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Glucose kinetics and substrate oxidation during exercise in the follicular and luteal phases

TED W. ZDERIC,[1] ANDREW R. COGGAN,[2] AND BRENT C. RUBY[1]
[1]*Human Performance Laboratory, University of Montana, Missoula, Montana 59812-1825; and* [2]*Division of Gerontology, Department of Medicine, University of Maryland School of Medicine, and Geriatric Research, Education, and Clinical Center, Geriatrics Service, Baltimore Veterans Affairs Medical Center, Baltimore, Maryland 21201*

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Zderic, Ted W., Andrew R. Coggan, and Brent C. Ruby. Glucose kinetics and substrate oxidation during exercise in the follicular and luteal phases. *J Appl Physiol* 90: 447–453, 2001.—The purpose of this investigation was to determine whether plasma glucose kinetics and substrate oxidation during exercise are dependent on the phase of the menstrual cycle. Once during the follicular (F) and luteal (L) phases, moderately trained subjects [peak O_2 uptake ($\dot{V}O_2$) = 48.2 ± 1.1 ml·min^{-1}·kg^{-1}; n = 6] cycled for 25 min at ~70% of the $\dot{V}O_2$ at their respective lactate threshold (70%LT), followed immediately by 25 min at 90%LT. Rates of plasma glucose appearance (R_a) and disappearance (R_d) were determined with a primed constant infusion of [6,6-^{2}H]glucose, and total carbohydrate (CHO) and fat oxidation were determined with indirect calorimetry. At rest and during exercise at 70%LT, there were no differences in glucose R_a or R_d between phases. CHO and fat oxidation were not different between phases at 70%LT. At 90%LT, glucose R_a (28.8 ± 4.8 vs. 33.7 ± 4.5 μmol·min^{-1}·kg^{-1}; $P < 0.05$) and R_d (28.4 ± 4.8 vs. 34.0 ± 4.1 μmol·min^{-1}·kg^{-1}; $P < 0.05$) were lower during the L phase. In addition, at 90%LT, CHO oxidation was lower during the L compared with the F phase (82.0 ± 12.3 vs. 93.8 ± 9.7 μmol·min^{-1}·kg^{-1}; $P < 0.05$). Conversely, total fat oxidation was greater during the L phase at 90%LT (7.46 ± 1.01 vs. 6.05 ± 0.89 μmol·min^{-1}·kg^{-1}; $P < 0.05$). Plasma lactate concentration was also lower during the L phase at 90%LT concentrations (2.48 ± 0.41 vs. 3.08 ± 0.39 mmol/l; $P < 0.05$). The lower CHO utilization during the L phase was associated with an elevated resting estradiol ($P < 0.05$). These results indicate that plasma glucose kinetics and CHO oxidation during moderate-intensity exercise are lower during the L compared with the F phase in women. These differences may have been due to differences in circulating estradiol.

carbohydrate oxidation; fat oxidation; estradiol; lactate threshold

WELL-KNOWN FACTORS THAT AFFECT plasma glucose kinetics and substrate oxidation during exercise include exercise intensity (32), duration (32), and training status (4). Ovarian hormones may also affect plasma glucose kinetics and substrate oxidation during exercise because estradiol has been shown to reduce plasma glucose rate of appearance (R_a) and rate of disappearance (R_d) in amenorrheic women (35), to reduce muscle glycogen utilization (22, 34) in rats, and to increase fatty acid oxidation (17) in rats. Because estradiol has been shown to mediate changes in carbohydrate and fat metabolism, it is possible that plasma glucose R_a and R_d, and carbohydrate and fat oxidation may be regulated differently across the menstrual cycle because of the large changes in circulating ovarian hormones throughout the cycle. Indeed, several reports indicate that substrate utilization is affected by menstrual phase because carbohydrate oxidation (14, 39) and plasma lactate production (20) and concentration (20, 25, 29) are lower and fat oxidation is elevated during the luteal phase (14, 39) when estradiol is elevated. However, several studies (1, 2, 20, 21, 31) concluded that there are no differences in fat or carbohydrate oxidation between menstrual phases. The aforementioned studies used indirect calorimetry to measure total carbohydrate and fat oxidation. Our laboratory has recently reported that transdermal estradiol administration reduces glucose R_a and R_d during moderate-intensity exercise in amenorrheic females who have naturally low endogenous estradiol concentrations (35). Although plasma glucose concentrations have been observed to be different across the menstrual cycle during exercise (10, 25), there are no reports of plasma glucose kinetics across the menstrual cycle.

For a more complete understanding of substrate utilization in exercising women, the purpose of this study was to determine whether plasma glucose R_a and R_d and carbohydrate oxidation are lower during exercise at two submaximal intensities [70% and 90% of O_2 uptake ($\dot{V}O_2$) at lactate threshold (70%LT and 90%LT), respectively], when estradiol is elevated in the luteal phase. The physiological responses to the two intensities were tested on the same day to avoid daily changes in the hormonal milieu. Because glucose R_a and R_d were determined by isotope dilution and we sought to minimize the effect of the preceding exercise stage on the subsequent stage, subjects exercised for 25 min at 70%LT followed by 25 min at 90%LT.

Address for reprint requests and other correspondence: B. C. Ruby, Dept. of Health and Human Performance, University of Montana, Missoula, MT 59812-1825 (E-mail: ruby@selway.umt.edu).

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METHODS

Subjects and procedures. Six regularly menstruating women who were recreational athletes served as subjects for this investigation (Table 1). Before participation, each subject completed a University of Montana Institutional Review Board-approved informed consent form. All subjects reported having a menstrual period once per month for at least the 6 mo before the study. Subjects recorded their days of menses and their morning oral temperature for 2 mo before all exercise trials to accurately predict the time of follicular and luteal phases. To estimate the time of ovulation, subjects recorded their oral temperature on awakening every morning. Serum estradiol was used to confirm the phase. None of the subjects had taken oral contraceptives for at least 3 mo preceding testing and for the duration of testing. Hydrostatic weighing was used to determine body fat percent (26). Cycling peak $\dot{V}O_2$ ($\dot{V}O_{2\,peak}$) and cycling lactate threshold were determined before the subjects completed two, two-staged submaximal cycling trials, once during the follicular phase (4–6 days after onset of menses) and once during the luteal phase (22–27 days after the onset of menses). Each of the two-stage trials took place at the same time of day to control for any diurnal effects on metabolism (10).

Cycling $\dot{V}O_{2\,peak}$ and lactate threshold tests. The $\dot{V}O_{2\,peak}$ testing protocol began with three 4-min steady-state stages of increasing power outputs (75, 125, and 175 W) on a Schwinn Velodyne cycle ergometer that was calibrated before each trial. Immediately after the third stage, the power output was increased 25 W every minute until volitional exhaustion. The criteria for $\dot{V}O_{2\,peak}$ were a plateau in $\dot{V}O_2$ and volitional exhaustion. The lactate threshold protocol consisted of an initial workload of 50 W for the first minute followed by an increase in power output of 25 W every minute until 100 W. The power output was increased 15 W every minute thereafter until ~90% maximal $\dot{V}O_2$ ($\dot{V}O_{2\,max}$). Power output at lactate threshold was defined as the last workload before a curvilinear increase in plasma lactate concentration was observed. Three subjects performed the lactate threshold and $\dot{V}O_{2\,max}$ tests during the follicular phase, and three performed these tests during the luteal phase.

Two-stage submaximal exercise trial. Subjects reported to the laboratory 10 h after their last meal. An indwelling Teflon catheter was inserted into an antecubital vein in each arm. After a blood sample was taken for background isotopic enrichment, a primed (30 μmol/kg) constant (0.42 $\mu mol \cdot min^{-1} \cdot kg^{-1}$) infusion of [6,6-^{2}H]glucose (Cambridge Isotopes Laboratories, Woburn, MA) was initiated into one arm. After 90 min of constant infusion, subjects cycled at a power output corresponding to 70%LT for 25 min immediately followed by 25 min of cycling at 90%LT. Expired gases were monitored during the last 5 min of each of the two stages for $\dot{V}O_2$ and respiratory exchange ratio (RER) using a TEEM 100 metabolic system (Aerosport, Ann Arbor, MI). The metabolic unit was equipped with a medium- to high-flow pneumotach depending on subject size. Before each test, the metabolic system was calibrated with a 3-liter calibration syringe and medical gases of known concentrations (15.8% O_2-4.2% CO_2-balance N_2). Metabolic data were recorded in 20-s intervals for all trials. $\dot{V}O_2$ and RER were used to calculate carbohydrate and fat oxidation (9). Blood samples for glucose and glucose isotopic enrichment were taken every 5 min during exercise and placed into tubes containing EDTA, whereas blood samples for all other metabolites and hormones were taken during the last 5 min of each 25-min stage. Three of the six subjects performed the submaximal test in the follicular phase first, and the other three women performed the test during the luteal phase first. The two submaximal trials were performed in adjacent phases (1–3 wk apart) so as to minimize the time between physiological testing. Subjects were asked to maintain their normal exercise routines in the time between the two submaximal trials and refrained from exercising at least 36 h before the submaximal exercise trials. Also, subjects ate the same diet in the 2 days preceding each of their two trials, and each subject submitted a 2-day dietary record before each submaximal exercise trial to ensure diet adherence. All subjects consumed at least 4 g carbohydrate·kg body $wt^{-1} \cdot day^{-1}$.

Metabolite and hormone assays. Plasma from the necessary blood samples for glucose, lactate, glycerol, insulin, human growth hormone (hGH), and estradiol assays were obtained and frozen at −20°C. Glucose and lactate concentrations from the submaximal trials were analyzed with a blood glucose and lactate analyzer (Yellow Springs Instrument, Yellow Springs, OH). Glycerol concentrations were determined with a spectrophotometric method. Insulin, estradiol, and hGH concentrations were measured with commercially available double-antibody radioimmunoassay kits (Diagnostic Products, Los Angeles, CA). All samples were analyzed in duplicate.

Isotopic enrichment and calculation of glucose kinetics. The ratio of [6,6-^{2}H]glucose to unlabeled glucose (isotopic enrichment) was determined by forming the pentaacetate derivative of glucose and using gas chromatography-mass spectroscopy to selectively monitor the peak abundances of mass-to-charge ratio 200, 201, and 202 (40). Glucose rates of R_a and R_d from the circulation were calculated with the non-steady-state equations of Steele (37) and spline fitting (41), and the average of 20 and 25 min and the average of 45 and 50 min were then determined. The volume of distribution was set at 150 ml/kg (5).

Statistical procedures. Dependent variables were compared using a priori planned comparison approach with the SuperAnova statistical package (Abacus, Berkeley, CA). The level of significance was set at an overall experimental alpha of 0.05. All data are presented as means ± SE.

Table 1. *Physical characteristics of subjects*

Age, yr	23.6 ± 1.1
Height, cm	162.9 ± 3.0
Body mass, kg	59.4 ± 3.5
Body fat, %	14.5 ± 1.4
Maximal heart rate, beats/min	186 ± 2.0
$\dot{V}O_{2peak}$, l/min	2.86 ± 0.17
$\dot{V}O_{2peak}$, $ml \cdot min^{-1} \cdot kg^{-1}$	48.2 ± 1.1
$\%\dot{V}O_{2peak}$ at lactate threshold	56.8 ± 3.8
Age at menarche, yr	13.2 ± 0.2
Length of menstrual cycle, days	28 ± 0.5

Values are means ± SE for 6 subjects. $\dot{V}O_{2peak}$, peak O_2 uptake.

RESULTS

Substrate oxidation. Table 2 lists the actual workloads as percentages of lactate threshold and $\dot{V}O_{2\,peak}$. There were no differences in work rates between phases. At 70%LT, there were no differences between the follicular and luteal phases in total carbohydrate and fat oxidation (Table 3). However, at 90%LT, total carbohydrate oxidation was 13% lower (82.0 ± 12.3 vs. 93.8 ± 9.7 $\mu mol \cdot min^{-1} \cdot kg^{-1}$; $P < 0.05$) and total fat oxidation was 23% higher (7.46 ± 1.01 vs. 6.05 ± 0.89 $\mu mol \cdot min^{-1} \cdot kg^{-1}$; $P < 0.05$) during the luteal phase.

Table 2. *Workload intensities for the two-stage submaximal trial menstrual phase comparison*

	70%LT		90%LT	
Intensity	Follicular	Luteal	Follicular	Luteal
$\%\dot{V}O_2$ at lactate threshold	69.8 ± 2.4	69.5 ± 2.2	85.3 ± 2.1	88.9 ± 1.5
$\%\dot{V}O_{2peak}$	41.8 ± 1.6	41.7 ± 1.7	51.1 ± 1.3	53.5 ± 2.3

Values are means ± SE. 70%LT, 70% of O_2 uptake ($\dot{V}O_2$) at lactate threshold; 90%LT, 90% of $\dot{V}O_2$ at lactate threshold. There were no differences between phases ($P > 0.05$).

Plasma glucose kinetics. Plasma enrichments are presented in Table 4. At rest and during 70%LT, there were no differences in glucose R_a or R_d between the follicular and luteal phases (Figs. 1 and 2). During 90%LT, glucose R_a was 14% lower in the luteal than follicular phase (28.9 ± 4.8 vs. 33.7 ± 4.5 $\mu mol \cdot min^{-1} \cdot kg^{-1}$; $P < 0.05$). Similarly, glucose R_d was 15% lower during the luteal phase (28.4.0 ± 4.8 vs. 33.4 ± 4.1 $\mu mol \cdot min^{-1} \cdot kg^{-1}$; $P < 0.05$) at 90%LT.

Plasma lactate and glycerol concentrations. At rest and during 70%LT, there were no differences in plasma lactate concentrations between phases (Table 5). At 90%LT, lactate concentration was lower during the luteal phase (2.48 ± 0.41 vs. 3.08 ± 0.39 mmol/l; $P < 0.05$). There were no differences in glycerol concentrations between the follicular and luteal phases at rest and during exercise (Table 5).

Estradiol, insulin, and hGH. Resting estradiol was significantly higher during the luteal phase than the follicular phase (172 ± 29 vs. 55 ± 7.5 nmol/l; $P < 0.05$). There were no significant menstrual phase differences in insulin concentrations at rest and during exercise (Table 5). hGH was not significantly different between phases, although human growth hormone tended to be higher during the luteal phase during both 70%LT and 90%LT (both $P = 0.1$; Table 5).

DISCUSSION

The purpose of this investigation was to determine whether plasma glucose R_a and R_d and carbohydrate oxidation are lower during exercise in the luteal phase of the menstrual cycle when estradiol is elevated. There are several reports in the literature indicating that carbohydrate metabolism, as reflected by carbohydrate oxidation (8, 14, 39) and lactate concentrations (20, 25, 29), is lower during the luteal phase, whereas fat oxidation is greater in the luteal phase (8, 14, 39). Although in female humans, there are reports of lower glucose uptake during a hyperglycemic clamp (7) in the luteal compared with the follicular phase and plasma glucose concentrations are reported to be lower (25) and higher (10) during exercise in the luteal phase compared with the follicular phase, no studies have examined glucose R_a and R_d during exercise across the menstrual cycle. The primary finding of this study is that plasma glucose R_a and R_d were lower during the luteal phase at an exercise intensity near the lactate threshold. With the lower glucose R_a and R_d, there was a concomitant reduction in carbohydrate oxidation and lactate concentrations, indicating that carbohydrate metabolism was suppressed during the luteal phase at an exercise intensity near the lactate threshold.

A possible mediator of the reduction in glucose R_a and R_d during the luteal phase may have been circulating estradiol, which was elevated during the luteal phase as expected. In a recent study, our laboratory reported that 3 and 6 days of estradiol administration transdermally reduces plasma glucose R_a and R_d during treadmill running at 65% $\dot{V}O_{2\,max}$ in amenorrheic women, who have low levels of endogenous estradiol (35). Interestingly, estradiol treatment has recently been observed to reduce glucose R_a and R_d during exercise in men as well (M. Tarnopolsky, personal communications).

The decrease in glucose R_a may have been due to potential direct effects of the changing hormonal milieu on hepatic glucose output or secondary to reductions in glucose R_d. Changes in glucose R_a may have been mediated by changes in gluconeogenesis because estradiol treatment of ovariectomized female rats decreases the activity of the gluconeogenic rate-limiting enzyme phospho*enol*pyruvate carboxykinase in liver preparations (27). In accord with this in vitro finding, estradiol treatment alone as well as estradiol in combination with the other significant luteal phase hormone, progesterone, reduce the conversion of alanine to glucose (28). In addition, estradiol treatment of amenorrheic women decreases the circulating epinephrine concentrations late in exercise (35), which may be the factor responsible for the lower observed glucose R_a in the luteal phase. Because the majority of glucose R_a is likely derived from hepatic glycogenolysis during 50 min (6) of exercise, it is also quite possible that the lower glucose R_a in the luteal phase is due to a reduction in hepatic glycogenolysis. Indeed, estradiol has been shown to reduce hepatic glycogen utilization dur-

Table 3. *Carbohydrate and fat oxidation during the two-stage submaximal trials*

	70%LT		90%LT	
	Follicular	Luteal	Follicular	Luteal
RER	0.836 ± 0.013	0.828 ± 0.018	0.867 ± 0.015	0.841 ± 0.017*
%CHO	44.6 ± 5.1	44.1 ± 7.3	55.3 ± 6.0	46.7 ± 6.9*
%Fat	55.4 ± 5.1	55.9 ± 7.3	44.7 ± 6.0	53.3 ± 6.9*
CHO, $\mu mol \cdot min^{-1} \cdot kg^{-1}$	61.4 ± 5.9	57.3 ± 8.7	93.8 ± 9.7	82.0 ± 12.3*
Fat, $\mu mol \cdot min^{-1} \cdot kg^{-1}$	6.11 ± 0.79	6.32 ± 0.91	6.05 ± 0.89	7.46 ± 1.01*

Values are means ± SE. RER, respiratory exchange ratio; CHO, carbohydrate. *Significantly different from follicular 90%LT, $P < 0.05$.

Table 4. *Plasma glucose enrichments at rest and during 50 min of exercise in the follicular and luteal phases*

	Time, min										
	0	5	10	15	20	25	30	35	40	45	50
Follicular											
Mean ± SE	3.04 ± 0.13	3.08 ± 0.13	3.02 ± 0.15	2.83 ± 0.13	2.71 ± 0.14	2.71 ± 0.11	2.56 ± 0.10	2.34 ± 0.12	2.25 ± 0.16	2.12 ± 0.14	1.97 ± 0.18
Luteal											
Mean ± SE	3.35 ± 0.12	3.32 ± 0.08	3.24 ± 0.08	3.22 ± 0.12	2.96 ± 0.20	2.99 ± 0.19	2.89 ± 0.20	2.81 ± 0.22	2.55 ± 0.23	2.47 ± 0.26	2.39 ± 0.27

Values are given in %.

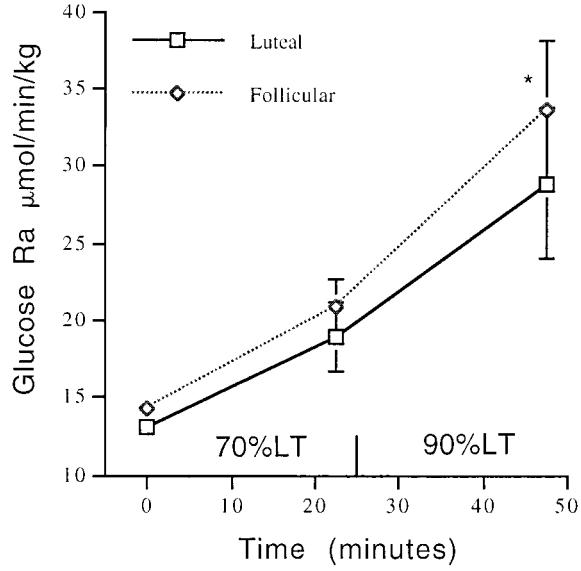

Fig. 1. Glucose rates of appearance (R_a) during the 2-stage submaximal trial menstrual phase comparison. Values are means ± SE for 6 subjects. 70%LT, ~70% of the O_2 uptake at lactate threshold; 90%LT, ~90% of the O_2 uptake at lactate threshold. *$P < 0.05$ between phases.

ing exercise (22, 34). Future research should investigate whether changes in hepatic gluconeogenesis and/or glycogenolysis are responsible for the lower glucose R_a observed in the luteal phase and during estradiol treatment. It is also possible that the lower glucose R_a in the luteal phase was not an effect mediated by hormonal action on the liver but rather a secondary effect to the lower glucose R_d in the luteal phase. Indeed, estradiol reduces glucose uptake in an in vitro rat diaphragm model (36). The reduction in glucose R_d may be due to reductions in glucose transport and/or glucose phosphorylation. In a recent and novel study,

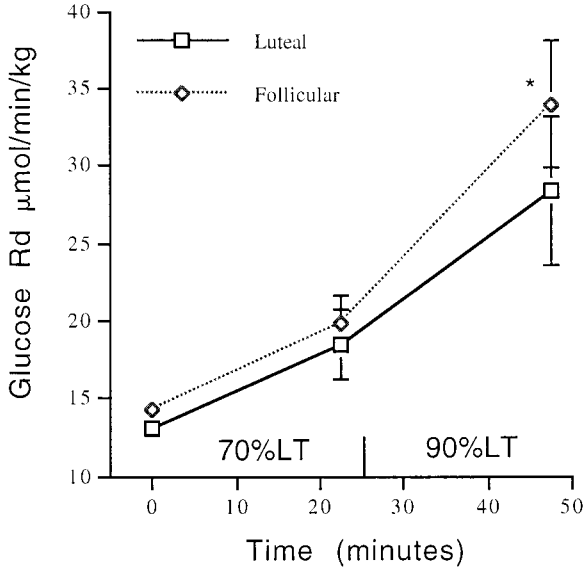

Fig. 2. Glucose rates of disappearance (R_d) during the 2-stage submaximal trial menstrual phase comparison. Values are means ± SE for 6 subjects. *$P < 0.05$ between phases.

Table 5. *Plasma metabolite and hormone concentrations during rest and exercise*

	Follicular			Luteal		
	Rest	70%LT	90%LT	Rest	70%LT	90%LT
Glucose, mM	4.23 ± 0.17	4.23 ± 0.17	4.38 ± 0.16	4.42 ± 0.10*	4.39 ± 0.15*	4.50 ± 0.16*
Lactate, mM	1.49 ± 0.20	2.01 ± 0.15	3.08 ± 0.39	1.22 ± 0.10	1.68 ± 0.14	2.48 ± 0.41*
Glycerol, mM	0.041 ± 0.002	0.048 ± 0.002	0.054 ± 0.004	0.034 ± 0.002	0.047 ± 0.004	0.052 ± 0.003
Insulin, μIV/ml	5.22 ± 0.63	4.47 ± 0.37	4.73 ± 0.53	5.07 ± 0.16	4.72 ± 0.16	4.11 ± 0.52
hGH, ng/ml	1.4 ± 0.03	8.8 ± 4.3	8.5 ± 2.6	1.6 ± 0.19	11.6 ± 4.2	11.1 ± 2.4

Values are means ± SE. hGH, human growth hormone. *$P < 0.05$ between phases.

ovariectomized female rats with low circulating estradiol were reported to have reduced contraction-stimulated glucose transport (15). Although these findings appear to be in contrast to the present findings, they do indicate that ovarian hormones have the ability to control glucose transport during exercise. Future research should examine whether the observed decrease in glucose R_d across the menstrual cycle is related to a reduction in glucose transport and GLUT-4 translocation. The small-in-magnitude but significantly greater blood glucose concentrations at rest and during exercise in the luteal phase are unexplained but are in agreement with studies that reported higher plasma glucose concentrations during rest (7) and during exercise in the luteal phase (10).

Dombovy et al. (8) reported a similar RER response to exercise intensity as this study (Table 3) in that RER was similar between phases at workloads at and below 50% $\dot{V}O_{2\,max}$, but lower during the luteal phase at workloads above 50% $\dot{V}O_{2\,max}$. Hackney et al. (14) also observed lower RER values during treadmill running at 60% $\dot{V}O_{2\,max}$ during the luteal phase; however, they also observed lower carbohydrate oxidation at 35% $\dot{V}O_{2\,max}$ during the luteal phase. In contrast to these findings we observed that carbohydrate oxidation was similar during 70%LT, which was ~40% $\dot{V}O_{2\,max}$ (Table 2). It is important to note that the lower carbohydrate oxidation in the luteal phase cannot be explained completely by a decrease in plasma glucose uptake because, whereas glucose R_d was 5.6 $\mu mol \cdot min^{-1} \cdot kg^{-1}$ lower in the luteal phase, total carbohydrate oxidation was 12 $\mu mol \cdot min^{-1}\ kg^{-1}$ lower, suggesting also a lower muscle glycogen oxidation during the luteal phase at 90%LT. It should be mentioned that carbohydrate and fat oxidation were calculated using RER and $\dot{V}O_2$ with the assumption that protein oxidation was negligible. Lamont et al. (24) reported that protein oxidation is higher during exercise in the luteal phase. A much higher protein oxidation in the luteal phase could be responsible for the significantly lower RER in the luteal phase because the respiratory quotient for protein oxidation is 0.82. However, on the basis of the reported values for the increase in protein oxidation (i.e., 3 g nitrogen over 60 min) in the luteal phase, RER would only be lowered by 0.004, which is much less than the 0.026 lower values observed in the luteal phase (Table 3) in the present study.

Decreased muscle glycogen stores may be an explanation for the decreased carbohydrate oxidation in the luteal phase because carbohydrate oxidation is directly related to muscle glycogen concentration in exercising men (15). Muscle glycogen concentrations were not measured in the present study. However, to avoid differences in preexercise muscle glycogen, subjects ate a similar diet for the 2 days preceding each trial and refrained from exercise 36 h before each trial. Furthermore, in both of the studies that compare resting muscle glycogen between the follicular and luteal phases, glycogen concentration are actually higher during the luteal phase (12, 13, 31). In addition, if there were differences in muscle glycogen concentration between the phases, we would have expected that carbohydrate oxidation would have been lower at the lower workload (i.e., 70%LT) as well. If differences in preexercise glycogen concentrations existed, they would be an unlikely explanation for the lower glucose R_d in the luteal phase because muscle glycogen concentration has no effect (16, 38) or an inverse (11) effect on plasma glucose utilization.

The lower lactate concentration in the luteal phase is in agreement with three studies (20, 25, 29) and was most likely due to lower lactate production and not increased lactate clearance because lactate clearance is not affected by the menstrual phase (20). These findings combined with the observation that glucose R_d, carbohydrate oxidation, and plasma lactate concentration were lower during the luteal phase suggest that glycolysis is reduced during the luteal phase near 50%$\dot{V}O_{2\,max}$.

It is important to note that the observed differences in carbohydrate metabolism across the menstrual cycle may not be completely exercise intensity dependent. It is possible that there is an interaction between exercise duration and menstrual phase that cannot be discerned by this present investigation. The different response between the menstrual phases during the 90%LT stage may be due to the fact that this stage was preceded by 25 min of exercise (i.e., 70%LT). Regardless of whether the different response between the phases is dependent on intensity and or duration, these data indicate that the menstrual phase affects carbohydrate and fat metabolism during moderate-intensity exercise.

Although the glycerol concentrations were similar between phases, there may have been greater fatty acid availability, because static glycerol concentrations do not represent glycerol rates of appearance or lipolysis and are approximate indicators of lipolysis. Future

studies in this area should employ free fatty acids (FFA) and glycerol tracers and muscle biopsies to determine the source (peripheral or intramuscular) of the greater fat oxidation during the luteal phase.

The elevated hGH ($P = 0.1$) and/or the estradiol in the luteal phase may have increased the availability of fatty acids to the mitochondria during the luteal phase (3). However, FFA are an unlikely candidate for the observed differences in glucose R_d because there were no differences in plasma FFA when estradiol administration reduces glucose turnover in amenorrheic women (35) and FFA are reported to be similar in the luteal and follicular phases in the fasted state (1). In addition, plasma FFA have no effect on glucose R_d in exercising men (19, 33).

Similar to the present observation of elevated hGH during exercise in the luteal phase when estradiol is elevated, recent studies report elevated hGH during exercise when estradiol is elevated during the late follicular phase (18) and during hormone replacement therapy (23). Elevated hGH may have been responsible for the lower glucose R_d because growth hormone is reported to reduce forearm glucose uptake during a hyperinsulinemic-euglycemic clamp independent of changes in plasma FFA or glycerol (30). However, we are unaware of any studies that have investigated the effect of growth hormone on plasma glucose kinetics during exercise.

In conclusion, the results of this study indicate that at exercise intensities near the lactate threshold, glucose R_a and R_d and carbohydrate oxidation are lower during the luteal phase. These differences may have been due to differences in circulating estradiol.

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