Thermic effect of food during each phase of the menstrual cycle1–3

Mary M Tai, Peter F Castillo, and F Xavier Pi-Sunyer

ABSTRACT The effect of the menstrual cycle on the thermic effect of food (TEF) was examined in eight healthy, normal-weight [x ± SD: 56.1 ± 5.6 kg and body mass index (in kg/m²) 21.3 ± 1.8] women aged 22–38 y. Their lean body mass and fat mass were 39.4 ± 2.7 kg and 16.9 ± 6.5 kg, respectively. TEF was measured on 4 separate days selected to match the four phases of a menstrual cycle: early follicular, follicular, luteal, and late luteal. The volunteers consumed a 3138-kJ liquid meal (54.5% carbohydrate, 14.0% protein, and 31.5% fat) on each test day. Resting metabolic rate was measured for 55 min before the meal and every 30 min after the start of the meal for 205 min. Although resting metabolic rate remained unchanged, there was a significant difference (P < 0.01 by ANOVA) in mean (± SEM) values for TEF among the four phases of the cycle: 0.94 ± 0.05 kJ/min during the early follicular phase, 0.86 ± 0.09 kJ/min during the follicular phase, 0.70 ± 0.10 kJ/min during the luteal phase, and 0.76 ± 0.07 kJ/min during the late luteal phase. TEF decreased significantly (P < 0.025 by paired t test) during postovulation (average of luteal and late luteal phases), when it was 0.73 ± 0.07 kJ/min, compared to preovulation (average of early follicular and follicular phases), when it was 0.90 ± 0.06 kJ/min. In conclusion, TEF decreased during the luteal phase of the menstrual cycle, possibly as a result of impairment of glucose uptake and slower transit of food through the upper gastrointestinal tract. Am J Clin Nutr 1997; 66:1110–5.

KEY WORDS Thermic effect of food, resting metabolic rate, menstrual cycle, glucose, women

INTRODUCTION

Interest in the possible variability in energy expenditure during the menstrual cycle has increased in recent years. Although studies to assess the effect of the menstrual cycle on basal metabolic rate were conducted as early as the 1920s (1–10), their findings were not conclusive. An increased basal metabolic rate during the luteal phase was found by some authors whereas others did not observe such a rise. More recent studies by Piers et al (11) and us (12) found no significant variations in resting metabolic rate (RMR) during the different phases of the cycle.

The effect of the menstrual cycle on the thermic effect of food (TEF) has not been studied as extensively as the influence of the menstrual cycle on RMR. Metha and Pande (13) compared TEF during the premenstrual and postmenstrual phases of the cycle in subjects who drank 200 mL milk and found no significant difference between the two phases. Weststrate (10) measured RMR and TEF in 23 women during the follicular and luteal phases over the course of three menstrual cycles and reported no significant differences between the two phases for either variable. However, Fiers et al (11) recently reported a significant increase in TEF during the luteal phase of the cycle.

Because of the difficulty of studying women at a particular phase of the menstrual cycle, most studies of TEF in women have not taken potential periodicity into consideration. However, any variation in TEF during the different phases of the menstrual cycle could be important in energy balance. Such a difference could have considerable implications for the validity of previous studies as well as an effect on future methods. We investigated possible variations in TEF in normal-weight women at four designated phases of the menstrual cycle.

SUBJECTS AND METHODS

Subjects

Eight women volunteers aged 22–38 y were recruited for the study. The women were not pregnant or breast-feeding; had a body weight within 5% of desirable body weight calculated from the midpoint of the 1983 height and weight tables of the Metropolitan Life Insurance Company (14); were free of known illness and gynecologic problems; had normal menstrual cycles over the previous year; were not taking oral contraceptive agents or other drugs, including nonsteroidal antiinflammatory agents; had not been dieting and had maintained a stable body weight during the previous 6 mo; were not smokers; had not participated in any physical-training programs for the previous 6 mo; and did not engage in regular exercise during the experimental period.

Each subject was required to continue consuming her regular weight-maintaining diet and follow her regular activity pattern

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during the study. All volunteers were graduate students who understood and followed the experimental protocol without known infringements. Subjects were required to attend preliminary sessions to become familiar with aspects of the experimental protocol, including body-temperature measurement and recording, blood collection and analysis, and measurements of body composition and metabolic rate. Subjects were instructed to fast overnight for 12–14 h before each experimental measurement.

Phases of the menstrual cycle

Each subject was instructed to record her rectal temperature early in the morning (before rising from bed) daily during the menstrual cycle before the RMR measurements to allow determination of the period of expected ovulation (15). The day of ovulation was identified as the low point on the base of the rise of the temperature curve into the hyperthermic phase, as defined by the World Health Organization (16). If the temperature remained at the same low point for > 1 d, the day of ovulation was defined as the final day of the low point at the base of the rise (17). On the basis of temperature curves of participants, experiments were conducted during the following four times: postmenstrual or early follicular (days 2–4 after menstruation began), follicular (days 7–10), luteal (days 19–22), and premenstrual or late luteal (days 25–28). This is illustrated in Figure 1, in which mean core body temperature at rest is plotted against day of menstruation and compared with the temperature curve established in the literature. The day of ovulation and phases of the cycle were also confirmed retrospectively by assuming that onset of the subsequent menstrual flow was the signal that ovulation had occurred as predicted (6).

Experimental design

The study was conducted in outpatient volunteers at the Obesity Research Center, St Luke’s–Roosevelt Hospital Center, New York. The protocol was approved by the institutional review board of the hospital.

On 4 d selected to match the range of the four phases of a single menstrual cycle, each subject arrived at the center in the morning after an overnight fast of 10–12 h. After the subject had rested for 40 min in a bed in a quiet, secluded temperature-controlled room (22–25 °C), her oxygen consumption and carbon dioxide production were measured during three 10-min periods over a 55-min period while she continued to rest. The chosen temperature range was thermonutral for lightly clothed individuals (18–20). After the initial three measurements, each subject consumed a 711-mL liquid test meal (Ensure; Ross Products Division, Abbott Laboratories, Columbus, OH) containing 3138 kJ (54.5% carbohydrate, 14.0% protein, and 31.5% fat). Measurements of oxygen consumption and carbon dioxide production continued after the meal. The beginning of meal consumption was assumed to be time 0. Measurements were obtained beginning at time 15 min for a 10-min period and then for the last 10 min of each 30-min period afterward during the 205 min after the test meal began.

Metabolic rate determination

An automated metabolic measurement cart system (Beckman Instruments, Schiller Park, IL) was used to measure oxygen and carbon dioxide. It included a polarographic oxygen analyzer, an infrared carbon dioxide analyzer, an electronic temperature monitor, two pressure transducers, a turbine volume meter, and automated sample-handling, data-collection, and computation capabilities. Oxygen consumption and carbon dioxide production were measured three times over the 55 min before the meal started and seven times over the 205 min after the beginning of the meal. Each measurement was made in a 1-min period during 10 min. The first two and the last determinations were discarded and the results from the remaining 7-min readings were averaged.

A three-way mouthpiece and a nose clip were used during the respiratory gas-exchange measurements, in which a continuous sample was drawn through the oxygen and carbon dioxide analyzers as in the Wilmore-Costill system (21). After 2 min, during which the system reached steady state, averaging

![Graph](image-url). // FIGURE 1. Core body temperature in relation to day of menstrual cycle. O—O, Subjects' mean values; •••••, curve established in the literature.
was achieved by sampling repeatedly the readings from the gas analyzers into the data system. Energy expenditure was determined by using the nonprotein energy equivalent for oxygen derived from Weir’s equation (22).

The equipment was recalibrated every testing day with standard gases of known concentration. Each individual measurement was taken during a 10-min period of stable oxygen consumption. The mean intraindividual SD for repeated RMR measurements in our laboratory is 238.5 kJ/d, which corresponds to an error CV of 3.8% (23). The RMR reported was the average value of results from the three RMR tests expressed as kJ/min. TEF was obtained from the difference in metabolic rate before and after the meal. Total TEF was calculated as the incremental area above the RMR level under the metabolic rate curve, with time 0 being the start of eating (24). There was no negative area in the TEF calculation. One-way analysis of variance (ANOVA) and paired t tests were used to assess statistical significance. The statistical analyses were performed with SAS (release 6.03; SAS Institute Inc, Cary, NC).

Blood biochemistry and body-composition analysis

Blood obtained while subjects were fasting was collected for analysis of plasma cholesterol (25), triacylglycerol (26), glucose (27), and insulin (28) concentrations. Thyroid hormones were measured with radioimmunoassay kits (Coat-A Count Total T₃ for triiodothyronine; Coat-A Count Total T₄ for thyroxine; and Coat-A Count TSH IRMA for thyrotropin; Diagnostic Products Corp, Los Angeles). Body weight was measured during each testing morning with an electronic digital scale and values were recorded to the nearest 100 g. The subjects wore standard clothing during body-weight determinations. Total body potassium was measured by γ spectrometry of ⁴⁰K. The SE of an estimate of total body potassium was determined by the statistical counting error of the subject’s net ⁴⁰K counting rate and the SE of the calibration factor. Lean body mass was calculated after ⁴²K calibration (29) by using a factor of 60 mmol K/kg lean body mass (30). Body fat was determined by subtracting lean body mass from body weight.

RESULTS

Physical and biochemical characteristics

The physical characteristics of the volunteers are shown in Table 1; fasting plasma values are shown in Table 2. All values were normal.

Temperature curve

Mean core body temperature at rest in relation to day of the menstrual cycle is shown in Figure 1. As expected, the changes

<table>
<thead>
<tr>
<th>Subject Characteristics¹</th>
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<tbody>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
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<tr>
<td>Lean body mass (kg)</td>
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<td>Fat mass (kg)</td>
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¹ x ± SD; n = 8.

in core temperature at rest reflected the cycle variations and were close to the temperature curve established in the literature.

Thermic effect of food

A summary of average RMR and TEF values during the designated phases of the menstrual cycle is given in Table 3. RMR is expressed in mean (± SEM) kJ/min. TEF is expressed in mean (± SEM) kJ/min, mean (± SEM) kJ/205 min, and percentage of energy consumed. TEF values expressed in kJ/205 min were obtained from the incremental area above the RMR level under the metabolic rate curve. Respiratory quotients before and after the meal are also shown in Table 1. Statistical analyses using one-way ANOVA showed no significant differences in RMR among the four phases of the menstrual cycle but significant differences in both TEF (P < 0.01) and respiratory quotients after the meal (P < 0.01). Respiratory quotients before the meal remained unchanged.

Mean TEF values at seven times after meal consumption during the four phases of the menstrual cycle are shown in Figure 2. TEF was highest during the early follicular phase and decreased gradually during the follicular phase. It reached its lowest point during the luteal phase and increased slightly during the late luteal or prefollicular phase. Preovulation values (average of early follicular and follicular values) and postovulation values (average of luteal and late luteal values) for RMR, TEF, and respiratory quotients before and after the meal are shown in Table 3. Statistical analyses using paired t tests found a significant difference between preovulation and postovulation values for TEF (P < 0.025) and respiratory quotients after the meal (P < 0.001). There were no significant differences between preovulation and postovulation values for RMR and respiratory quotients before the meal.

DISCUSSION

All subjects had normal menstrual cycles that ranged from 28 to 32 d. As expected, the elevation in core body temperature reflected the cycle variations (19). This study found a significant difference in TEF values among the four phases of the menstrual cycle.

There are relatively few studies of the effects of the menstrual cycle on TEF. Metha and Pande (13) measured preovulation and postovulation TEF in 10 subjects at 0, 5, and 15 min after they consumed 200 mL milk and found no significant difference between preovulation and postovulation values. The findings of Metha and Pande are best explained by the short postprandial period over which measurements were conducted. Use of a 15-min period resulted in exclusion of most of the
TABLE 3
Summary of results

<table>
<thead>
<tr>
<th>Phase of menstrual cycle</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Preovulation&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Postovulation&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting metabolic rate (kJ/min)</td>
<td>3.94 ± 0.17&lt;sup&gt;1&lt;/sup&gt;</td>
<td>3.92 ± 0.10</td>
<td>3.91 ± 0.17</td>
<td>3.85 ± 0.16</td>
<td>3.93 ± 0.12</td>
<td>3.88 ± 0.16</td>
</tr>
<tr>
<td>Thermic effect of food (kJ/205 min)</td>
<td>0.94 ± 0.05</td>
<td>0.86 ± 0.09</td>
<td>0.70 ± 0.10</td>
<td>0.76 ± 0.07&lt;sup&gt;4&lt;/sup&gt;</td>
<td>0.90 ± 0.06</td>
<td>0.73 ± 0.07&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>(% of energy ingested)</td>
<td>6.0</td>
<td>5.4</td>
<td>4.4</td>
<td>4.8</td>
<td>5.7</td>
<td>4.6</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>Before meal</td>
<td>0.79 ± 0.04</td>
<td>0.77 ± 0.02</td>
<td>0.78 ± 0.02</td>
<td>0.79 ± 0.02</td>
<td>0.78 ± 0.03</td>
</tr>
<tr>
<td>After meal</td>
<td>0.78 ± 0.04</td>
<td>0.82 ± 0.02</td>
<td>0.86 ± 0.02</td>
<td>0.86 ± 0.02&lt;sup&gt;4&lt;/sup&gt;</td>
<td>0.80 ± 0.03</td>
<td>0.86 ± 0.02&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup> ± SEM; n = 8.
<sup>2</sup> Average value of phases 1 and 2 (early follicular and follicular).
<sup>3</sup> Average value of phases 3 and 4 (luteal and late luteal).
<sup>4</sup> Significant difference among phases by one-way ANOVA, P < 0.01.
<sup>5-6</sup> Significantly different from preovulation (paired t test); <sup>5</sup> P < 0.025, <sup>6</sup> P < 0.001.

Total TEF, thereby precluding accurate estimation. More recently, Reed and Hill (31) found, in a 6-h measurement of TEF, that 60% of the total was measured after 3 h, 78% after 4 h, and 90% after 5 h. We measured TEF over 205 min (3.4 h). Because TEF values in our study peaked 2.25 h after the meal started, it is safe to assume, in accordance with the estimates of Reed and Hill, that the TEF values we observed encompassed ≈70.6% of the total. Segal et al (32) found that 60–70% of measured TEF is sufficient for comparisons of TEF in groups of subjects.

Piers et al (11) reported a significant increase in the thermic effect of a meal during the luteal phase of the menstrual cycle. However, they found no significant differences between the two phases of the cycle in postmeal total energy expenditure or substrate oxidation rates. The discrepancy between our study and that of Piers et al may be partly ascribed to the difference in the meals consumed. We provided 3138 kJ whereas Piers et al provided 1880 kJ. The composition of the meals varied considerably: 54.5% compared with 75% carbohydrate, 14% compared with 10% protein, and 31.5% compared with 15% fat. The volume and consistency of the meals were also different. Our study used a 711-mL liquid test meal with an appearance and consistency similar to milk whereas the study by Piers et al used a 200-mL acid, semisolid meal in which milk powder, rice cereal, and sugar were mixed with lemon juice and water. The lower energy content of the meal used by Piers et al may explain the much lower TEF values (0.42–0.5 kJ/min according to our calculations) in that study. However, when these values are expressed as a percentage of energy consumed, there was a 19.3% decrease in TEF between the follicular and luteal phase in our study and a 15.2% increase in the study by Piers et al. This may have been due to the different methods used in the two studies.

Another difference is the longer time (300 min) used by Piers et al to measure TEF. It could be argued that our study should have measured TEF for >205 min because our test meal contained twice the amount of fat and dietary fat influences and slows gastric emptying. However, Kinabo and Durin (33) showed that TEF is significantly influenced by the energy content but not the composition of a meal. Furthermore, a study of the effects of diet composition on nutrient balance in humans by Hill et al (34) concluded that diet composition can affect substrate oxidation without producing measurable effects on total energy expenditure.

![FIGURE 2. Mean (± SEM) thermic effect of food (TEF) at seven times after meal consumption during the four phases of the menstrual cycle (n = 8).](https://academic.oup.com/ajcn/article-abstract/66/5/1110/4655863)
In the study by Piers et al (11), three TEF measurements were obtained during the follicular phase of a menstrual cycle whereas only one was obtained during the luteal phase. A close look at the data from this study shows a greater increase in TEF as a percentage of energy consumed within the follicular phase (from 6.72% to 7.34% or 9.2%) than the increase between the follicular and luteal phases (from 7.34% to 7.96% or 8.4%). It is not known whether the lack of reproducibility within the follicular phase was also evident within the luteal phase because TEF was measured only once during the luteal phase. Piers et al attributed the increased energy expenditure during the luteal phase to elevated progesterone concentrations. They cited a study by Webb (6), who suggested that higher progesterone concentrations during the luteal phase are responsible for the increase in TEF. However, the existence of an increased thermogenic effect of progesterone during the luteal phase has not been firmly established.

Another factor may be impaired glucose uptake at the cellular level during the luteal phase of the menstrual cycle. Using hyperglycemic clamps, Diamond et al (35) showed that menstrual cyclicity had a profound effect on glucose homeostasis and that glucose uptake was impaired during the luteal phase of the cycle. This impairment was not explained by a defect in insulin secretion; instead, a defect in glucose uptake at the cellular level was suggested. These findings are consistent with the concept of deterioration in glucose homeostasis during the luteal phase indicated by elevated fasting glucose concentrations and impaired glucose tolerance during oral-glucose-tolerance tests (36, 37). Additionally, administration of progesterone to men resulted in hyperinsulinemia and an increased plasma insulin response to an oral-glucose-tolerance test (38).

Furthermore, several investigators found a deterioration in metabolic control and an increased incidence of diabetic ketoacidosis during the luteal phase of the cycle in women with diabetes mellitus (39–41). In our study, 54.5% of the total energy consumed was carbohydrate. Thus, a defect in glucose uptake and metabolism during the luteal phase of the menstrual cycle could have been responsible for a decrease in thermogenic output during this phase.

Upper gastrointestinal transit is prolonged during the luteal phase of the cycle. Wald et al (42) suggested that function of the small intestine might be altered during different phases of the menstrual cycle. Breath-hydrogen tests after a meal showed that upper gastrointestinal transit time was significantly prolonged during the luteal phase. Wald et al also showed that the putative effect of progesterone as a smooth-muscle relaxant responsible for intestinal hypomotility is not limited to pregnancy but also occurs, albeit to a lesser extent, during the luteal phase of a normal menstrual cycle. They further suggested that the increases in progesterone and estradiol that occur during the luteal phase lengthen gastrointestinal transit time by 25% compared with transit time during the follicular phase. Thus, the lowered TEF during the luteal phase observed in this study may have been due to slowed gastric emptying during the luteal phase (42). Because delayed gastric emptying slows the rate of nutrient absorption, it lowers TEF as a result of nutrients being oxidized or stored at a slower rate.

Previous studies showed that ovulatory amounts of circulating progesterone failed to elicit a thermogenic response during the luteal phase. For instance, Moghissi (43) studied the accuracy of basal body temperature in detecting ovulation and observed a decreased thermogenic response during the luteal phase in some subjects. The correlation between basal body temperature and serum ovulatory hormones during a single menstrual cycle showed that most women with normal menstruation had a biphasic (70%) or monophasic (20%) pattern for basal body temperature whereas 10% of women had anovulatory cycles or a deficient luteal phase. Moghissi suggested that in some women, for unknown reasons, ovulatory concentrations of circulating progesterone occasionally fail to elicit the thermogenic response during the luteal phase of an apparently normal menstrual cycle. Additionally, Piers et al (11) attributed the rise in TEF during the luteal phase to several factors, including a postovulatory increase in progesterone. The fact that RMR values remained unchanged during both the follicular and luteal phases suggests that the influence of progesterone is directed exclusively toward TEF, a discrepancy that is difficult to explain.

There is a preovulatory rise in progesterone concentration in normally ovulating women of reproductive age. Spiritos et al (44) studied the extent of preovulatory increases in follicle-stimulating hormone and progesterone in association with the luteinizing-hormone surge and observed a significant preovulatory rise in serum progesterone concentrations in women of reproductive age. Fritz and Speroff (45) suggested that the menstrual cycle is a highly complex integrated series of events that depends partly on a highly specific midcycle positive-feedback mechanism that potentiates and augments the ovulatory process. Spiritos et al (44) suggested that one such mechanism is the preovulatory rise in progesterone that ultimately enhances the gonadotropin surge from the anterior pituitary. These findings indicate that increased preovulatory concentrations of progesterone could counterbalance a postovulatory increase during the luteal phase.

We conclude that there is a significant decrease in TEF during the luteal phase of the menstrual cycle in normal-weight women. TEF decreased during the luteal phase whereas RMR remained unchanged because of slowed upper gastrointestinal transit and decreased glucose absorption and uptake during that phase. However, further studies are needed to explore the influence of hormones and the effect on TEF of meals with different nutrient densities and compositions during the different phases of the cycle.

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REFERENCES