Effects of the menstrual cycle and sex on postexercise hemodynamics

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Lynn BM, McCord JL, Halliwill JR. Effects of the menstrual cycle and sex on postexercise hemodynamics. Am J Physiol Regul Integr Comp Physiol 292: R1260–R1270, 2007. First published November 9, 2006; doi:10.1152/ajpregu.00589.2006.—Factors associated with the menstrual cycle, such as the endogenous hormones estrogen and progesterone, have dramatic effects on cardiovascular regulation. It is unknown how this affects postexercise hemodynamics. Therefore, we examined the effects of the menstrual cycle and sex on postexercise hemodynamics. We studied 14 normally menstruating women [24.0 (4.2) yr; SD] and 14 men [22.5 (3.5) yr] before and through 90 min after cycling at 60% \( \dot{V}O_2 \) peak for 60 min. Women were studied during their early follicular, ovulatory, and mid-luteal phases; men were studied once. In men and women during all phases studied, mean arterial pressure was decreased after exercise throughout 60 min \( (P < 0.001) \) postexercise and returned to preexercise values at 90 min \( (P = 0.089) \) postexercise. Systemic vascular conductance was increased following exercise in both sexes throughout 60 min \( (P = 0.005) \) postexercise and tended to be elevated at 90 min postexercise \( (P = 0.052) \), and femoral vascular conductance was increased following exercise throughout 90 min \( (P < 0.001) \) postexercise. Menstrual phase and sex had no effect on the percent reduction in arterial pressure \( (P = 0.360) \), the percent rise in systemic vascular conductance \( (P = 0.573) \), and the percent rise in femoral vascular conductance \( (P = 0.828) \) from before to after exercise, nor did the pattern of these responses differ across recovery with phase or sex. This suggests that postexercise hemodynamics are largely unaffected by sex or factors associated with the menstrual cycle.

exercise; blood flow; estrogen; progesterone; plasma volume; postexercise hypotension

BLOOD PRESSURE IS TYPICALLY reduced for ~2 h after a single bout of dynamic exercise in sedentary and endurance-trained humans (20, 31, 34). In general, this postexercise hypotension is characterized by a sustained increase in systemic vascular conductance that is not completely offset by ongoing elevations in cardiac output (20). Both sedentary and endurance-trained women and sedentary men follow this typical pattern of hemodynamics, but endurance-trained men exhibit postexercise hypotension with a different hemodynamic pattern characterized by reductions in cardiac output (44).

Several mechanisms appear to underlie the sustained peripheral vasodilation following exercise. Halliwill et al. (23) demonstrated the baroreflex is reset to defend a lower pressure following exercise; thus, sympathetic vasoconstrictor outflow is reduced postexercise in humans (23). In addition to this reduction in sympathetic nerve activity, there is reduced vascular responsiveness to a given level of sympathetic nerve activity (21, 23) and a sustained histamine-receptor dependent vasodilation (33, 35, 36). The overall effect on vascular conductance and arterial pressure will be determined by how these various mechanisms and pathways integrate at the level of the vascular smooth muscle; thus, factors that modify smooth muscle tone or vascular responses may modulate the pattern of postexercise hemodynamics.

Along these lines, estrogen receptors are located in the cells of the endothelium (12) and in smooth muscle in the peripheral vasculature (30) and can cause vasodilation (25, 42, 43), whereas progesterone appears to act antagonistically by opposing these actions (5, 43). Thus, it is plausible that changing levels of endogenous hormones during the menstrual cycle may alter the pattern of postexercise hemodynamics. Specifically, increased levels of estrogen around ovulation may enhance the peripheral vasodilation that underlies postexercise hypotension.

In addition to direct effects on the vasculature, estrogen and progesterone or other factors associated with the menstrual cycle affect arterial pressure regulation (39), temperature regulation (5), and extracellular fluid volume regulation (40, 45, 51). These three factors are affected by the menstrual cycle, and all have effects on cardiovascular function and/or regulation that may influence postexercise hemodynamics.

First, changes in arterial baroreflex control of sympathetic neural outflow results in elevated sympathetic nerve activity to skeletal muscle vascular beds during the midluteal phase (39). Thus, it is plausible that changes in arterial pressure regulation and sympathetic vasoconstrictor outflow associated with the menstrual cycle alter the pattern of postexercise hemodynamics. Specifically, enhanced baroreflex-mediated changes in sympathetic nerve activity in the midluteal phase could lead to lower overall skeletal muscle blood flow and diminished peripheral vascular conductance during recovery from exercise, diminishing postexercise hypotension.

Second, changes in temperature regulation during the menstrual cycle result in elevations of body core temperature of 0.3 to 0.5°C after ovulation has occurred corresponding with the rise in progesterone in the luteal phase (5). Such changes in body temperature are associated with elevations in the threshold and increased sensitivity for sweating and cutaneous vasodilation in the midluteal phase compared with the follicular phase during exercise and passive heating (27). Thus, it is plausible that shifts in thermoregulation associated with the menstrual cycle alter the pattern of postexercise cutaneous vasodilation. Specifically, an elevation in overall cutaneous blood flow in the midluteal phase may hinder the maintenance of stroke volume and cardiac output during recovery from exercise. These central hemodynamics alterations could translate into an increased postexercise hypotension response.

Third, changes in extracellular fluid volume regulation during the menstrual cycle result in plasma volume expansion

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when estrogen rises (17, 50), and volume contraction when progesterone rises (46). Thus, it is plausible that plasma volume changes associated with the menstrual cycle alter the pattern of postexercise hemodynamics. Specifically, expanded plasma volume around ovulation may enable better maintenance of stroke volume and cardiac output during recovery from exercise and may diminish the postexercise hypotension response.

To date, most of the studies involving postexercise hypotension have used men as subjects, tested women during a single phase of the menstrual cycle or oral contraceptive use (44), or not documented the menstrual phase (4, 13). Currently, a comprehensive comparison of postexercise hemodynamics between sexes is lacking.

Birch et al. (2) examined the effects of exogenous hormones and found no differences in postexercise hemodynamics during placebo and oral contraceptive use. However, in regard to cardiovascular regulation, the impact of exogenous hormones differ from that of the menstrual cycle (39, 48). Thus, the purpose of our study was to comprehensively describe the changes in postexercise hemodynamics and explore the potential influence of fluid balance and thermoregulation on recovery from exercise across the menstrual cycle in healthy women. As our study reached completion, Esformes et al. (15) reported that the pattern of postexercise hypotension was largely the same during the late follicular and midluteal phases in eight women but suggested postexercise hypotension was enhanced during the early follicular phase. However, the authors failed to measure estradiol and progesterone during this study. To properly characterize hormonal fluctuations of the menstrual cycle, a hormonal profile must be determined. In fact, in subject populations similar to those studied by Esformes et al. (15), between 10 and 55% of menstrual cycles will be abnormally short, inadequate, or anovulatory (11). In addition to this limitation, Esformes et al. (15) did not investigate the contribution of skeletal muscle vs. cutaneous blood flow to overall changes in limb blood flow. Finally, the ovulatory phase is a time of substantial changes in plasma volume and thermoregulation and postexercise hemodynamics have not been studied during this phase. A more comprehensive study is necessary to explore many of these issues.

Thus, we hypothesized that the postexercise response in the ovulatory phase would be associated with enhanced vasodilation in skeletal muscle vascular beds and would show unchanged vasodilation in cutaneous vascular beds relative to the early follicular phase. In addition, we hypothesized that the postexercise response in the midluteal phase would be associated with similar vasodilation in muscle vascular beds and elevated skin blood flow relative to the early follicular phase. Further, we hypothesized that the postexercise response in the midluteal phase would be associated with lower stroke volume and cardiac output relative to the other phases. Finally, we hypothesized that there would be similar postexercise hemodynamic responses between men and the early follicular phase, but that there would be differences between men and the ovulatory and midluteal phase.

Methods

This study was approved by the Institutional Review Board of the University of Oregon. Each subject gave written informed consent before participating in the study.

Subjects

We recruited and screened 23 women to participate in this study. Of these, nine were excluded from analysis because of either abnormally short, inadequate, or anovulatory cycles during the time of study. As a result, 14 women subjects between the ages of 19 and 33 yr completed all portions of this study. These subjects were healthy with no allergies, normally menstruating, nonsmoking, normotensive, and taking no medications. Subjects had regular menstrual cycles lasting 30 ± 2 days in duration and had no history of menstrual distress and had not utilized any form of hormonal contraception for a period of 6 mo or more before the study. All women subjects had negative pregnancy tests on each day of participation in the study.

From data previously collected (33, 35, 36), we matched 14 men to women subjects for age, body mass index (BMI), and relative aerobic capacity. Subjects were either sedentary or recreationally active, participating in no more than 2 h of aerobic activity each week. Subject characteristics for men and women are presented in Table 1. Men were included for sake of comparison to the women subjects but did not undergo all portions of the protocol.

Screening Visit

For each screening visit, subjects reported to the laboratory at least 2 h postprandially and abstained from caffeine for 12 h and from exercise, alcohol, and all medications for 24 h before the study. Subjects performed an incremental cycle exercise test (Lode Excalibur, Groningen, The Netherlands). The test consisted of 1-min of workload increments to determine peak oxygen uptake (VO2peak). Specifically, after a 2-min warm-up period of easing cycling (20–30 W), workload increased at 20, 25, or 30 W every min until volitional fatigue. Selection of the workload increment was subjective, with the goal of producing exhaustion within 8–12 min. Whole body oxygen uptake (VO2) was measured with a mixing chamber (Parvomedics, Sandy, UT) integrated with a mass spectrometry system (Marquette MGA 1100; MA Tech Services, St. Louis, MO). All subjects reached subjective exhaustion [Borg (3) rating of perceived exertion = 19–20] within the 8- to 12-min period. After the subjects rested for 15–20 min, they returned to the cycle ergometer for assessment of the workload corresponding to a steady state VO2 of 60% of VO2peak. This workload was used on the study day for the 60-min exercise bout. Subjects self-reported activity levels on two questionnaires (1, 32).

Study visits

Women subjects underwent identical study visits at the same time of day on three occasions; men underwent one study visit. The three

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women (n = 14)</th>
<th>Men (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>24.0 (4.2)</td>
<td>22.5 (3.5)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>165.5 (7.6)</td>
<td>180.8 (3.9)*</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>59.4 (6.8)</td>
<td>72.5 (6.2)*</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>21.7 (2.4)</td>
<td>22.2 (1.4)</td>
</tr>
<tr>
<td>VO2peak, ml/kg·min⁻¹</td>
<td>35.0 (8.5)</td>
<td>45.6 (9.3)*</td>
</tr>
<tr>
<td>VO2peak, ml/min</td>
<td>2062 (577)</td>
<td>3307 (722)*</td>
</tr>
<tr>
<td>Maximum workload, W</td>
<td>214 (54)</td>
<td>303 (64)*</td>
</tr>
<tr>
<td>Maximum heart rate, beats/min</td>
<td>185.1 (12.0)</td>
<td>183.9 (11.2)</td>
</tr>
<tr>
<td>Workload at 60% of VO2peak, W</td>
<td>92 (31)</td>
<td>141 (36)*</td>
</tr>
<tr>
<td>Baecke sport index, AU</td>
<td>10.4 (1.9)</td>
<td>9.9 (2.8)</td>
</tr>
<tr>
<td>Index of physical activity, MET·h⁻¹·wk⁻¹</td>
<td>107.4 (37.7)</td>
<td>109.5 (59.4)</td>
</tr>
</tbody>
</table>

Values are presented as means (SD). VO2peak, peak oxygen consumption; MET, metabolic equivalents; AU, arbitrary units. *P < 0.05.
separate study days for women were conducted in the following phases: 1) early follicular phase (1–3 days after the start of menstruation, when estrogen and progesterone are low); 2) ovulatory phase (within 48 h of the peak luteinizing hormone surge, when estrogen is increased but progesterone remains low); and 3) midluteal phase (8 to 10 days after the detection of the luteinizing hormone surge, when both estrogen and progesterone are elevated). At the end of the screening visit, women subjects gave a menstrual history and were taught how to document the start of a menstrual cycle and detect ovulation. Ovulation was determined individually with the use of an ovulation prediction kit, which measures urine luteinizing hormone (OvuQuick; Quidel, San Diego, CA). The menstrual phase for the study visits were randomized as five women were first tested during the early follicular phase, five women were first tested during the ovulatory phase, and four women were first tested in their midluteal phase.

For each study visit, subjects reported to the laboratory at least 2 h postprandially and abstained from caffeine for 12 h and from exercise, alcohol, and all medications for 24 h before the study. Subjects prehydrated the night before the study by drinking 7 ml/kg body weight of water. Subjects recorded all food and drink consumed after 5 PM the night before and the morning of each study visit. Subjects ingested a temperature-sensing pill at least 5 h before each study visit; subjects reporting to the laboratory in the morning swallowed the pill the night before. Core temperature was not measured in the men.

Upon arrival, subjects emptied their bladders, and a prestudy weight measurement to the nearest gram was obtained. In addition to prehydration the night before the study, subjects were asked to drink 7 ml/kg body wt of water before lying supine for instrumentation. A venous catheter was inserted into the right antecubital arm region to obtain blood samples and to infuse Evans blue dye. All samples and measurements were taken after 40 min of quiet rest in the supine position. After plasma volume was determined using Evans blue dye, subjects were encouraged to empty their bladders before the start of exercise. Venous blood samples were collected on each study visit for measurement of 17β-estradiol and progesterone to confirm menstrual cycle phase. Samples were immediately placed on ice, separated, and stored at −70°C until transport to Oregon Medical Laboratories for analysis (Eugene, OR).

Timing of the Measurements

All preexercise and postexercise measurements were taken after 30 min in the supine position to control for plasma volume shifts due to postural changes. Preexercise (baseline) measurements were obtained before and postexercise measurements were taken at 30, 60, and 90 min after the exercise bout. Preexercise and 30, 60, and 90 min postexercise measurements included blood samples for plasma volume determination, cardiac output, heart rate, arterial pressure, femoral artery blood flow, and skin blood flow. During exercise, blood pressure and heart rate were measured every 10 min. At the end of the protocol, maximum skin blood flow values were obtained through local heating to 43°C for 40 min or until achievement of a plateau in red blood cell flux (38). After the end of the complete protocol, subjects were again weighed to obtain a poststudy weight measurement to the nearest gram.

Exercise

The exercise bout consisted of a 60-min period of seated upright cycling ergometer exercise at 60% of VO2 peak determined on the screening day. This exercise duration and intensity has been proven to consistently produce a sustained (~2 h) postexercise hypotension in healthy normotensive subjects (20). Subjects were asked to drink 7 ml/kg body wt of water during the 60 min of exercise to replace water loss due to sweating. The ambient temperature of the laboratory was kept between 21 and 23°C and the humidity ranged from 23 to 48%.

Measurements

**Plasma and blood volume determination.** Evans blue dye (T-1824) dilution was used to measure plasma volume before exercise on each study visit in the women subjects by injecting 15 mg of dye (19). Although no samples were overtly turbid, we used an extrapolation of the 780–720 nm baseline absorbance to 619 nm to correct for artifact as suggested by Farjanel (16). Preexercise blood volume was calculated from plasma volume and hematocrit. Exercise and postexercise changes in blood and plasma volumes were calculated from changes in hematocrit and hemoglobin concentrations (14). Samples were immediately measured in triplicate for hematocrit (i-Stat Portable Clinical Analyzer; Abbott Laboratories, East Windsor, NJ) and hemoglobin concentration (Hemocue AB; Angelholm, Sweden) and were not corrected for venous sampling. Evans blue dye was not used in men due to limited availability; however, exercise and postexercise changes in blood and plasma volumes were determined as described above.

**Heart rate and arterial pressure.** Heart rate and arterial pressure were monitored throughout all experimental procedures. Heart rate was monitored using a 5-lead electrocardiogram (model Q710; Quinlon Instruments, Bothell, WA). Arterial pressure was measured in the arm by using an automated auscultometric device (Dinamap Pro100 vital signs monitor, Critikon, Tampa, FL).

**Cardiac output.** Cardiac output was estimated using an open-circuit acetylene washin method as described previously (28, 41). This method allows the noninvasive estimation of cardiac output. We chose an open-circuit method because subjects are exposed to stable oxygen and carbon dioxide levels throughout the measurement in contrast to rebreath techniques. In brief, subjects breathed 8 to 10 breaths of a gas mixture consisting of 0.6% acetylene-9.0% helium-20.9% oxygen and balance nitrogen. During the washin phase, breath-by-breath acetylene and helium uptake were measured by a respiratory mass spectrometer (Marquette MGA 1100; MA Tech Services) and tidal volume was measured via a pneumotach (model 3700; Hans Rudolf, Kansas City, MO) linearized by the technique of Yeh et al. (56) and calibrated by using test gas before each study. The pneumotach and valve system had a combined dead space of 24 ml. Cardiac output calculations have been described previously (28). Stroke volume was determined from cardiac output/heart rate expressed as ml/beat. Systemic vascular conductance was calculated as cardiac output/mean arterial pressure (ml/min−1•mmHg−1).

**Femoral artery blood flow.** Femoral blood flow was determined through measurements of femoral artery diameter and velocity using an ultrasound probe (10-MHz linear-array vascular probe; GE Vingmed System 5, Horton, Norway). The entire width of the femoral artery was insonated with an angle of 60°. Velocity measurements were recorded immediately before diameter measurements. Blood flow was then calculated as artery cross-sectional area multiplied by femoral mean blood velocity, doubled to represent both legs, and reported in milliliters per minute. Femoral vascular conductance was calculated as flow for both legs/mean arterial pressure (ml/min−1•mmHg−1).

**Index of skin blood flow.** An index of skin blood flow was derived from measuring red blood cell flux values via laser-Doppler flowmetry (model DRT4; Moor Instruments LTD, Devon, England). Laser-Doppler probes were placed on the forearm and the thigh. Skin blood flows were expressed as cutaneous vascular conductance, calculated as laser-Doppler flux/mean arterial pressure, and normalized to the maximal values achieved during local heating to 43°C at the end of the protocol (38).

**Core temperature.** Internal body temperature was assessed by an ingestible pill telemetry system (HQInc, Palmetto, FL) (9, 55). Core temperature was not measured in the men.
Table 2. Plasma hormonal concentration on each testing day

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early Follicular</th>
<th>Ovulatory</th>
<th>Midluteal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol, pg/ml</td>
<td>34.6 (15.0)</td>
<td>82.2 (41.2)</td>
<td>118.0 (51.1)ab</td>
</tr>
<tr>
<td>Progesterone, ng/ml</td>
<td>0.5 (0.2)</td>
<td>2.5 (1.4)</td>
<td>10.3 (5.0)</td>
</tr>
</tbody>
</table>

Values are presented as means (SD of 14 women); aP<0.05 vs. early follicular, bP<0.05 vs. ovulatory.
Exercise
tance between sexes (P = 0.322). There were no differences in thigh cutaneous vascular conductance across phases of the menstrual cycle (P = 0.391). There were no differences in thigh cutaneous vascular conductance between sexes (P = 0.110).

Exercise

Workload. Subjects exercised for 60 min at 60% of V\textsubscript{\text{Vo2 peak}} on all testing days. The average workload was 92.0 (31.6) W for normally menstruating women and 141.4 (36.4) W for the men on the study days. During the early follicular, ovulatory, and midluteal phases, average exercising heart rates were 143.2 (4.9), 147.9 (4.9), and 147.4 (4.9) beats/min. This represented a rate of 142.2 (2.2) beats/min, and this was not different compared with women (P = 0.735). Average heart rate reserve for men was 66.6 (1.8%), and this was not different compared with women (P = 0.926). Mean arterial pressure during exercise [early follicular, 79.0 (1.5); ovulatory, 76.8 (1.6); midluteal, 79.4 (1.9) mmHg] was not different across menstrual phases (P = 0.291). Men had a mean arterial pressure of 93.2 (2.6) mmHg during exercise, and this was higher compared with women at each phase of the menstrual cycle (P < 0.05). This sex difference in exercise blood pressure was reflective of preexercise values, as men had higher mean arterial pressure both prior to and during exercise.

Postexercise Hemodynamics

To simplify the presentation of results, postexercise responses are presented in Figs. 1 to 4 as the percent change from preexercise, at baseline for each phase of the menstrual cycle.

Arterial pressure. Figure 1A shows the percent changes in mean arterial pressure from preexercise to 30, 60, and 90 min postexercise. Mean arterial pressure was decreased following exercise in women throughout 60 min (P = 0.002) postexercise. The fall in pressure following exercise was not different between menstrual phase (P = 0.878), but the pattern tended to differ postexercise with phase (P = 0.092). Mean arterial pressure was reduced following exercise in men throughout 90 min (P < 0.008) postexercise. The fall in pressure following exercise was not different between sexes (P = 0.360) nor did the pattern differ postexercise with sex (P = 0.248).

Systemic hemodynamics. Figure 1B shows the percent changes in heart rate from preexercise to 30, 60, and 90 min postexercise. Heart rate was elevated following exercise in women throughout 60 min (P = 0.020) postexercise and tended to be elevated at 90 min postexercise (P = 0.092). The rise in heart rate following exercise was not different between menstrual phase (P = 0.194) nor did the pattern differ postexercise with phase (P = 0.391). Heart rate tended to be elevated following exercise in men at 30 min (P = 0.058) postexercise.

### Table 3. Preexercise hemodynamics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early Follicular</th>
<th>Ovulatory</th>
<th>Midluteal</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>102.7±2.5</td>
<td>101.5±2.1</td>
<td>100.6±2.9</td>
<td>116.6±2.6&lt;sup&gt;abc&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>64.9±1.4</td>
<td>64.5±1.3</td>
<td>62.3±1.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64.6±2.2</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>77.4±1.7</td>
<td>77.5±1.5</td>
<td>75.1±1.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>81.9±2.0&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>59.5±1.7</td>
<td>61.9±1.6</td>
<td>64.3±1.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60.9±2.1</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>4.16±0.33</td>
<td>4.31±0.33</td>
<td>4.81±0.24</td>
<td>5.46±0.32&lt;sup&gt;cd&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stroke volume, ml/beat</td>
<td>69.9±5.2</td>
<td>70.5±5.5</td>
<td>75.4±3.9</td>
<td>91.3±6.3&lt;sup&gt;de&lt;/sup&gt;</td>
</tr>
<tr>
<td>Systemic vascular conductance, ml/min±1·mmHg&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>53.9±4.3</td>
<td>56.2±4.6</td>
<td>64.3±3.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>67.2±4.4&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Femoral blood flow, ml/min</td>
<td>277±46</td>
<td>275±44</td>
<td>275±38</td>
<td>336±26</td>
</tr>
<tr>
<td>Femoral vascular conductance, ml/min±1·mmHg&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>3.19±0.53</td>
<td>3.11±0.44</td>
<td>3.20±0.46</td>
<td>4.08±0.28</td>
</tr>
</tbody>
</table>

Values are presented as means ± SE; n = 14 for women and men; <sup>a</sup>P < 0.05 vs. early follicular; <sup>b</sup>P < 0.05 vs. ovulatory; <sup>c</sup>P < 0.05 men vs. early follicular; <sup>d</sup>P < 0.05 men vs. ovulatory; <sup>e</sup>P < 0.05 men vs. midluteal. NA, not available.

### Table 4. Preexercise hemodynamics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early Follicular</th>
<th>Ovulatory</th>
<th>Midluteal</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit, %</td>
<td>33.4±0.9</td>
<td>33.9±0.8</td>
<td>33.7±0.8</td>
<td>40.7±0.6&lt;sup&gt;abc&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>11.7±0.4</td>
<td>12.0±0.3</td>
<td>12.0±0.3</td>
<td>14.5±0.7&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Plasma volume, ml</td>
<td>2559±161</td>
<td>2606±170&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2465±192&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NA</td>
</tr>
<tr>
<td>Blood volume, ml</td>
<td>3923±259</td>
<td>4106±259&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3753±290&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NA</td>
</tr>
<tr>
<td>Core temperature, °C</td>
<td>37.0±0.1</td>
<td>37.0±0.1</td>
<td>37.3±0.0&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>3.38±0.62</td>
</tr>
<tr>
<td>Forearm cutaneous vascular conductance, ml/min±1·mmHg&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>2.59±0.49</td>
<td>2.50±0.27</td>
<td>2.28±0.34</td>
<td>3.38±0.62</td>
</tr>
<tr>
<td>Thigh cutaneous vascular conductance, ml/min±1·mmHg&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>2.52±0.40</td>
<td>2.60±0.44</td>
<td>3.38±0.80</td>
<td>4.55±0.93</td>
</tr>
</tbody>
</table>

Values are presented as means ± SE; n = 14 for women and men; <sup>a</sup>P < 0.05 vs. early follicular; <sup>b</sup>P < 0.05 vs. ovulatory; <sup>c</sup>P < 0.05 men vs. early follicular; <sup>d</sup>P < 0.05 men vs. ovulatory; <sup>e</sup>P < 0.05 men vs. midluteal. NA, not available.
The rise in heart rate following exercise was not different between sexes \((P = 0.187)\) nor did the pattern differ postexercise with sex \((P = 0.787)\).

Figure 1C shows the percent changes in cardiac output from preexercise to 30, 60, and 90 min postexercise. Cardiac output was elevated following exercise in women at 30 min \((P < 0.001)\) postexercise and tended to be elevated at 60 min \((P = 0.084)\) postexercise. The rise in cardiac output following exercise was not different between menstrual phases \((P = 0.539)\) nor did the pattern differ postexercise with phase \((P = 0.313)\). Cardiac output following exercise was not different compared with preexercise in men \((P = 0.874)\). The rise in cardiac output following exercise was not different between the sexes \((P = 0.332)\) nor did the pattern differ postexercise with sex \((P = 0.516)\).

Figure 1D shows the percent changes in stroke volume from preexercise to 30, 60, and 90 min postexercise. Stroke volume following exercise was not different than preexercise in women \((P = 0.714)\). This lack of change was not affected by menstrual phase \((P = 0.519)\). Stroke volume following exercise was not different than preexercise in men \((P = 0.903)\). This lack of change was not affected by sex \((P = 0.542)\).

Figure 2A shows the percent changes in systemic vascular conductance from preexercise to 30, 60, and 90 min postexercise. Systemic vascular conductance was increased following exercise in women throughout 60 min \((P < 0.050)\) postexercise and tended to be elevated at 90 min \((P = 0.063)\) postexercise. The rise in systemic vascular conductance following exercise was not different between menstrual phases \((P = 0.521)\) nor did the pattern differ postexercise with phase \((P = 0.255)\). Systemic vascular conductance was increased following exercise in men at 30 min \((P < 0.038)\) postexercise. The rise in systemic vascular conductance following exercise was not different between sexes \((P = 0.573)\) nor did the pattern differ postexercise with sex \((P = 0.476)\).

**Leg hemodynamics.** Figure 2B shows the percent changes in femoral blood flow from preexercise to 30, 60, and 90 min postexercise. Femoral blood flow was increased following exercise in women throughout 90 min \((P < 0.001)\) postexercise. The rise in femoral blood flow following exercise was not different between menstrual phases \((P = 0.713)\) nor did the pattern differ postexercise with phase \((P = 0.763)\). Femoral blood flow was increased following exercise in men throughout 90 min \((P < 0.001)\) postexercise. The rise in femoral blood flow following exercise was not different between sexes \((P = 0.734)\) nor did the pattern differ postexercise with sex \((P = 0.534)\). Figure 2C shows the percent changes in femoral vascular conductance from preexercise to 30, 60, and 90 min postexercise. Femoral vascular conductance was increased following exercise in women throughout 90 min \((P < 0.001)\) postexercise. The rise in femoral vascular conductance following exercise was not different between menstrual phases \((P = 0.595)\) nor did the pattern differ postexercise with phase \((P = 0.717)\). Femoral vascular conductance was increased following exercise in men throughout 90 min \((all P < 0.001)\) postexercise. The rise in femoral vascular conductance following exercise was not different between sexes \((P = 0.828)\) nor did the pattern differ postexercise with sex \((P = 0.541)\).

**Core Temperature and Skin Blood Flow**

Figure 3A shows the absolute changes in body core temperature from preexercise to 30, 60, and 90 min postexercise. Core temperature was increased following exercise in women at 30 min \((P < 0.001)\) but not at 60 min \((P = 0.207)\) postexercise. The rise in temperature following exercise was not different between menstrual phase \((P = 0.708)\) nor did the pattern differ postexercise with phase \((P = 0.495)\). Core temperature was not measured in men.

Figure 3B shows the absolute changes in arm cutaneous vascular conductance (scaled as a percentage of maximal...
cutaneous vascular conductance) from preexercise to 30, 60, and 90 min postexercise. Arm cutaneous vascular conductance was increased in women following exercise at 30 min ($P < 0.001$) and 60 min postexercise ($P = 0.003$) but not at 90 min postexercise ($P = 0.778$). The rise in leg cutaneous vascular conductance following exercise was greater in men than women ($P = 0.010$), but the pattern did not differ across recovery with sex ($P = 0.224$).

**Body Weights, Plasma Volume and Blood Volume**

**Total body water loss.** Subjects were weighed pre- and postexercise in the same clothing to determine the overall change in body weight as a reflection of total body water loss. In an attempt to minimize dehydration during the study, subjects were hydrated three times with 7 ml/kg of water (night prior to study, morning of study, and during exercise). Despite these efforts, small losses in total body weight were seen from the beginning to the end of the study in the ovulatory phase $[0.29 (0.09) \text{ kg}; P < 0.001]$ and midluteal phases $[0.21 (0.06) \text{ kg}; P < 0.001]$ but not the early follicular phase $[0.06 (0.06) \text{ kg}; P = 0.427]$. Loss of weight did not differ between the ovulatory and midluteal phases ($P = 0.417$) but was less in the early

![Fig. 3](http://ajpregu.physiology.org/)

**Fig. 3.** The change in core temperature (A), arm cutaneous vascular conductance (B), and leg vascular conductance (C) from preexercise to 30, 60, and 90 min after exercise. Percent changes are grouped for each phase of the menstrual cycle and for men. *$P < 0.05$ vs. preexercise baseline, a $P < 0.05$ vs. early follicular, b $P < 0.05$ vs. ovulatory, c $P < 0.05$ men vs. early follicular, d $P < 0.05$ men vs. ovulatory, e $P < 0.05$ men vs. midluteal. Values are presented as means ± SE; $n = 14$ for each group.
Exercise. The blood volume loss and subsequent expansion following exercise was not different between sexes ($P = 0.366$) nor did the pattern differ postexercise with sex ($P = 0.120$).

**DISCUSSION**

We studied postexercise hemodynamics and explored aspects of the response related to thermoregulation and fluid balance in eumenorrheic women in three different phases of the menstrual cycle. Our main finding is that despite differences in endogenous concentrations of estrogen and progesterone and fluctuations in plasma volume and body temperature across the menstrual cycle, there was no modulation of the pattern of postexercise hypotension and postexercise hemodynamics. In contrast to our hypothesis, we found that leg vasodilation in the ovulatory phase and cutaneous vasodilation in the midluteal phase were not augmented compared with the early follicular phase. Also, we found no alteration in central hemodynamics following exercise in the midluteal phase. In addition, we observed that men have a similar postexercise hypotension pattern as the women, in agreement with prior work (44).

**Postexercise hemodynamics across the menstrual cycle.** We found preexercise differences in resting systemic vascular conductance, mean arterial pressure, and heart rate between menstrual phases, in such that the midluteal phase had elevated heart rates and lower mean arterial pressure compared with the other phases. These differences are consistent with previous literature (27) but are not always observed (39, 53). These differences in resting hemodynamics carry forward as differences in postexercise hemodynamics; however, they were not associated with differences in the postexercise response (i.e., the change in hemodynamics from before to after exercise).

**Postexercise hemodynamics across the menstrual cycle.** Postexercise hypotension is commonly characterized by a rise in systemic vascular conductance that is not completely offset by ongoing increases in cardiac output (20, 23, 24). The persistent vasodilation associated with postexercise hypotension does not occur solely in the exercising muscle, as forearm, calf, and leg vascular conductances are often increased in parallel with systemic vascular conductance (20, 41). Halliwell et al. (23) demonstrated that the baroreflex is reset to defend a lower pressure after exercise, which causes a decrease in sympathetic vasconstrictor outflow (23). In this context, Minsen et al. (39) found a greater sympathetic baroreflex sensitivity and resting muscle sympathetic nerve activity in the midluteal phase compared with the early follicular phase. We originally thought that such enhanced baroreflex sensitivity and elevated sympathetic neural outflow would result in lower muscle blood flow and diminished peripheral vascular conductance during recovery from exercise, but this was not observed. However, because baroreflex sensitivity was not measured in this study, we can only speculate on whether or not preexercise differences in baroreflex function across the menstrual cycle continue postexercise.

In addition to the reduced sympathetic outflow and impaired responsiveness to sympathetic nerve activity (20, 21, 23), the increased vascular conductance associated with postexercise hypotension can largely be explained by histamine H1 and H2 receptor-mediated vasodilation (33, 35). We originally thought that increased levels of estrogen during the ovulatory phase would enhance vasodilation following exercise by increasing
vascular responsiveness to these influences. The vasodilation seen in the presence of estrogen has been linked to enhancement of the production and release of basal nitric oxide in the endothelium (6, 49). Estrogen has been shown to decrease calcium entry into vascular smooth muscle cells (7), thus causing vascular smooth muscle relaxation. However, we saw no differences in skeletal muscle vasodilation or postexercise hypotension between menstrual phases, suggesting that high levels of estrogen do not enhance postexercise vasodilation. This may be due to the limited contribution of nitric oxide (a major pathway for the vascular effects of estrogen) to postexercise hemodynamics in humans (22).

In general, our results are similar but more comprehensive than those recently reported by Esformes et al. (15). They reported a similar pattern and magnitude of postexercise hypotension across the early follicular, late follicular, and midluteal phases. However, they reported pressures were lower throughout recovery, but not at rest, in the early follicular phase compared with the late follicular or midluteal phase. From this observation, they concluded that buffering of postexercise hypotension is enhanced during the late follicular and midluteal phases. In contrast, we found no evidence to support this conclusion or that the postexercise response varies across the menstrual cycle. However, we documented baseline differences in arterial pressure and systemic vascular conductance that carry forward postexercise. Esformes et al. (15), studying only eight women, appear to have lacked the statistical power to demonstrate differences in baseline pressure that were on the order of 6 mmHg; even these differences were similar in magnitude to their postexercise differences in pressure, 5 mmHg. Furthermore, they did not confirm the hormonal changes in estrogen and progesterone in their subjects, so one cannot rule out the possibility that some of their subjects were anovulatory or may not have undergone the expected fluctuations in estrogen and progesterone. This is a major limitation to their study, as in our experience 40% of women may have menstrual cycles that are abnormally short, inadequate, or anovulatory at the time of study and the incidence may be as high as 55% (11). Similar to our current findings, Birch et al. (2) found postexercise hemodynamics were not different between the active and placebo phases of oral contraceptive use. Thus, neither endogenous nor exogenous female sex hormones appear to substantially alter postexercise hemodynamics.

Carter et al. (4) found that women, without consideration of menstrual cycle, had greater decreases in mean arterial pressure than men following 3 min of cycling at 60% $\text{V}_\text{O}_2$ max, when studied in the seated upright position. In contrast, we did not find greater decreases in arterial pressure during recovery from exercise in women compared with men in this study or in our previous work (44) when studied in the supine position 30 to 90 min postexercise or when tilted upright at 45 min postexercise (44), and this is also consistent with work by Deschenes et al. (13). The findings of Carter et al. (4) in the first few minutes of recovery from exercise may be more closely related to the overall trend for women to be less orthostatic tolerant than men (8, 37).

**Thermoregulation and the menstrual cycle.** Because of shifts in thermoregulatory control, core body temperature is elevated during the midluteal phase, and this shift in control is associated with elevations in the threshold (26) and increased sensitivity for sweating and cutaneous vasodilation during exercise and passive heating (26, 27). In contrast, Stephenson and Kolkka (48) found no difference in the sensitivity for forearm blood flow and arm sweat rate with the menstrual phase compared with esophageal temperature. We originally thought that these changes might result in an augmented cutaneous vasodilation during recovery from exercise in the midluteal phase, which could result in reductions in stroke volume and cardiac output due to a greater amount of blood pooling in the compliant cutaneous vasculature. However, we found no differences in arm or leg cutaneous vascular conductance following exercise across the menstrual cycle. One possibility is that exercise appears to reset the threshold for cutaneous vasodilation such that cutaneous blood flow rapidly returns to preexercise levels despite continued elevations in core temperature (29), thus minimizing the influence of skin blood flow on postexercise hemodynamics (54).

**Plasma volume fluctuations and the menstrual cycle.** Plasma volume fluctuates throughout the menstrual cycle (17, 18, 40, 51, 52) due to transcapillary fluid shifts caused by changes in estrogen and progesterone levels (40, 45, 51). Specifically, elevated estrogen in the ovulatory phase appears to increase plasma volume (17, 45, 47, 50), whereas rising progesterone in the midluteal phase appears to decrease plasma volume (18, 46, 52). In general, these changes are related to protein gain and loss from the circulation and subsequent fluid shifts in and out of the vascular space. Along these lines, plasma volume rose and fell ~200 ml (~9%) across the menstrual cycle in our study. However, these baseline fluctuations in plasma volume did not appear to alter the plasma volume loss during exercise nor affect its restoration after exercise. This observation is consistent with one prior report in eumenorrheic trained females that changes in plasma volume at 4 and 40 min after submaximal exercise do not differ between the early follicular and midluteal phases (10).

**Perspectives**

In addition to direct effects on the vasculature, estrogen and progesterone or other factors associated with the menstrual cycle affect regulation of arterial pressure, temperature, and extracellular fluid volume. Our results suggest that, despite known cardiovascular alterations associated with endogenous hormones both at rest and following exercise, the variables associated with postexercise hemodynamics and the overall postexercise response are largely unaffected across the menstrual cycle. Thus, it appears that the pattern of the postexercise hemodynamic response, including aspects related to thermoregulation and fluid regulation, is tightly regulated to produce the pattern of response that is consistently observed in most individuals. Postexercise hypotension continues to be characterized as a systemic expression of sustained vasodilation in skeletal muscle, but not cutaneous, vascular beds of the legs (41, 54).

In conclusion, the influence of the menstrual cycle and sex on postexercise hemodynamics, thermoregulation, and fluid balance was examined in this study. Although there are pre-exercise differences in mean arterial pressure and heart rate, the overall pattern and magnitude of the postexercise hypotension response is unchanged throughout the menstrual cycle. Our data also suggest the pattern and magnitude of postexercise hypotension do not differ between sexes. Furthermore,
MENSTRUAL CYCLE AND POSTEXERCISE HEMODYNAMICS

regardless of the menstrual cycle, postexercise hemodynamics seem to be closely regulated. However, both menstrual cycle and sex are associated with baseline differences in resting hemodynamics that are critical to assessing postexercise responses.

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REFERENCES


