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Influence of Menstrual Cycle and Oral Contraceptives on Tolerance to  
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## ORIGINAL ARTICLE

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## Influence of menstrual cycle and oral contraceptives on tolerance to uncompensable heat stress

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**Abstract** In this study we examined the influence of menstrual cycle phase and oral contraceptive use on thermoregulation and tolerance during uncompensable heat stress. Eighteen women (18–35 years), who differed only with respect to oral contraceptive use ( $n = 9$ ) or non-use ( $n = 9$ ), performed light intermittent exercise at 40°C and 30% relative humidity while wearing nuclear, biological and chemical protective clothing. Their responses were compared during the early follicular (EF, days 2–5) and mid-luteal (ML, days 19–22) phases of the menstrual cycle. Since oral contraceptives are presumed to inhibit ovulation, a quasi-early follicular (q-EF) and quasi-mid-luteal (q-ML) phase was assumed for the users. Estradiol and progesterone measurements verified that all subjects were tested during the desired phases of the menstrual cycle. Results demonstrated that rectal temperature ( $T_{re}$ ) was elevated in ML compared with EF among the non-users at the beginning and throughout the heat-stress trial. For the users,  $T_{re}$  was higher in q-ML compared with q-EF at the beginning, and for 75 min of the heat-stress exposure. Tolerance times were significantly longer during EF [128.1 (13.4) min, mean (SD)] 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 both the q-EF [113.0 (5.8) min] and q-ML [116.8 (11.2) min] phases and did not differ from those of the

non-users. It was concluded that oral contraceptive use had little or no influence on tolerance to uncompensable heat stress, whereas tolerance was increased during EF for non-users of oral contraceptives.

**Key words** Protective clothing · Tolerance time · Thermoregulation · Rectal temperature

### Introduction

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. A thermal environment of compensable heat stress can become one of uncompensable heat stress by wearing clothing that restricts evaporative heat loss, and/or by increasing the ambient temperature or water vapour pressure (Kraning and Gonzalez 1991). During uncompensable heat stress the body's evaporative cooling requirement exceeds the maximum cooling capacity of the environment. As a result, individuals are unable to achieve thermal balance and will continue to store heat until exhaustion occurs (Montain et al. 1994).

A number of investigators have attempted to quantify the thermoregulatory strain experienced 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). However, there has been comparatively little research done to represent the physiological strain experienced by women under similar conditions. It has been well established, under conditions of compensable heat stress, that the menstrual cycle affects temperature regulation. 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 1985a, b; Horvath and Drinkwater 1982; Kolka and Stephenson 1989). Likewise, the core temperature thresholds for the onset of

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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 1985a, b; Kolka and Stephenson 1989). It is not known whether the same effects hold true under conditions of uncompensable heat stress.

The results from four subjects by Kolka and Stephenson (1997) suggest that at rest, and during 60 min of heavy exercise, core temperature is higher in the mid-luteal (ML) phase compared with the early follicular (EF) phase during uncompensable heat stress. Subjects in this study wore nuclear, biological and chemical (NBC) protective clothing, a clothing ensemble which severely reduces both evaporative and non-evaporative heat exchanges, to create an environment of uncompensable heat stress. Kolka and Stephenson (1997) found that despite the elevation in core temperature during the ML phase, tolerance times were similar among phases. Whether these results could be extrapolated to exercise of longer duration is not known. Studies performed on healthy young men wearing the NBC clothing have shown that factors which lower initial core temperature, such as fluid replacement (Cheung and McLellan 1998), heat acclimation (Aoyagi et al. 1994, 1995) and aerobic training (Aoyagi et al. 1994), exert a greater effect on heat tolerance during light exercise of long duration compared with heavy exercise of short duration (<60 min). Thus, it is conceivable that the luteal-phase-related elevation in core temperature may impair tolerance to longer-duration exercise during uncompensable heat stress.

It is also not known how oral contraceptive (OC) use affects temperature regulation during uncompensable heat stress. Recent investigations have shown that, similar to non-OC users, resting core temperature is higher during the quasi-luteal phase compared with the quasi-early-follicular (q-EF) phase (Charkoudian and Johnson 1997; Grucza et al. 1993, 1997; Rogers and Baker 1997). The phase-related elevation in core temperature is maintained during exercise in comfortable (Grucza et al. 1993; Rogers and Baker 1997) and warm (Martin and Buono 1997) environments, and during passive heat (Charkoudian and Johnson 1997) and passive cold (Grucza et al. 1997) exposure. The possible influence of OC use on thermoregulation during uncompensable heat stress has not been investigated.

The purpose of this study, therefore, was to quantify the heat strain and the physical work tolerance times experienced by female users and non-users of OC during uncompensable heat stress. It was hypothesised that both groups of women would have a decreased heat tolerance during the luteal phase of their menstrual cycle.

## Methods

### Subjects

Following approval from the Human Ethics Committees of the Defence and Civil Institute of Environmental Medicine and the

University of Toronto, 18 recreationally active, non-heat-acclimated females volunteered for the study. Participation in the experiment was subject to medical approval and to verbal confirmation, based on cycle length, of a regular menstrual cycle. The subjects were divided into two equal-sized groups that differed only with respect to OC use or non-use. Subject characteristics for the two groups (users: U, non-users: NU) are described in Table 1. Body fatness was estimated from skinfold measurements by using a gender-specific regression equation developed from hydrostatic measurements of body density (Forsyth et al. 1984), and body surface area was calculated according to DuBois and DuBois (1916). All of the women in U had been taking OC for a minimum of 3 months prior to involvement in the experiment. Seven of the nine U subjects were taking a monophasic contraceptive (the dose of the synthetic estrogen and progestin components remains constant during the 21-day pill-ingestion period of the menstrual cycle). The other two women were using a triphasic formulation (the dosages of the estrogen and progestin or both are altered during the 21-day pill-ingestion period of the menstrual cycle). The OC used by each subject in this group and the synthetic hormone components of the contraceptive are shown in Table 2. None of the women in NU had used OC in the past year. 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 early June, when outdoor temperatures rarely exceed 20°C, to limit heat acclimation through casual exposure to high ambient temperatures.

### Determination of peak aerobic power ( $\dot{V}O_{2peak}$ )

$\dot{V}O_{2peak}$  was determined on a motor-driven treadmill, using open-circuit spirometry. Subjects began running on a level treadmill at a

**Table 1** Subject characteristics for users ( $n = 9$ ) and non-users ( $n = 9$ ) of oral contraceptives. Values are the mean (SE). (BSA Body surface area,  $\dot{V}O_{2peak}$  peak oxygen uptake,  $HR_{peak}$  peak heart rate)

Characteristic	Non-users	Users
Age (years)	23.3 (1.9)	23.4 (0.7)
Height (m)	1.65 (0.03)	1.66 (0.03)
Mass (kg)	60.4 (3.0)	64.5 (1.8)
Body fat (%)	19.2 (1.4)	22.3 (1.6)
BSA (m <sup>2</sup> )	1.66 (0.05)	1.71 (0.04)
$\dot{V}O_{2peak}$ (ml · kg <sup>-1</sup> · min <sup>-1</sup> )	44.78 (2.55)	43.63 (2.70)
$HR_{peak}$ (beats · min <sup>-1</sup> )	191.8 (2.6)	194.9 (2.6)

**Table 2** Synthetic estrogen and progestin content and the dose regimen of the oral contraceptives used by subjects in this study, where  $n$  is the number of subjects using each contraceptive. Day 1 is the 1st day that the subjects begin a new cycle of pills. (EE ethinyl estradiol, LNG levonorgestrel, NET norethindrone, DG desogestrel)

Oral contraceptive	$n$	Pill	Estrogen (mg)	Progesterone (mg)
Minovral	1	1-21	0.030 EE	0.15 LNG
Marvelon	5	1-21	0.035 EE	0.03 DG
Ortho-cept	1	1-21	0.035 EE	0.03 DG
Synphasic	1	1-7	0.035 EE	0.5 NET
		8-16	0.035 EE	1.0 NET
		17-21	0.035 EE	0.5 NET
Triquilar	1	1-6	0.030 EE	0.05 LNG
		7-11	0.040 EE	0.075 LNG
		12-21	0.030 EE	0.125 LNG

self-selected pace of  $8.0\text{--}12.0 \text{ km} \cdot \text{h}^{-1}$  ( $2.22\text{--}3.33 \text{ m} \cdot \text{s}^{-1}$ ), depending upon the subject's aerobic fitness. After 3 min, the treadmill grade was increased by  $1\% \cdot \text{min}^{-1}$  until exhaustion.  $\dot{V}O_{2\text{peak}}$  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 Electro PE3000/Polar Vantage XL). The highest observed value was considered as the individual's peak heart rate ( $\text{HR}_{\text{peak}}$ ).

#### Experimental protocol

A minimum of 24 h following the determination of  $\dot{V}O_{2\text{peak}}$ , subjects were familiarized to light intermittent exercise in the heat ( $40^\circ\text{C}$ , 30% relative humidity, wind speed less than  $0.1 \text{ m} \cdot \text{s}^{-1}$ ) while wearing the Canadian Forces NBC protective clothing ensemble. Subjects alternated between 15 min of walking on a level treadmill at  $4 \text{ km} \cdot \text{h}^{-1}$  ( $1.11 \text{ m} \cdot \text{s}^{-1}$ ) and 15 min of seated rest, were allowed to drink one canteen (approximately 1 l) of water, and continued for a maximum exposure of 300 min in the climatic chamber or until: rectal temperature ( $T_{\text{re}}$ ) reached  $39.3^\circ\text{C}$ ;  $\text{HR} \geq 95\%$  peak for 3 min; dizziness or nausea precluded further exercise; the subject asked to be removed from the chamber; or based on the above criteria, the investigator or technician decided to end the trial. Subjects were then required to perform two trials during the menstrual cycle corresponding to the EF phase, days 2–5, and the ML phase, days 19–22. Since OC use is presumed to prevent ovulation, a q-EF and quasi-mid-luteal (q-ML) phase was assumed for the U subjects. The order of exposures was randomly assigned for all subjects to minimize the effects of training, acclimation and habituation on the dependent measures. The exercise protocol, experimental conditions and the end-point criteria were identical to those used during the familiarization session. All tests were performed at the same time of day (commencing at 8:00 a.m.) to minimize the influence of circadian rhythm on body temperature. Subjects were asked to eat a light breakfast before arriving at the laboratory on the morning of each trial. Subjects were also asked to refrain from heavy exercise and alcohol consumption on the day before, and caffeine for 12 h before each trial.

#### Clothing ensemble

The NBC protective clothing ensemble consisted of underwear, shorts, T-shirt, jog bra, socks, lightweight combat clothing and running shoes, impermeable rubber gloves, overboots, a mask with a respirator, and a semi-permeable NBC overgarment. The total thermal resistance of the NBC ensemble, determined using a heated copper manikin, was  $0.291 \text{ m}^2 \cdot ^\circ\text{C} \cdot \text{W}^{-1}$  (1.88 clo), and the Woodcock vapour permeability coefficient, determined with a completely wetted manikin, was 0.33 (Gonzalez et al. 1993).

#### Determination of menstrual cycle phase

Subjects reported to the investigator on day 1 of their cycle (i.e., the first day of menstrual flow). For NU, testing sessions for that cycle were scheduled to correspond to each of the desired phases (i.e., EF, days 2–5; and ML, days 19–22). For U, day 1 of their cycle (i.e., the 1st day of menstrual flow) usually corresponded to the 2nd or 3rd day during the 7-day period when no pill was ingested (all of these subjects were taking a 21-day OC). Testing sessions were scheduled to coincide with the same time frames as outlined for the NU subjects (i.e. q-EF, days 2–5; and q-ML, days 19–22). Plasma progesterone and estrogen levels were measured to verify that each subject was being tested in the correct phase. According to Hatcher et al. (1988), a progesterone level of more than  $3 \text{ ng} \cdot \text{ml}^{-1}$  ( $9.5 \text{ nmol} \cdot \text{l}^{-1}$ ) is good evidence that ovulation has occurred, and peak progesterone levels should reach between 8 and  $10 \text{ ng} \cdot \text{ml}^{-1}$  ( $25.4\text{--}31.8 \text{ nmol} \cdot \text{l}^{-1}$ ) during the ML phase. Data were discarded and trials were repeated if progesterone levels were not elevated during the ML phase for the NU subjects (indicating that ovulation had not occurred) or if progesterone levels were elevated during the

q-ML phase for the U subjects (indicating that ovulation had occurred).

#### Dressing and weighing procedures

Upon arrival at the laboratory, subjects changed into their shorts and T-shirt, and inserted a rectal probe to a depth of 15 cm beyond their anal sphincter. Subjects were requested to stand upright for a period of 10 min, and then a 5-ml sample of blood was drawn to allow the determination of hemoglobin, hematocrit, and estradiol and progesterone levels. Following this, subjects undressed (leaving the rectal thermistor in place) and their nude weight was recorded using an electronic scale that is sensitive to the nearest 10 g (Model 921, ElectroScale). Subjects put their undergarments, shorts and T-shirt back on, were fitted with the skin thermistors and HR monitor, donned the rest of the clothing and then their dressed weight was recorded. Upon entry into the climatic chamber, subjects were connected to the data acquisition system and then commenced walking on the treadmill. Gas exchange was measured for 3–4 min during the last portion of each 15-min walk/rest period. HR was recorded every 5 min. Since it was easiest to drink during the rest periods, subjects were allowed during these times to drink water ad libitum to a total volume of 1 l during each trial. Upon completion of each trial, the subjects' dressed weight was recorded within 1 min after exit from the chamber; nude weight was recorded within 5 min, after undressing and towel drying.

#### Physiological measurements

A computerized data acquisition system (Hewlett Packard 3497A data acquisition/control unit, 236-9000 computer, and 2934A printer) processed data from the  $T_{\text{re}}$  and skin temperature sensors at 1-min intervals.  $T_{\text{re}}$  was measured using a flexible vinyl-covered probe (Pharmaseal 400 Series rectal/esophageal probe, Baxter Healthcare). Skin temperatures were measured at 12 sites, using epoxy-covered thermistors (thermistor bead 44004, Yellow Springs Instruments). The mean skin temperature ( $\bar{T}_{\text{sk}}$ ) was calculated by weighting factors reflecting regional proportions of the total body surface area, according to the equation of Hody (1973). A transmitter/telemetry unit (Polar Electro PE3000/Polar Vantage XL) was used to monitor HR throughout the course of each trial. The transmitter was clipped to an elasticized 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, which was recorded manually every 5 min.

#### Metabolic rate and gas exchange

Open-circuit spirometry was used to determine  $\dot{V}O_2$  and carbon dioxide output from a 2-min average during the latter portion of every 15-min walk or rest period. An adapter attached to the exhaust valve of the respirator (for NBC clothing) directed expired gases into a 5-l mixing box and then through a ventilation module (Alpha Technologies VMM 110 Series). An aliquot of dried expired gases was pumped via a sampling line to an oxygen and carbon dioxide analyzer (Amtrek Instruments S-3A and CD-3A, respectively). The gas analyzers were calibrated using precision-analyzed 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),  $\dot{V}O_2$ , carbon dioxide output and the respiratory gas exchange ratio ( $R$ ) were calculated and printed on-line every 30 s using appropriate software. The rate of metabolic heat production ( $M$ ) was determined according to the equation of Nishi (1981).

#### Sweat production and evaporation

Differences in nude and dressed weights, before and after each trial, were corrected for fluid intake, and for respiratory and metabolic

weight loss. Respiratory water loss was calculated as in Mitchell et al. (1972). Weight loss due to gas exchange was estimated using the equation of Snellen (1966). 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.

### Blood analyses

Hemoglobin was determined in duplicate by spectrophotometry (Sigma Diagnostics Drabkin's Solution, 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 at 1500 g; plasma was removed and stored at  $-20^{\circ}\text{C}$  for later analysis of estradiol and progesterone. Estradiol and progesterone levels were determined in duplicate by radioimmunoassay (RIA; DSL-4800 Ultra-Sensitive Estradiol RIA Kit, and DSL-3900 ACTIVE Progesterone Coated-Tube RIA Kit, respectively, from Diagnostics Systems Laboratories). To reduce the error due to interassay variability, all samples for a given subject were measured using the same RIA kit.

### Statistical analyses

Data are presented as the mean (SE). A two-factor (menstrual cycle phase and time) repeated measures analysis of variance (ANOVA) with a grouping factor was used to compare the changes in  $T_{re}$ ,  $\bar{T}_{sk}$ , HR and gas exchange responses during the trials within and between groups. A one-factor (menstrual cycle phase) repeated measures ANOVA with a grouping factor was used to analyze differences in sweat rate, rate of evaporation, evaporative efficiency, and tolerance time. To correct for the violation of the sphericity assumption with the repeated factors, a Huynh-Feldt correction was applied to the  $F$ -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 level of statistical significance was set at  $P < 0.05$ .

## Results

### Subjects

There were no statistically significant differences in the subject characteristics presented in Table 1.

### Blood analyses

The mean plasma progesterone and plasma estradiol levels are presented in Table 3. Blood could not be obtained from two of the subjects in U. Hormonal analyses demonstrated that ovulation was inhibited in all of the remaining subjects using OC. Mean plasma progesterone was less than  $3 \text{ nmol} \cdot \text{l}^{-1}$  during both the q-EF and the q-ML phases in this group. Furthermore, the mean plasma progesterone levels observed in the q-EF and the q-ML phases were similar to those measured in the EF phase of the NU group. For the NU, mean progesterone levels were significantly elevated during ML compared with EF. Mean plasma progesterone was approximately  $22 \text{ nmol} \cdot \text{l}^{-1}$  in this group of subjects, indicating that ovulation had occurred.

**Table 3** Plasma progesterone and plasma estradiol in users ( $n = 7$ ) and non-users ( $n = 9$ ) of oral contraceptives prior to uncompensable heat stress for the early follicular (EF) and mid-luteal (ML) phases of the menstrual cycle. A quasi-early follicular (q-EF) and quasi-mid-luteal (q-ML) phase was assumed for the users. Values are the mean (SE)

	Users		Non-users	
	EF	ML	q-EF	q-ML
Progesterone ( $\text{nmol} \cdot \text{l}^{-1}$ )	1.68 (0.24)	21.86*† (5.02)	1.92 (0.35)	2.00 (0.28)
Estradiol ( $\text{nmol} \cdot \text{l}^{-1}$ )	0.074 (0.003)	0.154*† (0.013)	0.048 (0.010)	0.025** (0.004)

\* Significantly different from EF

\*\* Significantly different from q-EF

† Significantly different from q-EF and q-ML

Hormonal analyses also revealed that, for the U, mean plasma estradiol was significantly higher in the q-EF phase compared with the q-ML phase. Plasma estradiol declined throughout the 21-day pill cycle and then began to rise during the pill-free week. The concentration of plasma estradiol during the q-EF phase of U was similar to those values measured during the EF phase among NU. For the NU, mean plasma estradiol was significantly higher during ML compared with EF.

The values for hemoglobin and hematocrit, determined prior to each trial, did not differ among phases or between groups in either heat stress condition. Mean hemoglobin values ranged from  $14.1$  to  $15.0 \text{ g} \cdot \text{dl}^{-1}$ , and mean hematocrit values ranged from  $39.5$  to  $41.4\%$ .

### Indices of heat strain

#### Tolerance time

Mean tolerance times and reasons for trial termination are shown in Table 4. Among the NU, mean tolerance

**Table 4** Tolerance time and reason for test termination during uncompensable heat stress in users ( $n = 9$ ) and non-users ( $n = 9$ ) of oral contraceptives for the EF and ML phases of the menstrual cycle. A q-EF and q-ML phase was assumed for the users. Values for the tolerance times are the mean (SE), with range observations in brackets. The reason for test termination is presented as the number of subjects for rectal temperature ( $T_{re}$ ;  $39.3^{\circ}\text{C}$ ); heart rate ( $\text{HR} \geq 95\% \text{ HR}_{\text{peak}}$  for 3 min); subject's volition (SV); time limit (TL; 300 min)

	Non-users		Users	
	EF	ML	q-EF	q-ML
Tolerance time (min)	128.1 (13.4) [90–225]	107.4* (8.6) [85–169]	113.0 (5.8) [90–135]	116.8 (11.2) [75–187]
Reason				
$T_{re}$	3	3	1	0
$\text{HR}_{\text{peak}}$	0	0	2	3
SV	6	6	6	6
TL	0	0	0	0

\* Significantly different from EF

time was significantly longer during EF compared with ML. For the U, mean tolerance time was similar in both q-EF and q-ML. Mean tolerance time was not significantly different between the groups during any phase of the menstrual cycle. Due to the range of tolerance times observed during the uncompensable heat-stress trials, data are presented to 75 min for  $n = 9$  U and  $n = 9$  NU, to 85 min for  $n = 8$  U and  $n = 9$  NU, and to 90 min for  $n = 8$  U and  $n = 7$  NU.

### Metabolic rate and gas exchange

The value of  $\dot{M}$  did not differ between phases or between groups.  $\dot{M}$  was  $112.17 (3.16) \text{ W} \cdot \text{m}^{-2}$  and  $112.79 (3.29) \text{ W} \cdot \text{m}^{-2}$  for the NU during the EF and ML phases, respectively. For the U,  $\dot{M}$  was  $108.68 (3.03) \text{ W} \cdot \text{m}^{-2}$  during the q-EF phase and  $112.82 (3.43) \text{ W} \cdot \text{m}^{-2}$  during the q-ML phase. The average relative intensity at which the subjects performed exercise during uncompensable heat stress was approximately 20%  $\dot{V}\text{O}_{2\text{peak}}$  ( $0.54 \text{ l} \cdot \text{min}^{-1}$ ). This corresponded to a  $\dot{V}\text{O}_2$  of  $0.85 \text{ l} \cdot \text{min}^{-1}$  ( $\approx 31\% \dot{V}\text{O}_{2\text{peak}}$ ) during the walking portion, and a  $\dot{V}\text{O}_{2\text{peak}}$  of  $0.25 \text{ l} \cdot \text{min}^{-1}$  ( $\approx 9\% \dot{V}\text{O}_{2\text{peak}}$ ) during the sitting portion of the intermittent protocol.

### Heart rate

Figure 1 illustrates the HR response for both groups during the heat-stress trials. There were no phase-related or group-related differences in HR during the NBC clothing trials.

### Rectal temperature

Table 5 presents the data for initial, final, and delta  $T_{\text{re}}$ , and the time for a  $1.0^\circ\text{C}$  increase in  $T_{\text{re}}$  during the heat-stress trials. For the NU, the initial  $T_{\text{re}}$  was significantly higher in ML compared with EF. The phase-related elevation in  $T_{\text{re}}$  was significant throughout the uncompensable heat-stress trials (Fig. 2). Delta  $T_{\text{re}}$  was

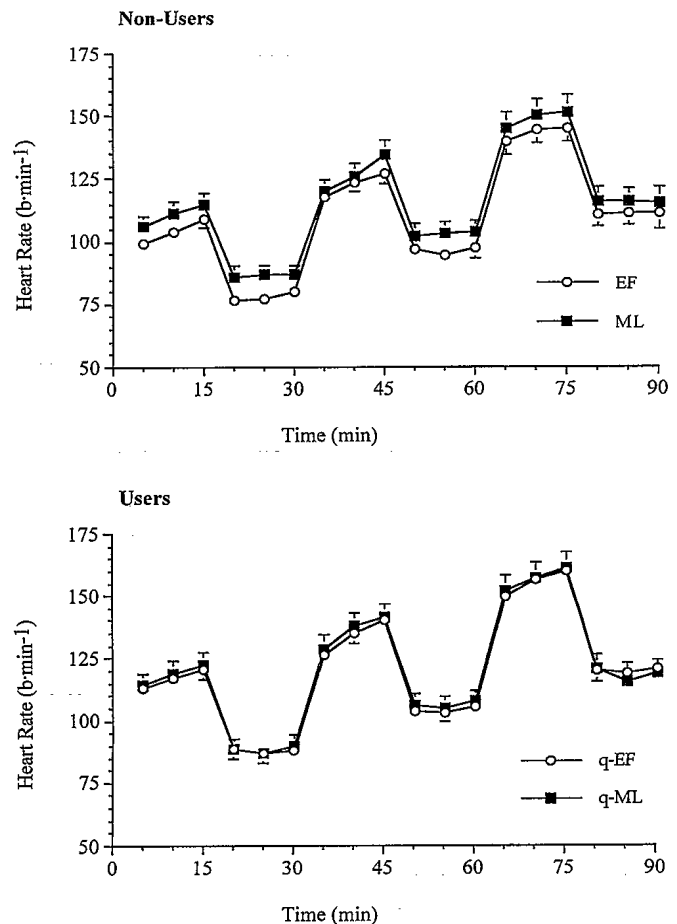


Fig. 1 Heart rate response in users ( $n = 9$  to 75 min,  $n = 8$  to 90 min) and non-users ( $n = 9$  to 85 min,  $n = 7$  to 90 min) of oral contraceptives for the early follicular (EF, open circle) and mid-luteal (ML, closed square) phases of the menstrual cycle. A quasi-early follicular (q-EF, open circle) and quasi-mid-luteal (q-ML, closed square) phase was assumed for the users. Values are the mean (SE)

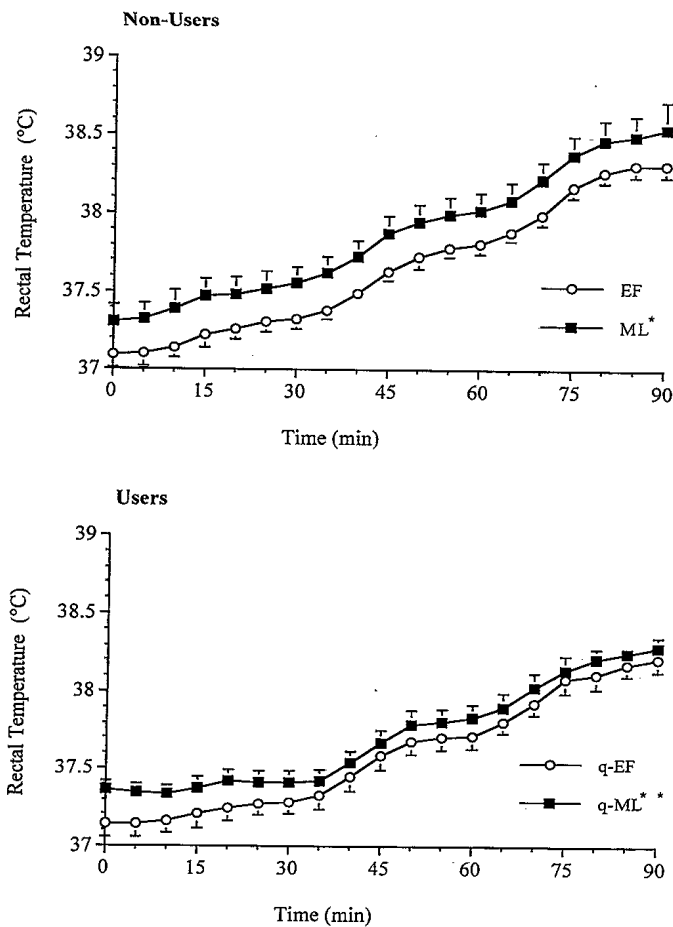
significantly greater in EF than in ML and, as a result, the final  $T_{\text{re}}$  was similar for both phases in this group (Table 5). There was also no phase-related difference in the time for a  $1.0^\circ\text{C}$  increase in  $T_{\text{re}}$  for the women in this group. For U, the initial  $T_{\text{re}}$  was significantly higher in q-ML than in q-EF.  $T_{\text{re}}$  remained significantly elevated

**Table 5** Initial, final and delta  $T_{\text{re}}$ , and the time required for a  $1.0^\circ\text{C}$  increase in  $T_{\text{re}}$  during uncompensable heat stress in users ( $n = 9$ ) and non-users ( $n = 9$ ) of oral contraceptives for the EF and ML phases of the menstrual cycle. A q-EF and q-ML phase was assumed for the users. Values are the mean (SE)

	Non-users		Users	
	EF	ML	q-EF	q-ML
Initial $T_{\text{re}}$ ( $^\circ\text{C}$ )	37.09 (0.08)	37.31* (0.08)	37.14 (0.08)	37.36** (0.06)
Final $T_{\text{re}}$ ( $^\circ\text{C}$ )	38.86 (0.14)	38.80 (0.14)	38.67 (0.13)	38.74 (0.10)
Delta $T_{\text{re}}$ ( $^\circ\text{C}$ )	1.77 (0.16)	1.49* (0.11)	1.52 (0.14)	1.39 (0.10)
Time (min) for $1.0^\circ\text{C}$ increase in $T_{\text{re}}$	72.2 (4.0)	73.9 (4.8)	79.7 (4.0)	86.0 (4.5)

\* Significantly different from EF

\*\* Significantly different from q-EF

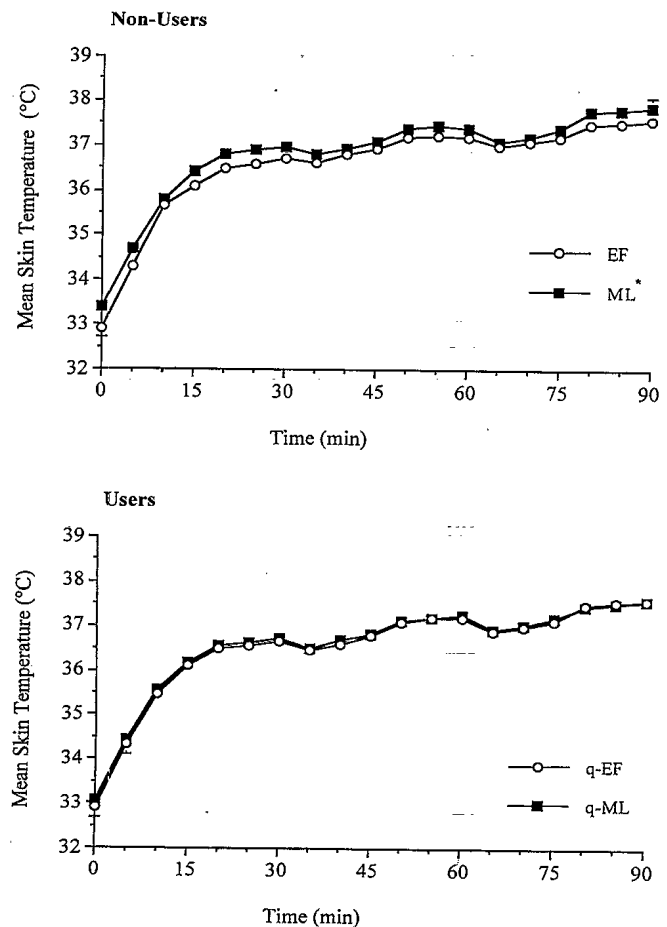


**Fig. 2** Rectal temperature in users ( $n = 9$  to 75 min,  $n = 8$  to 90 min) and non-users ( $n = 9$  to 85 min,  $n = 7$  to 90 min) of oral contraceptives for the EF (open circle) and ML (closed square) phases of the menstrual cycle. A q-EF (open circle) and q-ML (closed square) phase was assumed for the users. Values are the mean (SE). \* Significantly different from EF; \*\* significantly different from q-EF

during the q-ML phase over the first 75 min of uncompensable heat stress (Fig. 2). This phase-related elevation in  $T_{re}$  was still apparent for up to 90 min; however, the difference among phases was no longer statistically significant ( $n = 7$ ,  $P < 0.07$ ). Delta  $T_{re}$  was similar in both q-EF and q-ML and there was no phase-related difference in either the final  $T_{re}$  or the time for a  $1.0^{\circ}\text{C}$  increase in  $T_{re}$  for the women using OC. There were no group-related differences in  $T_{re}$  during the heat-stress trials.

#### Mean skin temperature

Initial  $\bar{T}_{sk}$  was significantly higher during ML [ $33.40$  ( $0.16^{\circ}\text{C}$ )] compared with EF [ $32.91$  ( $0.20^{\circ}\text{C}$ )] for the NU.  $\bar{T}_{sk}$  remained significantly higher in the ML phase throughout 85 min of heat exposure for the women in this group (Fig. 3).  $\bar{T}_{sk}$  did not differ among the phases for the U or between the two groups.



**Fig. 3** Mean skin temperature in 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 for the EF (open circle) and ML (closed square) phases of the menstrual cycle. A q-EF (open circle) and q-ML (closed square) phase was assumed for the users. Values are the mean (SE). \* Significantly different from EF to  $t = 85$  min

#### Sweat loss/evaporation

Sweat rates, which approximated  $0.35 \text{ kg} \cdot \text{m}^{-2} \cdot \text{h}^{-1}$ , were not different between phases for either group, nor was there any difference between groups for this measure. Similarly, the rate of sweat evaporation of  $0.125 \text{ kg} \cdot \text{m}^{-2} \cdot \text{h}^{-1}$  from the clothing ensemble was not affected by the phase of the menstrual cycle and was not different between groups.

#### Discussion

This study is one of the first to examine the effects of menstrual cycle phase and OC use on the cardiovascular and thermoregulatory responses to light exercise during uncompensable heat stress in healthy young women. As a significant percentage of young women utilize OC, research into this area is both important and relevant. The work intensity and the ambient environment chosen in the present investigation were similar to the condi-



tions used by McLellan (1996) and McLellan et al. (1994) to evaluate the heat strain and physical work tolerance times of healthy young men under equivalent conditions of uncompensable heat stress.

#### Influence of menstrual cycle during uncompensable heat stress

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 stress. Kolka et al. (1994) looked at thermoregulation in women during uncompensable heat stress in the EF phase alone. Since only one phase of the menstrual cycle was studied, conclusions cannot be drawn on possible differences between phases of the menstrual cycle. In a later investigation, Kolka and Stephenson (1997) examined the influence of different phases of the menstrual cycle under conditions of uncompensable heat stress. Their main findings indicate that while  $T_{re}$  remained significantly higher in the ML phase compared with the EF phase, tolerance times were similar in both phases (60 min and 55 min for the EF and ML phases, respectively). They also reported that HR,  $\bar{T}_{sk}$ , whole-body sweat rate and evaporative heat loss did not differ among phases during uncompensable heat stress (Kolka and Stephenson 1997).

The present study examined the influence of the EF and ML phases of the menstrual cycle on the cardiovascular and thermoregulatory responses of healthy young women performing light-intensity exercise during uncompensable heat stress. A lighter metabolic work rate was chosen because previous studies performed on healthy young men during uncompensable heat stress have demonstrated that manipulations which lower initial core temperatures exert more of an effect on heat tolerance during light-intensity exercise of long duration compared with high-intensity exercise of short duration (Aoyagi et al. 1994, 1995; Cheung and McLellan 1998).

Our findings have revealed that, similar to the results of Kolka and Stephenson (1997),  $T_{re}$  was significantly higher in the ML phase compared with the EF phase during uncompensable heat stress. We also observed that since  $\Delta T_{re}$  was greater during the EF phase than in the ML phase, and the time required for a 1.0°C increase in  $T_{re}$  was similar in both phases, there was no phase-related difference in final  $T_{re}$ . 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 heat stress 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. Our results for NU 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 uncompensable heat exposures, tolerance time was mainly affected by the starting core temperature. They resolved, from their research on healthy young men, that a reduction in the initial core temperature, achieved through endurance training and/or heat acclimation, resulted in prolonged tolerance times (Aoyagi et al. 1995; McLellan and Aoyagi 1996).

#### Influence of OC use during uncompensable heat stress

Recent investigations have demonstrated that  $T_{re}$  is significantly higher during pill use (q-ML) than during the week when no pill is ingested (q-EF), both at rest (Charkoudian and Johnson 1997; Grucza et al. 1993, 1997; Rogers and Baker 1997), and during exercise in comfortable (Grucza et al. 1993; Rogers and Baker 1997) and warm (Martin and Buono 1997) environments, as well as during passive heat (Charkoudian and Johnson 1997) and passive cold (Grucza et al. 1997) exposure. The results from the uncompensable heat-stress trials indicate that, similar to NU, core temperature is approximately 0.2°C higher during the q-ML phase of the menstrual cycle.

The present research represents, to our knowledge, the first report to discuss the influence of OC use during uncompensable heat stress. Our results indicate that OC use has little impact on the cardiovascular and thermoregulatory responses to uncompensable heat stress. Although  $T_{re}$  was approximately 0.2°C higher in q-ML than q-EF, the elevation in core temperature did not influence any of the other dependent measures. OC use did not affect  $\dot{V}O_2$ ,  $\dot{M}$  and HR under conditions of uncompensable heat stress. Likewise,  $\bar{T}_{sk}$ , sweat rate and the rate of evaporative heat loss were not affected by OC use during uncompensable heat stress. Furthermore, OC use did not influence heat storage or work tolerance times. Tolerance times were similar in both phases for the women within this group, and did not differ from those observed for the NU.

It appears as though a potential advantage of OC use is that it makes the thermoregulatory responses during uncompensable heat strain and the associated tolerance times more uniform across the different phases of the menstrual cycle. The possible mechanism of action of OC may be related to the hypothesis proposed by Grucza et al. (1993): that the elevation in resting core temperature among women using OC is the result of the strong effect of menstrual cycle phase. As such, the elevation in resting  $T_{re}$  during the ML phase of the menstrual cycle may represent a type of circadian rhythm that is not altered by the administration of synthetic hormones. Therefore, OC use may not result in the resetting of the thermoregulatory setpoint, as is believed to occur during the luteal phase in women with normal menstrual cycles.

In summary, the findings from the present study have shown that OC use has little or no influence on temperature regulation during uncompensable heat stress. In contrast, for women not using OC core temperature remains elevated in the luteal phase of the menstrual cycle and heat tolerance is reduced.

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