Women at altitude: energy requirement at 4,300 m

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Mawson, Jacinda T., Barry Braun, Paul B. Rock, Lorna G. Moore, Robert Mazzeo, and Gail E. Butterfield. Women at altitude: energy requirement at 4,300 m. J. Appl. Physiol. 88: 272–281, 2000.—To test the hypotheses that prolonged exposure to moderately high altitude increases the energy requirement of adequately fed women and that the sole cause of the increase is an elevation in basal metabolic rate (BMR), we studied 16 healthy women [21.7 ± 0.5 (SD) yr; 167.4 ± 1.1 cm; 62.2 ± 1.0 kg]. Studies were conducted over 12 days at sea level (SL) and at 4,300 m (high altitude [HA]). To test that menstrual cycle phase has an effect on energetics at HA, we monitored menstrual cycle in all women, and most women (n = 11) were studied in the same phase at SL and HA. Daily energy intake at HA was increased to respond to increases in BMR, and to maintain body weight and body composition. Mean BMR for the group rose 6.9% above SL by day 3 at HA and fell to SL values by day 6. Total energy requirement remained elevated 6% at HA [−670 kJ/day (160 kcal/day) above that at SL], but the small and transient increase in BMR could not explain all of this increase, giving rise to an apparent “energy requirement excess.” The transient nature of the rise in BMR may have been due to the fitness level of the subjects. The response to altitude was not affected by menstrual cycle phase. The energy requirement excess is at present unexplained.

LITTLE IS KNOWN ABOUT ENERGY requirements in women exposed to high altitude. In the 1960s, Hannon and colleagues (16–19) performed the most thorough study of the question to date. Their subjects demonstrated moderate anorexia and a transient elevation in basal metabolic rate (BMR) when taken to 4,300 m and provided an ad libitum diet. After the first week of altitude exposure, food intake and BMR returned to near sea level values. Hannon and co-workers (17) concluded that women required no more energy at high altitude to maintain body weight and composition than they required at sea level. However, the women they studied continued to lose weight slowly after the first week at high altitude, suggesting that an energy imbalance persisted and that, in actuality, energy require-

ments of women at high altitude may be elevated above those at sea level.

Similar studies in men illustrate that high altitude exposure is frequently accompanied by weight loss caused in part by energy imbalance (4, 11, 15, 21, 23, 28, 31, 38, 39) and increased basal energy requirement (15, 24, 26, 35). However, Butterfield et al. (8) have shown that it is possible to eliminate this weight loss in men at the moderately high altitude of 4,300 m simply by increasing energy intake to match changes in BMR. Under their experimental conditions, BMR increased over sea-level values after the first day at altitude and remained elevated throughout a 3-wk sojourn. Total energy required to maintain body weight and composition (defined as total energy requirement [TER]) at high altitude was ~1,256 kJ/day greater than that at sea level. Thus, in men, when the increased energy requirement associated with altitude exposure is met by increased food intake, energy balance can be achieved, but requirements remain elevated throughout exposure.

Building on this understanding of energy requirements in men taken to high altitude, we proposed to test the hypothesis that energy requirements of women exposed to similar conditions would remain elevated above sea-level values throughout the sojourn when energy intake was sufficient to maintain body weight and body composition. Furthermore, we hypothesized that increasing energy intake by an amount equal to the increase in BMR at high altitude would be sufficient to meet the increased energy requirement. Finally, because fluctuations of the ovarian steroid hormones estradiol and progesterone have been associated with changes in energy intake (3) and BMR (34) at sea level, we hypothesized that energy requirements at altitude would differ with respect to menstrual cycle phase.

MATERIALS AND METHODS

Experimental design. To test these hypotheses, we designed a study in which the TER of women was established at sea level and compared it with the energy requirement at high altitude. TER was defined as the energy intake required to maintain body weight and composition. BMR was measured as the primary component thought to determine the change in TER between sea level and high altitude. We attempted, when logistically possible, to test each individual in the same phase of the menstrual cycle (follicular or luteal) at sea level and high altitude.
Sea level (SL) studies were conducted in the metabolic unit at the Veterans Affairs Health Care System, Palo Alto, CA (15 m, SL); high altitude (HA) studies took place at the Maher Memorial Laboratory, Pike's Peak, CO (4,300 m, HA). Each study period lasted 12 days. At the time of the altitude studies, women were flown to Colorado and taken immediately by car to HA, with fewer than 12 h elapsing between leaving SL and achieving HA.

Food intake was enforced throughout both SL and HA study periods, with energy intake adjusted to minimize weight loss. Adequacy of energy intake and maintenance of body composition were estimated by the nitrogen (N) balance weight loss. Adequacy of energy intake and maintenance of body composition (9). Activity and fluid intake excretion, is the expected result if energy intake is adequate to maintain body composition (9). Activity and fluid intake were also monitored.

Subjects. Sixteen healthy women (21.7 ± 0.5 yr; 167.4 ± 1.1 cm; 62.2 ± 1.0 kg; 42.0 ± 1.5 ml·kg⁻¹·min⁻¹ peak oxygen consumption; see Table 1) with a history of normal menstrual cycles participated. The women were nonsmokers, of normal body weight and body mass index (wt/ht²), and moderately physically active, and all but one had not been exposed to altitudes >1,500 m within the preceding year. Physical examination, medical history, routine blood profile, blood glucose response to a standard meal, nutritional assessment, examination, medical history, routine blood profile, blood glucose response to a standard meal, nutritional assessment, and serum ferritin were used to determine health status for purposes of exclusion from the study; applicants with significant abnormalities in any parameter were excluded. Potential subjects with serum ferritin levels <20 mg/dl at the time of screening were asked to take a daily supplement of ferrous sulfate (325 mg FeSO₄ with 65 mg elemental iron) to bring serum ferritin up to the acceptable levels in fasting plasma collected on days 3, 6, 9, 10, and 11 at HA, as described previously (5). At SL, eight women were determined to be in the follicular phase of the menstrual cycle began testing at SL and HA on the day after the onset of menses. Women studied in the luteal phase began testing at SL or HA on the day after a surge of luteinizing hormone determined by the use of luteinizing hormone predictor kits (OvuQuick, Quidel, San Diego, CA). Cycle phase was confirmed by estradiol and progesterone levels in fasting plasma collected on days 3, 9, and 12 at SL and days 3, 6, 9, 10, and 11 at HA, as described previously (5). At SL, eight women were determined to be in the follicular phase (progesterone never exceeding 2.4 ng/ml) and eight subjects in the luteal phase (progesterone peaking at a level >2.5 ng/ml) (36) throughout the study period. At HA, 11 of the women were studied in the follicular phase, and five women in the luteal phase. Eleven of the women were studied in the same phase at both SL and HA (see Table 1).

Diet. Subjects were asked to consume specified quantities of a standardized diet for days 1–12 at SL and days 1–12 at HA. The basic diet contained the same food at SL and HA (Table 2), deriving 64% of kilocalories from carbohydrate, 24% from fat, and 12% from protein. Initial energy intake for each subject was determined based on the Harris-Benedict equation (20) and activity level. SL energy intake was adjusted to ensure weight maintenance. The energy intake that maintained body weight was defined as the SL TER, and adequacy of this intake was verified by using NB. Adjustments of energy intake were made by varying the amount of specific food items consumed (carbohydrate and electrolyte replacement drink, chocolate bar, nutrient bar, pasta, margarine, wheat bread). The absolute intake of protein was maintained relatively constant (1 g/kg) for each subject, and the intake of energy derived from carbohydrate and fat was adjusted to

### Table 1. Subject characteristics by phase of study at sea level

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Sea-Level Phase</th>
<th>High-Altitude Phase</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>V̇O₂peak, ml·kg⁻¹·min⁻¹</th>
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<td>F</td>
<td>F</td>
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<td>6</td>
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<td>L</td>
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<td>61.86</td>
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<td>F</td>
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<td>F</td>
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<td>56.55</td>
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<td>169.8</td>
<td>63.13</td>
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<tr>
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<td>66.00</td>
<td>39.42</td>
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<td>4.43</td>
<td>8.68</td>
<td>4.51</td>
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<td>21.7</td>
<td>167.4</td>
<td>62.20</td>
<td>42.00</td>
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<tr>
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<td>0.5</td>
<td>1.1</td>
<td>1.10</td>
<td>1.50</td>
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</table>

F, follicular phase; L, luteal phase; V̇O₂peak, peak oxygen consumption.
keep the proportion of each approximately consistent among all subjects.

Energy intake on day 1 at HA was set at the SL TER. For the remainder of HA, energy intake was adjusted commensurate with changes in BMR and body weight. Increasing energy intake to compensate for BMR [SL TER + increase in BMR at HA, defined as estimated energy requirement (EER)] was not always sufficient to maintain body weight, and additional energy was added as needed to minimize weight loss (total amount of energy required to maintain body weight defined as TER). Each woman filled in daily logs of all foods consumed. Estimation of energy intake from food tables was deemed accurate based on bomb calorimetric analysis of foods performed previously (8).

At SL, subjects drank water ad libitum. At HA, subjects were asked to consume a minimum of 3 liters of water/day (including fluid from food) and to measure and record all fluid consumed. "Crude" fluid balance (intake as food and water − urine volume) was computed to assist in the evaluation of body weight data. This value neglects the water produced by metabolic fuel oxidation, losses from feces, and insensible losses but has been used to estimate the latter (12).

Determination of BMR, body weight, and NB. At SL, subjects spent the night in the metabolic ward for days 7–11 of the study period. Determination of BMR with the use of indirect calorimetry, as reported previously (8), occurred on days 7–9. Measurements were made before the subjects arose, 8–10 h postprandial, and after 6–8 h of bed rest. Body weight was recorded immediately after the subjects arose and voided. Urine was collected for 24-h periods on days 7–11, beginning at 0700. Weight and volume of urine were recorded. Three-day fecal collections were made on days 7–9. To determine N intake, the equivalent of all foods consumed for 1 day by each subject was blended until homogeneous, and a determination of N intake, urinary N, and fecal N were analyzed and calculated at SL and HA (8), fecal collections were not conducted at HA.

At HA, measurements of BMR were made on days 2–12 under the same conditions as at SL. Body weight was recorded daily immediately after the subjects arose and voided. Urine collections for days 2–11 were made for 24-h periods. Urine weights and volumes were recorded daily, and aliquots were frozen at −20°C for later analysis of N content by the micro-Kjeldahl method (2). Additional urine samples were stored for analysis of catecholamines, as previously reported (25), and creatinine by using routine autoanalyzer methodology. Any urine collection with a creatinine value that deviated >10% from the mean for that individual was considered an incomplete collection and was eliminated from calculations.

At HA, measurements of BMR were made on days 2–12 under the same conditions as at SL. Body weight was recorded daily immediately after the subjects arose and voided. Urine collections for days 2–11 were made for 24-h periods. Urine weights and volumes were recorded daily, and aliquots were frozen at −20°C for subsequent analysis, as described above. On the basis of studies done in men that showed no difference in fecal N between SL and HA (8), fecal collections were not conducted at HA.

At SL, NB was calculated by using the formula 

\[NB = N \text{ intake} - (N\text{ intake} + N\text{ fecal} + N\text{ miscellaneous losses of N})\]

where N intake, urinary N, and fecal N were analyzed and calculated at SL and HA (8). Fecal collections were not conducted at HA.

Energy expenditure at activities. To ensure that activity was constant between SL and HA, subjects were queried as to their usual physical activity pattern at SL, and individualized activity programs of treadmill walking, stationary biking, and weight lifting were developed for use at HA. After the first day at HA, subjects were instructed to follow individualized exercise programs to maintain SL fitness and energy expended at activities and to record exercise more strenuous than walking. Daily energy expenditure was estimated by calculating energy expended while the subjects were sleeping (BMR/min × min sleeping) and energy expended while the subjects were awake [(1.5 × BMR/min) × min awake but not exercising] + [(BMR/min × energy factor for each activity) × min performing activity]. Energy factors used for activities were those of Mulligan and Butterfield (27).

Other measures. Acute mountain sickness (AMS) was monitored daily at HA by using the Environmental Symptoms Questionnaire at 0700 and 1900. Mean daily AMS-cerebral (AMS-C) values were used to determine the distinction between subjects with and without AMS. A score > 0.7 was taken as indicating the presence of AMS (32). Subjects were divided into those with and without AMS, by this definition, for statistical analysis. These data have been published elsewhere (30).

Levels of daily catecholamine (epinephrine and norepinephrine) excretion were determined on 24-h urine samples by using high pressure liquid chromatography as previously described (25).

Statistical analysis. Because the SL study period was the control condition, dependent variables recorded during that time were averaged to provide a comparison value for daily HA values. All values in the text and tables are expressed as means ± SD; figures were drawn by using means ± SE for visual clarity. Data were initially evaluated for significant differences between subjects studied in the follicular and the luteal phases of the menstrual cycle over time by using a two-way (menstrual cycle, time) repeated-measures ANOVA. When no significant differences were identified, data were pooled, and repeated-measures one-way ANOVA was used to identify significant changes over time with SL as one time point. ANOVA was performed by using SAS (SAS Institute, Cary, NC) or GB-Stat (Dynamic Microsystems, Silver Spring, MD) software with P < 0.05 as the level of significance. When main effects were found, significantly different means were identified by using Fisher’s least significant difference post hoc analysis. Regression analysis with the use of GB-Stat was performed to determine correlations.

RESULTS

SL (control). Body weight was maintained during SL (mean weight change days 2–12 = −0.16 ± 0.90 kg) with a mean TER of 10,541 ± 798 kJ/day (2,518 ± 191 kcal/day; Table 3). Results of the 4 days of NB studies at SL were positive for many women (mean NB = 0.605 ± 1.49 g N/day), and most women demonstrated at least N equilibrium, indicating that the SL TER was adequate to maintain body composition (9). Women studied in the follicular phase had a slightly lower TER (10,419 ± 707 kJ/day or 2,498 ± 169 kcal/day) than those studied in the luteal phase (10,796 ± 783 kJ/day or 2,579 ± 187 kcal/day), but the difference was not significant. Mean BMR for the group was 5,826 ± 494 kJ/day (1,392 ± 118 kcal/day or 196.4 ± 16.5 ml O₂/min; see Table 3). There was no significant difference between the BMR of the women studied in the follicular phase (5,626 ± 494 kJ/day or 1,344 ± 118 kcal/day; 196.4 ± 16.0 ml O₂/min) and those studied in the luteal phase (5,906 ± 352 kJ/day or 1,411 ± 84 kcal/day; 196.4 ± 16.0 ml O₂/min).
Table 3. Sea-level and daily high-altitude values for energy, nitrogen and fluid balances, and catecholamine levels

<table>
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<tr>
<th></th>
<th>Sea Level</th>
<th>HA2</th>
<th>HA3</th>
<th>HA4</th>
<th>HA5</th>
<th>HA6</th>
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<th>HA10</th>
<th>HA11</th>
<th>HA12</th>
</tr>
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<tbody>
<tr>
<td>BMR, kJ/day</td>
<td>5,826.1</td>
<td>6,028.9</td>
<td>6,227.7</td>
<td>6,188.0</td>
<td>6,054.3</td>
<td>5,847.7</td>
<td>5,860.1</td>
<td>5,925.2</td>
<td>5,879.2</td>
<td>5,917.0</td>
<td>5,954.3</td>
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<tr>
<td>± BMR, kJ/kg</td>
<td>± 493.8</td>
<td>± 434.4</td>
<td>± 558.5*</td>
<td>± 737.7</td>
<td>± 823.0</td>
<td>± 666.1</td>
<td>± 692.7</td>
<td>± 585.8</td>
<td>± 527.1</td>
<td>± 548.5</td>
<td>± 682.8</td>
<td>± 711.4</td>
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<tr>
<td>± BMR, ml O₂/min</td>
<td>± 8.7</td>
<td>± 8.8*</td>
<td>± 8.5*</td>
<td>± 8.6*</td>
<td>± 8.3*</td>
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<td>TER, kJ/day</td>
<td>10,541.4</td>
<td>10,740.2</td>
<td>10,844.9</td>
<td>10,923.1</td>
<td>11,086.9</td>
<td>11,243.9</td>
<td>11,358.4</td>
<td>11,423.3</td>
<td>11,463.1</td>
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<td>Daily EE, kJ/day</td>
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<td>9,471.2</td>
<td>9,915.2</td>
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<td>9,418.5</td>
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<td>8,995.7</td>
<td>8,560.4</td>
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<td>Fluid balance, ml/day</td>
<td>± 1,176.3</td>
<td>± 1,293.5</td>
<td>± 1,812.5</td>
<td>± 1,582.3</td>
<td>± 1,208.8</td>
<td>± 1,218.1</td>
<td>± 1,193.0</td>
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<td>± 690.7</td>
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<td>Body weight, kg</td>
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<td>63.09</td>
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<td>± 1.10</td>
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<tr>
<td>NE, µg/day</td>
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<td>± 1.017*</td>
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<td>± 0.645</td>
<td>± 0.041</td>
<td>0.163</td>
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<tr>
<td>± 1.487</td>
<td>± 2.851**</td>
<td>± 2.758*</td>
<td>± 1.792*</td>
<td>± 1.320</td>
<td>± 1.534</td>
<td>± 1.131</td>
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<td>AMS-C</td>
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<td>± 0.97</td>
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<td>± 0.12</td>
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<td>± 30.42*</td>
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<td>± 3.98</td>
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<td>± 4.08</td>
<td>± 2.93</td>
<td>± 4.12</td>
<td>± 5.33</td>
<td>± 6.09</td>
<td>± 4.61</td>
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Values are means ± SD. HA2–HA12, high altitude days 2–12; BMR, basal metabolic rate; TER, total energy requirement; daily EE, daily energy expenditure computed from activity diaries; NB, nitrogen balance; fluid balance, crude fluid balance; AMS-C, acute mountain sickness-cerebral score; NE, 24-h urinary norepinephrine; Epi, 24-h urinary epinephrine. *Significantly different from sea level (P < 0.05).
HA. Means of TER, the EER based only on the increase in BMR at HA, and the actual energy intake are reported in Fig. 1 for both SL and each day at HA. During the initial days of HA, actual energy intake was impaired in some subjects. Ten of the women experienced some degree of AMS (defined as a mean daily AMS-C score >0.7) during the first 3 days of exposure (mean AMS-C score for days 1–3 = 1.0 ± 0.96). For six subjects on day 1, five subjects on days 2 and 3, three subjects on day 4, and two subjects on day 5, the severity of AMS symptoms was sufficient to significantly reduce actual energy intake (see Fig. 1). As the symptoms subsided, actual energy intake increased, reaching the TER by day 6. The mean TER for the group was elevated over that at SL by day 3 (10,845 ± 855 kJ/day or 2,591 ± 204 kcal/day at HA vs. 10,541 ± 798 kJ/day or 2,518 ± 191 kcal/day at SL) and remained elevated throughout the rest of the sojourn. TER peaked at 11,463 ± 992 kJ/day (2,738 ± 237 kcal/day) on day 9, a value 1.97 times SL BMR. Mean TER over the 12-day period was 11,198 ± 946 kJ/day (2,675 ± 226 kcal/day), 1.92 times SL BMR. Weight loss was minimal at HA (0.46 ± 0.71 kg during the 12 days, an average of 41.8 ± 64.5 g/day; see Table 3). The majority of this weight loss (0.42 kg) occurred during days 1–5 at HA when the enforcement of food and fluid intake was often hampered because of AMS symptoms. Changes in body weight from day 2 to 12 of HA did not differ between the women studied in the follicular and those in the luteal phase. Crude fluid balance (see Table 3) was near equilibrium on day 1, suggesting a possible diuresis with acute exposure that may have contributed to some of the initial weight loss seen. Mean crude fluid balance became positive and constant with time, stabilizing at about +800 ml/day, a value that could be construed as equivalent to insensible losses (12).

Mean NB was negative and lower than SL on days 2–4 at HA (see Fig. 2). It reached a nadir on day 2, increased on days 3 and 4, and returned to equilibrium on day 5, a pattern that matched actual energy intake. NB became positive after day 5, suggesting a retention of N (and possibly a slight increase in lean tissue mass) after this time. The response of NB to altitude exposure was not significantly different between the women studied in the follicular and those studied in the luteal phase.

The EER (see Fig. 1) was computed from the SL energy requirement plus the change in BMR at HA. There was no significant difference in the response of BMR to HA between the women studied in the luteal and follicular phases of the menstrual cycle (see Fig. 3). BMR, when expressed in kilojoules per day was significantly different from SL only on day 3 (6,228 ± 558 kJ/day). When expressed in kilojoules per kilogram or basal oxygen consumption (ml O2/min), BMR was significantly different from SL on days 3–5. Basal oxygen consumption was greater at HA than SL on day 3 (SL = 196.4 ± 16.5 ml O2/min; HA = 212.94 ± 18.23 ml O2/min) and remained higher than SL only through day 5 (see Fig. 3). After that time, HA basal oxygen consumption was not different from that at SL. Thus the EER computed from the change in basal oxygen consumption did not match TER in these women after day 5. Rather, TER remained elevated, whereas the EER returned to SL values, creating an "energy requirement excess" of ~670 kJ/day (160 kcal/day) between estimated and real energy requirements at HA.

The energy requirement excess between EER and TER could be explained if activity level increased in the women while at HA. Individual exercise regimens, designed to match SL activities, were completed only ~72% of the time at HA, however. The total daily energy expenditure estimated from activity records was less than the energy required to maintain body weight (see Table 3), especially toward the end of the sojourn. Mean energy expended at exercise more strenuous than walking was 1,645 ± 452 kJ/day (393 ± 108 kcal/day).
DISCUSSION

In this study of women exposed to moderately HA (4,300 m) for 12 days, we determined that the TER to maintain body weight and composition (as monitored by NB) was elevated ~670 kJ/day above the requirement at SL and that this elevation extended throughout the sojourn at HA. Furthermore, the increase in energy requirement with moderately HA exposure could not be explained only by a rise in BMR, because the increase in BMR was transient and small, and HA BMR returned to SL values by day 5, whereas TER remained elevated. We discovered an energy requirement excess of ~670 kJ/day between estimated and actual energy requirement at HA (see Fig. 1), a finding not previously identified in other studies in women nor found in similar studies in men. These results were unaffected by the menstrual cycle phase in which the women were studied.

The TERs at HA reported here are of similar magnitude to those reported elsewhere for similar altitudes. The increase in TER in the women to 1.92 times SL BMR is slightly lower than the 2.05 (8) and 2.2 (7) times SL BMR found for TER in men under similar dietary, altitude, and activity conditions. Other studies evaluating energy requirements for a variety of activity patterns show a range of TER from 1.6 times SL BMR in men and women resting at 6,542 m (39) to 2.4 times BMR in the same individuals climbing to that elevation. Using doubly labeled water in soldiers, Hoyt and co-workers (21) found TER to range from 2.1 times SL BMR in individuals performing routine activities at 3,500 m, and Worme et al. (40) showed TER to be 3.5 times SL BMR in soldiers performing strenuous winter exercises at 2,500–3,100 m.

TER is the sum of energy required to sustain basic body functions (BMR), to digest and process food [ther-
mic effect of food (TEF), and to perform physical activity (thermic effect of activity (TEA)). Theoretically, the sum of these factors plus any changes in body weight should approximate the energy requirement of the individual. In this study, we evaluated the elements of energy balance and cannot completely account for the "excess" in energy requirement seen at HA in these women.

Body weight loss in this experiment was minimal (mean loss = 41.8 ± 64.5 g/day over the 12 days of the study) and much smaller than the loss shown in most other studies (see Ref. 7 for recent review), in which weight loss has been found to average ~150 g/day. In the only other report in women, Hannon and Sudman (19) found that subjects with a substantial initial energy deficit and a continuing deficit of ~712 kJ/day less at HA than at SL lost weight over 3 mo. In our experiment, as in the study by Hannon and Sudman, the majority of the weight loss occurred during the first 5 days at HA when energy intake was less than at SL for the group as a whole and N and crude fluid balances were negative. These data suggest that the weight loss was consequent to inadequate energy intake during that time (9), as well as to possible diuresis. Further weight loss was prevented (weight loss days 6–11 = 6 g/day) when sufficient energy was consumed after day 5. N equilibrium was reestablished, and crude fluid balance became positive and constant, suggesting that the subjects were in energy and fluid balance after the first week at HA. Thus the TER determined in this experiment maintained body weight and N equilibrium.

A small, transient increase in BMR was one factor contributing to the increased TER in these women during the first 5 days at HA. Transient increases in BMR at altitude are well documented in both women and men. This increase may be a response to the stress of altitude exposure or to the stress of inadequate energy intake. Urinary epinephrine levels in our study were elevated 93% above SL values on day 2 of exposure and fell to SL values by day 5 (see Table 3), where they stayed for the remainder of the exposure (25). Levels of norepinephrine, however, increased throughout the HA exposure, peaking at 79% above SL values on day 11. Both epinephrine and norepinephrine affect BMR and total energy expenditure at SL (13, 29). In addition, SL studies have demonstrated acute increases in oxygen consumption during the first few days of fasting or inadequate energy intakes (37). Whereas short-term fasting studies commonly exhibit diuresis (37), several of these studies also demonstrate increased levels of epinephrine and/or norepinephrine.

The relatively small increase in BMR seen in this experiment may reflect the small energy deficit experienced by these subjects. In work at the same facility, Hannon and Sudman (19) reported much larger increases in BMR of 28% by day 3 of exposure in women with a greater energy deficit (2,930 kJ/day below SL intake). BMR in their subjects fell to SL values by day 7 at HA. Studies in men fed ad libitum and consuming less energy than required have shown increases in BMR of a magnitude similar to that seen in the Hannon and Sudman study (28%), followed by a decline to SL values within 3 wk (24, 26). However, Butterfield et al. (8) found only a 17% increase in BMR, which was maintained throughout 3 wk at HA in men fed adequate energy to maintain body weight in an experimental design similar to that used in our study.

Further support for the hypothesis that initial energy deficit drives an increase in BMR may be found by dividing our subjects into groups of those who consumed adequate energy from the beginning of HA ("eaters," n = 7) and those who were unable to eat adequately initially ("noneaters," n = 9). The peak increase in BMR in the noneaters was greater by ~314 kJ/day than that of the eaters (Fig. 4A), although the differences in these data are not statistically significant. Higher BMRs in the noneaters do not appear to be mediated by catecholamine levels, however, as levels of epinephrine and norepinephrine were lower in the noneaters compared with the eaters. Only the levels of epinephrine were significantly lower. About one-half of the subjects with AMS were unable to eat adequately at some point during the first few days at HA. Among all subjects with AMS (n = 10), however, there was a trend (P = 0.09) toward smaller increases in BMR from SL values (HA BMR – SL BMR) than in subjects without AMS.

The decline in BMR observed here after day 5, and in other studies (24), may be explained by the fitness level of the subjects. When the women in this study are divided by the results of their SL maximum oxygen consumption (VO_{2max}) tests into "fit" (SL VO_{2max} >42 ml·kg^{-1}·min^{-1}, n = 10) and "less fit" (SL VO_{2max} <42 ml·kg^{-1}·min^{-1}, n = 6; Ref. 6; Fig. 4B), the data suggest that the BMR fell to SL values in the fit women, whereas it remained elevated by 10% (~544 kJ/day) above SL values in women who were less fit. Although the BMR values for the two groups were not significantly different, norepinephrine levels were significantly greater in the fit women than in the less fit. Armstrong (1), comparing the effect of repeated cold challenges in fit and unfit women, demonstrated that fit women showed a smaller increase in BMR and an increase in norepinephrine that was twice as large as that seen in the unfit women. Perhaps fit women are better able to adapt metabolically to the stress of altitude than less fit women are. The men studied by Butterfield et al. (8) who maintained an elevated BMR throughout 21 days at 4,300 m would have been defined primarily as less fit by the same criteria (6).

The TEF was not studied directly in our experiment. However, the TEF associated with SL energy intake is part of the SL TER. Stock et al. (35) reported that this component of energy output decreased 17% with acute exposure to altitude but rose to normal values within 3 days when food intake was ad libitum. In circumstances in which energy intake is greater than at SL, as in our experiment, TEF may be elevated (14). The subjects in this experiment found it necessary to eat five or more times a day to consume all food required, and thus TEF may have been greater at HA than at SL.
However, the magnitude of the increase in TEF in response to an extra 670 kJ/day intake (at most 10% or 67 kJ/day) would not in itself be sufficient to explain the 670-kJ energy requirement excess.

The final element in the determination of TER is the TEA. If TEA increases at HA compared with SL, TER could be increased concomitantly. However, our women were not able to maintain the activity programs developed to mimic their SL activities 72% of the time at HA, and the daily energy expenditure calculated from activity diaries did not approach the TER. Even if these activity diaries represent an underreporting, these data suggest that the women were probably less active at HA than at SL. A similar reduction in activity at altitude has been shown in men (8). Thus the change in activity from SL to HA is in opposition to the energy requirement excess.

That the elevated TER at altitude cannot completely be accounted for by increases in BMR, TEF, or TEA suggests two possibilities: either there may be other factors affecting energy requirement in these women, or there may be methodological errors that give rise to the energy requirement excess. Considering the first, early reports in men suggested that impaired digestibility and/or absorption of nutrients may play at least a minor role in energy imbalance at altitude (4, 28), but these reports have not been substantiated by more recent reports specifically targeting protein (23) or fat absorption (22). The impact of absorption in women is unknown, but there is no reason to suspect that there is a gender difference in digestibility of food components.

Considering the second possibility, potential sources of error in the methods used here include failure to include energy derived from weight change in the

Fig. 4. A: BMR for subjects eating adequately (Eaters, n = 7) and not eating adequately (Noneaters, n = 9) for days 2–12 at HA. B: BMR for subjects with SL maximum oxygen consumption >42 ml·kg⁻¹·min⁻¹ (Fit, n = 10) and <42 ml·kg⁻¹·min⁻¹ (Less Fit, n = 6) for days 2–12 at HA. Values are means ± SE.
calculation of energy requirement, inaccuracies in intake and activity records, and problems in determination of BMR. Inclusion of the energy derived from changes in body tissue (mean weight loss over the 12 days was 0.46 ± 0.71 kg, which could be equivalent to 690–1,570 kJ/day, depending on the composition of the tissue lost) would increase the energy requirement excess by increasing the TER. Inaccuracy in record keeping is one of the main problems in determination of energy requirements by the balance method (33). In this experiment, food intake was supervised and enforced so that, with few exceptions, these data should reflect true intakes required to maintain body weight. However, the possibility of occasional overreporting of intake cannot be completely ruled out. Because the intake records were in part self-reports, if the women reported eating foods they did not actually consume, TER could be artificially inflated. On the output side, activity energy expenditure may have been somewhat underestimated here because of boredom, but the trend seen is similar to that seen in other studies (8), with a gradual decrease in activity over time. This trend does not explain the continued increase in TER toward the end of the 12-day stay. Finally, because BMR was used to calculate the theoretical energy requirement and thus the energy requirement excess, its determination is important. However, the possible sources of error in this measurement, such as elevation due to sleeplessness or failure to be truly resting at the time of the measurement, would only serve to decrease the energy expenditure excess, not create it. Thus, although potential inaccuracies in the self-reports used to calculate the energy requirement excess may have contributed in part to that parameter, we feel that these potential errors were minimized because of the dedication of the subjects. In addition, other potential methodological errors may have actually diminish the effect, suggesting that the energy requirement excess reported here could be underestimated.

This discrepancy between EERs and actual TER is not easily explained. Although the pattern of norepinephrine levels during the exposure appears to mimic the increase and sustained elevation in TER, the statistical correlation is weak (r = 0.01), nor does epinephrine correlate significantly with TER or BMR. Thus we have no definitive explanation for the energy requirement excess.

Finally, we found that the potential effect of the menstrual cycle phase, as defined by ovarian hormone levels, on BMR and energy requirement seen in some studies at SL was not seen in these women at SL or HA. Women studied in the follicular phase (progesterone never < 2.4 ng/ml) did not differ significantly from the women studied in the luteal phase (progesterone peaking at > 2.5 ng/ml) with respect to TER, BMR, NB, or weight loss. The small number of subjects studied in the luteal phase at HA may have precluded identification of a significant effect. However, time of measurements within the cycle may have contributed more significantly to the lack of detectable response in our study. Previously, when differences have been shown in BMR (34) or energy intake (3) between follicular and luteal phases, they have been apparent only in the first days of the luteal phase in women followed across an entire cycle. The subjects in the study reported here were not studied in both phases of the menstrual cycle at SL and thus did not act as their own controls for menstrual cycle comparisons. In addition, SL BMR measurements were made toward the end of the menstrual phase when differences between phases are generally undetected, and HA measurements were made across the whole cycle phase, with its range of hormone levels. Thus, comparison of the values across the same approximate time of the cycle at SL and HA would not be expected to provide significantly different results because of cycle phase, because HA BMR had returned to SL values by the time in the menstrual cycle when comparisons would be appropriate.

Conclusion. Young women with normal menstrual cycles taken to 4,300-m elevation experience a small and transient increase in BMR and a sustained increase in TER. Maintenance of body weight requires a continued energy intake equivalent to 1.92 times SL BMR, although HA BMR drops to SL values after 5 days. If this increased requirement is met with enforced food intake, NB and water balance can be attained and body composition maintained. The menstrual cycle phase in which the women were studied appeared not to affect this response to HA. The excess energy required to maintain body weight, even after BMR had returned to SL values, is unexplained by an increase in TEF or TEA.

We thank, first and foremost, the subjects for their cooperation and positive attitude. We thank the nursing and dietary staffs of the Aging Study Unit, Palo Alto Veterans Affairs Health Care System, for careful handling of the protocol at sea level. We thank the United States Army Research Institute of Environmental Medicine for the use of the Maher Memorial Laboratory on Pikes Peak. Special thanks go to Gene and Rosann McCullough for 24-h technical support in all aspects of the study, and to Shannon Dominick, Allison Giltrap, and Janna Gordon-Elliot. Finally, we thank Hershey Foods (Hershey, PA) and Shaklee Corporation (San Francisco, CA) for donation of food items.

This experiment was supported by Army Contract DAMD 17-95-C-9110 and National Institutes of Health Grants HL-14985 and RR-00051.

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Received 19 May 1999; accepted in final form 14 September 1999.

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