Changes in energy expenditure during the menstrual cycle

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1. Eight women were studied under metabolic-ward conditions while consuming a constant diet throughout a single menstrual cycle. Basal body temperature, salivary and urinary hormone concentrations were used in monitoring the cycle and designing the study so that whole-body calorimetry for 36 h was conducted at four phases of the cycle in relation to the time of ovulation.

2. The metabolic rate during sleep showed cyclical changes, being lowest in the late follicular phase and highest in the late luteal phase. The increase amounted to 6·1 (SD 2·7) %. Energy expenditure (24 h) also increased but the change was not statistically significant ($P > 0·05$). Exercise efficiency did not change during the cycle.

3. There were no significant changes in plasma thyroxine, 3, 5, 3′-triiodothyronine or free 3, 5, 3′-triiodothyronine concentrations to explain the metabolic rate changes; nor did they relate to urinary luteinizing hormone, pregnanediol-3α-glucuronide or oestrone-3-glucuronide excretion rates. No link with salivary cortisol or progesterone concentrations was observed, but there was a small inverse relation between the individual increase in sleeping metabolic rate and the subjects' falling ratio of urinary oestrone-3-glucuronide: pregnanediol-3α-glucuronide.

The variability in energy balance of women during the menstrual cycle has been of interest since research workers in the 1920s examined the problem. At first there was little appreciation that changes might occur at times other than menstruation itself and whether systematic changes did occur was disputed (Snell *et al.* 1920; Blunt & Dye, 1921; Wiltshire, 1921; Wakeham, 1923; Hafkesbring & Collett, 1924; Smith & Doolittle, 1925; Benedict & Finn, 1928; Griffith *et al.* 1928–9; Hitchcock & Wardwell, 1929). Some authors failed to find any effect, whereas others showed an increase in basal metabolic rate (BMR) during the premenstrual phase of the menstrual cycle. In all these early studies the dietary intake was uncontrolled so that any changes in food intake could have affected BMR. More recently, Solomon *et al.* (1982) overcame this problem by measuring BMR in the course of studies which involved changing the protein intake in sequential menstrual cycles. Thus, the diet was maintained constant during a single cycle but the protein intake varied from cycle to cycle. The BMR was found to increase significantly during the luteal phase of the cycle.

METHODS

The purpose of the present study was to maintain food intake constant throughout the cycles of eight women who remained under metabolic-ward conditions. Total faecal and urine collections were made to quantify energy and protein losses, and thyroidal, cortisol and sex hormones were also monitored throughout the cycles to assess whether they might influence energy expenditure. Energy expenditure itself was measured under a variety of

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resting and exercise conditions during the 36 h periods spent in a whole body indirect calorimeter; these metabolic rate measurements were repeated at weekly intervals.

Eight adult women aged 19–32 years (mean 26·3 years) volunteered to take part in this prolonged study which involved 9–13 weeks of monitoring at home before entering the Centre in Cambridge where they were then maintained on a precisely controlled diet for a period lasting from 33 to 39 d. The pre-residential phase was used to assess the length of the menstrual cycle, whether the cycles were usually ovulatory, to monitor normal food intake, and to assess the weight stability, pattern of physical activity and BMR of each subject. All the women were postgraduate students or professionals except for the youngest who was completing her education at school. Table 1 provides details of the women. Three of the women exceeded the upper limit of acceptable weights (Royal College of Physicians, 1983) by 5·5, 3·4 and 1·5% only. Skinfold thicknesses were measured at four sites as described by Durnin & Womersley (1974) to obtain an estimate of body fat by the use of their equations.

The length of the post-ovulatory phase was estimated from the change in basal body temperature monitored intravaginally at home with a series of specially calibrated clinical thermometers. The average of the daily basal temperature from 5 to 11 d after the onset of menstruation was designated as the reference temperature for the follicular phase, extra days being included if any single temperature was classified as invalid, i.e. exceeding a 0·3° swing in comparison with the adjoining readings (Royston & Abrams, 1980). This was found to be more useful than the running mean technique proposed by McCarthy & Rockette (1983) as it was readily applicable to charts with a step-like shift in temperature as well as those where the temperature increase was persistent but more gradual. A biphasic response occurred when six readings in the latter part of the cycle were 0·2° or more above the follicular reference level. Ovulation was then defined as taking place on the day that the temperature increased from a nadir (Hilgers & Bailey, 1980). The ovulatory day was designated as day 1 of the luteal phase of the cycle, and the approximate lengths of the luteal phases of consecutive cycles were then used to predict the most appropriate timing for calorimeter tests in the residential phase of the study. All women were examined medically before the study, had no complicating illnesses and neither smoked nor took oral contraceptives or any other drugs. Their consent was obtained to the study, which was approved by the Dunn Nutrition Laboratory's Ethical Committee.

On entry to the Centre the women were placed on a meat-free diet both to cope with the dietary preferences of some of the volunteers and to help in monitoring creatinine excretion without the additional variation ascribable to meat eating (Bingham & Cummings, 1985). The energy intake was adjusted in accordance with each woman's physical activity, three proving to engage in light, four medium and one heavy activity (competitive rowing). It was arranged for all the women to maintain their habitual physical activity throughout the residential period except when they were confined to the calorimeter. The first calorimetric test, conducted on arrival, was used to habituate them to the complex schedule and to check on the likely validity of the energy intake; as a result three of the group had their intakes increased. Once the energy intake had been adjusted in the first 3–4 d of residence no further changes in intake were made. The principal nutrients in the diet were based on the average for Cambridge women (Bingham *et al.* 1981), i.e. with 40% energy as fat, 13% as protein and the remainder as carbohydrate. Given the meat-free design of the study and the dietary preference of the group, however, the estimated fibre content of the diet (Paul & Southgate, 1978), amounted to approximately 42 g/d. Daily intake was provided as three meals of equal energy content and as far as possible with the same composition as the whole day's diet. Meals were taken at standard times and a 3 d rotating menu was used. Duplicate meals were obtained for each menu for subsequent chemical analysis. Fig. 1 shows the

Table 1. *The anthropometric characteristics of the women studied*

Subject	Age (years)	Height (m)	Unclothed wt (kg)	Ideal wt* (%)	Estimated body fat† (%)	Estimated muscle mass‡ (kg)
1	32	1·62	60·70	112·4	36·67	22·90
2	32	1·66	68·60	120·8	33·08	24·46
3	19	1·69	68·27	117·5	32·72	28·80
4	24	1·65	57·68	104·1	26·99	17·96
5	26	1·64	64·97	117·3	31·26	16·28
6	23	1·64	56·65	102·3	27·18	18·10
7	23	1·66	61·58	108·4	23·02	21·66
8	31	1·72	63·26	103·2	29·23	21·78
Mean	26·3	1·66	62·71	110·8	30·02	21·48
SD	4·9	0·03	4·45	7·3	4·30	4·08

* Ideal weight taken as mean acceptable weight-for-height (Royal College of Physicians, 1983).
† Estimated from sum of four skinfolds (Durnin & Womersley, 1974).
‡ Estimated from total urinary creatinine (g/d). 1 g urinary creatinine/d = 20 kg muscle (Heymsfield *et al.* 1983).

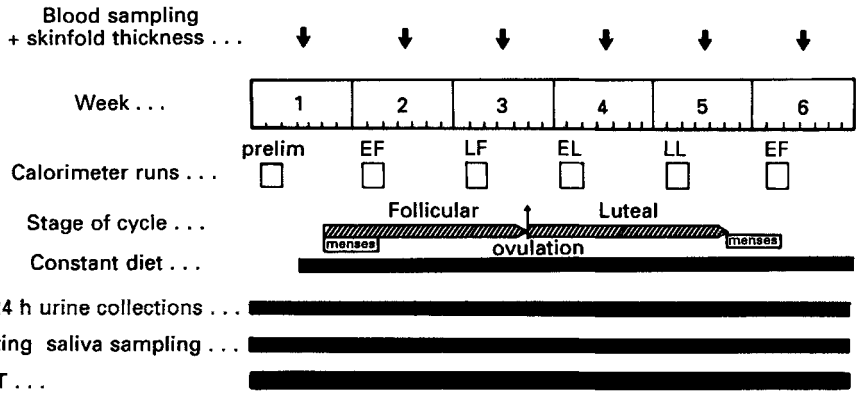

Fig. 1. The protocol for the residential phase of the study. The protocol is set out for simplicity as though all the volunteers were admitted on the same phase of their menstrual cycle. In practice the women entered the study at any phase of the cycle. EF, early follicular; LF, late follicular; EL, early luteal; LL, late luteal; for details, see pp. 188–189. BBT, basal body temperature.

features of the residential period. For simplicity the volunteer is depicted as starting at the beginning of her cycle, i.e. on the first day of menstruation. In practice the women began their residential monitoring at a time to suit their work or social convenience and to fit the calorimeter schedule.

The definition of the time of ovulation while in the Centre did not depend on monitoring basal temperature but on measuring the peak excretion of luteinizing hormone (LH). LH concentrations in 24 h urine collections were monitored for 7 to 10 d around the time of ovulation, predicted from the changes in basal temperature while in the Centre. Ovulation was defined as occurring on the day after the peak LH concentration and taken as the first day of the luteal phase. The follicular and luteal phases were then arbitrarily divided into early and late components, the follicular phase beginning on the first day of menstrual loss. Fig. 1 shows that the subjects collected all urine throughout the study in 24 h portions; complete faecal collections were also made and checked for completeness with the use of

radio-opaque markers provided in capsule form and taken three times daily with meals (Branch & Cummings, 1978). Body-weight and vaginal temperature were measured each morning.

Hormonal assessment

Oestrone-3-glucuronide was assayed in urine by the immunoassay method of Baker *et al.* (1979) using an antiserum with a cross-reactivity of 2·7% with oestrone, 10·2% with oestradiol-17β, 6·1% with oestradiol-17α and 2·6% with epi-oestriol. This represented minimal cross-reactivity given the very small amount of oestrone and oestradiol-17β in human urine (Bolton & Rutherford, 1976). The sensitivity of the assay was 9 pg per assay tube equivalent to 3·8 nmol/l, with intra- and interassay coefficients of variation of 13·1 and 12·9%. These values were similar to those of Baker *et al.* (1979). Urinary pregnanediol-3α-glucuronide was assayed with the antiserum and immunoassay technique of Samarajeewa *et al.* (1979) which showed a 19·5% cross-reactivity with pregnanediol (present in insignificant amounts in human urine) but showed no detectable cross-reactivity to seven other progestogens, to nine oestrogens or to androsterone derivatives. Assay sensitivity was 30 pg equivalent to 0·6 μmol/l, and intra- and interassay variations were 9·3 and 7·9% respectively. Urinary LH was measured by radioimmunoassay kit supplied by Amersham International plc, Amersham, Bucks. No dilution or pretreatment of the samples was necessary. Cross-reactivity was designated as 2·4% against follicular-stimulating hormone, 3·8% against thyroid-stimulating hormone with an intra- and interassay variability of 12·0 and 5·1%.

Fasting salivary samples were used to measure progesterone and cortisol concentrations. Volunteers washed their mouths out first with water and then collected salivary samples 15 min later. The time for collection was standardized to the same time each morning. Samples were frozen immediately at $-20°$ in plastic containers before transport to Cardiff for assay by techniques which have been fully described by Walker *et al.* (1978, 1979). Assay sensitivity for progesterone was 7 pg with an intra- and interassay variability of 11 and 8%. The reason for the intra-assay variability being greater than the interassay variability was that the measurements fell at the low end of the standard response curve, giving more variability than would otherwise be expected within assays. For cortisol the lower sensitivity limit was 4 pg with an intra- and interassay variation of less than 7·1 and 12·2%. Plasma samples obtained weekly at the end of each calorimetric session were used to assay progesterone, thyroxine (T_4), and free and total 3, 5, 3′-triiodothyronine (T_3) concentrations using immunoassay kits obtained from Nuclear Medical Systems Inc (for progesterone) and from RIA (UK) Ltd for thyroid hormones. Sensitivity of the progesterone assay was 25 pg, with an intra-assay variation of 10·3% in the single assay used. Cross-reactivity with other progestogens, oestrogen and corticosteroids was below 1% in all cases. Intra-assay variability for T_4 was less than 5%, for T_3 below 10% and for free T_3 within the 3% limit specified by the manufacturers of the kit.

Calorimeter analysis of energy expenditure

The two smaller indirect calorimetric chambers built at the Dunn Clinical Centre were used for this research, each chamber having a size of approximately 11·6 m^3. The design of these chambers has been described by Dauncey *et al.* (1978) and the basis of the protocol was that described by Dallosso & James (1984). The calorimeter was maintained at $26 \pm 0·2°$. This temperature is considered to represent thermoneutrality for lightly clothed individuals (Itoh, 1974; Wilkerson *et al.* 1972; Dauncey, 1981). The women, wearing clothes of their own choice, entered the calorimeter in the evening at 21.00 hours having had their last meal of the day at 18.00 hours. The details of the calorimetric schedule are shown in Fig. 2, which indicates that the women had set periods of activity with defined work loads doing bicycling

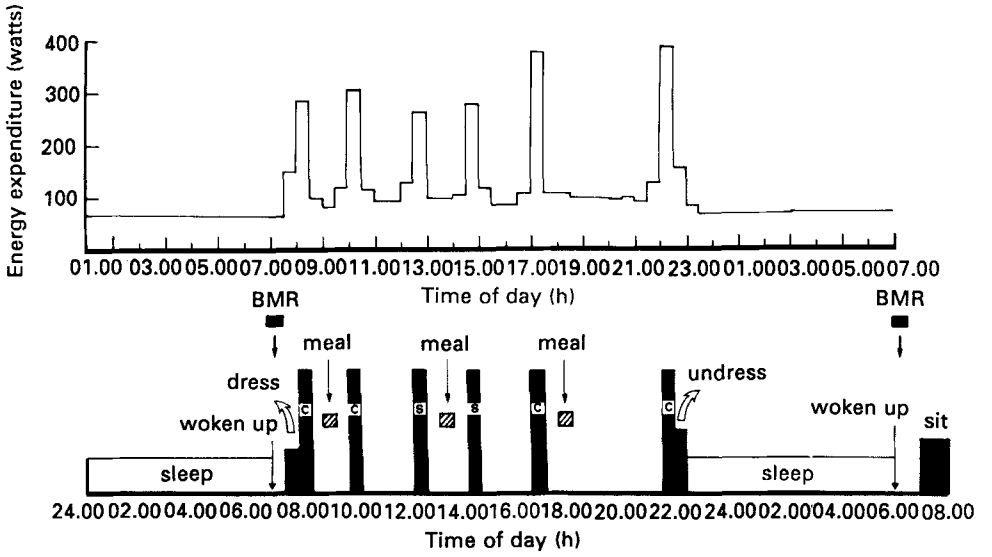

Fig. 2. Timetable of events in the calorimeter. BMR, basal metabolic rate; c, cycling; s, step test.

and step tests at a set rate maintained by the use of a metronome. Meals were eaten at specified times. A period of 30 min was designated as a time for measuring BMR between 07.00 and 07.30 hours, the women being woken immediately before that so that they could be measured in the awake, fasting and resting states. The women left the calorimeter after the BMR period of the second morning and were then weighed, had their skinfolds measured and a blood sample taken before returning to their normal daily schedule. All the women had the same standardized activity in the chambers, but for the rest of the time continued, as far as possible, with their normal pursuits.

Mechanical efficiency of physical activity

Two approaches were used in assessing the possible impact of changes in the energetic efficiency of physical activity during the menstrual cycle. In the first, changes in cost of daytime activities were considered separately from resting levels during the night. This approach necessarily included any changes in diet-induced thermogenesis on the time allocated to physical activity, and any amplification of thermogenesis by co-existent dietary and exercise-induced effects as well as changes in the mechanical efficiency of physical activity. A more precise analysis of the efficiency of physical activity entailed extracting the values for the cycling period from 22.00 to 22.30 hours which was 3·5 h after the last meal. From this 30 min energy value was subtracted the energy output while sitting in a chair between 21.00 and 21.30 hours. The net cost (E) was then related to the mechanical work (W) demand of 73·5 watts against the braking force of 1·5 kp on one cycle, the efficiency (F) being expressed as a percentage where $F = (W/E) \times 100$.

Calculations

The findings were considered for the four phases of the menstrual cycle which were classified on the basis of results of urinary LH excretion. The first calorimetric session was discarded as a training session and not included in the analysis of cyclical changes in metabolism.

The calorimetric calculations are set out in detail by Brown *et al.* (1984) who provided

the equations which made allowances for the delay in achieving a steady-state of chamber gases because of the volume of the calorimeter. The energy equivalence of the measured oxygen uptake and carbon dioxide production was based on Weir's (1949) formulas. Analysis of variance was used to assess any order effect and the statistical significance of any changes in energy expenditure during the menstrual cycle.

RESULTS

All the women had evidence of ovulatory cycles as shown by the pattern of basal body temperature changes in both the preliminary assessment and during the residential study phase. The day of ovulation was readily specified in all the women since a clear peak in LH excretion occurred on a single day. The pattern of hormonal secretion is shown in Fig. 3. Changes in salivary cortisol were unremarkable, but salivary progesterone and urinary pregnanediol-3α-glucuronide showed a highly consistent pattern with a progressive rise during the early luteal phase. The pattern of oestrone-3-glucuronide excretion was also consistent and showed, on average, a peak in the 24 h urine collection corresponding to the day of ovulation. When the ratio, oestrone-3-glucuronide: pregnanediol-3α-glucuronide was used as an index of ovulation then, as expected from the pattern of individual hormone responses, there was a peak which in this case was, on average, a little more prominent on the same day as the urinary LH peak, i.e. 1 d before the estimated day of ovulation. Changes in thyroidal hormone concentrations were within the normal range for all women and showed no consistent pattern during the menstrual cycle (Table 2).

The mean length of the luteal phase was 13·3 (SD 1·7) d during the residential study. This compared with an average of 13·5 (SD 1·2) d estimated from changes in the basal body temperature in eighteen cycles when the eight women were living at home.

Energy expenditure and its variation within the group

The principal values obtained from the calorimetry study are shown in Table 3. The total energy expenditure varied from 5·6 to 7·5% between subjects at different phases of the cycle. Although some of this variation might be ascribable to differences in metabolic mass, the values, when expressed as the 24 h energy output per kg fat-free mass, still had a coefficient of variation of 5·2% in the early follicular phase and 6·3% in the late luteal phase. This, therefore, signifies small differences in the metabolic activity of the body, or subtle differences in physical activity, despite the standardized activity schedule. This can be assessed to some extent by the analysis of the sleeping metabolic rate (SMR) measured between midnight and 06.00 hours. In this case the absolute SMR had, within the group, a coefficient of variation of 7·1% in the early follicular phase rising to 9·1% in the late luteal measurement; these values fell to 4·7 and 6·1% respectively when expressed in terms of fat-free mass.

The calorimeter computer analysis provided values every 5 min throughout the day and night and this was assessed in 30-min blocks. It was, therefore, possible to assess the degree of variation in energy expenditure during the night in each volunteer. The intra-individual variation was small, varying from 3·8% in subject 7 to 7·8% in subject 4. The small intra- and interindividual variation in SMR does seem, however, to account for most of the interindividual variation in daytime energy expenditure since these again were small, i.e. 5·9% in the early follicular rising to 7·2% in the late luteal phase, and amounting to only 5·8–7·0% when expressed in terms of the volunteers' fat-free mass. This emphasized how well the volunteers adhered to the protocol. It is noteworthy that almost all the analyses show that the time of greatest intra-individual variability occurred in the latter part of the luteal phase of the cycle.

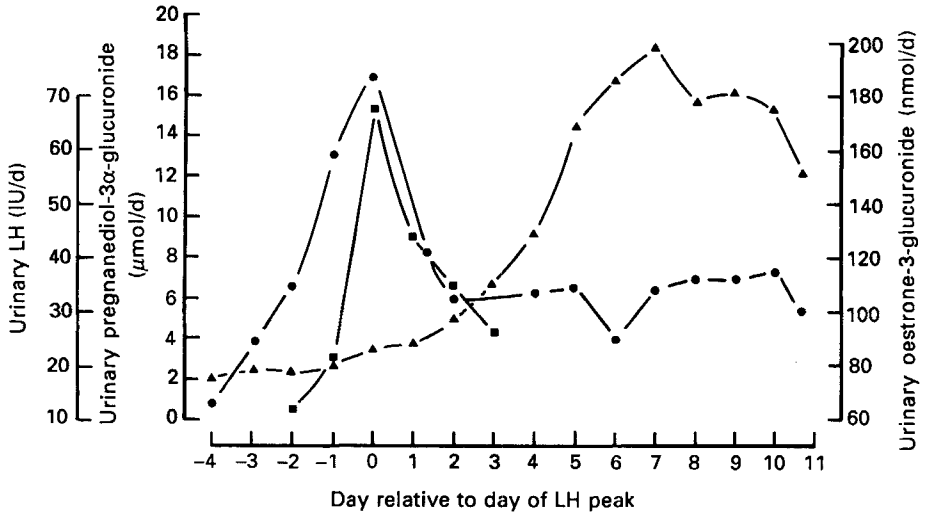

Fig. 3. Summary of mean hormonal profiles for the group during the residential phase of the study. (■—■), Luteinizing hormone (LH); (▲—▲), pregnanediol-3α-glucuronide; (●—●), oestrone-3-glucuronide.

Table 2. *Mean plasma thyroidal concentrations (nmol/l) in women during the menstrual cycle*
(Mean values and standard deviations)

Phase of cycle*...	Early follicular		Late follicular		Early luteal		Late luteal	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Thyroxine (nmol/l)	82	6·1	88	6·4	86	6·1	86	11·4
3,5,3′-Triiodothyroxine (nmol/l)	2·4	0·2	2·1	0·5	2·4	0·2	2·3	0·3
Free 3,5,3′-triiodothyronine (pmol/l)	4·6	0·5	4·6	0·4	4·8	0·6	4·6	0·6

* For details, see pp. 188–189.

Values for the half-hour period used for measuring the BMR are given in Table 4. Given the much shorter duration of measurement than those listed in Table 3, it is perhaps not surprising that the variations in metabolic rate are much higher, with a coefficient of variation for the interindividual values ranging from 5·8 to 12·3%. The BMR and SMR measurements can both be expressed for simplicity of comparison in terms of 24 h values and it is clear that the BMR readings are, on average, 2–7% above the SMR at different times of the cycle, the greatest difference again being in the late luteal phase. The activity ratios, i.e. the 24 h total energy expenditure as a proportion of the BMR, amount to a mean of 1·76 (SD 0·10), slightly lower than the 1·84 (SD 0·09) calculated on the basis of the SMR.

Cyclical variation in energy expenditure

The average values for 24 h energy expenditure, for SMR, BMR and for daytime activities all show a consistent pattern of change throughout the menstrual cycle, with a fall in energy expenditure in the late follicular phase followed by a rise to maximum values in the late luteal stage. These changes are, however, small, amounting to about 1·5% for the daytime and 6·0% for the SMR, with an overall increase in total 24 h energy expenditure

Table 3. *Energy expenditure at different phases of the menstrual cycle (kJ/d)*

Phase of cycle*... Subject	Early follicular	Late follicular	Early luteal	Late luteal
	Total 24 h energy expenditure			
1	10514	10261	10178	10003
2	11310	10927	11571	—
3	11845	11453	11483	11899
4	11117	11537	11723	12161
5	10875	11152	11120	10761
6	9774	9843	10006	10252
7	11369	11378	11320	11526
8	10873	10729	10994	11548
Mean	10960	10910	11049	11164
SD	623	605	637	832
	Sleeping metabolic rate (midnight to 06.00 hours)			
1	5812	5504	5722	5853
2	6092	5700	6338	—
3	6505	6291	6871	6873
4	5574	5597	5943	6002
5	5900	5622	5742	6109
6	5298	5265	5242	5340
7	6525	6586	6781	6930
8	5923	5933	6040	6204
Mean	5954	5775	6085	6187
SD	422	368	554	562
	Daytime energy expenditure (09.30 to 21.30 hours)			
1	12033	11670	11502	11427
2	13177	12516	13435	—
3	13607	12966	13022	13463
4	12593	13377	13413	13920
5	12600	12923	12724	12434
6	11189	11238	11232	11687
7	13033	13253	12738	12857
8	12439	12066	12599	13093
Mean	12584	12501	12583	12697
SD	744	775	815	910

* For details, see pp. 188–189.

of about 2·5% between the late follicular and late luteal phases. The differences in the SMR were highly significant ($P < 0{\cdot}001$). Despite the small variability of the values both between-subjects and within-subjects, the statistical significance of the increase does not emerge in either the daytime values or the total 24 h energy output values. Fig. 4 shows the mean increase in SMR in terms of the individuals' fat-free mass. All the differences between the phases proved to be statistically significant when considered separately (paired t test) except that between early follicular and early luteal phases; there was a sharp increase in metabolic rate between the late follicular and early luteal phases.

The absence of any appreciable changes in the efficiency of physical activity was confirmed by an analysis of the energy cost of cycling at different times of the menstrual cycle (Table 5). These findings and the very small differences between daytime rates of energy expenditure argue against the cyclical changes in energy expenditure being due to differences in exercise or diet-induced thermogenesis or their potential interactions.

Table 4. *Basal metabolic rate (BMR; kJ/d) measured at four phases of the menstrual cycle and related to the 24 h energy expenditure*

Subject	Phase of cycle*				Mean activity rate for 24 h: BMR
	Early follicular	Late follicular	Early luteal	Late luteal	
1	5786	5556	5469	5979	1·80
2	6126	6100	6817	—	1·78
3	7119	7119	7344	6653	1·65
4	5573	6039	5478	7422	1·90
5	5979	6402	6152	7214	1·71
6	4890	5426	5530	5314	1·88
7	6722	6947	7137	7534	1·61
8	6437	5944	6281	6385	1·76
Mean	6079	6024	6276	6643	1·76
SD	696	351	759	817	0·10

* For details, see pp. 188–189.

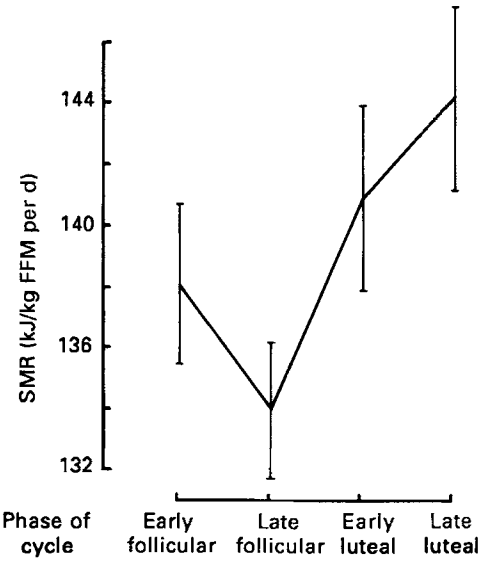

Fig. 4. Mean sleeping metabolic rate (SMR) (kJ/kg), fat-free mass (FFM) (per d) at four phases of the menstrual cycle (for details of phases, see pp. 188–189). Values are means with their standard errors represented by vertical bars.

DISCUSSION

The present study has attempted to bring together the latest hormonal and calorimetric techniques for assessing accurately the different phases of the menstrual cycle and the various components of total 24 h energy expenditure in normal women. Some variation in the pre-residential cycle length (mean 29 (SD 2·7) d with a range from 25 to 33 d) was observed within individual volunteers as well as between the subjects, but the mean length of the cycles during the residential phase was little different at 27·8 (SD 2·2) d. Identifying ovulation by measuring basal body temperature also suggested that the luteal part of the cycle was 13·5 (SD 1·2) d during the pre-residential phase compared with 13·3 (SD 1·7) d

Table 5. *Exercise efficiency* (%) *during four phases of the menstrual cycle*

Subject	Phase of cycle*				Average efficiency† (%)
	Early follicular	Late follicular	Early luteal	Late luteal	
1	29·7	27·7	26·7	28·1	28·0
2	26·4	28·7	28·7	—	27·9
3	24·9	25·2	27·7	23·2	25·2
4	21·4	19·7	19·6	21·1	20·4
5	30·0	33·1	26·9	33·5	30·7
6	27·4	26·9	26·7	29·3	27·5
7	29·2	31·5	31·0	27·6	29·7
8	24·8	24·7	24·3	21·8	23·8
Mean	26·7	27·2	26·5	26·4	26·7
SD	3·0	4·2	3·4	4·5	3·4

* For details, see pp. 188–189.

† Efficiency values were obtained during the cycling period between 22.00 and 22.30 hours; for details, see p. 191.

during the intensive period of residential observations. This suggests that the change in diet to a meat-free, high-fibre regimen and the intensity of the study did not materially alter the cycle length. Nevertheless, the differences in the lengths of the luteal and follicular phases of the cycle necessarily required that the calorimeter measurements, organized to take place 3 to 5 d and 10 to 12 d after ovulation and menstruation, were not conducted at identical times of the cycle in all the volunteers. That precision of timing is necessary became evident from the cyclical change in metabolic rate, and what appeared to be a sharp increase in energy expenditure at about the time of ovulation.

These changes in energy expenditure could explain only in part the differences in basal body temperature (BBT) between the follicular and luteal phases of the cycle. There seemed to be no close relation, since the BBT during the follicular phase did not drop progressively and there was only a single day's nadir in BBT which appeared to correspond to the oestrogen surge immediately before ovulation. We did not measure energy expenditure daily around the time of ovulation so a sharp increase in metabolic rate could have occurred, but in the later luteal phase there was a further increase in metabolic rate without a corresponding increase in BBT. This implies that there are changes in vasomotor function and heat storage during the course of the cycle which are likely to contribute to the resetting of BBT in the luteal phase.

The basis for the changes in energy metabolism remains uncertain. Progesterone, administered to both normal and ovariectomized women has been shown to be hyperthermic (Barton & Wiesner, 1945; Kappas & Palmer, 1965) and this led Solomon *et al.* (1982) to conclude that increased progesterone output was responsible, particularly with the known increase in progesterone during the luteal phase.

A direct link between progesterone secretion and the control of BBT seems unlikely, given the sharp rise and then stable BBT in the luteal phase and the progressive rise in progesterone secretion, although a significant ($P < 0{\cdot}001$) relation was found in our study between the BBT at eight phases of the cycle and the log of mean urinary pregnanediol-3α-glucuronide levels for the same periods when all the women's values were assessed together by linear regression analysis. The amplitude of the increase in SMR did not relate significantly to the magnitude of the increases in pregnanediol-3α-glucuronide, but a statistically significant relation ($P < 0{\cdot}05$) was observed when the SMR changes were

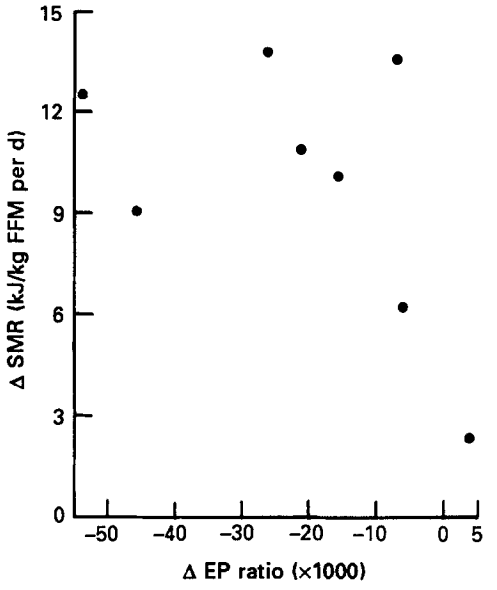

Fig. 5. The relation between the change in sleeping metabolic rate (△SMR) over the menstrual cycle and the difference between the ratio, oestrone-3-glucuronide: pregnanediol-3α-glucuronide (△EP ratio) excretion at these times. FFM, fat-free mass.

$$\triangle SMR = 5{\cdot}57 - 1{\cdot}77 \log_n \triangle EP \quad (r - 0{\cdot}7638, P < 0{\cdot}05).$$

related to the ratio, oestrone-3-glucuronide: pregnanediol-3α-glucuronide output (Fig. 5). This relation may not be causal, but simply reflects the correlation between two indices of a change in hypothalamic regulation during the course of the menstrual cycle. Extensive animal experiments have attempted to unravel the effects of sex hormones on energy balance, perhaps the most relevant being the studies of the effects of ovarian hormones on food intake and body-weight in primates (Czaja & Goy, 1975; Rosenblatt *et al.* 1980; Kemnitz *et al.*1982; Bielert & Busse, 1983).

The present study strongly suggests that the small changes in total energy expenditure amounting to only about 2·5% are dependent on larger alterations in resting metabolic rate rather than on any changes in diet- or exercise-induced changes in energy balance. Webb (1986), in his recent analyses of 24 h energy expenditure during the menstrual cycle, observed a 9% increase in energy output, but studied subjects in an extremely sedentary state while wearing a calorimetric suit. The magnitude of the swing is, therefore, more akin to that observed during sleep in our studies; nevertheless, Webb (1986) did observe a more clearcut increase in daytime values during the post-ovulatory period, but made no direct assessment of diet-induced thermogenesis.

These subtle shifts in energy expenditure imply a complex control system for energy balance. If food intake normally increases by 12·5% (Pliner & Fleming, 1983) to 38% (Dalvit, 1981) in normal women during the menstrual cycle, then this may reflect a biphasic change in energy balance during the menstrual cycle, with women being in positive energy balance during the luteal phase and negative balance during the follicular phase. How long-term energy balance is controlled under these circumstances is unclear, but the small shifts in energy output may be important. If contraceptives, by inhibiting ovulation, also inhibit the increase in energy expenditure, then this could represent about a 1% decline in average energy output, and perhaps account for a slow increase in body fat in women taking

contraceptives or after the menopause. Webb (1986) found in a single subject a stability of energy output when she was taking an oral contraceptive, and in preliminary studies we have observed a decline in BMR in women on oral contraceptives compared with the non-pill cycles, and there was no significant difference in BMR at different stages of the cycle (McNeill *et al.* 1988). This emphasizes the importance of hormonal changes in determining the observed phasic pattern of energy expenditure in young women.

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