Thermoregulation in Women: Effect of the Menstrual Cycle

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Twelve women participated in seven different experimental protocols which characterized the effect of the mid-luteal phase elevation in core temperature during exercise and heat exposure. Experiments were conducted at ambient temperatures between 30°C and 50°C at both low and high ambient water vapor pressures when test subjects were not naturally acclimatized or artificially acclimated to the heat. In all experiments, the separation of temperatures between the early follicular and mid-luteal phases was apparent, with temperature in the mid-luteal phase averaging 0.3 to 0.5°C higher than in the early follicular phase. This significant difference observed in resting core (esophageal) temperature between the two menstrual cycle phases studied in these experiments was maintained during exercise during both cycling and walking exercise, in both hot and very hot ambient temperatures, in both humid and dry conditions, and when heavy or light clothing was worn. Heart rate, skin temperatures and sweating rates were variable between test protocols. In summary, the change in resting and exercise core temperature between the mid-luteal and early follicular phases of the menstrual cycle was significant and of the same magnitude as observed as a result of changes in circadian timing, heat acclimation, exercise training or during dehydration.
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Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to Army Regulation 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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FOREWORD

Results from early studies of thermoregulation indicated that women were less tolerant to environmental stress than men, especially during exposure to hot environments. Generally, it was observed that women had higher core temperatures, higher skin temperatures, higher heart rates and lower sweating rates compared to men during exposure to identical environmental or exercise conditions. This results because on average, cardiorespiratory fitness in women is approximately 70% that of men of a similar age, so if work or exercise is at a similar absolute intensity, women must work at a level closer to their maximal aerobic power, which increases both core temperature and heart rate. More recent studies comparing thermoregulation between men and women have stressed the importance of controlling for physical fitness, heat acclimation, body fat and size. Specifically, if aerobic fitness is similar, differences previously observed between men and women during heat exposure are minimized. In the last ten years, it has been re-emphasized that for any evaluation of thermoregulation in women, “control” for aerobic fitness, acclimation status, time of day, hydration status and menstrual cycle phase must be considered in the experimental design. This report describes a series of studies done at the U.S. Army Research Institute of Environmental Medicine which characterizes the thermoregulatory effects associated with menstrual cycle changes in circulating reproductive hormones. Publication and discussion of these studies is timely as recent funding and administrative efforts by Federal Agencies, including the Department of Defense, have centered on physiologic responses of women during clinical trials. It must be noted that controlling for menstrual cycle phase in thermoregulatory studies is essential. Thermoregulation in women of reproductive age (post-menarche to pre-menopausal) is characterized by an elevation in the core temperature threshold for the onset of all thermoregulatory effectors (sweating, vasodilation, shivering and vasoconstriction) during exercise, heat exposure and cold exposure during the mid-luteal phase of the menstrual cycle compared to the early follicular phase of the menstrual cycle.
ACKNOWLEDGEMENTS

This work would not have been possible without the volunteers who participated in the tests described in this report. We wish to thank them for their time and effort. We especially thank Dr. T. Doherty, L. Trad, L. Levine, Dr. C. Gabarée and Dr. R.R. Gonzalez for their contributions to these studies. We especially thank Dr. A.B. DuBois for the use of facilities at the John B. Pierce Foundation Laboratory.
EXECUTIVE SUMMARY

Twelve women participated in seven different experimental protocols which characterized the effect of the mid-luteal phase elevation in core temperature during exercise, heat exposure or combination of exercise and heat exposure. One subject participated in all seven protocols; one subject participated in six of the protocols; two subjects were in three protocols; and eight subjects participated in one protocol each. Experiments were conducted at ambient temperatures between 30°C and 50°C at both low and high ambient water vapor pressures when test subjects were not naturally acclimatized or artificially acclimated to the heat. In all experiments, the separation of temperatures between the early follicular and mid-luteal phases was apparent, with temperature in the mid-luteal phase averaging 0.3 to 0.5°C higher than in the early follicular phase. This significant difference observed in resting core (esophageal) temperature between the two menstrual cycle phases studied in these experiments was maintained during exercise during both cycling and walking exercise, in both hot and very hot ambient temperatures, in both humid and dry conditions, and when heavy or light clothing was worn. Heart rate, skin temperatures and sweating rates were variable between test protocols. In summary, the change in resting and exercise core temperature between the mid-luteal and early follicular phases of the menstrual cycle was significant and of the same magnitude as observed as a result of changes in circadian timing, heat acclimation, exercise training or during dehydration.
INTRODUCTION

Thermoregulation in men and women was well-studied in the 1940's, 1960's and again in the 1980's (see reviews by Kolka, 1992; Stephenson and Kolka, 1993). The early consensus was that women were less heat tolerant than men. In the earliest studies, the women tested were much less fit than the men, which in itself would decrease tolerance to hot environments. However, during light to moderate exercise in men and women "matched" for fitness level, body fat and body surface area, these differences were minimized, although sweating rates remain higher in men even when fitness and acclimation states were similar.

Heat exposure demands active thermoregulatory effector mechanisms to maintain core temperature. If core and skin temperatures increase, heat loss mechanisms are activated and increased sweat secretion and increased blood flow to the skin surface occur and body heat is eliminated. Evaporative heat loss (sweating) is determined by air flow surrounding the outer surface area and the water vapor pressure gradient between the skin and the environment while dry heat loss (skin blood flow) is determined by the temperature gradient between the skin and the air (Gonzalez et al., 1978).

In women of reproductive age thermoregulation is characterized by higher core temperature thresholds for onset of all thermoregulatory effectors (sweating, vasodilation, vasoconstriction, and shivering) during exercise, heat exposure and cold exposure during the mid-luteal phase of the menstrual cycle (Cunningham and Cabanac, 1971; Haslag and Hertzman, 1965; Hessemer and Brück 1985; Kolka and Stephenson, 1989; Stephenson and Kolka, 1985). These elevated core temperature thresholds are consistent with a higher regulated core temperature in the mid-luteal phase of the menstrual cycle. The increased regulated core temperature during the mid-luteal phase may be a consequence of altered levels of the reproductive hormones (Rothchild, 1952) or a change in the balance of immuno-modulators (Cannon and Dinarello, 1985).

The mid-luteal phase of the menstrual cycle is characterized by elevated circulating estradiol and progesterone concentrations. The post-ovulatory increase in body
temperature only occurs when circulating progesterone levels are significantly elevated, generally for more than two to three days (Barton and Wiesner, 1945; Cagnacci et al., 1992; Cargille et al., 1969; Davis and Fugo, 1945; Rothchild and Barnes, 1952). The intravenous injection of progesterone increases core temperature in rabbits (Nakayama et al., 1975), but not consistently in monkeys (Cunningham et al., 1975). However, intravenous injection of progesterone decreased the firing rate of pre-optic warm sensitive neurons and increased the firing rate of pre-optic cold sensitive neurons. These effects would result in an upward shift of the thermoregulatory set point as indicated by an increased regulated body temperature.

STATEMENT OF PURPOSE

The common purpose for this series of protocols was to provide much needed data regarding heat stress, heat strain and heat transfer in females during exercise, including exercise while clothed in chemical protective garments. The phase of the menstrual cycle was strictly documented during these studies so that the experiments were done in either early follicular or mid-luteal phases. Esophageal temperature was measured to document the change in regulated body temperature between the two menstrual cycle phases as well as to indicate heat storage during exercise. Sweating rate, heart rate and skin temperature responses were also measured.
METHODS

Twelve women participated in seven different experimental protocols. One subject was in all seven protocols; one subject was in six of the protocols; two subjects were in three protocols; and eight subjects were in one protocol each. The characteristics of the subjects for each of the seven protocols are shown in Table 1. Experiments were conducted when test subjects were not naturally acclimatized or artificially acclimated to the heat. Experiments were conducted at ambient temperatures between 30°C and 50°C at both low and high ambient water vapor pressures. The seven experimental protocols are briefly described in Table 2.

Prior to actual testing, peak or maximal aerobic power was assessed during cycling or treadmill walking in a temperate environment. This testing was essential to accurately assess the relative work intensity on all test days, and ensured similar conditions for each test subject.

Interviews were done to assure that each female volunteer had a normal menstrual cycle as defined by regular periodicity and was not taking oral contraceptives. To verify ovulatory menstrual cycles, daily basal body temperature (BBT) was recorded by each subject upon awakening. Oral temperature was measured at the same time each morning for at least five minutes using a clinical thermometer. Data from an entire menstrual cycle was collected and graphed prior to the study to determine whether BBT increased after ovulation (Kleitman and Ramsaroop, 1948). Although BBT is not a wholly sufficient method to predict ovulation time, higher BBT is closely correlated with the higher plasma progesterone concentration in the luteal phase of the menstrual cycle (Cargille et al. 1969). Consequently, elevated BBT in the luteal phase was an adequate post hoc method of determining that ovulation occurred and enabled the investigators to schedule experiments in the appropriate menstrual cycle phase. Testing in the mid-luteal phase was done on days when the resting core temperature was elevated (approximately days 19-22 which are temporally associated with elevated serum estradiol and progesterone concentrations). Testing in the follicular phase was done on days 3-6 (day 1 = first day of menstrual flow; low serum estradiol and progesterone concentrations), and in some experiments testing was done on days 10-12 (elevated serum estradiol and low serum progesterone concentrations). Prior to testing,
volunteers were thoroughly familiarized with all experimental techniques. On test days pre-experiment body weights were within 1% of the mean body weight measured during preliminary testing to avoid the possible effects of dehydration.

Upon arriving at the laboratory each morning, a 10 ml blood sample was taken in some protocols (6&7) for the measurement of progesterone and estradiol (RIA) to accurately define menstrual cycle phase. After this, the volunteer swallowed the esophageal probe for core temperature measurement. This esophageal probe was adjusted (by the volunteer) to heart level, based on an insertion distance of 25% of her height. Surface thermocouples were placed at eight skin sites area weighted to estimate mean skin temperature ($T_{sk}$, Nishi and Gagge, 1970) as:

$$
T_{sk} = 0.07 T_{forehead} + 0.175 T_{chest} + 0.175 T_{back} + 0.07 T_{upperarm} \\
+ 0.07 T_{forearm} + 0.05 T_{hand} + 0.19 T_{thigh} + 0.20 T_{calf}
$$

Whole body sweating was determined as the change in body weight from pre- to post-exercise. Metabolic heat production calculated from the oxygen utilized was measured by an automated method (SensorMedics™) at rest and during exercise. Heart rate was measured from the EKG. In the clothing study (Protocol 6) after instrumentation, each subject dressed in chemical protective clothing (modified MOPP 4: BDU, overgarment, overboots, hood, gloves, mask was open for metabolic rate measurements and to accommodate the esophageal thermocouple). After complete instrumentation and dressing, rest began. After equilibration with the environment (15-30 min), cycle or treadmill exercise began and continued for 10-75 minutes depending on the specific protocol (Table 2).

Subject Safety

All of the procedures in this study fell within the framework, restrictions and safety limitations of the USARIEM Type Protocol for Human Research Studies in the areas
of Thermal, Hypoxic and Operational Stress, Exercise, Nutrition and Military Performance, which was in effect at the time when the research was done.¹

STATISTICAL ANALYSES

All data (core and surface temperatures, heart rate, blood flows and sweating rate) were analyzed by analysis of variance techniques with repeated measures. Whenever a significant F ratio occurred (P ≤ 0.05), Tukey's critical difference was used for post hoc analysis.

Approved 14 Dec 1994. The type protocol provides information and explanations about conditions, standards and safeguards, in order to serve as an encompassing framework for specific in-house studies in its general subject area. It is to be used as a reference to facilitate the understanding and review of specific study protocols which conform to its provisions, and thus do not exceed the degree of risk, and safety limits herein stipulated (reference para 18, USAMRDC Reg 70-25).
Table 1: Mean ± SD characteristics for the subjects in the seven experimental protocols.

<table>
<thead>
<tr>
<th>PROTOCOL DESCRIPTION</th>
<th>Age (yr)</th>
<th>Ht (m)</th>
<th>Mass (kg)</th>
<th>SA (m²)</th>
<th>VO₂ (L·min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1; Tₐ=35°C, T_d=13°C; n=4</td>
<td>29.5 (4.2)</td>
<td>1.66 (0.08)</td>
<td>59.2 (7.4)</td>
<td>1.65 (0.14)</td>
<td>2.50 (0.54)</td>
</tr>
<tr>
<td>2; Tₐ=50°C, T_d=12°C; n=5</td>
<td>27.2 (4.2)</td>
<td>1.67 (0.05)</td>
<td>63.2 (3.4)</td>
<td>1.71 (0.05)</td>
<td>2.62 (0.07)</td>
</tr>
<tr>
<td>3; Tₐ=50°C, T_d=12°C; n=5</td>
<td>27.2 (4.2)</td>
<td>1.67 (0.05)</td>
<td>63.2 (3.4)</td>
<td>1.71 (0.05)</td>
<td>2.62 (0.07)</td>
</tr>
<tr>
<td>4; Tₐ=35°C, T_d=11°C; n=3</td>
<td>27.7 (5.9)</td>
<td>1.69 (0.05)</td>
<td>63.7 (4.5)</td>
<td>1.73 (0.05)</td>
<td>2.63 (0.08)</td>
</tr>
<tr>
<td>5; Tₐ=35°C, T_d=11°C; n=5</td>
<td>27.0 (4.2)</td>
<td>1.68 (0.05)</td>
<td>66.0 (7.4)</td>
<td>1.75 (0.10)</td>
<td>2.87 (0.54)</td>
</tr>
<tr>
<td>6; Tₐ=30°C, T_d=12°C; n=5</td>
<td>28.0 (11.0)</td>
<td>1.69 (0.05)</td>
<td>60.0 (12.0)</td>
<td>1.68 (0.17)</td>
<td>2.57 (0.25)</td>
</tr>
<tr>
<td>7; Tₐ=38°C, T_d=29°C; n=3</td>
<td>32.5 (9.7)</td>
<td>1.65 (0.07)</td>
<td>66.7 (3.4)</td>
<td>1.74 (0.08)</td>
<td>2.13 (0.25)</td>
</tr>
<tr>
<td>ALL PROTOCOLS, MEAN±SD</td>
<td>28.4 (6.2)</td>
<td>1.67 (0.06)</td>
<td>63.1 (5.9)</td>
<td>1.71 (0.09)</td>
<td>2.57 (0.26)</td>
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Table 2: Description of the seven protocols.

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>Ambient Temperature (°C)</th>
<th>Dew-point Temperature (°C)</th>
<th>Target Exercise Intensity (%VO₂)</th>
<th>Target Duration (min)</th>
</tr>
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<tbody>
<tr>
<td>1; Exercise</td>
<td>35</td>
<td>13</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>2; Rest</td>
<td>50</td>
<td>20</td>
<td>rest</td>
<td>180</td>
</tr>
<tr>
<td>3; Exercise</td>
<td>50</td>
<td>12</td>
<td>80</td>
<td>10</td>
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<tr>
<td>4; Exercise</td>
<td>35</td>
<td>12</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>5; Exercise</td>
<td>35</td>
<td>11</td>
<td>80</td>
<td>30</td>
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<td>6; Exercise</td>
<td>30</td>
<td>12</td>
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<td>75</td>
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<tr>
<td>7; Exercise</td>
<td>38</td>
<td>29</td>
<td>40-50</td>
<td>75</td>
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RESULTS AND DISCUSSION

Esophageal temperature at rest and during moderate exercise (steady-state) for four subjects tested in the early follicular and mid-luteal phases of the menstrual cycle (Protocol 1) is shown in Figure 1. Data are shown for experiments run in both the early morning and the late afternoon. These data show significantly increased resting and exercise esophageal temperatures (p<0.05) during the mid-luteal phase of the menstrual cycle compared to the early follicular phase of the menstrual cycle. The change in esophageal temperature from rest to exercise was similar in all four experiments averaging 0.8°C. Figure 1 also shows the circadian elevation in core temperature which occurs in the late afternoon or early evening (pm experiments) compared to the early morning hours (am experiments).

Esophageal temperature during approximately three hours of resting heat exposure of five subjects in the early follicular and mid-luteal phases of the menstrual cycle in very hot environmental conditions (50°C; Protocol 2) is shown in Figure 2. These data show the statistically significant mid-luteal phase elevation in esophageal temperature at zero time which is maintained over the three hour heating period. The increase in esophageal temperature in these experiments was similar between the early follicular and mid-luteal exposures as this was part of the experimental design. Figure 3 shows esophageal temperature during heavy exercise in the same five subjects from Figure 2 in both the early follicular and mid-luteal phases of the menstrual cycle in very hot environmental conditions (Protocol 3). Again, the statistically significant mid-luteal phase elevation in esophageal temperature is apparent during the entire, albeit short, exercise period. The exercise-induced increase in esophageal temperature was similar between experiments which was the intent of the experimental design.

Esophageal temperature of three women during moderate exercise in the early follicular and mid-luteal phases of the menstrual cycle in hot environmental conditions (Protocol 4) is shown in Figure 4. These data show a statistically significant elevation in both resting and exercise core temperature in the luteal phase experiments. Again, the increase in esophageal temperature during exercise is similar for the two experiments. Figure 5 shows esophageal temperature during heavy exercise of five women in the early follicular and mid-luteal phases of the menstrual cycle in hot
environmental conditions (35°C; Protocol 5). Resting esophageal temperature is significantly higher in the luteal phase experiments. The exercise period in these experiments was approximately thirty minutes with significant heat storage as indicated by the increased esophageal temperature. Esophageal temperature remained significantly higher throughout exercise in the luteal phase compared to the follicular phase.

Esophageal temperature during moderate exercise for four women wearing chemical protective clothing in the early follicular and mid-luteal phases of the menstrual cycle in warm environmental conditions (Protocol 6) is shown in Figure 6. Resting and exercise esophageal temperatures are higher in the mid-luteal phase experiments. Even under these conditions where heat exchange with the environment is severely limited by the clothing layers worn, the difference in exercise esophageal temperature between the menstrual cycle phases studied is apparent throughout the exercise period. Data are also presented from the USARIEM Heat Strain Model predicted from data collected from male subjects in an identical scenario. It is evident that the data from Protocol 6 of these experiments fit the prediction line rather well. In Protocol 7, which simulated the conditions inside the protective clothing, the esophageal temperature at rest in this hot, humid environment averaged 37.07±0.36°C and 37.27±0.32°C for the early follicular and mid-luteal phases, respectively. During exercise, esophageal temperature increased between 1.00 and 1.65°C depending on the duration of the experiment. This increase in esophageal temperature was consistent within a specific subject in all tests. These data represent only three subjects and are part of an ongoing study.

In all figures, the separation of temperatures between the early follicular and mid-luteal phases is apparent. The significant difference in resting core (esophageal) temperature in these experiments is maintained during exercise during both cycling and walking exercise, in both hot and very hot ambient temperatures, in both humid and dry conditions, and with heavy or light clothing. This difference is readily apparent and statistically significant with as few a three test subjects in some of the experimental protocols.
The elevation in resting core temperature was the *a priori* criterion for the luteal phase experiments. Circulating estradiol and progesterone, when measured (Protocol 6&7), were elevated significantly in the luteal phase experiments in those subjects with elevated resting esophageal temperatures. The average values for the early follicular and mid-luteal for estradiol were 46.6 (18.6) pg/ml and 128.7 (59.2) pg/ml and for progesterone were 0.7 (0.2) ng/ml and 17.4 (5.7) ng/ml for nine subjects in two protocols with elevated mid-luteal phase core temperature. Resting core temperature was not elevated without an increase in progesterone concentration, although it is possible that progesterone could be elevated before an increased core temperature occurs (Barton and Wiesner, 1945; Davis and Fugo, 1945; Rothchild and Barnes, 1952).

Whole body sweating rates were not different between early follicular and mid-luteal phases of the menstrual cycle in any of the protocols. In Protocol 1, sweating rates were 12.1±3.6 and 10.8±1.3 g/min in the early follicular and mid-luteal experiments. At rest in 50°C (Protocol 2), sweating rate averaged 7.4 (1.3) and 6.5 (2.8) g/min in early follicular and mid-luteal phases. During heavy exercise at 50°C (Protocol 3), sweating rates averaged 16.9 (3.6) and 17.2 (2.8) g/min, respectively. In Protocol 4, sweating rates averaged 20.6 (5.6) and 19.3 (4.2) g/min, respectively during moderate exercise at 35°C. During heavy exercise at 35°C (Protocol 5), sweating rates averaged 20.6 (5.6) and 19.3 (4.2) g/min, respectively. During Protocol 6 at 30°C during uncompensable heat stress in heavy clothing, sweating rates averaged 13.2 (4.3) and 13.3 (4.7) g/min in the early follicular and mid-luteal phases of the menstrual cycle. During uncompensable heat stress at 38°C (Protocol 7), sweating rates averaged 11.3±2.6 and 11.8±1.9 g/min, respectively. In some of these protocols, total sweat loss was at a rate of 1-2 L·h⁻¹. In Protocols 2, 6 and 7, the lower sweating rates are a result of the experimental conditions. These specific sweating rates can be explained by the fact that the subjects were resting, not exercising, in Protocol 2 and there was limited evaporative potential due to the clothing layers or the high water vapor pressure in the environmental chamber during Protocols 6 and 7.

Heart rates were higher (p<0.05) in the mid-luteal phase at rest in Protocol 1 and after three hours of heat exposure in Protocol 2. In all other experiments, heart rate
was not different between mid-luteal and early follicular experiments. These data are shown in Table 3.

The calculation of a mean weighted skin or surface temperature was accomplished in these studies with mixed results. These data are incorporated in Figures 1-6. In the hot, dry experiments (Protocols 2 and 3), skin temperature was 0.3 to 0.5 °C higher during exposure in the mid-luteal phase compared to the early follicular phase, a statistically significant difference. However, in other experiments, for example the clothing studies or studies at 35°C, skin temperatures were not different between the menstrual cycle phases studied with the exception being the skin temperature response during rest in Protocol 5. No attempt was made in these studies to examine temporal changes in the local skin temperatures during exercise or rest in hot environments. At an ambient temperature of 35°C, skin temperature remains close to 35°C throughout exposure. This ambient condition was used by design to maintain the surface temperature during exercise and to "force" internal (esophageal temperature in these experiments) to "drive" the heat loss mechanisms. Additional experiments, conducted in the thermoneutral zone for vasomotor regulation, are necessary to fully understand what, if any, impact the changing hormonal environment may have on the control of skin temperature during exercise. In essence, the skin temperature was driven by the ambient conditions used (Gonzalez et al., 1978). In some conditions, the increased skin temperature response associated with the reproductive hormonal changes of the luteal phase was masked. These results are consistent with earlier reports (Kenshalo et al., 1966).

As stated in the methods, some experiments (in Protocols 6&7) were conducted on days 10-12 of the menstrual cycle. During this late follicular phase, serum estradiol concentrations were high and progesterone levels were low. This combination was different from the early follicular experiments where both estradiol and progesterone concentrations were low, and was different from the mid-luteal experiments where both progesterone and estradiol were elevated. The resting esophageal temperature in these experiments was approximately 0.3°C lower than that observed in the early follicular phase, and 0.6 to 0.8°C lower than the mid-luteal phase resting esophageal temperatures. Systemic estrogen treatment was shown to decrease body temperature (Magallon and Masters, 1950), and estrogen replacement therapy decreased both core
temperature and the set-point temperature for thermoregulatory effector onset in post-menopausal women (Tankersley et al. 1992). Furthermore, evidence from pre-optic hypothalamic tissue slices suggests that estradiol increases the firing rate of warm sensitive neurons (Silva and Boulant, 1986). Since neuronal models for thermoregulation suggest that heat loss responses are facilitated by warm sensitive neurons (Boulant, 1980; Hammel, 1965), enhanced firing rates after estradiol would increase heat loss mechanisms and lower the regulated core temperature.

Heart rate, sweating rates and mean skin temperatures were not different in the late follicular (pre-ovulatory) experiments from those observed in either the early follicular or the mid-luteal phase experiments. It should be noted however that the skin temperature responses were affected by the environmental and clothing conditions of the protocols, and different skin temperature responses might be observed under more temperate environmental conditions in the late follicular phase.

The implications concerning resting core temperature are clear. Resting core temperature in a women with the hormonal patterns of a "normal" menstrual cycle can range up to 0.8°C during a 25 to 35 day cycle. If, for example, a late follicular experiment under the conditions of high circulating estradiol (an effect lowering the core temperature ~0.3°C) was compared to a mid-luteal experiment under the conditions of high circulating estradiol and progesterone (an effect raising the core temperature ~0.5°C) such great variability in core temperature measurements could mask the effect of, or falsely indicate an effect of, a treatment.

A summary of what is currently known and thought regarding thermoregulation in humans is shown in Figure 7. The control of body temperature is dependent on peripheral and central inputs depicted on the left side of the figure as internal temperature, skin temperature, exercise or baroreflexes. These inputs are integrated centrally resulting in the appropriate response shown in the right side of the figure. For example, shivering is initiated to produce heat, vasoconstriction to conserve heat, and sweating and vasodilation to dissipate heat. Various modifiers of this thermoregulatory concept exist in this human model of temperature regulation. These are shown in the figure and include aerobic fitness, acclimation status, time of day,
Figure 1: Mean ± SD esophageal temperature at rest and during exercise for four subjects tested in the early follicular and mid-luteal phases of the menstrual cycle (Protocol 1). Data are further divided into early morning and late afternoon experiments at 35°C. Mean skin temperatures are shown above the bars.
Figure 2: Mean ± SD esophageal temperature at selected time periods over approximately 160 minutes of passive heating for five subjects in the early follicular and mid-luteal phases of the menstrual cycle at 50°C (Protocol 2). Mean skin temperatures are shown above the bars.
Figure 3: Mean ± SD esophageal temperature during a short bout of heavy exercise for five subjects in the early follicular and mid-luteal phases of the menstrual cycle at 50°C (Protocol 3). Mean skin temperatures are shown above the bars.
Figure 4: Mean ± SD esophageal temperature during a period of moderate exercise for three women in the early follicular and mid-luteal phases of the menstrual cycle at 35°C (Protocol 4). Mean skin temperatures are shown on the figure.
Figure 5: Mean ± SD esophageal temperature during a period of heavy exercise for five women in the early follicular and mid-luteal phases of the menstrual cycle at 35°C (Protocol 5). Mean skin temperatures are shown on the figure.
Figure 6: Mean ± SD core temperature during moderate exercise for four women wearing chemical protective clothing in the early follicular and mid-luteal phases of the menstrual cycle at 30°C (Protocol 6). Data from the USARIEM Heat Strain Model for unacclimated men under the same conditions are also shown. Mean skin temperatures are shown.
Table 3: Mean ± SD heart rate at rest and during exercise or heat exposure during the seven protocols.

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>Early-follicular phase resting heart rate</th>
<th>Mid-luteal phase resting heart rate</th>
<th>Early-follicular phase exposure heart rate</th>
<th>Mid-luteal phase exposure heart rate</th>
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<tbody>
<tr>
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<td>56 (3)</td>
<td>67 (11)</td>
<td>144 (16)</td>
<td>147 (11)</td>
</tr>
<tr>
<td>2</td>
<td>-----</td>
<td>-----</td>
<td>83 (8)</td>
<td>92 (8)</td>
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<tr>
<td>3</td>
<td>-----</td>
<td>-----</td>
<td>166 (15)</td>
<td>165 (11)</td>
</tr>
<tr>
<td>4</td>
<td>68 (3)</td>
<td>65 (3)</td>
<td>145 (11)</td>
<td>146 (12)</td>
</tr>
<tr>
<td>5</td>
<td>67 (3)</td>
<td>70 (4)</td>
<td>156 (10)</td>
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<td>6</td>
<td>74 (3)</td>
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<tr>
<td>7</td>
<td>75 (3)</td>
<td>73 (6)</td>
<td>163 (9)</td>
<td>162 (5)</td>
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</tbody>
</table>
Figure 7: Summary of thermoregulation with modifiers (hormonal status).
and hydration status. The data presented in this report adds menstrual cycle phase to these modifiers.

**CONCLUSIONS**

In summary, there is little support for the theory that gender affects thermoregulatory ability if *all* factors that independently and collectively affect thermoregulation, such as maximal aerobic power, state of training, hydration status or heat acclimation are controlled. This report adds to that list the altered core temperature associated with elevated serum progesterone which occurs in the mid-luteal phase of the menstrual cycle. The protocols described in this report were conducted on unacclimated women in various combinations of exercise and heat stress. All studies were done matching the exercise intensity from test to test and from subject to subject. The majority of women studied in these protocols were fit and active and consequently should reflect the fitness characteristics of women in the military. In the clothing study, the prediction of responses for men unacclimated to the heat fit well with the data from the female subjects. No data are presented here for women acclimated to the heat in any of the protocols, although the women were "active" which confers some degree of heat acclimation. These conclusions are based only on the data presented in this report.


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