clothing that restricts the evaporation of sweat or a result of increasing $P_A$, resting and exercise core temperature are higher in the mid luteal phase compared with the early follicular phase (Kolka and Stephenson, 1995). The difference in exercise esophageal temperature between the early follicular and mid luteal phases is apparent throughout the exercise period (Kolka and Stephenson, 1995). Whole body sweating rates, mean skin temperature and heart rate did not differ among the phases (Kolka and Stephenson, 1995). The data from their experiment, when compared to the USARIEM Heat Strain Model which was derived from data collected from male subjects in an identical scenario, showed that women experience similar strain during uncompensable heat stress as predicted for men (Kolka and Stephenson, 1995). It is not known whether similar conclusions would be obtained with women performing lighter exercise where tolerance times approach 100 min.

### 2.6.8.4 Menstrual Cycle and Exercise

Results of studies using hormonal documentation to verify menstrual cycle phase have shown that, in general, maximal aerobic capacity and submaximal exercise responses do not differ between the follicular and luteal phases of the menstrual cycle (Horvath and Drinkwater, 1982; Jurkowski et al., 1981; Lebrun, 1994; Stephenson et al., 1982). Horvath and Drinkwater (1982) observed that there were no phase-related differences in oxygen consumption ($\dot{V}O_2$), heart rate (HR), blood pressure (BP) or stroke volume (SV) in women performing exercise at 30% $\dot{V}O_{2\text{max}}$. Stephenson et al. (1982) found that $\dot{V}O_2$, carbon dioxide production ($\dot{V}CO_2$), and respiratory exchange ratio (RER) did not differ at any exercise intensity (mild through severe) or phase of the menstrual cycle, and time to exhaustion did not differ by phase. Some investigators have reported that women experience a slight decrease in aerobic capacity during the luteal phase (Lebrun et al., 1995); however, others have found an enhancement of endurance performance in this phase (Jurkowski et al., 1978; Jurkowski et al., 1981).
Lebrun et al. (1995) looked at exercise performance in 16 women during the early follicular and mid luteal phases of the menstrual cycle and found that although both absolute (L·min⁻¹) and relative maximal oxygen (mL·kg⁻¹·min⁻¹) uptake were slightly lower during the luteal phase of the menstrual cycle, there was no significant effect of menstrual cycle phase on anaerobic performance, aerobic endurance or isokinetic muscle strength. As well, they reported that there was no significant difference in ventilatory function, maximum heart rate, maximum respiratory exchange ratio, or body composition. Bemben et al. (1995) did not find any alteration in blood lactate, aerobic power or maximal ventilatory parameters during the luteal phase compared with the early follicular and late follicular phases of the menstrual cycle in women performing maximal treadmill exercise.

In contrast to these observations, Jurkowski et al. (1978) and Jurkowski et al. (1981) found that the time to exhaustion during maximal exercise performance was longer in the luteal phase (2.97 min) compared with the follicular phase (1.57 min) in women with a normal menstrual cycle. Blood pH decreased during exhaustive exercise; however, the decline from resting pH was only significant during the follicular phase (Jurkowski et al., 1981). In addition, mean lactate concentration was 30% higher in the follicular phase compared with the luteal phase (Jurkowski et al., 1981). Maximum power output, maximum heart rate, oxygen consumption, carbon dioxide production, and stroke volume did not differ between the two phases (Jurkowski et al., 1981).

It appears as though the menstrual cycle has a minimal impact on exercise performance, with the possible exception of aerobic capacity. The magnitude of this effect varies substantially among women, and may be more important on an individual basis (Lebrun, 1993).
2.6.9 Oral Contraceptives

2.6.9.1 Oral Contraceptives and the Menstrual Cycle

Oral contraceptives (OCs) modify normal menstrual function in at least four ways. The most significant impact of oral contraceptive therapy is the inhibition of ovulation. Since oral contraceptives inhibit the surge of LH, they also negate the rise in progesterone levels associated with the luteal phase of the menstrual cycle. Some of the other effects of oral contraceptive usage are that they cause changes in the endometrium which thwarts implantation of the blastula; they modify the physical and chemical properties of the cervical mucus, consequently inhibiting sperm penetration; and they produce subtle changes in the hypothalamic-pituitary-ovarian axis that are believed to alter corpus luteum function (Health Canada, 1995).

Contraceptive technology has changed substantially in the last twenty years. The first generation of oral contraceptives contained high doses of the progestins norethynodrel or norethidrone (Health Canada, 1995). The new generation of oral contraceptives contain a lower dosage of progestin (either norethidrone, norethidrone acetate, norethynodrel, ethynodial diacetate, dl-norgestrel, levonorgestrel, noregestimate, desogestrel or gestodene) and estrogen (either ethinylestradiol or mestranol) (Health Canada, 1995). The newer progestins were developed in an attempt to produce agents with more selective progestational activity that would improve cycle control and minimise metabolic changes and adverse effects while effectively preventing pregnancy (Wilde and Balfour, 1995). The most widely used combination pills today contain 1 mg or less of a progestogen and 30 to 35 μg of an estrogen (Hale, 1987). It is believed that the new low-dose formulations have far fewer side effects and complications than do the earlier high-dose pills.

Improvements in oral contraceptive technology have also led to the introduction of triphasic combination formulas, in which the dose of estrogen or progestogen or both are altered during the month. Three basic
formulations of the triphasic pill have been developed. In two of these formulations, the dosage of the progestin is varied, while the estrogen component remains constant throughout the entire cycle (Hale, 1987). In the third formulation, both the estrogen and progestin is altered (Hale, 1987).

The progestins used in oral contraceptives are derived from one of two parent compounds, either progesterone or testosterone. Two important progestins structurally related to testosterone are norethidrone and levonorgestrel. The new generation of progestins used in oral contraceptives (desogestrel, norgestimate and gestodene) are derivatives of levonorgestrel. A general comparison of the pharmacokinetics of norethindrone, levonorgestrel, desogestrel and gestodene show that large intersubject and intrasubject variability exists in serum levels and pharmacokinetics of the progestins. Studies have demonstrated that gestodene and levonorgestrel are essentially completely bioavailable, whereas the average absolute bioavailabilities of 3-keto-desogestrel and of norethindrone are 75% and 65%, respectively (Lobo and Stanczyk, 1994). The time to reach maximum serum levels is similar among the four progestins (1.4 to 1.7 h) (Lobo and Stanczyk, 1994) and the plasma concentrations of these progestins are higher on day 21 than on day 1 (Shenfield and Griffin, 1991). For example, mean trough (24-hour) serum concentrations for subjects using a 150 μg desogestrel/30 μg ethinylestradiol combination pill increased from 0.24 ± 0.15 μg·L⁻¹ on day 1 to 0.86 ± 0.45 μg·L⁻¹ on day 21 (Kuhl et al., 1988a). For subjects using a 75 μg gestodene/30 μg ethinylestradiol combination pill, mean trough serum concentrations rose from 1.4 ± 1.7 μg·L⁻¹ on day 1 to 4.9 ± 2.3 μg·L⁻¹ on day 21 (Kuhl et al., 1988b). The increase in their serum concentration over the course of the cycle is presumably due to the progressive rise in sex hormone binding globulin (SHBG). Ethinylestradiol enhances SHBG levels, resulting in an increase in progestin bound to the protein (Shenfield and Griffin, 1991).

The most common estrogen used in contraceptive formulations is ethinylestradiol (EE). EE is formed by the structural modification of the
estradiol molecule by the insertion of an ethynyl group at carbon 17. Mestranol was widely used in earlier oral contraceptive formulations, but since it has been shown the estrogenic effect of mestranol is the result of its demethylation in the liver, forming ethinylestradiol, it is no longer used (Lobo and Stanczyk, 1994). Pharmacokinetics studies show that there are large intraindividual and interindividual differences in ethinylestradiol levels which are mainly dependent on variations in metabolic capacity (Kuhl, 1990). After oral administration, EE is rapidly absorbed in the gastrointestinal tract. Peak levels are observed between 1 and 2 h after oral intake and its bioavailability is between 40% to 50% (Kuhl, 1990). The average peak level of EE after a single oral dose of 20 µg in combination with 150 µg desogestrel is 25 pg·mL⁻¹ and after 30 µg EE and 150 µg desogestrel this value is 60 pg·mL⁻¹ (Jung-Hoffmann and Kuhl, 1989). The serum concentrations of ethinylestradiol rise during multiple intake to levels of up to 60 pg·mL⁻¹ and 110 pg·mL⁻¹, respectively (Jung-Hoffmann and Kuhl, 1989). The mean value for its half-life of elimination is 10 hours (Lobo and Stanczyk, 1994). Ethinylestradiol is bound almost exclusively to albumin, and not SHBG.

The efficacy of oral contraceptives stems mainly from the action of the progestin component. The inhibition of follicular development, as indicated by follicle size and estradiol levels, is dependent on the progestin dose rather than on the ethinylestradiol component (Kuhl, 1990). The doses of EE used in oral contraceptive formulations are insufficient to consistently produce an antiovulatory effect (Lobo and Stanczyk, 1994). Rather, EE potentiates the action of the progestin component and it stabilizes the endometrium so that irregular shedding and breakthrough bleeding are minimised (Lobo and Stanczyk, 1994).

The primary site of action of oral contraceptive steroids is at the level of the hypothalamus. Pituitary LH and FSH are suppressed. The midcycle cycle LH and FSH surges, as well as the preovulatory estradiol peak do not occur and consequently ovulation is inhibited. As well, the pituitary
response to gonadotropin-releasing hormone (GnRH) stimulation is significantly depressed in oral contraceptive users. Mishell et al. (1977) looked at the short-term (3 months) and long-term (> 9 months) effect of oral contraceptive use on hypothalamic-pituitary function. They observed that LH and FSH release were significantly lower in both the short-term and long-term users. Endogenous estradiol levels were low and relatively constant, similar to those found in the early follicular phase (Mishell et al., 1977). Progesterone levels were also low (less than 1 ng.mL$^{-1}$ on day 22), indicating that ovulation was inhibited in all of the subjects (Mishell et al., 1977). As well, most of the short-term and long-term users displayed a diminished gonadotropin response to GnRH stimulation. The results of their study demonstrate that oral contraceptives have a direct effect on the pituitary gland resulting in the inhibition of pituitary gonadotropin function (Mishell et al., 1977).

Likewise, the results of Fitzgerald et al. (1994) and Jung-Hoffmann et al. (1988) demonstrated that mean LH and FSH concentrations were significantly reduced during oral contraceptive use. LH was diminished by almost 50% and FSH by 70% by day 10 of each cycle (Jung-Hoffmann et al., 1988). The results of both studies also indicated that FSH and LH began to rise after day 21 (i.e., during the pill-free interval). FSH and LH levels were normalised by day 1 of the following cycle, indicating that pituitary function had recovered during the pill-free interval (Jung-Hoffmann et al., 1988).

The results of Fitzgerald et al. (1994) and Jung-Hoffmann et al. (1988) also demonstrate that there is a decrease in ovarian steroidogenesis with oral contraceptive use. Both studies compared the effects of different oral contraceptive preparations on ovarian function, showing that there is no significant difference in the clinical effects or in the influence on the serum hormone parameters between the formulations studied. Serum estradiol is significantly reduced between days 1 and 21 of the cycle. Fitzgerald et al. (1994) observed that serum estradiol declined after pill intake started, reaching its
lowest level on day 12. Estradiol levels remained low throughout the remainder of the 21 day cycle and then began to rise again during the pill-free week (Fitzgerald et al., 1994). Similarly, Jung-Hoffmann et al. (1988) reported a decline in serum estradiol levels; however, estradiol was lower on day 21 than on day 10 in their study. They also observed an increase in serum estradiol levels during the pill-free interval. The concentration of serum estradiol on day 1 of the oral contraceptive cycles was similar to those values measured on day 1 of the control cycle (prior to the initiation of oral contraceptive use) (Jung-Hoffmann et al., 1988). In addition, serum progesterone is suppressed during oral contraceptive use. The results of Jung-Hoffmann demonstrate that progesterone levels on day 21 are similar to those observed on day 1. Furthermore, the serum progesterone levels measured on day 21 of the cycles during oral contraceptive use are similar to those values measured on day 1 of the control cycle. The low levels of serum progesterone and estradiol indicate that ovarian steroidogenesis is suppressed during oral contraceptive use.

2.6.9.2 Influence of Oral Contraceptives on Thermoregulation

While there has been considerable research on the influence of the menstrual cycle on temperature regulation, very few investigators have looked at the influence oral contraceptive use on thermoregulation. Results from the only two studies published to date elucidate that, similar to women with normal menstrual cycles, resting core temperature and the threshold for the onset of thermoregulatory sweating are higher during the luteal phase compared with the early follicular phase (Grucza et al., 1993; Rogers and Baker, 1997). In both investigations, thermoregulation was studied during exercise in a comfortable ambient environment (22°C to 24°C). The possible influence of oral contraceptives on thermoregulation in a warmer ambient environment and during uncompensable heat stress has not been investigated.
Grucza et al. (1993) examined the influence of the menstrual cycle and oral contraceptives on thermoregulatory responses to maximal and submaximal (50% $\dot{V}O_{2\text{max}}$) exercise during the follicular and luteal phases. A quasi-follicular phase (q-F) and a quasi-luteal phase (q-L) were assumed for the women using oral contraceptives. Eight of their subjects were using a triphasic formulation (the dose of the progestin component is raised over the course of the cycle) and two of their subjects were taking a monophasic preparation (the dose of the both the estrogen and progestin are consistent throughout the cycle). Grucza et al. (1993) found that, similar to women who were not taking oral contraceptives, resting core temperature was significantly greater in the quasi-luteal phase than in the quasi-follicular phase, and the rectal temperature threshold for sweating was significantly higher in q-L than in q-F. However, final $T_r$ did not differ between the two phases (Grucza et al., 1993). Changes in $T_{sk}$ during exercise were similar in both phases and there was no significant difference in the increase in $T_{sk}$ between the two phases (Grucza et al., 1993). Heart rate increased in response to exercise similarly in both q-F and q-L, and the dynamics of sweating did not differ between the two phases (Grucza et al., 1993). They concluded that the administration of oral contraceptives did not change the greater core temperature threshold for sweating among women in the luteal phase but reduced the phase-related differences in the gains for sweating, making the thermoregulatory responses to exercise more uniform during the menstrual cycle. The upward shift in core temperature and in the threshold onset of sweating in the quasi-luteal phase are most likely the result of the strong effect of cycle phase of the menstrual cycle on the thermoregulatory system since they were not affected by oral contraceptive use (Grucza et al., 1993).

Rogers and Baker (1997) compared the thermoregulatory response of seven women to treadmill exercise (1.33 m·s\(^{-1}\), 10% grade) during the third week of pill use (P) and the week when no pill was ingested (N). Five of their seven subjects were using a triphasic combination oral contraceptive and two of their subjects were using a monophasic combination pill. They found that
resting core temperature was 0.31°C higher and the threshold for the onset of evaporative water loss was 0.32°C higher in P than in N, respectively (Rogers and Baker, 1997). Rectal temperature remained higher throughout the entire exercise period during P compared with N (Rogers and Baker, 1997). Also, exercise heart rate was 6.5 b-min⁻¹ higher in P than in N (Rogers and Baker, 1997). Packed cell volume and plasma osmolality did not differ between P and N, and thus it was not likely that changes in body fluid balance contributed to the upward shift in the threshold for the onset of evaporative water loss or heart rate during P (Rogers and Baker, 1997). They concluded from their results that the progestin component of the pill has a dominant effect on thermoregulation (Rogers and Baker, 1997).

### 2.6.9.3 Oral Contraceptives and Exercise

Once again, there is comparatively less information known about the influence of oral contraceptive use on exercise performance than there is on the effect of the menstrual cycle on exercise performance. Huisveld et al. (1985) found that exercise performance did not differ between users and non-users of oral contraceptives. They compared the responses of 10 trained OC users and 10 trained OC non-users to incremental cycle exercise until exhaustion. Maximal heart rate, maximal respiratory exchange ratio, maximal lactate acid concentration, \( \dot{V}O_{2\text{max}} \) and time to exhaustion did not differ between the two groups. Similarly, Grucza et al. (1993) found that \( \dot{V}O_{2\text{max}} \) did not differ between users and non-users of oral contraceptives. Bonen et al. (1991) examined the substrate and hormonal responses of 7 OC users and 8 OC non-users during 30 min of treadmill exercise at 40% \( \dot{V}O_{2\text{max}} \), followed by 30 min of treadmill exercise at 85% \( \dot{V}O_{2\text{max}} \). From their results, they concluded that OC use alters the availability of free fatty acid at rest and during mild exercise, but not during heavy exercise. During heavy exercise, carbohydrate metabolism, free fatty acid use and lactate production are similar in both groups (Bonen et al., 1991). Bemben et al. (1992) found that contraceptive steroids exert significant metabolic and endocrine effects that
alter substrate utilisation during exercise. The growth hormone response was greater, and blood glucose levels and carbohydrate utilisation were lower in OC users compared with non-users during 90 min of treadmill exercise at 50% \( \dot{V}O_{2\max} \) (Bemben et al., 1992). Their results support those of Bonen et al. (1991) who found a preference for lipid metabolism among OC users during light exercise.

It appears as though exercise performance does not differ between users and non-users of oral contraceptives, aside from slight alterations in some substrate and hormonal parameters. This conclusion, however, seems premature due to the limited amount of information available with respect to OC use and exercise. Numerous investigations have carefully analysed the influence of menstrual cycle phase and estrogen/progesterone levels on various parameters of exercise performance, over a wide range of exercise intensities and exercise protocols. The same cannot be said of the research performed to date with respect to OCs and exercise. There is much that is not known about the potential influence of oral contraceptives during exercise and/or heat stress. For example, it is not known to what extent oral contraceptives may modify the physiological responses to exercise and/or heat stress over a wide range of exercise intensities and ambient conditions. The influence of oral contraceptives during uncompensable heat stress remains to be explored. Finally, the influence of oral contraceptive ingestion and synthetic ethinyl estradiol/progestin levels on the established menstrual phase-related alterations in exercise performance and thermoregulatory function are not clearly understood.
Chapter 3

STUDY OBJECTIVES AND HYPOTHESES

3.1 OBJECTIVES

The objectives of this study were to:

i. Document the heat strain experienced by women wearing combat clothing and Canadian Forces NBC protective clothing during light intermittent exercise in the heat.

ii. Determine the influence of the early follicular, late follicular and mid luteal phases of the menstrual cycle during compensable and uncompensable heat strain.

iii. Evaluate the influence of oral contraceptive use during compensable and uncompensable heat strain.

3.2 HYPOTHESES

The hypotheses tested in this study were that:

i. Women who are not using oral contraceptives will experience greater heat strain during the luteal phase of their menstrual cycle compared with the early follicular and late follicular phases while wearing the NBC protective clothing.

ii. Since oral contraceptives negate the surge in progesterone associated with the luteal phase, women who are using oral contraceptives will be at a thermoregulatory advantage compared with women not using this method of birth control during the luteal phase.
Chapter 4

METHODS

This study was carried out at the Defence and Civil Institute of Environmental Medicine (DCIEM) from January to June, 1996. The study was approved by the Human Ethics Committees of the University of Toronto and DCIEM.

4.1 SUBJECTS

Eighteen healthy female volunteers, between the ages of 18 and 35 yrs, were recruited from DCIEM, the university community and the military reserves to participate in this study. Participation in the experiment was subject to medical approval and to verbal confirmation of a regular menstrual cycle. Prior to inclusion in the study, all subjects were apprised of the details of the experimental procedures and the associated risks and discomforts and were required to sign an informed consent statement. Testing was conducted from January to June to limit heat acclimation through casual exposure to high ambient temperatures.

The subjects were divided into two equal sized groups which differed only with respect to oral contraceptive use or non-use. All of the women in the user group had been taking oral contraceptives for a minimum of three months prior to involvement in the experiment. Seven of the 9 users were taking a monophasic contraceptive (the dose of the synthetic estrogen and progestin components remain constant during the 21 day pill-ingestion period of the menstrual cycle). The other two users were taking a triphasic formulation (the dosage of the estrogen or progestin or both are altered during the 21 day pill-ingestion period of the menstrual cycle). The oral contraceptive used by each subject in this group and the synthetic hormone components of the contraceptive are shown in Table 1.
Table 1: Synthetic estrogen and progestin content and dosage regimen of the oral contraceptives used by subjects in this study. (EE, ethinyl estradiol; LNG, levonorgestrel; NET, norethindrone; DG, desogestrel).

<table>
<thead>
<tr>
<th>Oral Contraceptive</th>
<th>n</th>
<th>Pill</th>
<th>Estrogen (mg)</th>
<th>Progestin (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minovral</td>
<td>1</td>
<td>1-21</td>
<td>0.030 EE</td>
<td>0.15 LNG</td>
</tr>
<tr>
<td>Marvelon</td>
<td>5</td>
<td>1-21</td>
<td>0.035 EE</td>
<td>0.03 DG</td>
</tr>
<tr>
<td>Ortho-cept</td>
<td>1</td>
<td>1-21</td>
<td>0.035 EE</td>
<td>0.03 DG</td>
</tr>
<tr>
<td>Synphasic</td>
<td>1</td>
<td>1-7</td>
<td>0.035 EE</td>
<td>0.5 NET</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8-16</td>
<td>0.035 EE</td>
<td>1.0 NET</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17-21</td>
<td>0.035 EE</td>
<td>0.5 NET</td>
</tr>
<tr>
<td>Triquilar</td>
<td>1</td>
<td>1-6</td>
<td>0.030 EE</td>
<td>0.05 LNG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-11</td>
<td>0.040 EE</td>
<td>0.075 LNG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-21</td>
<td>0.030 EE</td>
<td>0.125 LNG</td>
</tr>
</tbody>
</table>

4.2 DETERMINATION OF PEAK AEROBIC POWER (\(\dot{V}O_2^{peak}\))

\(\dot{V}O_2^{peak}\) was determined on a motor-driven treadmill using open-circuit spirometry. Subjects began running on a level treadmill at a self-selected pace of 8.0 - 12.0 km·h\(^{-1}\) (2.22 - 3.33 m·s\(^{-1}\)), depending on the subject's aerobic fitness. After 3 min, the treadmill grade was increased by 1 %·min\(^{-1}\) until exhaustion. \(\dot{V}O_2^{peak}\) was defined as the highest 30-s oxygen consumption (\(\dot{V}O_2\)) observed during the incremental test. Heart rate (HR) was monitored throughout the test via a transmitter/receiver telemetry unit (Polar Vantage XL, Polar Electro PE3000). The highest observed value was considered as the individual's peak heart rate (HR\(_{peak}\)).
4.3 EXPERIMENTAL PROTOCOL

4.3.1 Familiarisation

A minimum of 24 h following the determination of $\dot{V}O_2$peak, subjects were familiarised to light intermittent exercise in a hot environment (40°C and 30% relative humidity; 2.2 kPa, wind less than 0.1 m·s⁻¹) while wearing the Canadian Forces NBC protective ensemble. During the familiarisation session, subjects alternated between 15 min of walking on a level treadmill at 4 km·h⁻¹ (1.11 m·s⁻¹) and 15 min of seated rest and were allowed to drink one canteen (approximately 1 litre) of water. Rectal temperature, mean skin temperature, heart rate and gas exchange were monitored and the end-point criteria were identical to those listed below.

4.3.2 Experimental Design

Subjects were required to perform six trials over the course of a minimum of two menstrual cycles. Three trials were performed while wearing normal operational military clothing (i.e., combat clothing) and three trials were done while wearing the Canadian Forces NBC protective ensemble. For each clothing configuration, the scheduling of the trials during the menstrual cycle corresponded to early follicular (EF), days 2-5, late follicular (LF), days 9-12, and mid luteal (ML), days 19-22. The order of exposure, in terms of phase and clothing ensemble, was randomly assigned for all subjects to minimise the effects of training, acclimation, and habituation on the dependent measures. During each trial, subjects alternated between 15 min of walking on a level treadmill at 4 km·h⁻¹ (1.11 m·s⁻¹) and 15 min of seated rest, until one of the end-point criteria was met.
4.3.3 End-point Criteria

Each trial continued for a maximum exposure of 300 min in the climatic chamber or until:

(i) rectal temperature reached 39.3 °C;
(ii) heart rate ≥ 95% peak for 3 min;
(iii) dizziness or nausea precluded further exercise;
(iv) the subject asked to be removed from the chamber; or,
(v) based on the above criteria, the investigator or technician decided to end the trial.

4.3.4 Dressing and Weighing Procedures

All tests were performed at the same time of day (commencing at 8:00 a.m.) to minimise the influence of circadian rhythm on body temperature. Upon arrival at the lab, subjects changed into their shorts and T-shirt and inserted a rectal thermistor to a depth a 15 cm beyond the anal sphincter. Subjects were then requested to stand upright for a period of 10 min prior to the venipuncture. A 5-mL sample of blood was taken to allow the determination of hemoglobin, hematocrit, osmolality, estradiol and progesterone levels. Following this, subjects undressed (leaving the rectal thermistor in place) and their nude weight was recorded. Subjects put their undergarments, shorts and T-shirt back on and they were then fitted with the skin thermistors and heart rate monitor. Subjects donned one of the two clothing configurations and their dressed weight was recorded.

Upon entry into the climatic chamber, subjects were connected to the data acquisition system and they commenced walking on the treadmill. Gas exchange was measured for 3-4 min during the last portion of each 15 min walk/rest period. Heart rate was recorded every 5 min. Since it was easiest to drink during the rest periods, subjects were allowed during these times to
drink *ad libitum* to a total volume of 1 L during each trial. The subjects' dressed and nude weights were remeasured upon removal from the chamber.

4.3.5 Clothing Ensembles

The normal operational clothing configuration consisted of underwear, shorts, T-shirt, jog bra, socks, lightweight combat clothing and running shoes. The NBC protective clothing ensemble consisted of impermeable rubber gloves, overboots, and mask with a respirator, and a NBC overgarment, layered over the combat clothing configuration. The total thermal resistances of the combat clothing and NBC ensemble, determined using a heated copper manikin, were 0.169 m²°C·W⁻¹ (1.09 clo) and 0.291 m²°C·W⁻¹ (1.88 clo), respectively, and the Woodcock vapour permeability coefficients ($i_m$), determined with a completely wetted manikin, were 0.58 and 0.33, respectively (Gonzalez et al., 1993).

4.4 PHYSIOLOGICAL MEASUREMENTS
4.4.1 Rectal and mean skin temperatures

A computerised data acquisition system (Hewlett Packard 3497A data acquisition/control unit, 236-9000 computer, and 2934A printer) processed data from the $T_{re}$ and $T_{sk}$ temperature sensors at 1-min intervals. Rectal temperature, in °C, was measured using a flexible vinyl-covered probe (Pharmaseal 400 Series rectal/esophageal probe, Baxter Healthcare Corporation) inserted 15 cm beyond the anal sphincter. Skin temperatures, in °C, were measured at 12 sites, using epoxy-covered thermistors (thermistor bead 44004, Yellow Springs Instruments). The mean skin temperature, $T_{sk}$, was calculated by weighting factors reflecting regional proportions of the total body surface area, according to the equation of Hody (1973):
\[ T_{sk} = 0.07 \cdot \text{(forehead)} + 0.085 \cdot \text{(chest)} + 0.065 \cdot \text{(calf)} + 0.085 \cdot \text{(abdomen)} \]  
+ 0.14 \cdot \text{(lower arm)} + 0.05 \cdot \text{(wrist)} + 0.095 \cdot \text{(front thigh)} + 0.065 \cdot \text{(shin)} 
+ 0.07 \cdot \text{(foot)} + 0.09 \cdot \text{(upper back)} + 0.09 \cdot \text{(lower back)} + 0.095 \cdot \text{(rear thigh)} \]  

4.4.2 Heart Rate

A transmitter/telemetry unit (Polar PE3000/Polar Vantage XL) was used to monitor heart rate throughout the course of each trial. The transmitter was clipped to an elasticised electrode belt that was fitted around the chest. The receiver was taped to the outside of the clothing to provide a continuous display of HR. HR was recorded manually every 5 min.

4.4.3 Metabolic Rate and Gas Exchange

Open-circuit spirometry was used to determine oxygen consumption (\( \dot{V}O_2 \)) (in STPD) and carbon dioxide output (\( \dot{V}CO_2 \)) (in STPD) from a 2-min average during the latter portion of every 15 min walk or rest period. A low-resistance Hans-Rudolf respiratory valve (for combat clothing) or an adapter attached to the exhaust valve of the respirator (for protective clothing) directed expired gases into a 5-L mixing box and then through a ventilation module (Alpha Technologies VNN 110 Series) for the determination of minute ventilation (\( \dot{V}_E \)). An aliquot of dried expired gases was pumped via a sampling line to an \( O_2 \) and \( CO_2 \) analyser (Amtek Instruments S-3A and CD-3A, respectively). The gas analysers were calibrated using precision-analysed gas mixtures in cylinders and the ventilation meter was calibrated with a 3-L syringe. After analogue-to-digital conversion (Hewlett Packard 59313A A/D converter), \( \dot{V}_E \), \( \dot{V}O_2 \), \( \dot{V}CO_2 \) and respiratory gas exchange ratio (R) were calculated and printed on-line every 30 s (Vista with Turbofit Cart). The rate of metabolic heat production (\( W \cdot m^{-2} \)) was determined as (Nishi, 1981):

\[ \dot{M} = 352(0.23 \cdot R + 0.77) \cdot (\dot{V}O_2 \cdot A_d^{-1}) \]  

Eq. 6
where $R$ is the respiratory exchange ratio, $\dot{V}O_2$ is the measured rate of oxygen consumption in $L \cdot min^{-1}$, and $A_d$ is the Dubois surface area.

### 4.4.4 Sweat Production and Evaporation

Subjects were weighed, nude and dressed, before and immediately after the trials, using an electronic scale sensitive to the nearest 10 g (Model 921, Electroscale Corporation). Differences in nude and dressed weights before and after each trial were corrected for respiratory and metabolic weight loss. Respiratory water loss ($\dot{m}_w$ in g min$^{-1}$) was calculated from the measured $\dot{V}O_2$ (L min$^{-1}$) during the trial, $P_A$, and the respired mouth water vapour pressure ($P_{resp}$) in kPa as (Mitchell et al., 1972):

$$\dot{m}_w = 0.1425 \cdot \dot{V}O_2 (P_{resp} - P_A) \quad \text{Eq. 7}$$

A $P_{resp}$ of 5.32 kPa was chosen based on the work of Livingstone et al. (1994), which measured the respired mouth vapour pressure of subjects exercising under similar experimental and ambient conditions.

Weight losses due to CO$_2$-O$_2$ exchange ($\dot{m}_r$ in g min$^{-1}$) was estimated from $\dot{V}O_2$ (L min$^{-1}$) and the respiratory exchange ratio ($R$) using the equation of Snellen (1966):

$$\dot{m}_r = \dot{V}O_2 (1.9769 \cdot R - 1.42904) \quad \text{Eq. 8}$$

The rate of sweat production was calculated as the corrected difference between the pre-trial and post-trial nude weights, divided by tolerance time. Tolerance time was defined as the difference in time between removal from and entry into the climatic chamber. Evaporative sweat loss was calculated from the corrected differences in pre- and post-trial dressed weights. Evaporative efficiency was calculated as the amount of sweat evaporated (SE) divided by the amount of sweat produced (SP) or $(SE \cdot SP^{-1}) \cdot 100$. 


4.5 CALCULATION OF BODY HEAT CONTENT

The calculation of body heat gain was done using the method presented by McLellan et al. (1996). Body heat gain for each subject was calculated by subtracting the body heat content before the trial (HC_N) from the body heat content after the trial (HC_H) as follows:

\[
\text{HG} = \text{HC}_H - \text{HC}_N \tag{9}
\]

\[
\text{HC}_H = (0.90 \cdot T_{re(i)} + 0.10 \cdot T_{sk(i)}) \cdot m_{b(i)} \cdot 3.47 \tag{10}
\]

\[
\text{HC}_N = (0.79 \cdot T_{re(i)} + 0.21 \cdot T_{sk(i)}) \cdot m_{b(i)} \cdot 3.47 \tag{11}
\]

where \(0.90 \cdot T_{re(i)} + 0.10 \cdot T_{sk(i)}\) represents the mean body temperature at the end of the heat exposure, \(T_{re(i)}\), \(T_{sk(i)}\), and \(m_{b(i)}\) represent the final rectal temperature, mean skin temperature and body mass at the end of the trial, respectively, and 3.47 is the average specific heat of body tissues (in kJ·kg\(^{-1}\)·°C\(^{-1}\)). The mean body temperature at the beginning of the trial was estimated as \(0.79 \cdot T_{re(i)} + 0.21 \cdot T_{sk(i)}\), where \(T_{sk(i)}\), \(T_{re(i)}\), and \(m_{b(i)}\) represent the initial mean skin and rectal temperatures, and the initial body mass, respectively.

4.6 DETERMINATION OF MENSTRUAL CYCLE PHASE

Subjects reported day 1 of their cycle (i.e., the first day of menstrual flow) to the investigator. Testing sessions for that cycle were then scheduled to correspond to each of the desired phases (i.e., EF, days 2-5; LF, days 9-12; and ML, days 19-22). For the subjects taking oral contraceptives, day 1 of their cycle (i.e., the first day of flow) usually corresponded to the second or third day during the seven day period when no pill was ingested (all of our subjects were on a 21-day oral contraceptive). Testing sessions were scheduled to coincide with the same time frames as outlined for the non-users (i.e., days 2-5, days 9-12 and days 19-22 of the menstrual cycle). A 5-mL blood sample was drawn prior to each session to determine each subject's progesterone and
estrogen levels and to verify that the subject was being tested in the correct phase. Data was discarded and trials were repeated if progesterone levels were not elevated during the mid luteal phase for the non-users (indicating that ovulation had not occurred) or if progesterone levels were elevated during the mid luteal phase for the users (indicating that ovulation had occurred).

4.7 BLOOD ANALYSES

Hemoglobin was determined in duplicate by spectrophotometry, using Sigma Diagnostics Drabkins Solution, Catalog No. 525-2 and a Stasar III Spectrophotometer, Ser. 4033. Hematocrit was measured in triplicate, using an Autocrit Ultra 3 Centrifuge, Model 575. The remainder of the sample was centrifuged and an aliquot of plasma was removed and stored at -20°C for later analyses of osmolality, estradiol and progesterone. Estradiol and progesterone levels were determined in duplicate by radioimmunoassay (DSL-4800 Ultra-Sensitive Estradiol Radioimmunoassay Kit, and DSL-3900 ACTIVE Progesterone Coated-Tube Radioimmunoassay Kit, respectively, from Diagnostics Systems Laboratories, Inc.). To reduce the error due to interassay variability, all six of each subject's plasma samples were measured using the same radioimmunoassay kit. Osmolality was calculated using Nova Biomedical's Stat Profile Ultra, which calculates osmolality (mOsm·kg⁻¹) as a zero-order approximation consisting of only the most important contributors. The calculation used is as follows (Nova Biomedical Corp., 1996):

\[
\text{Osm} = 1.86\cdot [\text{Na}^+] + [\text{Glu}]\cdot 18^{-1} + [\text{BUN}]\cdot 2.8^{-1} + 9
\]

Eq. 12

Sodium units are mmol·L⁻¹, glucose units are mg·dL⁻¹, and blood urea nitrogen (BUN) units are mg·dL⁻¹.
4.8 STATISTICAL ANALYSES

Data are presented as mean (± SE). A three-factor repeated measures analysis of variance (ANOVA) [group x (menstrual cycle phase x time)] was used to compare the changes in rectal and mean skin temperature, heart rate and gas exchange responses during the trials for each clothing configuration within and between groups. A two-factor repeated measures ANOVA [group x (menstrual cycle phase)] was used to analyse differences in sweat rate, evaporative efficiency, body heat content, and tolerance time. To correct for the violation of the sphericity assumption, a Huynh-Feldt correction was applied when selecting a critical F-ratio. When a significant F-ratio was obtained, a Newman-Keuls post-hoc analysis was used to isolate differences among treatment means. For all statistical analyses, the 0.05 level of significance was used. All ANOVAs were performed using statistical software (Super ANOVA v 1.11 (1991), Abacus Concepts Inc.).
Chapter 5

RESULTS

5.1 SUBJECTS

Subject characteristics for the two groups are described in Table 2. There were no significant differences in anthropometric or physiological variables between the two groups.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-Users</th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>23.3 (1.9)</td>
<td>23.4 (0.7)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65 (0.03)</td>
<td>1.66 (0.03)</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>60.4 (3.0)</td>
<td>64.5 (1.8)</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>19.2 (1.4)</td>
<td>22.3 (1.6)</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.66 (0.05)</td>
<td>1.71 (0.04)</td>
</tr>
<tr>
<td>BSA:Mass (m²·kg⁻¹)</td>
<td>0.03 (0.00)</td>
<td>0.03 (0.00)</td>
</tr>
<tr>
<td>VO₂peak (mL·kg⁻¹·min⁻¹)</td>
<td>44.78 (2.55)</td>
<td>43.63 (2.70)</td>
</tr>
<tr>
<td>HRₚₑᵃᵏ (b·min⁻¹)</td>
<td>191.8 (2.6)</td>
<td>194.9 (2.6)</td>
</tr>
</tbody>
</table>

Table 2: Mean values (± SE) for age, height, weight, % body fat, body surface area (BSA), VO₂peak, and HRₚₑᵃᵏ for users (n=9) and non-users (n=9) of oral contraceptives.

Due to a combination of subjects' personal time constraints, the scheduling of menstrual cycle phase, and experimental time constraints, one of the non-users and two of the users were unable to complete all three of the trials while wearing the combat clothing configuration. As a result, the data for these three subjects were not included in the analyses of the compensable heat strain trials. Also, the data for a second non-user were excluded from the statistical analyses of the compensable heat strain trials because hormonal verification revealed that progesterone levels were not elevated during the mid luteal phase while wearing the combat clothing configuration.
5.2 BLOOD ANALYSES

5.2.1 Progesterone

The mean plasma progesterone levels are presented in Table 3 for both groups. Hormonal verification of menstrual cycle phase demonstrated that ovulation was inhibited in all of the subjects using oral contraceptives. In both clothing configurations mean plasma progesterone was less than 1 ng·mL⁻¹ during the mid luteal phase. The progesterone levels observed in this phase were similar to those measured during the early follicular and late follicular phases for both groups. Among the non-users, mean progesterone levels were significantly elevated during the ML phase. Progesterone levels were approximately 7 ng·mL⁻¹, indicating that ovulation had occurred. Hormonal analyses revealed that progesterone levels were not elevated in two of the non-users during one of their ML trials. The data from these two runs were discarded and the trials were repeated in a subsequent cycle.

Table 3: Plasma progesterone (ng·mL⁻¹) for users and non-users of oral contraceptives during compensable and uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE) for n=7 users and n=9 non-users during uncompensable and n=5 users and n=7 non-users during compensable heat strain.

<table>
<thead>
<tr>
<th></th>
<th>Compensable Heat Strain</th>
<th>Uncompensable Heat Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td>Non-Users</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.62</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>(0.12)</td>
<td>(0.04)</td>
</tr>
<tr>
<td>Users</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.75</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>(0.11)</td>
<td>(0.07)</td>
</tr>
</tbody>
</table>

† Significantly different from other phases.

Daily basal body temperature was monitored in both of these subjects during the subsequent cycle to enable a better estimation of cycle phase. While this method proved successful in one of the subjects (progesterone analysis confirmed that the subject was hormonally in the mid luteal phase), the same cannot be said for the second subject. Although the second subject
experienced a rise in basal body temperature during what should have been the mid luteal phase, hormonal analysis revealed progesterone levels were once again quite low. Due to study time limitations, the data from this subject was excluded from the statistical analyses of the compensable heat strain trials.

5.2.2 Estradiol

The mean estradiol levels during the EF, LF and ML phases for both groups are described in Table 4. Plasma estradiol levels declined throughout the 21 day pill cycle among the OC users. The decrease in estradiol was significant between EF and ML during the compensable heat strain trials. Estradiol level began to rise in the pill-free week and the concentration of plasma estradiol during the EF phase of the OC users was similar to those values measured during the EF phase among the OC non-users. Mean plasma estradiol levels differed significantly among all three phases for the non-users during the NBC clothing trials. Estradiol was lowest during the EF phase and highest during the ML phase. Estradiol levels followed a similar trend during the combat clothing trials, although only the difference between the EF and ML phases achieved statistical significance.

Table 4: Plasma estradiol (pg·mL⁻¹) for users and non-users during compensable and uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE) for n=7 users and n=9 non-users during uncompensable and n=5 users and n=7 non-users during compensable heat strain.

<table>
<thead>
<tr>
<th></th>
<th>Compensable Heat Strain</th>
<th>Uncompensable Heat Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td>Non-Users</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19.7*</td>
<td>37.8</td>
</tr>
<tr>
<td></td>
<td>(3.2)</td>
<td>(9.3)</td>
</tr>
<tr>
<td>Users</td>
<td>17.4*</td>
<td>12.0</td>
</tr>
<tr>
<td></td>
<td>(2.4)</td>
<td>(3.4)</td>
</tr>
</tbody>
</table>

* Significantly different from ML.
‡ Significantly different from other phases.
5.2.3 Relative Ratio of Estradiol to Progesterone

The relative ratios of estradiol (pg·mL⁻¹) to progesterone (ng·mL⁻¹) during the EF, LF and ML phases during compensable and uncompensable heat strain are described in Table 5 for both groups. For the non-users, the relative ratio of estradiol to progesterone was significantly greater during the LF phase compared with both the EF and ML phases in both clothing configurations. During uncompensable heat strain the ratio of estradiol to progesterone was significantly higher during EF compared with ML for the women in this group. Likewise, the ratio of estradiol to progesterone was greater during EF compared with ML for the non-users during compensable heat strain; however, the difference among the two phases was not statistically significant. For the users, there were no significant differences in the ratios of estradiol to progesterone among phases in either clothing configuration. However, the ratio of estradiol to progesterone during the LF phase for the users was significantly different from that of the non-users during the same phase. There were no other phase-related differences in the ratios of estradiol to progesterone between the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Compensable Heat Strain</th>
<th>Uncompensable Heat Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td>Non-Users</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>34.6</td>
<td>88.6</td>
</tr>
<tr>
<td></td>
<td>(4.3)</td>
<td>(18.2)</td>
</tr>
<tr>
<td>Users</td>
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</tr>
<tr>
<td></td>
<td>24.6</td>
<td>18.7</td>
</tr>
<tr>
<td></td>
<td>(4.1)</td>
<td>(4.3)</td>
</tr>
</tbody>
</table>

\* Significantly different from other phases.
\*d Significantly different from LF phase for the users.
5.2.4 Hemoglobin, hematocrit and osmolality

There were no significant differences in hemoglobin, hematocrit or osmolality between the groups, among phases or between the two clothing configurations. The measured values are presented in Table 6 for the combat clothing trials and in Table 7 for the NBC clothing trials.

Table 6: Hemoglobin, hematocrit, and osmolality for users (n=5) and non-users (n=7) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE).

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th></th>
<th></th>
<th></th>
<th>Users</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g·dL⁻¹)</td>
<td>14.8</td>
<td>14.0</td>
<td>14.2</td>
<td>14.6</td>
<td>14.2</td>
<td>14.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.4)</td>
<td>(0.9)</td>
<td>(0.2)</td>
<td>(0.2)</td>
<td>(0.4)</td>
<td>(0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit (%BV)</td>
<td>41.0</td>
<td>39.2</td>
<td>40.4</td>
<td>41.6</td>
<td>41.3</td>
<td>39.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.0)</td>
<td>(2.0)</td>
<td>(0.4)</td>
<td>(0.6)</td>
<td>(1.4)</td>
<td>(1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmolality (mOsm·kg⁻¹)</td>
<td>265.4</td>
<td>265.1</td>
<td>263.6</td>
<td>260.1</td>
<td>257.1</td>
<td>263.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.8)</td>
<td>(2.2)</td>
<td>(1.3)</td>
<td>(3.7)</td>
<td>(4.8)</td>
<td>(1.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 7: Hemoglobin, hematocrit and osmolality values for users (n=7) and non-users (n=9) of oral contraceptives during uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE).

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th></th>
<th></th>
<th></th>
<th>Users</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g·dL⁻¹)</td>
<td>14.7</td>
<td>14.7</td>
<td>15.0</td>
<td>14.6</td>
<td>14.0</td>
<td>14.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.5)</td>
<td>(0.2)</td>
<td>(0.5)</td>
<td>(0.4)</td>
<td>(0.5)</td>
<td>(0.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit (%BV)</td>
<td>39.4</td>
<td>41.6</td>
<td>41.4</td>
<td>40.8</td>
<td>40.5</td>
<td>40.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.9)</td>
<td>(0.5)</td>
<td>(0.9)</td>
<td>(0.9)</td>
<td>(1.3)</td>
<td>(1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmolality (mOsm·kg⁻¹)</td>
<td>264.9</td>
<td>263.4</td>
<td>264.4</td>
<td>262.8</td>
<td>256.8</td>
<td>264.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2.2)</td>
<td>(0.9)</td>
<td>(1.7)</td>
<td>(3.2)</td>
<td>(4.3)</td>
<td>(1.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5.3 INDICES OF HEAT STRAIN

5.3.1 Metabolic Rate and Gas Exchange

There were no phase-related or group-related differences in the rate of metabolic heat production, oxygen consumption or minute ventilation during either the combat clothing trials or the NBC clothing trials. The values for $\dot{M}$, $\dot{V}O_2$, and $\dot{V}e$ are presented in Table 8 for the compensable heat strain trials and in Table 9 for the uncompensable heat strain trials. $\dot{V}O_2$ was approximately 0.68 L·min^{-1} (11 mL·kg^{-1}·min^{-1}) and 0.86 L·min^{-1} (13 - 14 mL·kg^{-1}·min^{-1}) during the walking portion of the compensable and uncompensable heat trials, respectively. These values correspond to a relative exercise intensity of 25% and 30% $\dot{V}O_{2\text{peak}}$, accordingly. During the sitting portion of both the compensable and uncompensable heat trials, $\dot{V}O_2$ was approximately 0.25 L·min^{-1} (3 - 4 mL·kg^{-1}·min^{-1}) or 7 - 9% $\dot{V}O_{2\text{peak}}$.

Table 8: Gas exchange data for users (n=7 to 215 min; n=6 to 300 min) and non-users (n=7 to 240 min; n=5 to 300 min) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values for $\dot{V}O_2$ and $\dot{V}e$ are mean (± SE) for seven 15-min walking or sitting periods. Values for $\dot{M}$ are mean (± SE) averaged over the entire exposure.

<table>
<thead>
<tr>
<th></th>
<th>EF</th>
<th>LF</th>
<th>ML</th>
<th>EF</th>
<th>LF</th>
<th>ML</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\dot{V}e$ - walking (L·min^{-1})</td>
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<td>16.48</td>
<td>17.29</td>
<td>16.13</td>
<td>15.83</td>
<td>15.84</td>
</tr>
<tr>
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<td>(0.72)</td>
<td>(0.42)</td>
<td>(0.47)</td>
<td>(0.34)</td>
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<tr>
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<td>7.51</td>
<td>6.54</td>
<td>7.02</td>
<td>6.93</td>
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<tr>
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<td>(0.39)</td>
<td>(0.16)</td>
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<tr>
<td>$\dot{V}O_2$ - walking (L·min^{-1})</td>
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<td>0.69</td>
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<td>0.69</td>
<td>0.67</td>
<td>0.68</td>
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<tr>
<td></td>
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<td>(0.05)</td>
<td>(0.04)</td>
<td>(0.02)</td>
<td>(0.02)</td>
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<td>0.23</td>
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<td>0.24</td>
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<td>(0.01)</td>
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<td>(0.02)</td>
<td>(0.01)</td>
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<tr>
<td>$\dot{M}$ (L·min^{-1})</td>
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<td>0.45</td>
<td>0.46</td>
<td>0.46</td>
<td>0.45</td>
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<tr>
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<td>(0.01)</td>
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<tr>
<td>$\dot{M}$ (W·m^{-2})</td>
<td>93.63</td>
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<td>94.46</td>
<td>90.97</td>
<td>91.13</td>
<td>90.62</td>
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<tr>
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<td>(2.53)</td>
<td>(2.83)</td>
<td>(2.80)</td>
<td>(2.52)</td>
<td>(2.54)</td>
<td>(2.47)</td>
</tr>
</tbody>
</table>
Table 9: Gas exchange data for users (n=9 to 75 min; n=8 to 90 min) and non-users (n=9 to 85 min; n=7 to 90 min) of oral contraceptives during uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values for $\dot{V}O_2$ and $\dot{V}e$ are mean (± SE) for three 15-min walking or sitting periods. Values for $\dot{M}$ are mean (± SE) averaged over the entire exposure.

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</thead>
<tbody>
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<td>ML</td>
<td>EF</td>
</tr>
<tr>
<td>$\dot{V}e$ - walking (L·min$^{-1}$)</td>
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<td>(1.04)</td>
<td>(0.54)</td>
</tr>
<tr>
<td>$\dot{V}e$ - sitting (L·min$^{-1}$)</td>
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<td>7.36</td>
<td>7.98</td>
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<td>(0.77)</td>
<td>(0.45)</td>
</tr>
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</tr>
<tr>
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<td>(0.04)</td>
<td>(0.02)</td>
<td>(0.02)</td>
</tr>
<tr>
<td>$\dot{VO}_2$ - sitting (L·min$^{-1}$)</td>
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<td>0.24</td>
<td>0.27</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>(0.02)</td>
<td>(0.02)</td>
<td>(0.03)</td>
<td>(0.01)</td>
</tr>
<tr>
<td>$\dot{M}$ (L·min$^{-1}$)</td>
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<td>0.55</td>
<td>0.55</td>
<td>0.55</td>
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<tr>
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<td>(0.03)</td>
<td>(0.02)</td>
<td>(0.02)</td>
</tr>
<tr>
<td>$\dot{M}$ (W·m$^{-2}$)</td>
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<td>115.21</td>
<td>116.40</td>
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<tr>
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<td>(3.10)</td>
<td>(2.94)</td>
<td>(2.48)</td>
<td>(3.41)</td>
</tr>
</tbody>
</table>

5.3.2 Heart Rate

a) Compensable Heat Strain (Combat Clothing)

Figure 2 presents the heart rate response during the compensable heat strain trials for both groups. For the users, during the first 215 min of compensable heat exposure (n=7) heart rate tended to be higher during EF compared with LF and ML (p<0.06). Following 240 min of heat exposure (n=6), this difference achieved significance. The difference in heart rate was apparent during either the walking or the resting phases of the intermittent protocol. There were no phase-related differences in mean heart rate in the non-user group (Table 10).
Figure 2: Heart rate response for users (n=7 to 215 min, n=6 to 300 min) and non-users (n=7 to 240 min, n=5 to 300 min) of oral contraceptives performing light intermittent exercise during compensable heat strain for the early follicular (O), late follicular (▲) and mid luteal (□) phases of the menstrual cycle. Values are mean (±SE).
Table 10: Heart rate response for users (n=7 to 215 min; n=6 to 300 min) and non-users (n=7 to 240 min; n=5 to 300 min) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF), and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE) for seven 15-min walking or sitting periods, as well as the overall mean (±SE) value for the entire exposure (240 min).

<table>
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</tr>
</thead>
<tbody>
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<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td>HR - walking (b·min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>104.5</td>
<td>104.0</td>
</tr>
<tr>
<td></td>
<td>(4.9)</td>
<td>(2.5)</td>
</tr>
<tr>
<td>HR - sitting (b·min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>79.9</td>
<td>82.9</td>
</tr>
<tr>
<td></td>
<td>(4.2)</td>
<td>(2.6)</td>
</tr>
<tr>
<td>Mean HR (b·min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>92.5</td>
<td>93.7</td>
</tr>
<tr>
<td></td>
<td>(4.4)</td>
<td>(2.3)</td>
</tr>
</tbody>
</table>

† Significantly different from other phases.

b) Uncompensable Heat Strain (NBC Clothing)

Figure 3 illustrates the heart rate response for both groups during the uncompensable heat strain trials. There were no phase-related or group-related differences in heart rate response during the NBC clothing trials (Table 11).

Table 11: Heart rate response for users (n=9) and non-users (n=9) of oral contraceptives during uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE) for three 15-min walking or sitting periods, as well as the overall mean (±SE) value for the entire exposure (90 min).

<table>
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<tr>
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</tr>
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<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td>HR - walking (b·min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>123.2</td>
<td>126.2</td>
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<tr>
<td></td>
<td>(3.7)</td>
<td>(5.2)</td>
</tr>
<tr>
<td>HR - sitting (b·min⁻¹)</td>
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<tr>
<td></td>
<td>95.3</td>
<td>97.8</td>
</tr>
<tr>
<td></td>
<td>(2.8)</td>
<td>(4.4)</td>
</tr>
<tr>
<td>Mean HR (b·min⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>108.0</td>
<td>110.4</td>
</tr>
<tr>
<td></td>
<td>(3.0)</td>
<td>(4.6)</td>
</tr>
</tbody>
</table>
Figure 3: Heart rate for users (n=9 to 75 min, n=8 to 90 min) and non-users (n=9 to 85 min, n=7 to 90 min) of oral contraceptives performing light intermittent exercise during uncompensable heat stress for the early follicular (O), late follicular (▲) and mid luteal (■) phases of the menstrual cycle. Values are mean (± SE).
5.3.3 Rectal Temperature

a) Compensable Heat Strain (Combat Clothing)

Initial $T_{re}$ was higher in the mid luteal phase compared with the early follicular and late follicular phases among the non-users, although this difference was not statistically significant (Table 12, p<0.08). Mean rectal temperatures during the compensable heat strain trials are illustrated in Figure 4 for both groups. The elevation in $T_{re}$ during the ML phase was apparent throughout the duration of the compensable heat exposures; however, again this difference did not achieve statistical significance (p<0.08).

Initial and final $T_{re}$ were similar in all three phases within the group using oral contraceptives (Table 12). Likewise, $T_{re}$ was similar throughout the three compensable heat trials within this group (Figure 4). Delta $T_{re}$ ($\Delta T_{re}$), which represents the difference between final $T_{re}$ and initial $T_{re}$, did not differ among phases or between groups (Table 12). Compensable heat stress resulted in an increase in core temperature of less than 0.6°C in the non-users and less than 0.5°C in the users.

| Table 12: Initial, final, and delta $T_{re}$ for users (n=7) and non-users (n=7) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE). |
|---------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|
|                                 | Non-Users        | Users            |
|                                 | EF               | LF               | ML               | EF               | LF               | ML               |
| **Initial $T_{re}$ (°C)**       | 37.11 ± 0.10     | 37.11 ± 0.10     | 37.30 ± 0.08     | 37.23 ± 0.08     | 37.24 ± 0.06     | 37.27 ± 0.06     |
| **Final $T_{re}$ (°C)**         | 37.74 ± 0.08     | 37.67 ± 0.06     | 37.83 ± 0.14     | 37.70 ± 0.12     | 37.66 ± 0.07     | 37.71 ± 0.05     |
| **Delta $T_{re}$ (°C)**         | 0.60 ± 0.09      | 0.56 ± 0.11      | 0.53 ± 0.12      | 0.47 ± 0.08      | 0.41 ± 0.03      | 0.44 ± 0.05      |
Figure 4: Rectal temperature for users (n=7 to 215 min, n=6 to 300 min) and non-users (n=7 to 240 min, n=5 to 300 min) of oral contraceptives performing light intermittent exercise during compensable heat strain for the early follicular (O), late follicular (▲) and mid luteal (□) phases of the menstrual cycle. Values are mean (± SE).
b) Uncompensable Heat Strain (NBC Clothing)

The values for initial $T_{re}$, final $T_{re}$, $\Delta T_{re}$, and the time for a $1.0^\circ C$ increase in $T_{re}$ for both the users and non-users of oral contraceptives during uncompensable heat strain are presented in Table 13. For the users, initial $T_{re}$ was significantly higher during ML (37.36°C) compared with EF (37.14°C), but not LF (37.24°C). However, there was no significant effect of phase during the uncompensable heat exposures for the women in this group, and final $T_{re}$ did not differ among phases. The overall increase in $T_{re}$ ($\Delta T_{re}$) for the users was greatest in EF (1.52°C), although this value was not statistically different from LF (1.39°C) and ML (1.34°C). Subjects using oral contraceptives appeared to store heat more slowly during ML compared with EF, as the time for a $1.0^\circ C$ increase in $T_{re}$ was longer during the ML phase, although once again this difference was not statistically significant.

| Table 13: Initial, final, and delta $T_{re}$, and the time required for a $1.0^\circ C$ increase in $T_{re}$ for users (n=9) and non-users (n=4) of oral contraceptives during uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE). |
|-----------------|------------------|------------------|-----------------|------------------|------------------|------------------|
|                 | Non-Users        |                 |                 | Users            |                 |                 |
|                 | EF               | LF              | ML              | EF               | LF              | ML              |
| Initial $T_{re}$ (°C) | 37.09 (0.08) | 37.16 (0.07) | 37.31 (0.11) b | 37.14 (0.08) a * | 37.24 (0.08) | 37.36 (0.06) b |
| Final $T_{re}$ (°C)   | 38.86 (0.14) | 38.81 (0.13) | 38.80 (0.14) | 38.67 (0.13) | 38.63 (0.11) | 38.74 (0.10)   |
| $\Delta T_{re}$ (°C)  | 1.77 (0.16) a  | 1.66 (0.13)    | 1.48 (0.11)    | 1.52 (0.14) a   | 1.39 (0.12)    | 1.34 (0.11)    |
| Time (min) for 1.0°C  | 72.2 (4.0)     | 72.4 (5.0)     | 73.9 (4.8)     | 79.7 (4.0)      | 82.6 (4.4)     | 86.0 (4.5)     |

a For groups combined, significantly different from ML.
b For groups combined, significantly different from other phases.
* Significantly different from ML.
Figure 5: Rectal temperature for users (n=9 to 75 min, n=8 to 90 min) and non-users (n=9 to 85 min, n=7 to 90 min) of oral contraceptives performing light intermittent exercise during uncompensable heat strain for the early follicular (O), late follicular (▲) and mid luteal (□) phases of the menstrual cycle. Values are mean (± SE).
For the non-users, initial $T_{re}$ was greatest during ML (37.31°C) compared with EF (37.09°C) and LF (37.16°C) for the non-users, although the difference among phases was not statistically significant ($p<0.08$) in this group. During the uncompensable heat exposures, $T_{re}$ was significantly higher in ML compared with EF (Figure 5). However, following 90 minutes of exercise in the heat when the number of subjects included in the data analyses decreased from 9 to 7, the phase-related difference in $T_{re}$ was no longer apparent. Final $T_{re}$ was similar among all three phases for this group (Table 13). Delta $T_{re}$ ($\Delta T_{re}$) was significantly greater during the EF phase compared with the ML phase. The time for a 1.0°C increase in $T_{re}$ was not significantly different for any of the phases.

Analyses of $T_{re}$ for the groups combined demonstrated that rectal temperature did not differ between the two groups during the NBC clothing trials. Initial $T_{re}$ was higher in ML (37.33°C) compared with EF (37.12°C) for the two groups combined. $\Delta T_{re}$ for the groups combined was greater during the EF phase (1.64°C) compared with the ML phase (1.41°C). Final $T_{re}$ and the time for a 1.0°C increase in $T_{re}$ for the two groups combined did not differ.

5.3.4 Mean Skin Temperature

a) Compensable Heat Strain (Combat Clothing)

Initial and final $T_{sk}$ during the combat clothing trials are presented in Table 14. During the trials, $T_{sk}$ did not differ among phases for either group or between the two groups. Figure 6 represents the change in $T_{sk}$ for both groups during the compensable heat strain trials.
Table 14: Initial and final $\bar{T}_{sk}$ for users (n=7) and non-users (n=7) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE).

<table>
<thead>
<tr>
<th></th>
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<th>Users</th>
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<th></th>
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<td>LF</td>
<td>ML</td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
</tr>
<tr>
<td>Initial $\bar{T}_{sk}$ (°C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td>Final $\bar{T}_{sk}$ (°C)</td>
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<tr>
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</table>

b) Uncompensable Heat Strain (NBC Clothing)

Although initial $\bar{T}_{sk}$ was significantly higher during ML compared with both LF and EF (Table 15), there was no effect of phase on $\bar{T}_{sk}$ during the uncompensable heat exposures for the women not using oral contraceptives. Likewise, $\bar{T}_{sk}$ did not differ among phases for the women using oral contraceptives or between the two groups during the uncompensable heat exposures (Figure 7).

Table 15: Initial and final $\bar{T}_{sk}$ for users (n=9) and non-users (n=9) of oral contraceptives performing light intermittent exercise during uncompensable heat strain. Values are mean (± SE).

<table>
<thead>
<tr>
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</thead>
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<td>ML</td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
</tr>
<tr>
<td>Initial $\bar{T}_{sk}$ (°C)</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
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<td>32.91</td>
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<tr>
<td>Final $\bar{T}_{sk}$ (°C)</td>
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</tr>
<tr>
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<td>37.63</td>
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<td>(0.20)</td>
<td>(0.17)</td>
<td>(0.14)</td>
<td>(0.13)</td>
<td>(0.07)</td>
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</tbody>
</table>

‡ Significantly different from other phases.
Figure 6: Mean skin temperature for users (n=7 to 215 min, n=6 to 300 min) and non-users (n=7 to 240 min, n=5 to 300 min) of oral contraceptives performing light intermittent exercise during compensable heat strain for the early follicular (O), late follicular (△) and mid luteal (□) phases of the menstrual cycle. Values are mean (± SE).
Figure 7: Mean skin temperature for users (n=9 to 75 min, n=8 to 90 min) and non-users (n=9 to 85 min, n=7 to 90 min) of oral contraceptives performing light intermittent exercise during uncompensable heat strain for the early follicular (○), late follicular (▲) and mid luteal (□) phases of the menstrual cycle. Values are mean (± SE).

Non-Users

Users

† ML greater than EF and LF at t=0.
5.3.5 Body Heat Content

The gain in body heat content did not differ among phases or between groups during compensable heat strain (Table 16). During uncompensable heat strain, the gain in body heat content was significantly greater in EF than ML for the non-users and for the two groups combined. There were no phase-related differences in the gain in body heat content during the uncompensable heat strain trials for the users.

Table 16: Gain in body heat content (kJ) during compensable (users n=7 and non-users n=7) and uncompensable (users n=9 and non-users n=9) heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE).

<table>
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<td>LF</td>
<td>ML</td>
<td>EF</td>
</tr>
<tr>
<td>Compensable Heat Strain</td>
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<td>192.11</td>
<td>174.60</td>
<td>174.34</td>
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<td>(28.46)</td>
<td>(16.50)</td>
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<td>(34.75)</td>
<td>(33.58)</td>
<td>(17.54)</td>
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</tbody>
</table>

* Significantly different from ML.

5.3.6 Sweat Loss/Evaporation

a) Compensable Heat Strain (Combat Clothing)

The values for the rate of sweat loss, the rate of sweat evaporation and evaporative efficiency for users and non-users of oral contraceptives while performing light intermittent exercise during compensable heat strain are presented in Table 17. There were no phase-related or group-related differences in these variables.
Table 17: The rate of sweat loss, the rate of sweat evaporation, and evaporative efficiency for users (n=7) and non-users (n=7) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE).

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td><strong>Sweat Rate (kg·m⁻²·h⁻¹)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.179</td>
<td>0.181</td>
</tr>
<tr>
<td></td>
<td>(0.006)</td>
<td>(0.008)</td>
</tr>
<tr>
<td><strong>Evaporation Rate (kg·m⁻²·h⁻¹)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.166</td>
<td>0.168</td>
</tr>
<tr>
<td></td>
<td>(0.003)</td>
<td>(0.005)</td>
</tr>
<tr>
<td><strong>Evaporative Efficiency (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>92.9</td>
<td>93.4</td>
</tr>
<tr>
<td></td>
<td>(1.6)</td>
<td>(1.6)</td>
</tr>
</tbody>
</table>

b) Uncompensable Heat Strain (NBC Clothing)

For the groups combined, sweat rate during ML was higher than LF (Table 18). There were no other differences in sweat rate among phases or between groups. Evaporation rate and evaporation efficiency did not differ among phases or between groups during the uncompensable heat strain trials.

Table 18: The rate of sweat loss, the rate of sweat evaporation, and evaporative efficiency for users (n=9) and non-users (n=9) of oral contraceptives during uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values are mean (± SE).

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th>Users</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
</tr>
<tr>
<td><strong>Sweat Rate (kg·m⁻²·h⁻¹)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.335</td>
<td>0.338</td>
</tr>
<tr>
<td></td>
<td>(0.042)</td>
<td>(0.038)</td>
</tr>
<tr>
<td><strong>Evaporation Rate (kg·m⁻²·h⁻¹)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.134</td>
<td>0.123</td>
</tr>
<tr>
<td></td>
<td>(0.009)</td>
<td>(0.007)</td>
</tr>
<tr>
<td><strong>Evaporative Efficiency (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>43.2</td>
<td>39.0</td>
</tr>
<tr>
<td></td>
<td>(3.6)</td>
<td>(3.6)</td>
</tr>
</tbody>
</table>

C For the groups combined, significantly different from ML.
5.3.7 Tolerance Time

a) Compensable Heat Strain (Combat Clothing)

Mean tolerance time was not affected by menstrual cycle phase or by use or non-use of oral contraceptives during the compensable heat strain trials. The mean tolerance times for both groups while wearing the combat clothing configuration are presented in Table 19. Five of the seven non-users and six of the seven users completed the 300 min of light intermittent exercise during all three phases. Of the three subjects who did not complete the full 300 min exposure, one left after 270 min during the EF phase due to hunger, another left after 239 min during the ML phase as a result of dizziness, and the third left after 240 min and 217 min during the EF and LF phases, respectively, due to dizziness and nausea.

Table 19: Tolerance time and reasons for test termination for users (n=7) and non-users (n=7) of oral contraceptives during compensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values for tolerance time are mean (±SE), with range of observations in square parentheses. Reasons for test termination are presented as number of subjects for $T_{re}$, rectal temperature (39.3°C); HR, heart rate ($\geq$ 95% $HR_{peak}$ for 3 min); SV, subject's volition; TL, time limit (300 min).

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th></th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
</tr>
<tr>
<td>Tolerance Time (min)</td>
<td>295.6 (4.4)</td>
<td>300.0 (0.0)</td>
<td>291.3 (8.7)</td>
</tr>
<tr>
<td>[range]</td>
<td>[269-300]</td>
<td>[300]</td>
<td>[239-300]</td>
</tr>
<tr>
<td>Reason</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_{re}$</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HR</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SV</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>TL</td>
<td>6</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>
Mean tolerance times while wearing the NBC clothing configuration and reasons for trial termination are shown in Table 20. Among the non-users, mean tolerance time was significantly longer during EF (128.1 ± 13.4 min) compared with ML (107.4 ± 8.6 min). For the users, mean tolerance times were similar among all three phases. Mean tolerance time was not significantly different between the groups during any phase of the menstrual cycle. None of the subjects completed the 300 min of light intermittent exercise while wearing the NBC protective ensemble.

Table 20: Tolerance time and reasons for test termination for users (n=9) and non-users (n=9) of oral contraceptives during uncompensable heat strain for the early follicular (EF), late follicular (LF) and mid luteal (ML) phases of the menstrual cycle. Values for tolerance time are mean (± SE), with range of observations in square parentheses. Reasons for test termination are presented as number of subjects for $T_{re}$, rectal temperature (39.3°C); HR, heart rate (≥ 95% $HR_{peak}$ for 3 min); SV, subject's volition; TL, time limit (300 min).

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th></th>
<th>Users</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF</td>
<td>LF</td>
<td>ML</td>
<td>EF</td>
</tr>
<tr>
<td>Tolerance Time (min)</td>
<td>128.1* (13.4)</td>
<td>114.2 (8.7)</td>
<td>107.4 (8.6)</td>
<td>113.0 (5.8)</td>
</tr>
<tr>
<td>[range]</td>
<td>[90-225]</td>
<td>[91-158]</td>
<td>[85-169]</td>
<td>[90-135]</td>
</tr>
<tr>
<td>Reason</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>$T_{re}$</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>HR</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>SV</td>
<td>6</td>
<td>7</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>TL</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Significantly different from ML.
Chapter 6

DISCUSSION

6.1 MAIN FINDINGS

This study quantified and documented the heat strain and the physical work tolerance times associated with light exercise in the heat while wearing combat clothing and NBC protective clothing in healthy young women. The two clothing configurations were chosen because they represent different types of physiological heat strain. The combat clothing configuration represents an environment of compensable heat strain, since in this clothing configuration subjects are able to effectively exchange heat with the environment and achieve a thermal steady-state. The NBC clothing configuration represents an environment of uncompensable heat stress. The permeability and insulation characteristics of the NBC clothing ensemble restrict both non-evaporative and evaporative heat exchange between the body and the environment and, as a result, subjects are unable to achieve thermal balance, continuing to store heat until exhaustion occurs. The work intensity and the ambient environment chosen in the present investigation were similar to the conditions used by McLellan et al. (1992 and 1994) to evaluate the heat strain and physical work tolerance times of healthy, young men under equivalent conditions of compensable and uncompensable heat strain.

Two groups of women were chosen who differed with respect to oral contraceptive use or non-use. The thermoregulatory responses of these women were compared during three different phases of the menstrual cycle. The three phases studied were the early follicular (days 2-5), the late follicular (days 9-12), and the mid luteal (days 19-22) phases. It was hypothesised that women not using oral contraceptives would experience greater heat strain during the mid luteal phase of their menstrual cycle compared with the early
follicular and late follicular phases during uncompensable heat strain. The second hypothesis stated that since oral contraceptives negate the surge in progesterone associated with the luteal phase, women who are using oral contraceptives would be at a thermoregulatory advantage during this phase of their menstrual cycle compared with women not using this method of birth control.

Several observations were made. The first was that menstrual cycle phase and oral contraceptive use did not affect temperature regulation during compensable heat strain. Work tolerance times and the physiological indices of heat strain were similar between the two groups in all three phases. A second observation was that women not using oral contraceptives experienced greater heat strain during the mid luteal phase of their menstrual cycle while wearing the NBC protective ensemble. Work tolerance time was significantly lower during the mid luteal phase compared with the early follicular phase among the women in this group and core temperature was elevated throughout the trial. A third observation was that oral contraceptive use did not influence temperature regulation during uncompensable heat strain. The physiological responses and work tolerance times of the women in this group were similar in all three phases and did not differ from the thermoregulatory responses of the non-users in any of the phases. Our results demonstrate that oral contraceptive use appears to make the thermoregulatory responses to uncompensable heat stress more uniform over the course of the menstrual cycle.

6.2 ANALYSIS OF PROGESTERONE AND ESTRADIOL LEVELS

In order to gain an understanding of how the menstrual cycle and oral contraceptive use impact thermoregulation, endogenous levels of estradiol and progesterone were measured in both groups during the three different phases studied. Hormonal verification of cycle phase demonstrated that ovulation was inhibited in all of the women using oral contraceptives.
Progesterone levels were low throughout the 21 day pill cycle. In both clothing configurations mean plasma progesterone was less than 1 ng·mL⁻¹ during the mid luteal phase, signifying that the rise in progesterone normally associated with this phase did not occur. Mean progesterone levels observed in all three phases within this group were similar to those measured during the early follicular phase in the non-users (Table 3). Likewise, mean estradiol levels were low throughout the 21 day pill cycle in the women using oral contraceptives. The concentration of plasma estradiol measured during the EF phase for the users was similar to those values measured during the EF phase for the non-users (Table 4). Estradiol levels declined between the EF and ML phases and then began to rise during the 7 day period when no pill was ingested. These results indicate that ovarian steroidogenesis was suppressed in the women using oral contraceptives. The endogenous levels of estradiol and progesterone were similar to those observed during the early follicular phase among women with normal menstrual cycles. Several other investigators have observed similar changes in the levels of endogenous estradiol and progesterone with oral contraceptive use (Fitzgerald et al., 1994; Jung-Hoffmann et al., 1988; Mishell et al., 1977).

The trends in the plasma concentrations of estradiol and progesterone measured during the EF, LF and ML phases within the women not using oral contraceptives were similar to those reported elsewhere (Carr, 1993; Hatcher et al., 1988; Hamm, 1991). Mean plasma estradiol levels were significantly different in all three phases during the uncompensable heat strain trials (Table 4). Estradiol levels were lowest during the EF phase and highest during the ML phase. Plasma estradiol levels followed a similar trend during the compensable heat strain trials, although only the difference between the EF and ML phases achieved statistical significance. Mean plasma progesterone levels were low during both the EF and LF phases (less than 0.6 ng·mL⁻¹) and were significantly elevated during the ML phase. Mean progesterone levels during the mid luteal phase were approximately 7 ng·mL⁻¹, indicating that ovulation had occurred.
The plasma concentrations of synthetic estrogen and progestin were not measured in this study. The reason for this was because of the methodological difficulties and cost involved in measuring and comparing the varying estrogen and progestin components of the different oral contraceptive formulations used by the women in our study. While six of our subjects were using an oral contraceptive with the same synthetic steroid content and dosage regimen (0.035 mg ethinyl estradiol/0.03 desogestrel), the other three subjects in this group were taking OCs with a different progestin component (levonorgestrel or norethindrone). Comparisons among different oral contraceptive formulations is difficult because there is large intersubject and intrasubject variability in the pharmacokinetics and serum levels of different progestins (Lobo and Stanczyk, 1994).

Generally, the serum concentrations of ethinyl estradiol and progestin increase rapidly following pill ingestion, reaching peak levels within 0.5 to 4 h, and then begin to decline back to baseline (Jung-Hoffmann and Kuhl, 1989). Typical values for the half-life of elimination of the synthetic hormones range from 7.5 h to 22 h, depending on the progestin component in the oral contraceptive and on the dosage regimen (Wilde and Balfour, 1995). Measurement of serum concentration 24 h after pill ingestion shows that most of synthetic hormone has been eliminated from the system (Kuhl, 1990). However, a certain amount of accumulation of the synthetic hormones does occur over the course of the pill intake cycle and, in general, the plasma concentrations of synthetic progestin and estrogen are higher on day 21 of pill intake than on day 1 (Jung-Hoffmann and Kuhl, 1989; Kuhl et al., 1988a; Kuhl et al., 1988b; Shenfield and Griffin, 1991). For example, serum levels of ethinyl estradiol increase significantly between day 1 and 10 of pill intake, and remain significantly elevated until day 21 (Jung-Hoffmann and Kuhl, 1989). During the 7 day pill-free interval, the concentration of exogenous hormones decline. In subsequent cycles, the serum concentrations on day 1 may be elevated compared with those measured on day 1 of the first cycle. There may
be a significant increase in concentration on day 1 from cycle to cycle, but over the course of 12 months of pill use, the typical day 1 value is similar to that of the first cycle (Kuhl et al., 1988a&b). It is not known how changes in the serum concentrations of the synthetic hormones affect temperature regulation.

6.3 THERMOREGULATORY SET POINTS ($T_{mr}$, $T_{sk}$)

6.3.1 Initial Rectal Temperature

Initial core temperature was approximately 0.2°C higher during the mid luteal phase compared with the early follicular phase among the non-users during the compensable heat strain trials (Table 11, p<0.08). Similarly, initial core temperature was elevated during the ML phase compared with the EF phase among the non-users during the uncompensable heat strain trials (Table 12, p<0.07). The observation of an elevation in resting core temperature during the luteal phase of the menstrual cycle compared with the follicular phase is consistent with the findings of several other investigators (Bemben et al., 1995; Frascarolo et al., 1990; Hessemer and Bruck, 1985a&b; Horvath and Drinkwater, 1982; Kolka and Stephenson, 1995; Stephenson and Kolka, 1993). The rise in basal body temperature during the luteal phase is generally attributed to the thermogenic effect of the increase in progesterone levels following ovulation (Lebrun, 1994).

There may be several reasons why our results do not show as significant a division in resting core temperature as compared with the reports of these other investigators. First of all, the statistical significance of this measure may have been influenced by the number of women studied. To illustrate, if we combine the data for initial rectal temperature from both clothing configurations for the non-users (thus increasing the sample size to n=16), the difference between the EF (37.10 ± 0.06°C) and ML (37.31 ± 0.07°C) phases achieves statistical significance.
Second, intersubject variations may have influenced the statistical significance of initial rectal temperature. One of the subjects in the non-user group did not experience the rise in basal body temperature normally associated with the luteal phase during the compensable heat strain trials, even though hormonally it was confirmed that progesterone was significantly elevated. Likewise, during the uncompensable heat strain trials, initial $T_{re}$ was lower in two of the non-users during the ML phase compared with the EF phase even though hormonal analysis verified that ovulation had occurred.

A third reason why our results do not show as significant a division in resting core temperature as compared with the reports of other investigators may have been due to differences in the determination of menstrual cycle phase. Many investigators monitor basal body temperature for a number of cycles prior to the actual experiment (Horvath and Drinkwater, 1982; Hessemer and Bruck, 1985a; Hessemer and Bruck, 1985b; Kolka and Stephenson, 1989; Kolka and Stephenson, 1995). The selection of cycle day is then based on changes in body temperature, and later verified by hormonal analysis. In this manner, investigators are testing their subjects on days when basal temperature is at a maximal displacement and thus, are pre-selecting for a difference in resting core temperature between the two phases. In the present study, difficulties recruiting subjects and study time limitations did not accommodate the monitoring of subjects' cycles prior to involvement in the experiment. Testing days were chosen based on the knowledge of the first day of flow and average cycle length. Consequently, although cycle phase was confirmed by hormonal analysis, subjects may have been tested on a day in the mid luteal phase when basal body temperature was not necessarily at a maximal displacement.

Finally, Hessemer and Bruck (1985a) relate that the small temperature differences found during the day between different phases of the menstrual cycle under strictly resting conditions may easily disappear because of minor
differences in physical activity and other factors prior to the experimental session. Thus, it is possible that variances in pre-trial posture and activity may have influenced our measure of initial $T_{re}$.

A post hoc calculation of power was performed for initial $T_{re}$. A power $(1 - \beta)$ of 0.80 is usually considered as an acceptable value when ensuring that one has correctly determined that there was no significant difference between or among treatment means. Since the power for the statistical analyses of initial $T_{re}$ in the present study was determined to be 0.45 for the combat clothing configuration and 0.48 for the NBC configuration, I believe we are committing a Type II error in concluding that there was no significant effect of phase on initial $T_{re}$ for the non-users. One method of reducing the risk of making a Type II error would be to increase the number of subjects tested. However, with the number of subjects involved in the present study, testing was conducted daily over a 6 month time period. Thus, to double the number of subjects would have required a full year of data collection. This brings to light the issue of statistical significance versus practical significance. Given the fact that there was a strong tendency ($p<0.08$) for $T_{re}$ to be elevated during the mid luteal phase in comparison with the early follicular phase for the non-users, and the fact the initial $T_{re}$ was not measured under controlled resting conditions, it would be impractical to invest the extra time and money required to achieve statistical significance for this one measure of rectal temperature.

The influence of oral contraceptive use on resting core temperature is unclear. Initial $T_{re}$ was similar in all three phases for the women using oral contraceptives in the combat clothing configuration. Values were 37.23 ± 0.8°C during EF, 37.24 ± 0.06°C during LF and 37.27 ± 0.06°C during ML. In contrast to this observation, the results from the uncompensable heat strain trials demonstrated that resting core temperature was significantly elevated during the ML phase (37.36 ± 0.06°C) compared with the EF phase (37.14 ± 0.08°C). Similar to the non-users, basal body temperature was approximately
0.2°C higher during the ML phase in the NBC clothing configuration. However, this phase-related difference in $T_{re}$ was not evident during uncompensable heat exposure.

The observation of a difference in the resting core temperature response between the two clothing configurations was not expected. Initial core temperature is independent of the treatment and therefore should not be influenced by the type of clothing worn. Analysis of initial $T_{re}$ in the NBC clothing configuration for the same seven women as in the combat clothing configuration revealed that the variance in the resting $T_{re}$ response was still apparent. A closer inspection of our methodology verified that the order of exposure, in terms of clothing configuration and menstrual cycle phase, was randomised for all of the subjects, and thus the difference in initial $T_{re}$ was not the result of a training effect or partial heat acclimation. There was no difference in the handling of the subjects, i.e., subjects were not sitting around for an extended period of time in their NBC suit before the ML trial as compared with the other uncompensable heat stress trials. Also, blood analyses demonstrated that there were no differences in plasma osmolality or hematocrit among phases or between the two clothing configurations for the users. Consequently, the variance in initial $T_{re}$ cannot be attributed to differences in body fluid balance. Furthermore, although we did not control for the posture of the subjects during the dressing period and prior to entry into the thermal chamber, it is unlikely that changes in pre-trial posture can explain the disparity in our results.

While there has been considerable research on the influence of the menstrual cycle on temperature regulation, very few investigators have looked at the influence of oral contraceptive use on thermoregulation. Results from the only two studies published to date elucidate that, similar to women with normal menstrual cycles, resting core temperature is higher during the luteal phase compared with the early follicular phase (Grucza et al., 1993; Rogers and Baker, 1997). Likewise, both investigations reported that
the separation of initial core temperature between the two phases was maintained during exercise in a comfortable ambient environment (22°C to 24°C). Grucza et al. (1993) suggested that the upward shift in core temperature was the result of the strong effect of menstrual cycle phase on the thermoregulatory system. Alternatively, Rogers and Baker (1997) postulated from their results that the progestin component of oral contraceptives has a dominant effect on thermoregulation.

When considering this last hypothesis as a possible explanation for the existence of an elevation in resting core temperature during the luteal phase of the menstrual cycle in women using oral contraceptives, it is important to note that in the investigations by Grucza et al. (1993) and Rogers and Baker (1997), although the subjects were using different formulations, the majority of the women were using a triphasic oral contraceptive. The dosage regimen of triphasic oral contraceptives is such that the dose of the progestin component is varied during the 3-week period of pill ingestion. As a result, during the luteal phase these women are ingesting a higher dosage of the progestin as compared with the follicular phase. In the present study, six of the seven women in the combat clothing configuration, and seven of the nine women in the NBC clothing configuration were using a monophasic pill (the dose of both the estrogen and progestin components are constant throughout the cycle). Analyses of initial $T_c$ for the monophasic users in our study demonstrated that there still was no difference in resting core temperature among the three phases in the combat clothing configuration. Alternatively, once again there was a significant effect of phase on resting $T_c$ during the NBC clothing trials. Thus, we are uncertain whether the type of oral contraceptive formulation used (i.e., monophasic versus triphasic) has an impact on resting core temperature.

Since so little is known about the influence of synthetic progestins on temperature regulation it is difficult to draw conclusions from the studies by Rogers and Baker (1997) and Grucza et al. (1993) to ours. Furthermore, there
are substantial between and within subject variabilities in the pharmacokinetics and the serum levels of different synthetic progestins (Lobo and Stanczyk, 1994). Therefore, if basal body temperature is influenced by the synthetic progestin component, as Rogers and Baker (1997) suggested, the existence of large differences in the pharmacokinetics and serum levels of these hormones may help explain the disparity in our results. Further research is required to ascertain the influence of oral contraceptive use on resting core temperature. Specifically, research is required to elucidate the potential influence of triphasic oral contraceptives in comparison with monophasic oral contraceptives on resting T<sub>re</sub>.

6.3.2 Initial Mean Skin Temperature

Analysis of initial T<sub>sk</sub> for the non-users in both clothing configurations revealed contradictory results. During the compensable heat strain trials, initial T<sub>sk</sub> was similar in all three phases of the menstrual cycle (Table 13). In contrast, initial T<sub>sk</sub> was significantly higher during ML compared with EF and LF during the uncompensable heat strain trials (Table 14). A difference in this response between the two clothing configurations was not anticipated.

A review of literature revealed that a number of investigators have observed that there is no significant difference in initial T<sub>sk</sub> between the luteal and follicular phases of the menstrual cycle (Frascarolo et al., 1990; Gruca et al., 1993; Hirata et al. 1986; Horvath and Drinkwater, 1982; Pivarnik et al., 1992; Wells and Horvath, 1973). Alternatively, Carpenter and Nunneley (1988) found that initial T<sub>sk</sub> was 0.3°C higher during the luteal phase compared with the early follicular phase. Likewise, Hessemer and Bruck (1985a&b) observed that mean skin temperature was 0.5 to 0.6°C higher during the luteal phase compared with the follicular phase in resting subjects. In agreement with our observations, Kolka and Stephenson (1995) reported that mean skin temperatures were variable between different test protocols. They observed that T<sub>sk</sub> was 0.3 to 0.5°C higher during the ML phase compared with the EF phase in two of their protocols, whereas, in several other
protocols there was no significant difference in $\bar{T}_{sk}$. Kolka and Stephenson (1995) did not offer an explanation for the disparity in their results.

Once more, a review of methodology substantiated that the order of exposure, in terms of clothing configuration and menstrual cycle phase, was randomised for all of the subjects, and thus the difference in initial $\bar{T}_{sk}$ was not the result of a training effect or partial heat acclimation. Blood analysis revealed that plasma osmolality did not differ among phases or between the two clothing configurations for the non-users. Therefore, the difference in initial $\bar{T}_{sk}$ cannot be ascribed to an alteration in body fluid balance. Again, there was no difference in the handling of the subjects, i.e., subjects were not sitting around for an extended period of time in their NBC suit before the ML trial as compared with the other trials.

It is important to note that the temperatures reported for both initial $T_{re}$ and $\bar{T}_{sk}$ represent the values measured once the subject was completely dressed and connected to the data acquisition system within the thermal chamber. Since the purpose of this study was to determine the influence of menstrual cycle phase and oral contraceptive use on temperature regulation during compensable and uncompensable heat strain, our primary investigative concern was to document this strain during alternating exercise and rest periods in a hot environment rather than to record $T_{re}$ or $\bar{T}_{sk}$ in a thermoneutral environment under controlled resting conditions.

Oral contraceptive use did not affect initial mean skin temperature among phases in either clothing configuration (Tables 13 and 14). To our knowledge, there has been only one other paper published to date that has examined mean skin temperature among different phases of oral contraceptive use. Consistent with our findings, Grucza et al. (1993) observed that resting $\bar{T}_{sk}$ was similar during the follicular and luteal phases in women using oral contraceptives.
6.4 INDICES OF HEAT STRAIN

6.4.1 Metabolic Rate and Gas Exchange

Menstrual cycle phase did not influence the rate of metabolic heat production, $\dot{V}O_2$ or $\dot{V}_E$ during the compensable heat strain trials for either group. Likewise, neither menstrual cycle phase nor oral contraceptive use significantly influenced $M$, $\dot{V}O_2$, or $\dot{V}_E$ during the uncompensable heat strain trials.

Consistent with the observations made in the present study for the non-users, Hirata et al. (1986) found that there was no difference in $\dot{V}O_2$, $\dot{V}CO_2$, and $\dot{V}_E$ between the luteal (L) and follicular (F) phases, at rest in a 20°C environment or during exercise at 40% and 70% $\dot{V}O_{2max}$. Likewise, Stephenson et al. (1982) and Wells and Horvath (1973) reported that $\dot{V}O_2$ and $\dot{V}_E$ were not influenced by menstrual cycle phase, and Jurkowski et al. (1981) found that HR, SV, $\dot{V}O_2$, $\dot{V}CO_2$ and cardiac output did not differ between L and F. Also in agreement with our observations, Carpenter and Nunneley (1988) and Frascarolo et al. (1990) both reported that there was no difference between phases of the menstrual cycle for metabolic rate. In contrast, Hessemer and Bruck (1985a&b) found that basal metabolic rate and exercise $\dot{V}O_2$ were increased by approximately 5% during the luteal phase.

While there has been considerable research on the influence of menstrual cycle phase during compensable heat stress, there has been comparatively little research examining its affect during uncompensable heat strain. Kolka et al. (1994) looked at thermoregulation in women during uncompensable heat strain in the EF phase alone. Since only one phase of the menstrual cycle was studied, conclusions can not be drawn on possible differences in oxygen consumption between phases of the menstrual cycle. In a later investigation, Kolka and Stephenson (1995) examined the influence of the early follicular, late follicular and mid luteal phases of the menstrual cycle on thermoregulation under conditions of uncompensable heat stress.
However, no information was presented with respect to differences in \( \dot{V}O_2 \) or \( M \) among the phases.

To the best of our knowledge, the present research represents one of the first reports to discuss the influence of OC use on metabolic rate and oxygen consumption among different phases of the menstrual cycle, and between different types of physiological heat strain. Huisveld et al. (1995) compared the responses of 10 trained OC users and 10 trained OC non-users during incremental exercise to exhaustion. They found that maximal heart rate, maximal respiratory exchange ratio and \( \dot{V}O_{2\text{max}} \) did not differ between users and non-users of oral contraceptives (Huisveld et al., 1995). However, a comparison of these variables between different phases of the menstrual cycle was not performed. Grucza et al. (1993) observed that \( \dot{V}O_{2\text{max}} \) and the \( O_2 \) cost of exercise at 50% \( \dot{V}O_{2\text{max}} \) were similar among the follicular and luteal phases and between users and non-users of oral contraceptives. Thus, it appears as though oral contraceptive use does not influence \( \dot{V}O_2 \) and \( \dot{V}O_{2\text{max}} \) during mild exercise-heat stress. There has yet to be literature disclosed on the potential influence of oral contraceptive use on \( \dot{V}O_2 \) and \( M \) under conditions of uncompensable heat strain.

6.4.2 Heart Rate

There were no phase-related differences in heart rate among the non-users during either the compensable (Figure 2) or the uncompensable (Figure 3) heat strain trials. This observation is consistent with the findings of several other investigators (Hirata et al., 1986; Horvath and Drinkwater, 1982; Jurkowski et al., 1981; Kolka and Stephenson, 1995; Lebrun et al., 1995; Phillips, 1968; and Sato et al., 1995).

Similar to the women not using oral contraceptives, heart rate did not differ significantly among phases for the users during the uncompensable heat strain trials. However, this was not the case during the compensable
heat strain trials. Heart rate tended to be higher during EF compared with LF and ML after 215 min of compensable heat exposure for the women within this group \((n=7, \ p<0.06)\). Following 240 min of heat exposure, this difference achieved statistical significance \((n=6)\). Further analyses revealed that the heart rate response during the first 215 min was statistically significant when the one subject who dropped out after 215 min was excluded from the analysis. The difference in HR was apparent during both the walking and the sitting phases of the experimental protocol and was evident \((p<0.07)\) from the start of the compensable heat strain trial (Figure 2).

There was no difference in \(\dot{M}\) among the phases for the users. Likewise, oxygen consumption and minute ventilation did not differ among phases during the compensable heat strain trials. Thus, the increase in heart rate was not due to an increased cost of exercise or an increased rate of metabolic heat production. A comparison of the HR response of these seven women with their HR response during the EF phase in the NBC clothing configuration did not reveal a similar trend. Other possible explanations for a difference in the heart rate response among the EF and the LF and ML phases include: (1) hydration status; (2) training status; (3) partial heat acclimation; (4) elevated core temperature and skin temperature; (5) influence of either endogenous or exogenous hormones; and (6) alteration in autonomic control.

Hydration level during exercise in the heat is of particular importance because hypohydration (a body water deficit of 3-4%) results in an increased core temperature response, an increased HR, and a decreased stroke volume relative to euhydration \((\text{Sawka et al., 1996})\). However, blood analyses revealed that there were no phase-related differences in osmolality, hematocrit or hemoglobin in either clothing configuration (Table 5). Also, although no attempt was made to control for hydration status, subsequent analyses revealed that there was no significant difference in pre-trial body weight among the three phases during the combat clothing trials. Therefore,
it is not likely that changes in body fluid balance contributed to the increase in HR during the EF phase.

The improvements acquired through physical training or heat acclimation reduce the strain imposed on the cardiovascular system during exercise-heat stress (Nadel et al., 1974). One of the most prominent changes associated with either physical training or heat acclimation is a decreased heart rate during submaximal exercise in the heat (Aoyagi et al., 1997). Thus, it is possible that the lower HR observed during the LF and ML phases may have been due to an improvement in cardiovascular fitness or partial heat acclimation. However, a review of methodology verified, once again, that there was no bias in the order of exposures (i.e., all the subjects did not complete the EF trial first). Therefore, the lower HR observed during LF and ML was not the result of a training effect or partial heat acclimation.

An elevation in core temperature and skin temperature can result in an increase in heart rate (Aoyagi et al., 1997). However, both core temperature (Figure 4) and mean skin temperature (Figure 6) did not differ among the phases during the compensable heat strain trials. Thus, a difference in these variables does not explain the higher heart rate observed during the early follicular phase.

It is plausible to attribute the difference in the heart rate response to variances in the levels of either endogenous or exogenous hormones during the different phases of the menstrual cycle studied. Since the endogenous levels of estradiol and progesterone were similar in both the users and the non-users during the early follicular phase, and an elevation in heart rate was not observed in the EF phase among the non-users during the compensable heat strain trials, the increase in HR was not likely due to the influence of the endogenous hormones. Therefore, the elevated heart rate during the early follicular phase may be related to some aspect of oral contraceptive use, or more specifically, to OC non-use since during the EF phase in the users no pill
is ingested. The removal of the exogenous steroids may exert an influence on the autonomic control of HR.

An elevation in HR can be brought about by either an increase in sympathetic activity or a decrease in parasympathetic activity, or a combination of both. Consideration of the possible interaction between the removal of exogenous hormones and an alteration in the autonomic control of heart rate led to the hypothesis that during the EF phase among OC users, the decline in the plasma levels of the exogenous steroid hormones results in a decrease of parasympathetic outflow to the heart. Consequently, HR is elevated during the EF phase in comparison with the LF and ML phases. The reason the same effect on HR is not observed during the uncompensable heat strain trials is because the demand of the activity masks or overrides the alteration in parasympathetic tone. During the NBC clothing configuration trials, sympathetic outflow is greater in response to the conditions of uncompensable heat strain. Thus, a corollary to our hypothesis was that the influence of the removal of the synthetic hormones on the HR response may be only visible at light metabolic rates, since under conditions that demand a greater HR, the sympathetic drive in response to the activity would override the parasympathetic contribution.

There are two major weaknesses with this explanation. First, the elevation in HR during EF was still apparent during the later stages of the compensable heat strain trial when values were comparable to the HR recorded at the beginning of the uncompensable condition where no effect of cycle phase was observed. Second, HR during the rest period in the NBC trials was similar to the HR observed at the onset of exercise in during the compensable heat strain trials, and yet, no phase-related difference in HR was apparent in the former clothing configuration.

Gruca et al. (1993) observed that there was no difference in the HR response between the follicular and luteal phases during submaximal (50%
\( \dot{V}O_2 \text{max} \) and maximal cycle exercise in a comfortable ambient environment (24°C, 50% relative humidity; 1.5 kPa). Conversely, Rogers and Baker (1997) found that HR was 6.5 b-min\(^{-1}\) higher in subjects walking on a treadmill for 60 min at 4.8 km·h\(^{-1}\) at a 10% gradient in a 22°C environment during the third week of pill use compared with the week when no pill was taken. These time frames correspond to ML and EF, respectively, in our study. Thus, we are unable to account for the elevated HR response during the EF phase for the users during the compensable heat strain trials. Given the limited amount of research in this area, and the fact that this is the first study performed where the majority of subjects were using a monophasic oral contraceptive, more research is warranted.

6.4.3 Rectal Temperature

For the women not using oral contraceptives, initial \( T_{re} \) was higher during ML compared with EF in the combat clothing configuration (p<0.08). The elevation in \( T_{re} \) during the ML phase was apparent throughout the compensable heat strain trials (Figure 4). Over 240 min of light intermittent exercise in the heat (n=7), the difference in \( T_{re} \) between EF and ML was still discernible (p<0.08). Referring back to our earlier discussion on initial \( T_{re} \) for the non-users, the statistical significance of this measure may have been influenced by the small number of subjects (n=7) who participated in the compensable heat exposure trials, and thus may have resulted in the commission of a Type II error. Another possible reason why our results do not show as significant a division in exercise core temperature as compared with the reports of other investigators may be differences in the determination of menstrual cycle phase. Difficulties recruiting subjects and study time limitations did not accommodate the monitoring of subjects' cycles prior to involvement in the experiment. Thus, although cycle phase was confirmed by hormonal analysis, subjects may have been tested on a day in the mid luteal phase when basal body temperature was not necessarily significantly elevated in comparison with the early follicular phase.
The observation that the separation in core temperature between the EF and ML phases is maintained throughout exercise is consistent with the findings of several other investigators (Carpenter and Nunneley, 1988; Hessemer and Bruck, 1985b; Hirata et al., 1986; Jurkowski et al., 1981; Kolka and Stephenson, 1989 and 1995; and Pivarnik et al., 1992). The concept that a small difference in internal temperature can be maintained throughout exercise without a significant change in heat production or heat loss implies that the thermoregulatory setpoint is reset to a higher level during the luteal phase of the menstrual cycle.

During the uncompensable heat strain trials, initial core temperature was lower, ΔT_re was greater, and both final T_re and the time for a 1.0°C increase in T_re were similar for the EF phase compared with the ML phase for the women not using oral contraceptives. This suggests that because the women within this group started at a lower initial T_re in the EF phase, and gained heat at the same rate as in the ML phase, they were able to continue under the uncompensable conditions for a longer period of time during the EF phase before reaching their core temperature threshold for heat tolerance. This conjecture was affirmed by the observation that tolerance times were significantly longer during the EF phase compared with the ML phase for the non-users. Kolka and Stephenson (1995) also found that resting and exercise esophageal temperature were higher in ML than in EF for women wearing chemical protective clothing in a warm environment. However, the data presented in their report were for only a small number of subjects (n=4) and are part of an ongoing investigation.

Our findings for the women not using oral contraceptives are in agreement with the work of Aoyagi et al. (1995) and McLellan and Aoyagi (1996) who observed that if the rate of heat storage did not differ between conditions, and if core temperature was similar at the end of the exposures, tolerance time was mainly affected by the starting core temperature. They resolved from their research that a reduction in initial core temperature,
achieved through endurance training and/or heat acclimation, resulted in prolonged tolerance times (Aoyagi et al., 1995; McLellan and Aoyagi, 1996).

The rectal temperature response of the users was similar among phases during both heat strain conditions. Aside from the elevation in $T_{re}$ at the onset of the NBC clothing trials in ML, rectal temperature did not differ among phases during the exercise-heat trials in either clothing configuration (Figures 4 and 5). Likewise, neither delta $T_{re}$ nor final $T_{re}$ were significantly different among phases in either clothing ensemble for the women using oral contraceptives. Additionally, the results for $\Delta T_{re}$ and final $T_{re}$ from both the heat conditions did not differ from those of the non-users.

Since the rectal temperature response did not differ among phases for the users during the compensable heat strain trials, and the lower initial $T_{re}$ in the EF phase during the NBC trials did not result in longer tolerance times, it is unlikely that oral contraceptive use has a significant phase-related effect on the core temperature response during uncompensable heat strain. It appears as though the initial elevation in $T_{re}$ in the ML phase during the NBC trials was transient. Thus, the potential advantage of oral contraceptive use is that it makes the thermoregulatory response more uniform during both compensable and uncompensable heat strain. The possible mechanism of action of oral contraceptives may be related to the hypothesis proposed by Grucza et al. (1993) that the elevation in resting core temperature among women using oral contraceptives was the strong effect of menstrual cycle phase. As such, the elevation in resting $T_{re}$ during the mid luteal phase of the menstrual cycle may represent a type of circadian rhythm that is not altered by the administration of synthetic hormones. Therefore, oral contraceptive use may not result in the resetting of the thermoregulatory set-point, as is believed to occur during the luteal phase in women with normal menstrual cycles. Consequently, the elevation in $T_{re}$ during the ML phase is not maintained during a significant thermoregulatory challenge.
Similar to initial $T_{re}$, our findings on the $T_{re}$ response in women using oral contraceptives during compensable exercise-heat stress are not in agreement with Grucza et al. (1993) and Rogers and Baker (1997), who found that $T_{re}$ remained significantly elevated in the ML phase throughout submaximal exercise. It is possible that the ensuing thermoregulatory strain was not a sufficient enough challenge to override the natural menstrual cycle rhythm in core temperature in these former studies where subjects exercised in a comfortable ambient environment (22 - 24°C). However, subjects exercised at a higher relative intensity (40 - 50% $\dot{V}O_{2max}$) which would be expected to offset the differences in environmental conditions between these two investigations and this study.

6.4.4. Mean Skin Temperature

Menstrual cycle phase did not influence $\overline{T}_{sk}$ during the compensable heat exposures (Figure 6). This observation is consistent with the results of Frascarolo et al. (1990), Hirata et al. (1986), Horvath and Drinkwater (1982), Pivarnik et al. (1992) and Wells and Horvath (1973). Conversely, Carpenter and Nunneley (1988), Hessemer and Bruck (1985b), Kolka and Stephenson (1993) and Stephenson et al. (1982) found that $T_{sk}$ was higher throughout exercise in the luteal phase compared with the follicular phase.

Although initial $\overline{T}_{sk}$ was significantly higher during ML compared with both LF and EF in the NBC clothing configuration, there was no effect of phase on $\overline{T}_{sk}$ during the uncompensable heat strain trials for the women not using oral contraceptives. This finding is in agreement with the results of Kolka and Stephenson (1995), who reported that $\overline{T}_{sk}$ was similar among the EF and ML phases while performing continuous exercise in NBC clothing.

Oral contraceptive use does not appear to influence the $T_{sk}$ response during heat stress. Similar to the findings of Grucza et al. (1993) there were no phase-related difference in the mean skin temperature responses during
compensable heat strain for the women using oral contraceptives. Likewise, $\bar{T}_{sk}$ did not differ among phases for the users during uncompensable heat strain.

6.4.5 Gain in Body Heat Content

There were no phase-related or group-related differences in body heat storage during the compensable heat strain trials (Table 15). Similarly, there was no phase-related difference in the gain in body heat content for the users during the NBC clothing trials. In contrast, the gain in body heat content was significantly greater in EF than ML for the non-users during the NBC clothing trials. This finding is consistent with the changes observed in $\Delta T_{re}$ among phases for the non-users during the NBC trials. To the best of our knowledge, there have been no reports published to date which have examined the changes in body heat content among different phases of the menstrual cycle during uncompensable heat strain.

6.4.6 Sweat Production and Evaporation

The rate of sweat production and the rate of evaporative heat loss were similar in all three phases among the non-users in the combat clothing configuration (Table 16). Evaporative efficiency (the ratio of evaporative heat loss to sweat production) was approximately 93%, signifying that the subjects were able to effectively exchange heat with the environment. During the uncompensable heat strain trials, sweat rate tended to be greater during ML compared with EF and LF, although this difference was not statistically significant ($p<0.11$). Similar to the combat clothing trials, neither evaporation rate nor evaporative efficiency were influenced by menstrual cycle phase while wearing the NBC ensemble (Table 17). However, evaporative efficiency was considerably reduced in all three phases while wearing the NBC clothing (approximately 38%) indicating that the ability to dissipate heat via the
evaporation of sweat was severely reduced during the uncompensable heat strain trials.

The lack of phase-related differences in the rate of sweat production and evaporative heat loss during compensable heat strain are in agreement with the work of Carpenter and Nunneley (1988), Horvath and Drinkwater (1982), Pivarnik et al. (1992) and Wells and Horvath (1973). Carpenter and Nunneley (1988) reported that there were no differences in either total sweat loss or chest and thigh sweat rate between the follicular and luteal phases of the menstrual cycle during exercise at 30% VO\textsubscript{2peak} in a 48°C environment. Similarly, Horvath and Drinkwater (1982) found that evaporative heat loss and sweating rates were similar during the EF, LF and ML phases in women performing exercise at 30% VO\textsubscript{2max} for 2 h at 28°C, 35°C, and 48°C. Pivarnik et al. (1992) found that sweat loss was not affected by menstrual cycle phase during endurance exercise (60 min at 65% VO\textsubscript{2peak}) performed at 22°C and 60% relative humidity (1.6 kPa). Finally, Wells and Horvath (1973) found that total body sweating rates and evaporative heat loss did not differ between the luteal and follicular phases in subjects who were exposed for 2 h to an environment of 48°C and 11 mm water vapour pressure (1.5 kPa). In contrast with these results, Hessemer and Bruck (1985a) observed that chest sweat rate was higher in the luteal phase than in the follicular phase in subjects at rest in the heat (ambient temperature increased 1-2°C·min\textsuperscript{-1}, up to 59°C). However, Hessemer and Bruck (1985b) found that overall chest sweat rate was not different during exercise.

To the best of our knowledge, there has been only one other report published which examined the potential influence of menstrual cycle phase during uncompensable heat strain. Kolka and Stephenson (1995) observed, similar to our findings, that whole body sweating rates did not differ between the early follicular and mid luteal phases of the menstrual cycle in women performing continuous exercise (40% VO\textsubscript{2max}) in the heat while wearing the United Stated NBC protective clothing. However, no information was
disclosed in this report with respect to evaporation rate and evaporative efficiency. In an earlier study by Kolka et al. (1994) that looked at thermoregulation in women during uncompensable heat stress in the EF phase alone, evaporative efficiency was reported to average $45 \pm 14\%$ while wearing the NBC clothing.

The rate of sweat production and the rate of evaporative heat loss were similar among all three phases during compensable heat strain for the women using oral contraceptives (Table 16). Likewise, sweat rate and evaporation rate did not differ among phases during the uncompensable heat strain trials for the women within this group (Table 17). Evaporative efficiencies were approximately 91% and 37% for the combat clothing and NBC clothing configurations, respectively. Furthermore, there were no differences in these variables in comparison with the group not using oral contraceptives. Thus, oral contraceptive use did not influence the rate of sweat production or evaporative heat loss.

Once again, given the limited amount of information, the potential influence of oral contraceptive use on the dynamics of sweating and the rate of sweat evaporation during exercise-heat stress is poorly understood. In addition, our findings represent the first attempt to quantify the dynamics of sweating and evaporative heat loss during uncompensable strain among women using oral contraceptives. In comparison with the work of Grucza et al. (1993) and Rogers and Baker (1997), the present investigation did not look at the temperature threshold for the onset of sweating or the sensitivity of the sweating response between the luteal and follicular phases of the menstrual cycle. Grucza et al. (1993) demonstrated that the dynamics of sweating did not differ significantly between the quasi-follicular and quasi-luteal phases of the menstrual cycle. They found that although the threshold for the onset of sweating occurred at a higher core temperature during the quasi-luteal phase, the gain for the sweating response was similar in both phases. Likewise, Rogers and Baker (1997) reported that the core temperature threshold for the
onset of evaporative water loss was significantly greater in the ML phase compared with the EF phase. The changes in evaporative water loss with time were not different between the two phases (Rogers and Baker, 1997).

6.4.7 Tolerance Time

There was no significant difference in tolerance time between the two groups during the compensable heat strain trials. Neither menstrual cycle phase nor oral contraceptive use influenced heat strain and work tolerance time during light exercise in the heat while wearing the combat clothing configuration.

The results from the uncompensable heat strain trials are consistent with those of a number of investigators (Armstrong et al., 1991; McLellan et al., 1992, McLellan, 1993; McLellan et al., 1996; Montain et al., 1994; White et al., 1991). The use of NBC protective clothing during light exercise in the heat resulted in continued heat storage and severely reduced physical work tolerance time. Tolerance time to the heat stress was determined by time, ethically imposed end-points, or subject exhaustion. None of the subjects completed the 300 min of light intermittent exercise while wearing the NBC protective ensemble. The initial familiarisation session served to accustom subjects to the protocol and any associated discomforts prior to the actual test. Therefore, the subjects were experienced with wearing the clothing and appeared highly motivated. Of the 54 NBC test trials, 37 were terminated due to exhaustion. Of the remainder, 10 were terminated due to $T_{re}$ reaching 39.3°C and 7 due to HR reaching 95% of peak value. In all of these cases, subjects reported they were very near the point of exhaustion.

Menstrual cycle phase had a significant effect on work tolerance time during uncompensable heat strain among the non-users. Women tolerated heat better during the EF phase ($128.1 \pm 13.4$ min) compared with the ML phase ($107.4 \pm 8.6$ min). As was discussed previously, women within this
group started at a lower initial $T_r$ in the EF phase, and because they gained heat at the same rate as in the ML phase, they were able to store heat for a longer period of time during the EF phase before reaching their core temperature threshold for heat tolerance. This finding is in agreement with the observations of Aoyagi et al. (1995) and McLellan and Aoyagi (1996) who concluded that differences in tolerance time are mainly affected by the starting core temperature. A comparison with the results of Kolka and Stephenson (1995) is not possible because they do not report tolerance times for their subjects. It appears (from the graph in their report) as though tolerance times were longer in the EF phase compared with the ML phase; however, because no data were presented, this is only a qualitative assumption that has not been validated.

Oral contraceptive use did not influence heat storage or work tolerance times during uncompensable heat strain. Tolerance times were similar in all three phases for the women within this group. Furthermore, tolerance times were not significantly different from those observed for the group of women not using this method of birth control and were similar to tolerance times reported by McLellan et al. (1992 and 1994) for healthy, young men, under equivalent experimental conditions. Although initial core temperature was significantly different between the ML and EF phases, this difference was not evident during the uncompensable heat exposure and, therefore, $T_r$ did not influence any of the other physiological indices of heat strain or physical work tolerance time. It appears as though the potential advantage of oral contraceptive use is that it makes the thermoregulatory responses during uncompensable heat strain and the associated work tolerance times more uniform across the different phases of the menstrual cycle.
Chapter 7

LIMITATIONS OF THE STUDY

The factors which have limited interpretation of the results of this study follow:

1. Not all of the women in the group using oral contraceptives were taking the same oral contraceptive formulation. This was, in large part, a factor of recruiting a sufficient number of subjects willing to participate fully in all aspects of the study.

2. The serum concentrations of the synthetic estrogen and progestin were not measured. The reason for this was because of the methodological difficulties and cost involved in measuring and comparing the varying estrogen and progestin components of different oral contraceptive formulations.

3. The temperatures reported for initial $T_{re}$ and $T_{sk}$ represent the values measured once the subject was completely dressed and connected to the data acquisition system within the thermal chamber and therefore do not represent $T_{re}$ and $T_{sk}$ in a thermoneutral environment under controlled resting conditions.

4. Due to subjects' time constraints, the scheduling of cycle phase and study time constraints, the data for two non-users and two users were not included in the analyses of the compensable heat strain trials. The reduction in sample size for these trials influenced the statistical significance of the effect of menstrual cycle phase on $T_{re}$ during these trials.
1. Menstrual cycle phase and oral contraceptive use did not affect temperature regulation during compensable heat strain. Work tolerance time and the physiological indices of heat strain were similar between the two groups in all three phases studied.

2. Women not using oral contraceptives experienced greater heat strain during the mid luteal phase of their menstrual cycle while wearing the NBC protective ensemble. Work tolerance time was significantly lower during the mid luteal phase compared with the early follicular phase among the women in this group and core temperature was elevated throughout the trial.

3. There were no significant differences in the indices of heat strain or work tolerance time between the mid luteal and the late follicular phases of the menstrual cycle for the women not using oral contraceptives.

4. Oral contraceptive use did not influence temperature regulation during uncompensable heat strain. The physiological responses and work tolerance times of the women in this group were similar in all three phases and did not differ from the thermoregulatory responses of the non-users in any of the phases. Our results demonstrate that oral contraceptive use appears to make the thermoregulatory responses to uncompensable heat strain more uniform over the course of the menstrual cycle.
Chapter 9

RECOMMENDATIONS FOR FUTURE STUDY

Directions for further study should include the following:

1. To investigate the influence of monophasic oral contraceptives in comparison with triphasic oral contraceptives on thermoregulation.

2. To better understand the effect of oral contraceptive use on the core temperature response during different phases of the menstrual cycle, it is recommended that levels of synthetic ethinyl estradiol and progestin be measured along with endogenous estradiol and progesterone.

3. To determine the influence of estrogen therapy as a possible ergogenic aid during the mid luteal phase of the menstrual cycle for women who must perform work under conditions of uncompensable heat strain.


McLellan TM (1991). Influence of metabolic rate at 40°C ambient temperature on work tolerance times with varying levels of Canadian Forces NBC protective clothing. Technical report no. 91-27, DCIEM.


McLellan TM (1994). Tolerance times for continuous work tasks while wearing NBC protective clothing in warm and hot environments and the strategy of implementing rest schedules. Technical report no. 94-62, DCIEM.

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