Menstrual dysfunction in female athletes
A review for clinicians
T. D. NOAKES, MARIE VAN GEND

Summary
A critical review of factors considered to cause menstrual dysfunction is women athletes with no overt organic cause for the abnormality is presented. Evidence suggests that although regular exercise can produce a specific change in hypothalamic-pituitary function, in particular reduced pulsatile luteinising hormone secretion, this is not associated with amenorrhoea or oligomenorrhoea in the majority of female athletes, most of whom continue to menstruate cyclically. Thus additional factors must be operative. It seems probable that severe menstrual dysfunction occurs in a specific predisposed subset of women athletes who have a particular personality type or body build and are attracted to a lifestyle including regular vigorous exercise. The biochemical basis may be related to hypothalamic, pituitary or even ovarian dysfunction possibly due to elevated levels of anti-reproductive hormones, including β-endorphins, dopamine, prolactin and catechol oestrogens, induced by exercise; dopamine appears the most likely candidate. Chronic hypo-oestrogenic or eu-oestrogenic amenorrhoea or oligomenorrhoea may not be benign and should probably be treated in order to reduce the risk of osteoporosis or endometrial hyperplasia and adenocarcinoma.

Low percentage body fat
Frisch and McArthur have proposed that a critical percentage of body fat is required for both the onset of menarche (17%) and its maintenance (22%). With improved nutrition and increased body fat at an early age in North America, there has been a parallel decrease in age of menarche providing indirect support for this theory. Frisch et al. reported a high incidence of amenorrhoea among ballet dancers with a percentage body fat lower than 22%, further supporting this theory.

Studies of female distance runners have also found a relationship between body weight, as distinct from percentage body fat, and menstrual dysfunction. Young women weighing less than 52 kg and who lost more than 4.5 kg after they began running were most likely to develop menstrual dysfunction. Frisch and McArthur have proposed that a critical percentage of body fat is required for both the onset of menarche (17%) and its maintenance (22%). With improved nutrition and increased body fat at an early age in North America, there has been a parallel decrease in age of menarche providing indirect support for this theory.

Dale et al. and Dale and Goldberg divided 168 women into a control group, joggers who ran between 8-47 km/week, and runners who ran more than 48 km/week. Each group had almost identical average heights but differed greatly with respect to percentage body fat and also body weight. The runners were approximately 6 kg below average body weight for height and their higher incidence of menstrual dysfunction correlated with their lower percentage body fat. Other studies have shown that amenorrheic runners are lighter than eumenorrheic runners or controls. Ame

In this review, normal menstrual cycles (eumenorrhoea) are considered to be of less than 35 days duration but longer than 23 days. Menstrual dysfunction is considered to include the following: (i) primary amenorrhoea — absence of any previous menstrual cycles; (ii) secondary amenorrhoea — menstrual cycles lasting longer than 90 days after previous menstruation; (iii) oligomenorrhoea — menstrual cycles lasting between 35 and 90 days; and (iv) short luteal phase — menstrual cycles lasting less than 23 days.

The following parameters have so far been related to some or all of the above in sportswomen: (i) low percentage body fat; (ii) late onset menarche; (iii) heavy training load; (iv) history of previous menstrual irregularities; (v) parity; (vi) nutrition; (vii) hypothalamic-pituitary dysfunction; and (ix) ovarian dysfunction.

As more women have become physically active in the past decade, special interest has been shown in the medical problems peculiar to women athletes. A majority of studies have found that physically active women have an increased incidence of menstrual dysfunction. It is therefore opportune to review contemporary ideas in this field and to comment on their application to clinical practice.

Menstrual dysfunction in athletes must initially be evaluated as it would be in non-athletes; athletic females are not immune to pathological conditions causing abnormalities in menstrual function. This review focuses specifically on menstrual dysfunctions in athletes in whom no other cause can be found and in whom normal menstruation returns with avoidance of exercise and its associated stresses.

Sport Science Centre, Department of Physiology, University of Cape Town
T. D. NOAKES, M.D.
MARIE VAN GEND, B.S.C. (MED.) HONS (SPORT SCI.)

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Reprint requests to: Professor T. D. Noakes, Sport Science Centre, University of Cape Town Medical School, Observatory, 7925 RSA.

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more, heavily training athletes may have elevated circulating 
estradiol oestrogen levels even without an accompanying marked 
weight loss. 53

However, the percentage body fat theory has been criti-
cised, 34,40,43,57,59 on the basis of the methods used to determine 
percentage body fat by Frisch and her colleagues; by the 
failure of many studies to find an association between this 
variable and amenorrhoea; and, in particular, by the finding 
that many eumenorrheic runners have body-fat levels signif-
ically lower than that at which menstrual dysfunction is 
believed to develop. For example, some patients with anorexia 
nervosa become amenorrhoeic before they lose significant 
amounts of weight and therefore body-fat and therefore 
menstruation even when normal weight is attained. 59 The 
reverse phenomenon has been found in ballet dancers 14,22,23 
and swimmers 53 whose menstrual cycles became increasingly 
irregular during training and more regular in the off-season 
even without significant changes in body weight. However, 
one study found that individuals with low body weight and 
decreased body fat were more likely to develop amenorrhoea,
suggesting a synergistic effect of exercise and low body weight 69 as 
found in girls with anorexia nervosa. 61

Furthermore, some amenorrhoeic runners are of normal 
body weight 11 and other studies found no difference in height 
or weight, 9,10,40 percentage body fat, 34 lean body mass, 49 fat 
weight or skinfold thickness 62 between amenorrhoeic and 
eumenorrhoeic runners or controls. These studies were, 
however, cross-sectional with no control for other variables 
that may influence susceptibility to exercise-related menstrual 
dysfunction. However, a recent longitudinal study 34 showed 
changes in hypothalamic-pituitary function without changes in 
body weight in 19 women, 18 of whom developed oligo-
menorrhoea during a 15-month endurance training programme. 
The authors concluded that the hypothalamic basis for this 
exercise-related oligomenorrhoea was different from that 
induced by simple weight loss.

Similarly, the percentage body fat of a group of amenorrhoeic 
ballet dancers was more than that claimed to be necessary for 
normal menstruation, 22 a finding which could be interpreted as 
evidence of both importance of exercise and increase in set 
point for weight with heavy energy expenditure. Alternatively, 
the rapidity of weight loss may be more important than the 
amount lost, 53,64 since evidence suggests that a rapid loss of 
15% body weight (equivalent to approximately 30% body fat 
loss) influences menstruation. Peripheral conversion of androgens to oestrone occurs equally 
in thin amenorrhoeic and eumenorrhoeic runners; 36 both have 
normal serum oestrone levels. Thus the postulated biochemical 
mechanism whereby a reduced body-fat content influences 
menstrual function occurs has not been established. This implies a wide 
relationship between percentage body fat and menstrual dys-
fuction. However, most of them also had histories 
primary amenorrhoea. However, most of them also had histories 
of menstrual dysfunction may not have been directly related to exercise 
alone. 28

Age

Younger athletes appear to be more prone to menstrual dys-
fuction. 13,25,34,40 In two large surveys of 900 35 and 550 35 
runners, proportionally more young women developed sec-
dary amenorrhoea. However, most of them also had histories 
of menstrual dysfunction before taking up running, so the 
dysfunction may not have been directly related to exercise 
alone. 28

Previous menstrual irregularity

The scientific validity of determining a subject's previous 
menstrual status is questionable since it relies on her recall and
also her concept of a normal menstrual pattern. However, if the role of exercise is inducing menstrual dysfunction is to be established, the previous menstrual status of subjects must be known.24

In a survey of women completing the 1979 New York City Marathon, Shangold and Levine26 found that an incidence of oligomenorrhoea and amenorrhoea in respondents was 19% before training and 24% at the time of the marathon. Indeed, the best predictor of each woman’s menstrual pattern during training was her pre-training menstrual status. Similarly, Schwartz et al.18 found that, even before they began running, amenorrhoeic runners had a higher incidence of menstrual irregularity than eumenorrhoeic runners or controls. The same finding has been reported in ballet dancers22 and in ultra-marathon runners24 pre-training menstrual status predicted menstrual functions after training had begun.43

These findings suggest that in these groups factors unrelated to physical activity may be of particular importance in determining menstrual dysfunction. Shangold and Levine26 suggest that some factor which promotes menstrual dysfunction may inspire women to start running, just as women who have a late menarche may also be attracted to running.34

Attention to pre-training menstrual status has uncovered a further fact suggesting that exercise is not the sole factor determining menstrual dysfunction. Shangold and Levine26 found that whereas only 7% of their marathon runners who had regular menses before training began subsequently developed oligomenorrhoea or amenorrhoea, fully 25% of those with either of these menstrual abnormalities before they commenced training, became eumenorrhoeic after starting running. Thus exercise was more likely to regularise rather than disturb menstrual patterns. A similar finding was reported in ultra-marathon runners.88

Parity

Baker et al.15 and Dale et al.11 found that nulliparous women were more likely to develop running-related amenorrhoea than parous runners.

Nutrition

There is no published evidence relating a single nutritional deficiency to menstrual dysfunction in exercising women. Dale et al.,44 found no significant variations in the dietary intake of marathon runners, joggers and controls, whose menstrual patterns differed. Schwartz et al.18 found that the daily kilojoule intake of amenorrhoeic runners was higher than that of other runners and controls although their protein intakes were less. They also reported that 2 athletes first developed amenorrhoea when they became strict vegetarians. Vegetarianism was also considered to be associated with menstrual dysfunction in the study of Carlberg et al.47 Brooks et al.36 have also reported that amenorrhoeic runners are one-fifth the amount of meat ingested by eumenorrhoeic runners. Eighty-two per cent of amenorrhoeic runners ate less than 200 g/week meat (poultry or red meat) and were classified as vegetarians, as against 13% of normally menstruating runners. Total animal protein intake was, however, not different since the amenorrhoeic runners took more dairy produce. Fat consumption was also lower in amenorrhoeic runners, but total daily kilojoule intake was the same. Frisch37 has indicated that a vegetarian low-fat diet can reduce plasma oestrogen levels.

However, these studies preceded newer findings showing that dietary kilojoule restriction and pathogenic weight-control behaviour24 are widespread among ballet dancers,17,25,46 gymnasts17,25 and runners,43 precisely the groups of athletes prone to menstrual dysfunction. Thus Rosen et al.72 have reported that 74% of gymnasts and 47% of runners practised at least one pathogenic weight-control behaviour, either self-induced vomiting, binge eating or the use of laxatives, diet pills or diuretics. Mean daily kilojoule intakes of 5 700,72,74 7 0275 and 7 93676 representing 72-84% of the Recommended Dietary Allowance (RDA) for kilojoules have been reported in ballet dancers. In one study,75 the kilojoule intake of amenorrhoeic dancers (5 813) was lower than that of eumenorrhoeic dancers (7 551). In Benson et al.’s58 study, 11% of dancers consumed less than 5 040 kJ/d (53% of RDA). Similarly low daily kilojoule intakes of 7 32577 and 8 07778 have been reported in gymnasts. It would be surprising if such low kilojoule intakes were not without effect on menstrual patterns, particularly with the very low intakes.

Very low intakes have also been reported in runners despite the heavy energy drain imposed by regular training; lower daily kilojoule intakes have been reported in amenorrhoeic than in eumenorrhoeic runners.

Drinkwater et al. found that despite running 66 km/week in training, amenorrhoeic runners had a lower daily energy intake (6 817 v. 8 253 kJ) than eumenorrhoeic runners who ran only 40 km/week. Marcus et al.80 also reported a lower daily kilojoule intake in amenorrhoeic runners (5 352 v. 7 203 kJ/d), who also had markedly reduced serum tri-iodothyronine levels; 3 (of 11) admitted to bulimic episodes in the past. Nelson et al.81 and Zierath et al.82 have also reported daily kilojoule intakes of amenorrhoeic runners (7 266 and 6 647) significantly lower than those of eumenorrhoeic runners (9 450 and 10 458) respectively. In their study of amenorrhoeic women runners, McArthur et al.83 had to exclude 4 of 7 subjects because of ‘undernutrition and personality features suggestive of anorexia nervosa’.

Our own studies have complemented these findings. We incidentally found that 3 of 7 amenorrhoeic or oligomenorrhoeic ultramarathon runners had previously been treated for anorexia nervosa; these runners were also the better performers.84 Next we showed that younger, more competitive runners — precisely those most likely to have menstrual dysfunction — had higher Eating Attitude Test (EAT) and Eating Disorders Inventory (EDI) scores than did less competitive runners,85 high EAT and EDI scores are suggestive but not diagnostic of the emotional, psychological and behavioural characteristics of anorexia nervosa and bulimia. Finally, we have found that an elevated EAT score is the single best predictor of menstrual dysfunction in lean females, some of whom are athletic.86 In this group menstrual dysfunction was unrelated to either body weight or the amount of habitual exercise taken.

These studies therefore suggest that unrecognised nutritional factors, in particular chronic energy malnutrition, may play an essential role in development of menstrual dysfunction in athletes. Future studies will be incomplete if they do not include accurate analyses of habitual dietary intakes.

Hypothalamic-pituitary dysfunction

The precise endocrinological abnormalities associated with exercise-related menstrual dysfunction have yet to be defined.37,55 In general, amenorrhoeic runners have been found to exhibit the same hormonal profile as prepubertal girls,6,16,49,41,85 return of menstruation being accompanied by resumption of normal hormonal patterns. One possibility is that exercise-related hormonal abnormalities progress from disturbed folliculogenesis86 to luteal-phase deficiency;36 to hypo- or eu-oestrogenic anovulation;87,88 and finally to hypo-oestrogenic amenorrhoea,89 but firm scientific evidence for this is lacking.7,59
Current interest centres on the possible aetiological role of altered pulsatile release of GnRH from the arcuate nucleus of the hypothalamus (Fig. 1). Thus pulsatile LH release from the pituitary is reduced in both eumenorrhoic and amenorrhoic runners, presumably because of either decreased pulsatile GnRH release from the hypothalamus or pituitary refractoriness to GnRH stimulation. Studies to distinguish between these two possibilities have been inconclusive since pituitary responsiveness to GnRH in amenorrheic and oligomenorrhoic runners has been found to be increased, normal or reduced. Interestingly, extreme weight loss in anorexia nervosa also impairs hypothalamic function, which could result from the action of several neurotransmitters on the arcuate nucleus, thereby influencing GnRH release.

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Fig. 1. If brain β-endorphin levels are increased by exercise training combined with a kilojoule-restricted diet, they could impair GnRH release from the arcuate nucleus in the median eminence of the hypothalamus by inhibiting the stimulatory effect of noradrenaline, and by stimulating the inhibitory effect of dopamine on the GnRH neuron. Low oestrogen levels facilitate the latter effect. Since LH release is dependent on a GnRH surge, impaired LH release will cause a loss of pulsatile LH release from the pituitary, possibly the commonest endocrinological abnormality found in athletic females (adapted from Yen). 100

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Fig. 1 shows that β-endorphin, noradrenaline and dopamine all have nerve terminals in the arcuate–median eminence of the hypothalamus — the site of the GnRH neuron, and all are thought to play a role in the release of GnRH. 98,99,100,101,102,103,104,105 Endorphins suppress pulsatile LH release either by suppressing noradrenaline stimulation of GnRH release or by stimulation of dopamine secretion. 100 Dopamine also inhibits GnRH release since administration of an antagonist, metoclopramide, causes elevated levels of LH in women suffering from non-athletic amenorrhoea (Fig. 1). 70,98,106 In the presence of normal oestrogen levels, dopamine appears to stimulate GnRH release. 85

The evidence that β-endorphins, blood — but not necessarily brain — levels of which rise during exercise, influence menstruation is that administration of the endorphin antagonist, naloxone, causes an LH surge in non-athletic hypogonadotropic amenorrhoeic women, implying that high levels of endogenous opiates may have been one cause of amenorrhoea. 107 One of 3 amenorrhoeic runners showed the same response suggesting that endorphins may play a role in some but not all cases of exercise-related amenorrhoea. Increased hypothalamic dopamine levels may be the more likely cause of impaired LH release in these athletes. 108

Other substances that could influence menstruation via the hypothalamus include catechol oestrogens, 109 melatonin and serotonin. 110 Russel et al. reported that serum β-endorphin and catechol oestrogen levels rose significantly in swimmers who became oligomenorrhoic during periods of very heavy training (< 90 km swimming per week). They postulate that the elevated catechol oestrogen levels compete with catecholamines and dopamine for degradation by catecholmethyl-transferase. This causes hypothalamic dopamine levels to rise which, in the presence of β-endorphin, suppresses GnRH release.

Melatonin levels rise during exercise and could conceivably play some role in menstrual dysfunction if intracerebral levels are also chronically elevated. The effect of exercise on serotonin levels does not appear to have been studied.

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**Ovarian dysfunction**

A recent study has shown that a subset of women who developed oligomenorrhoea during a longitudinal exercise programme had low mid-cycle oestrogen and progesterone levels despite the normal mid-cycle follicle-stimulating hormone (FSH) and LH surge suggesting an ovarian rather than a hypothalamic-pituitary cause of their hypo-oestrogenism. 111 This group was unusual in having an extremely high incidence of menstrual dysfunction, possibly because of the very stressful nature of training, especially when undertaken by previously untrained women. This abnormality may therefore not be representative of all forms of menstrual dysfunction. Possibly this form of menstrual dysfunction parallels the short-term menstrual irregularity identified in a high percentage of ultramarathon runners during heavy training and competition. 112

Elevated prolactin levels can influence ovarian function by reducing follicle sensitivity to steroid stimulation. 105,106 Blood prolactin levels are higher in athletes than non-athletes 107 and training increases the prolactin response to thyrotrophin releasing hormone (TRH). 108 Blood prolactin levels are elevated during and immediately after exercise 109 and this rise may also be due to elevated intracerebral β-endorphin levels 110 since naloxone reduces the prolactin rise during exercise. 111 Oestradiol also controls prolactin release by reversal of the inhibitory effect of dopamine. 114 However, it appears unlikely that such transient changes in blood prolactin levels could influence menstruation materially, particularly as amenorrhoic runners have a reduced, not increased, prolactin response to exercise. 115,116 The impaired prolactin response may be due to extreme ovarian failure since oestradiol stimulates prolactin release in response to TRH stimulation. 117 The same applies to changes in blood androgen levels; exercise-induced changes are neither large nor sustained 118 and blood androgen levels may not differ between amenorrhoeic runners and eumenorrhoic runners. 119

**Clinical considerations**

Prolonged amenorrhoea in sportswomen is no longer considered to be totally benign. Women with short luteal phase or eu-oestrogenic anovulation are considered to be at risk of endometrial hyperplasia and adenocarcinoma although this association has not been proven in women with exercise-related menstrual dysfunction. 120 Women with hypo-oestrogenic amenorrhoea risk the development of osteoporosis, atrophic vaginitis and urethritis. 121,122,123,124 Hormonal replacement therapy should probably be considered in athletic women with hypo-oestrogenic amenorrhoea or oligomenorrhoea if attention to possible dietary causes fails to restore normal menses. 125,126 Women with eu-oestrogenic anovulation whose oestrogen levels are > 40 pg/ml should be treated with a 10-day course of progesterone at monthly intervals to protect the endometrium from unopposed oestrogen action. 126

**Conclusions**

This review shows that the cause of athletic amenorrhoea is complex and in some ways has suffered from previous over-
simplification. Today there is evidence that even very vigorous exercise alone does not greatly reduce body weight, particularly in females.\textsuperscript{11}\textsuperscript{8} Thus it is almost certainly incorrect to assume that the low body mass of amenorrheic runners, gymnasts and ballet dancers is due purely to the ‘energy drain’ of those activities,\textsuperscript{9}\textsuperscript{7} especially since the energy expended in ballet dancing\textsuperscript{11}\textsuperscript{8} and gymnastics\textsuperscript{20} is in reality rather low. It is more likely that chronic energy malnutrition, not exercise, explains both the low body mass found in a large percentage of these women and their menstrual dysfunction. Our finding that as many as 50% of lean ballet dancers and runners have elevated EAT and EDI scores\textsuperscript{44} almost certainly indicates an alarming incidence of disturbed eating patterns in these groups.

We postulate that chronic dietary restriction is the additional essential ingredient necessary to convert the impaired pulsatile E:uth.\textsuperscript{7} and is relatively uncommon even despite heavy training in less competitive sportswomen who presumably restrict their diets less, lose less weight, are of a different body build, and are not exposed to similar competitive stresses. It would also explain why avoidance of exercise causes a return to normal menstrual function in only a minority of runners with amenorrhea.\textsuperscript{47}

The prevention and adequate therapy of menstrual dysfunction are essential to prevent long-term complications, in particular osteoporosis. In general, the likelihood of developing exercise-related menstrual dysfunction would appear to be very small in all but the select group of women described above. Thus exercise can safely be prescribed for the majority of women without the risk that chronic menstrual dysfunction will develop.

\textbf{REFERENCES}


