Physical work causes suppression of ovarian function in women

G. Jasieńska[*] and P. T. Ellison

Department of Anthropology, Harvard University, 11 Divinity Avenue, Cambridge, MA 02138, USA
(*jasienska@post.harvard.edu, pellison@fas.harvard.edu*)

The suppression of reproductive function is known to occur in women engaging in activities that require high energetic expenses, such as sport participation and subsistence work. It is still unclear, however, if reproductive suppression is a response to high levels of energy expenditure, or only to the resulting state of negative energy balance. To our knowledge, this study provides the first evidence that work-related energy expenditure alone, without associated negative energy balance, can lead to the suppression of reproductive function in women. We document suppression of ovarian function expressed as lowered salivary progesterone levels in women from an agricultural community who work hard, but remain in neutral energy balance. We propose two alternative evolutionary explanations (the 'pre-emptive ovarian suppression' hypothesis and the 'constrained down-regulation' hypothesis) for the observed results.

Keywords: female reproductive function; energy expenditure; energy balance; ovarian suppression

1. INTRODUCTION

High levels of energy expenditure have been typical features of human ecology since before the emergence of anatomically modern *Homo sapiens* (Leonard & Robertson 1997). Factors affecting energy availability influence ovarian function in human females, owing to high energetic demands of female reproduction (Ellison 1994). Indices of ovarian suppression, e.g. amenorrhoea, anovulatory cycles and inadequate luteal phases, are associated with dieting and exercise in women from developed countries, and with low-calorie diet and intense workload in women from developing countries (Warren 1983; Prior 1985; Green *et al*. 1986; Howlett 1987; Henley & Vaitu-kaitis 1988; Ellison *et al*. 1989; Cumming 1993; Rosetta 1993; Panter-Brick & Ellison 1994). However, interpreting the functional significance of ovarian suppression induced by physical activity has been difficult for two principal reasons. First, patterns of aerobic activity typical of most sports may not be representative of subsistence-related energy expenditure. Second, in traditional agricultural communities, suppressive effects of intense work are often confounded with those of poor diet and negative energy balance (Ellison *et al*. 1989; Panter-Brick *et al*. 1993).

In this study we have attempted to determine if work-related energy expenditure alone, without associated negative energy balance, can lead to the suppression of reproductive function in women. We have conducted a comprehensive study of Polish rural women who were involved in agricultural, domestic and child-care work. Data were collected on seasonal changes in energy expenditure, energy intake, body composition and ovarian function. In these women, hard physical work had a suppressive effect on salivary progesterone levels.

[*]Author for correspondence.

This relationship was independent of nutritional status and energy balance.

2. MATERIAL AND METHODS

Twenty women from the village of Chyszówki, which is located in southern Poland (near the city of Limanowa), participated in this study (table 1). Women were aged between 24 and 39 years. For at least six months before the study and while collecting the samples, the subjects had not been using steroid-based contraception or been pregnant or lactating. Data on reproductive function of women were supplemented by profiles of energy expenditure, energy intake and anthropometric data. Measurements of body weight and fat percentage were taken every two weeks, between the beginning of July and the end of August. Subcutaneous body fat was measured over mid-arm triceps to the nearest 0.5% with an infrared reflectometer (Futrex 1000) (Heyward *et al*. 1992).

Total daily energy expenditure (TEE) was assessed by weekly 24-h recall interviews and by focal observations during fieldwork in July and August. TEE was estimated by multiplying total time spent at each activity by the energy cost of that particular activity (expressed as a multiple of predicted basal metabolic rate (BMR) of a subject). BMR was estimated from individual weights using age-specific predictive equations (FAO/WHO/UNU Expert Consultation 1985). Energy expenditure estimates of each activity were derived from published values (FAO/WHO/UNU Expert Consultation 1985). Data on total daily energy intake (TEI) were gathered by weekly 24-h recall interviews and were analysed using the Nutritionist III database, supplemented by data on Polish foods (Łos-Kuczera 1990).

Ovarian function was assessed by measuring levels of salivary progesterone, which are sensitive indicators of ovarian responsiveness to ecological stress (Ellison 1991). A rise in progesterone levels in the second half of the menstrual cycle indicates ovulation; elevated levels of progesterone in the luteal

Table 1. *Age and anthropometric characteristics of study subjects* ($n=20$)

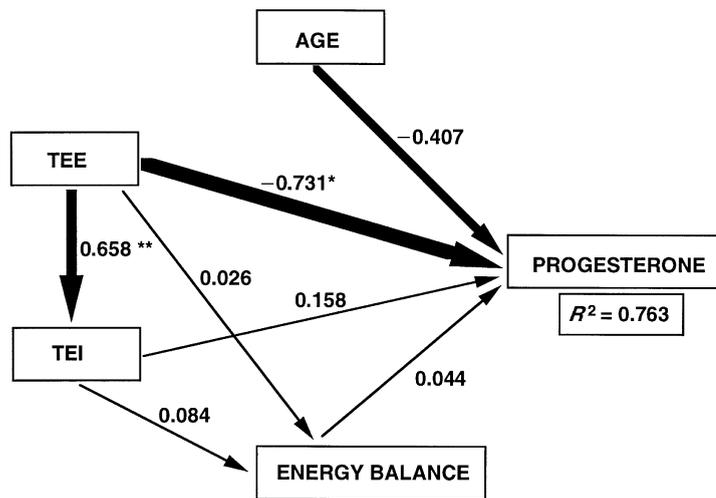|	age (years)	age at menarche (years)	height (cm)	body weight (kg)		body fat (%)	
				July	August	July	August
mean	31.4	14.5	162.1	64.2	64.1	27.5	26.2
s.d.	4.55	0.66	3.80	8.42	8.85	6.60	6.67
range	24–39	13–16	154–170	50–87	49–89	15.5–37.0	14.5–36.1

Figure 1. A path-analysis model of the relationship between luteal progesterone levels and age, energy expenditure, energy intake and energy balance. Arrow thickness is proportional to the magnitude of the path coefficient. Statistical significance of the direct and indirect effects was determined by a randomization procedure in which the full path analysis was repeated 2000 times. * indicates significance at $p<0.01$, and ** at $p<0.001$. The TEI and TEE values for each subject represent the sum of the average values for July and August.

phase contribute to the successful implantation of the blastocyst (Stouffer 1988). Subjects collected daily saliva samples for four months, starting in July 1992. Progesterone concentration in saliva was measured by radioimmunoassay, according to published protocols (Ellison 1988).

3. DATA ANALYSES: CAUSAL MODELS

A causal model has been developed to test the relative effects of energy intake, energy expenditure and energy balance on the changes in ovarian function, expressed as mean luteal progesterone (figure 1). The choice of variables in the causal model is based on previous research that demonstrated the influence of age, diet and exercise on levels of ovarian steroids (Ellison 1994). To represent those factors, the following variables are used in the model: age, TEI, TEE, and change in body fat percentage between the beginning and the end of the harvest season (fat% change). The July–August change in the subcutaneous fat is used to represent energy balance, as the data indicate that ovarian function is sensitive to changes in body composition (Lager & Ellison 1990). Other body composition variables (mean body weight and body mass index) did not change from July to August with increased TEE and were not incorporated in analyses. The subjects' age is included in the model, because even within the chosen age range, age-related differences in progesterone indices are likely (Lipson & Ellison 1992). The model assumes that TEI may affect progesterone levels directly and/or indirectly, when changes in energy intake cause positive or negative changes in energy balance. Similarly, TEE may have direct effects on ovarian function, or indirect effects via changes in the energy balance. TEE affects TEI, as

women expending more energy are likely to demonstrate compensatory changes in energy intake. A causal effect of TEI on TEE is unlikely, as the TEE of an individual results from demands of field- and housework and is not limited in this population by food availability (Jasieńska 1996). The magnitudes of the direct and indirect effects were evaluated by path analysis (Sokal & Rohlf 1995) with the significance of direct and indirect effect determined through bootstrapping (see Jasieńska (1996) for details).

4. RESULTS

Agricultural work in this village is conducted in a very traditional manner; the use of mechanical equipment is limited on fragmented, family-owned, mountain-side fields, and most activities are done by hand. Agricultural work varies seasonally, with peak activities occurring during the summer haying and harvest season (table 2). TEE differed among months: mean TEE significantly increased by 9% between July and August, and decreased by 22% between both summer months and January (two-way ANOVA, $F_{2,38}=36.268$, $p<0.0001$; followed by Tukey–Kramer tests, $p<0.05$; table 2). Mean TEE in the first two weeks of August, the most demanding time of the harvest, exceeded that of the following January by 37%. In contrast to many agricultural populations with similar patterns of subsistence-related workload, women in this study do not experience nutritional stress. The diet is adequate, especially in terms of caloric intake (table 2). Mean TEI did not differ significantly between seasons (12.2 MJ day^{-1} in summer and 11.8 MJ day^{-1} in winter; $F_{1,19}=1.791$, $p>0.05$). When months were analysed separately, there was a significant difference among

Table 2. *Mean total daily energy expenditure (TEE) and mean total daily energy intake (TEI) for July and August 1992 and January 1993*

	TEE (MJ day^{-1})			TEE expressed as a multiple of BMR			TEI (MJ day^{-1})		
	July	August	January	July	August	January	July	August	January
mean	10.954	11.758	9.403	1.877	2.019	1.562	11.591	12.599	11.841
s.d.	1.876	2.437	0.880	0.347	0.384	0.103	1.936	1.598	0.966
min.	7.59	7.99	8.04	1.33	1.51	1.40	8.09	10.83	10.14
max.	14.32	15.90	11.72	2.43	2.47	1.78	14.73	15.24	13.92

months in mean TEI ($F_{2,38}=13.508$, $p=0.0001$) with higher mean TEI in August than in either July or January (Tukey–Kramer tests, $p<0.05$). Energy intake thus tended to increase with energy expenditure in this population.

Mean luteal progesterone levels (P_{lut}) were significantly suppressed in the summer (July and August: the months characterized by the highest activity levels) when compared with the autumn (especially October, when agricultural work for the year ends). There was significant variation among months in P_{lut} (two-way ANOVA, $F_{3,49}=10.256$, $p=0.0001$), characterized by a significant linear trend of rising P_{lut} levels from July to October ($F_{1,983}=24.891$, $p=0.0001$). Mean P_{lut} values were 177.2 pmol l^{-1} in July (s.d. $=72.754$, range 83.9–361.2, $n=17$ subjects), 189.9 pmol l^{-1} in August (s.d. $=76.385$, range 29.6–359.0, $n=20$), 211.0 pmol l^{-1} in September (s.d. $=79.737$, range 111.3–426.0, $n=20$), and 227.4 pmol l^{-1} in October (s.d. $=66.061$, range 143.6–414.3, $n=15$) (figure 2).

Results from the causal model tested by path analysis indicate that the energy expenditure was the only factor with a significant direct effect on ovarian function ($p<0.01$), causing a reduction in luteal progesterone levels (figure 1). Energy balance did not have significant effect on ovarian function. Similarly, indirect effects of TEE (via energy balance) on progesterone levels were not significant. Results of this analysis also show that energy expenditure had a significant positive effect on TEI ($p<0.001$), suggesting compensatory increase in caloric intake in women with highest expenditure (figure 1).

The hypothesis that women with higher energy expenditure are expected to have lower levels of salivary progesterone was also confirmed in comparisons of mean progesterone profiles of two groups of women characterized by different levels of summer workload (figure 3). For the summer of 1991 (pilot project), the cumulative progesterone profile for the high-workload group (with mean P_{lut} 174.0 pmol l^{-1}, s.d. $=82.72$, $n=7$) was significantly lower than the profile for the moderate-workload group (with mean P_{lut} of 266.0 pmol l^{-1}, s.d. $=141.92$, $n=13$; repeated-measures ANOVA, $F_{1,25}=16.882$, $p=0.0001$). In the 1992 study, the cumulative progesterone profiles for both groups were also significantly different during the summer (repeated-measures ANOVA, $F_{1,18}=6.155$, $p=0.0001$). Mean P_{lut} was 162.2 pmol l^{-1} (s.d. $=109.39$, $n=12$) for the high-TEE group and 212.9 pmol l^{-1} (s.d. $=106.69$, $n=8$) for the moderate-TEE group. Furthermore, a regression analysis indicated a significant influence of workload on the suppression of ovarian function (figure 4). Women with higher average
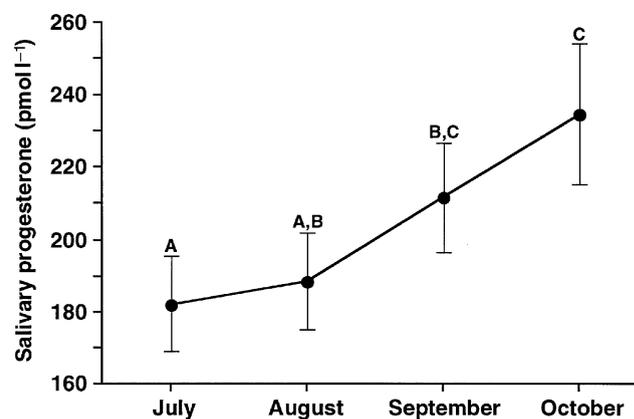
Figure 2. Mean (with 95% confidence intervals) luteal progesterone levels for the four months of 1992. Means marked by the same letter are not significantly different (Tukey–Kramer, $p<0.05$). The 14 days preceding menstrual onset were defined as the luteal phase for the purpose of calculating mean luteal progesterone (P_{lut}) for each cycle.

summer workloads showed greater suppression of P_{lut} in August relative to their own P_{lut} values in October.

5. DISCUSSION

Studies of Western women have shown that intense aerobic exercise is associated with ovarian suppression even when caloric intake is increased to match energy expenditure (Bullen *et al.* 1985). However, it is debatable whether short-term, intense, aerobic exercise can serve as a basis for extrapolating to the effects of longer-duration, but less intense, physical activities that are characteristic of subsistence work among traditional and prehistoric human populations. There is direct evidence that seasonal increases in energy expenditure resulting from agricultural work are associated with ovarian suppression in Nepali women, but only when accompanied by weight loss (Panter-Brick *et al.* 1993).

This study is, to our knowledge, the first to show that high energy expenditure associated with subsistence work can cause ovarian suppression in women, even in the absence of a negative energy balance. These results point to energy expenditure as an important energetic factor shaping adaptive responses of female reproductive function during the course of human evolution (Ellison 1994). We suggest two evolutionary explanations for the functional significance of ovarian suppression observed in
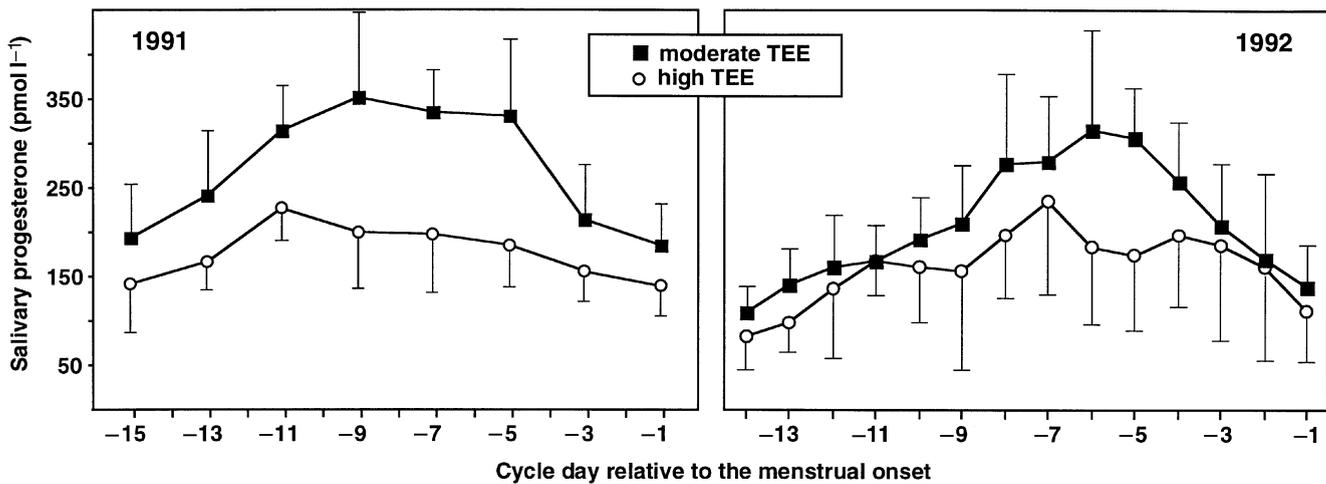
Figure 3. Mean (with 95% confidence intervals) salivary progesterone profiles of women characterized by different levels of workload. In 1992, subjects were divided into two groups: one with above-mean and another with below-mean summer TEE values. The progesterone profiles are derived from daily samples over the last 14 days of the menstrual cycle. The August 1991 data come from a pilot field study conducted in the same population. Twenty subjects (of which 15 participated in the 1992 study) were assigned to either a high-workload or a moderate-workload group based on the average number of hours spent on agricultural work in July and August. Samples from the luteal phase of each cycle were assayed for progesterone using the same method as in the 1992 study.
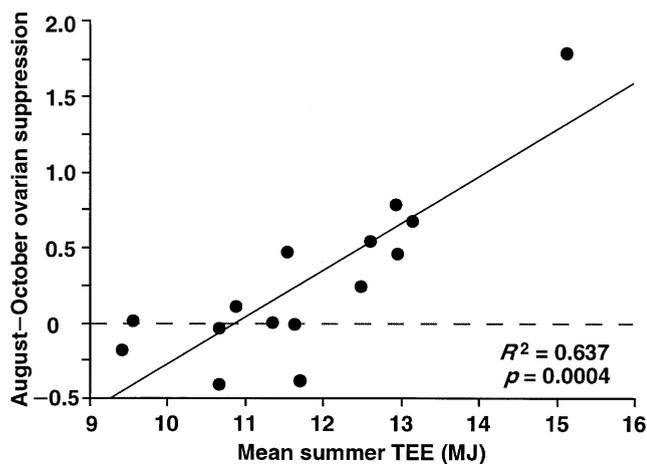

Figure 4. The relationship between mean summer TEE and the index of ovarian suppression (quantified as the difference in mean progesterone levels between October and August). This relationship remains significant when the subject with the highest mean summer TEE is removed from the analysis ($R^2 = 0.408$, $p = 0.014$, $n = 14$).

women who experience a heavy workload, but maintain energy balance.

According to the first scenario, which could be called the hypothesis of the 'pre-emptive ovarian suppression', compensatory increases in energy intake at times of high workload were uncommon in our evolutionary past. Therefore, a substantial increase in workload usually led in human ancestors to the state of negative energy balance. Such limited ability to increase energy intake might have been caused by low food availability or, more likely, by physiological constraints to energy assimilation and production (i.e. metabolic ceilings to energy budgets (Hammond & Diamond 1997)). It can be hypothesized that the particular diet composition of human ancestors

entailed metabolic ceilings that are much lower than those allowed today by high-quality diets. In fact, in industrial societies, metabolic ceilings may be relevant only for professional athletes experiencing very high levels of energy expenditure (Peterson *et al*. 1990). Consequently, an increase in workload for human ancestors was a reliable predictor of an imminent energetic hardship, and therefore functioned as a cue for pre-emptive ovarian suppression.

According to the alternative scenario (the 'constrained down-regulation' hypothesis), remaining, as a result of high workload, in the state of high energy flux (i.e. high energy expenditure and a simultaneous compensatory high energy intake) may constrain a woman's physiological capacity to allocate energy to reproduction (Jasieńska 1996). In the context of a traditional subsistence ecology, a woman's ability to meet the metabolic costs of pregnancy and lactation often depends on her ability to down-regulate her own metabolic requirements (Poppitt *et al*. 1993). When high workload constrains this ability (Sjodin *et al*. 1996), a temporary suppression of ovarian function may be adaptive.

Reproductive patterns in contemporary societies are determined by both cultural and biological factors. Consequently, the phenomenon of ovarian suppression described here does not necessarily explain fertility differences among modern populations (Bentley *et al*. 1993). However, workload-related ovarian suppression might have had an important determining effect on female fecundity, and therefore fertility, during human evolution. It may also remain an important factor influencing reproductive health in contemporary societies. For example, because ovarian suppression involves lowering of the steroid hormone concentrations, it may help explain low rates of reproductive cancers in women from populations with traditional modes of subsistence (Eaton *et al*. 1994).

REFERENCES

Bentley, G. R., Goldberg, T. & Jasieńska, G. 1993 The fertility of agricultural and non agricultural traditional societies. *Pop. Stud.* **47**, 269–281.

Bullen, B. A., Skrinar, G. S., Beitins, I. Z., von Mering, G., Turnbull, B. A. & McArthur, J. W. 1985 Induction of menstrual disorders by strenuous exercise in untrained women. *N. Engl. J. Med.* **312**, 1349–1353.

Cumming, D. C. 1993 The effects of exercise and nutrition on the menstrual cycle. In *Biomedical and demographic determinants of reproduction* (ed. R. Gray, H. Leridon & A. Spira), pp. 132–156. Oxford: Clarendon Press.

Eaton, S. B., Pike, M. C., Short, R. V., Lee, N. C., Trussell, J., Hatcher, R. A., Wood, J. W., Worthman, C. M., Jones, N. G. & Konner, M. J. 1994 Women's reproductive cancers in evolutionary context. *Q. Rev. Biol.* **69**, 353–367.

Ellison, P. T. 1988 Human salivary steroids: methodological issues and applications in physical anthropology. *Yb. Phys. Anthropol.* **31**, 115–142.

Ellison, P. T. 1991 Reproductive ecology and human fertility. In *Applications of biological anthropology to human affairs* (ed. G. W. Lasker & C. G. N. Mascie-Taylor), pp. 14–54. Cambridge University Press.

Ellison, P. T. 1994 Advances in human reproductive ecology. *A. Rev. Anthropol.* **23**, 255–275.

Ellison, P. T., Peacock, N. R. & Lager, C. 1989 Ecology and ovarian function among Lese women of Ituri Forest, Zaire. *Am. J. Phys. Anthropol.* **78**, 519–526.

FAO/WHO/UNU Expert Consultation 1985 *Energy and protein requirements. Tech. Rep. Ser. 724.* Geneva: World Health Organization.

Green, B. B., Daling, J. R., Weiss, N. S., Liff, J. M. & Koepsell, T. 1986 Exercise as a risk factor for infertility with ovulatory dysfunction. *Am. J. Publ. Health* **76**, 432–436.

Hammond, K. & Diamond, J. 1997 Maximal sustained energy budgets in humans and animals. *Nature* **386**, 457–462.

Henley, K. & Vaitukaitis, J. L. 1988 Exercise-induced menstrual dysfunction. *A. Rev. Med.* **39**, 443–451.

Heyward, V. H., Jenkins, K. A., Cook, K. L., Hicks, V. L., Quatrochi, J. A., Wilson, W. L. & Going, S. B. 1992 Validity of single-site and multi-site models for estimating body composition of women using near-infrared interactance. *Am. J. Hum. Biol.* **4**, 579–593.

Howlett, T. A. 1987 Hormonal responses to exercise and training: a short review. *Clin. Endocr.* **26**, 723–742.

Jasieńska, G. 1996 Energy expenditure and ovarian function in Polish rural women. PhD thesis, Harvard University.

Lager, C. & Ellison, P. T. 1990 Effect of moderate weight loss on ovarian function assessed by salivary progesterone measurements. *Am. J. Hum. Biol.* **2**, 303–312.

Leonard, W. R. & Robertson, M. L. 1997 Comparative primate energetics and hominid evolution. *Am. J. Phys. Anthropol.* **102**, 265–281.

Lipson, S. F. & Ellison, P. T. 1992 Normative study of age variation in salivary progesterone profiles. *J. Biosocial Sci.* **24**, 233–244.

Łos-Kuczera, M. 1990 *Food products. Composition and nutritive value.* Warszawa: Instytut Zywnosci i Zywienia. [In Polish.]

Panter-Brick, C. & Ellison, P. 1994 Seasonality of workloads and ovarian function in Nepali women. *Ann. N.Y. Acad. Sci.* **709**, 234–235.

Panter-Brick, C., Lotstein, D. S. & Ellison, P. T. 1993 Seasonality of reproductive function and weight loss in rural Nepali women. *Hum. Repr.* **8**, 684–690.

Peterson, C. C., Nagy, K. A. & Diamond, J. 1990 Sustained metabolic scope. *Proc. Natn. Acad. Sci. USA* **87**, 2324–2328.

Poppitt, S. D., Prentice, A. M., Jequier, E., Schutz, Y. & Whitehead, R. G. 1993 Evidence of energy sparing in Gambian women during pregnancy: a longitudinal study using whole-body calorimetry. *Am. J. Clin. Nutr.* **57**, 353–364.

Prior, J. C. 1985 Luteal phase defects and anovulation: adaptive alterations occurring with conditioning exercise. *Sem. Reprod. Endocr.* **3**, 27–33.

Rosetta, L. 1993 Female reproductive dysfunction and intense physical training. *Oxf. Rev. Repr. Biol.* **15**, 113–141.

Sjodin, A. M., Forslund, A. H., Westerterp, K. R., Andersson, A. B., Forslund, J. W. & Hammbraeus, L. H. 1996 The influence of physical activity on BMR. *Med. Sci. Sports Exerc.* **28**, 85–91.

Sokal, R. R. & Rohlf, F. J. 1995 *Biometry*, 3rd edn. New York: W. H. Freeman.

Stouffer, R. L. 1988 Perspectives on the corpus luteum of the menstrual cycle and early pregnancy. *Sem. Repr. Endocr.* **6**, 103–113.

Warren, M. 1983 Effects of undernutrition on reproductive function in the human. *Endocr. Rev.* **4**, 363–377.