Athletic Amenorrhea: A Review

Barbara L. Drinkwater
University of Washington

The strenuous training regimens associated with endurance sports have numerous positive effects on physiological function. Women, as well as men, benefit from training by increasing their cardiovascular endurance, reducing body fat, and developing muscular strength and endurance. However, the effect of these programs on the reproductive hormones of the female is much more obvious than in the male and has become the subject of some concern among women, their coaches, and their physicians.

The basic anatomical and physiological differences between the sexes have long been used to explain why women shouldn't—or couldn't—participate in the same activities or at the same level of effort as male athletes. One major point of contention has always been the effect of physical activity on reproductive function or possibility of trauma to the reproductive organs. When a number of survey studies (Åstrand, Eriksson, Nylander, Engström, Karlberg, Saltin, & Thoren, 1963; Erdelyi, 1962) were published in the 1960s showing that women athletes had less dysmenorrhea, easier labor, and no evidence of serious damage to uterus or breast, most of the concern dissipated. It appeared that women athletes were well on their way toward equal opportunity in the athletic world. Today that picture has become clouded with reports of an increased incidence of menstrual irregularities and delayed menarche among female athletes.

The reaction to these reports of menstrual dysfunction has varied from speculation that exercise per se may not be the causative agent (Shangold, 1982) to the suggestion that the hormonal response is a form of “endocrine conditioning” similar to that seen in the cardiovascular or skeletal system with training (Prior, 1982). For the most part the reaction has been cautious, an interest and concern about the etiology of the phenomenon, but no suggestion that women cease participating in en-
durance sports or diminish the intensity of their training. The general

tenor of most articles dealing with this topic is that the condition appears
to be reversible and that there is no evidence to suggest any long-term ef-
However, there is also the often repeated caveat that long-term prospec-
tive studies are needed to be completely assured that the condition is
reversible and that there are no deleterious effects on reproductive func-

While the term menstrual irregularities covers a wide spectrum of
problems, the concern of athletes centers on amenorrhea (absence of
menses) or oligomenorrhea (infrequent menses) (Shangold, 1982).
Amenorrhea may be either "primary," meaning that menses has never oc-
curred, or "secondary," a cessation of menses following a period of nor-
mal cycles. Different investigators define secondary amenorrhea in
various ways, ranging from 3 consecutive months without a period
(Frisch, Wyshak, & Vincent, 1980), to 6-months intervals (Frisch, Gotz-
Welbergen, McArthur, Albright, Witsch, Bullen, Birnholz, Reed, & Her-
man, 1981; Wakat, Sweeney, & Rogol, 1982) to 10 months with only one
period (Shangold & Levine, 1982), or 12 months without menses (Lutter
& Cushman, 1982). The basic definition of oligomenorrhea is "infre-
quent" periods, but infrequent can mean intervals of 38 days to 3 months
(Frisch et al., 1980), 36 days or longer (Lutter & Cushman, 1982), 37
days to 6 months (Shangold & Levine, 1982), or cycles that vary ± 9 days
month to month. Since a woman can be classified as amenorrheic in one
study and oligomenorrheic in another, acceptance of a standard classifi-
cation by all investigators would aid in identifying patterns descriptive of
each group.

The incidence of oligo/amenorrhea reported in the literature varies
widely (Table 1). Part of this variability may reflect how the conditions
are defined, but one might also expect the incidence to vary with the
population studied. The primary research tool has been the retrospective
questionnaire. The respondents varied from women who jog 1 to 5 miles
a week (Speroff & Redwine, 1980) to 1,841 entrants in the New York City
Marathon (Shangold & Levine, 1982) and professional ballerinas
(Cohen, Kim, May, & Ertel, 1982). They ranged in age from the prepu-
bertal to postmenopausal years (Frisch et al., 1980; Speroff & Redwine,
1980). Nevertheless, it is obvious that the incidence of oligo/amenorrhea
among these athletes far exceeds the population norm of 2-3%. Nor is
the phenomenon limited to running. Swimming, cycling, crew, ballet and
other activities involving strenuous physical activity all have a higher
than average number of oligo/amenorrhea participants (Baker, 1981;
Erdelyi, 1976).

Investigations into the etiology of this form of menstrual dysfunc-
tion have relied primarily on survey data to identify those factors
Table 1

Incidence of Oligo/Amenorrhea Among Women Athletes

<table>
<thead>
<tr>
<th>Reference</th>
<th>Activity</th>
<th>% Oligo/Amenorrhea</th>
<th>% Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohen et al., 1982</td>
<td>Ballet</td>
<td>6.6/36.6</td>
<td>43.2</td>
</tr>
<tr>
<td>Dale et al., 1979</td>
<td>Running</td>
<td></td>
<td>34.0</td>
</tr>
<tr>
<td></td>
<td>Jogging</td>
<td></td>
<td>23.0</td>
</tr>
<tr>
<td>Sanborn et al., 1982</td>
<td>Running</td>
<td></td>
<td>25.7</td>
</tr>
<tr>
<td></td>
<td>Swimming</td>
<td></td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Cycling</td>
<td></td>
<td>12.1</td>
</tr>
<tr>
<td>Frisch et al., 1980</td>
<td>Ballet</td>
<td>30.0/15.0</td>
<td>45.0</td>
</tr>
<tr>
<td>Lutter &amp; Cushman, 1982</td>
<td>Running</td>
<td>19.4/3.4</td>
<td>22.8</td>
</tr>
<tr>
<td>Schwartz et al., 1981</td>
<td>Running</td>
<td>4.8/15.4</td>
<td>20.2</td>
</tr>
<tr>
<td>Shangold &amp; Levine, 1982</td>
<td>Running</td>
<td>18.0/6.0</td>
<td>24.0</td>
</tr>
<tr>
<td>Speroff &amp; Redwine, 1980</td>
<td>Running</td>
<td>/6.0</td>
<td></td>
</tr>
<tr>
<td>Wilmore, Brown, &amp; Davis, 1977</td>
<td>Running</td>
<td>19.0/23.0</td>
<td>42.0</td>
</tr>
</tbody>
</table>


From these studies have emerged three theories to explain the association between strenuous physical exercise and oligo/amenorrhea: decrease in percent body fat, hormonal fluctuations resulting from sustained intense exercise, and psychological stress. To understand how each of these factors might influence the cycle, one must understand the normal pattern of hormonal events that culminates in a monthly menses. The normal menstrual cycle is the result of a complex interplay of hormonal events involving the hypothalamus, the pituitary, and the ovaries (Shangold, 1982). The following brief description is based on an extensive review of the literature by Knobil (1980).

Under normal conditions the arcuate nucleus of the hypothalamus discharges a bolus of gonadotropin-releasing hormone (GnRH) approximately once per hour. This bolus reaches the pituitary via the portal cir-
culation and stimulates the secretion of the gonadotropins, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), in a pulsatile fashion—also at a rate of once per hour. During the follicular phase of the cycle, this constant but low-level gonadotropin secretion stimulates the growth and maturation of the immature follicles in the ovary. Early in the follicular stage, relatively low levels of estradiol (E₂) act as a negative feedback at the pituitary to limit the release of LH while low levels of progesterone encourage the secretion of FSH. As the follicles grow they secrete increasing amounts of estradiol. Once the concentration of estradiol reaches approximately 150 pg/ml and remains at that level for 36 hours, its previous negative effect on the pituitary reverses and becomes positive. The result is the typical mid-cycle LH surge that precedes ovulation by a few hours. An increase in GnRH at the same time suggests that the positive feedback effect of estrogen extends to the hypothalamus (Turgeon, 1980).

Following the LH surge, the follicle ruptures and the ovum enters the oviduct on its way to the uterus. The follicular remains evolve into the corpus luteum and produce large amounts of estradiol and progesterone. Immediately following ovulation the concentration of FSH and LH decrease to the levels in the follicular stage, but the maturation of a new follicle is inhibited by the high level of progesterone. As the corpus luteum regresses, the level of progesterone falls, FSH rises, and follicular growth begins again. If all components of the hypothalamic-pituitary-ovarian axis contribute when and as expected, the follicular phase lasts 14 days, ovulation occurs, there is a 14-day luteal phase, and menses follows.

The very complexity of the system ensures that a variation of the norm in one part of the cycle can have a marked effect on other cycle events. For example, a change in the pulsatile release pattern of GnRH at the hypothalamus may result in failure of the ovarian follicle to mature. There will be no ovulation, no progesterone stimulus to the endometrium, and no menses. Any theory relating exercise to oligo/amenorrhea must demonstrate where and how these cyclic events are altered.

The concept that athletic amenorrhea may be related to a decrease in percent body fat is an outgrowth of the Frisch & Revelle (1970) hypothesis that the onset of menarche depends on a “critical weight.” Frisch and her co-workers (Frisch, Revelle, & Cook, 1973; Frisch & McArthur, 1974) later modified the hypothesis to emphasize body composition rather than weight per se as the important factor, suggesting 17% body fat as a requirement for menarche and 22% as the level necessary to maintain a regular cycle. At first glance the theory had considerable “face validity” because distance runners and ballet dancers, who have the highest incidence of oligo/amenorrhea, are lean women. Also, a number of survey studies (Dale et al., 1979; Lutter & Cushman,
1982; Sanborn et al., 1982; Shangold & Levine, 1982; Speroff & Redwine, 1980) have reported either a significant relationship between body weight or composition and oligo/amenorrhea, or have found significant differences in weight, weight loss, or percent body fat between normally cycling women and oligo/amenorrheic athletes.

There are several problems with accepting this theory as the sole explanation for the oligo/amenorrhea associated with exercise. An obvious difficulty arises with the determination of body fat. The technique used by Frisch (1974), predicting body composition by using height and weight to estimate total body water (TBW), has been criticized by Trussell (1978) and Reeves (1979) as an imprecise instrument for predicting fatness. Other investigators have used skinfolds (Baker et al., 1981; Schwartz, Cumming, Riordan, Selye, Yen, & Rebar, 1981; Wakat et al., 1982) or simple body weight (Abraham, Beumont, Fraser, & Llewellyn-Jones, 1982; Feicht et al., 1978; Shangold & Levine, 1982) in making comparisons between eumenorrheic and oligo/amenorrheic women. It is unlikely that any of these studies have presented valid estimates of percent body fat. Of the two studies using hydrostatic weighing to estimate fatness, both found a lower fat weight in the oligo/amenorrheic condition (Boyden et al., 1982; Carlberg & Riedesel, 1979).

A number of studies have also failed to show any relationship between weight and/or body composition and oligo/amenorrhea in athletes. Three studies (Baker et al., 1981; Feicht et al., 1978; Wakat et al., 1982) reported no significant difference in weight or body fat between amenorrheic and regularly cycling runners. If body fat were the deciding factor one would expect active women who become inactive, either by choice or injury, to begin normal cycling only with a gain in body weight. However, both Warren (1980) and Abraham et al. (1982) reported that ballet dancers improved menstrual status during vacations or periods of enforced rest without appreciable change in body weight. Both investigators concluded that strenuous exercise, rather than body weight or composition, was the important factor in determining menstrual regularity.

One difficulty in delineating the role of body composition in athletic amenorrhea is that thin runners also tend to be the better runners. These women train more intensely, run faster, and are more competitive, confounding the effect of low body fat with a high physical and psychic energy drain. To further confuse the issue Lutter & Cushman (1982) reported that of 14 women in their survey who had low body weight and high mileage, 50% were oligo/amenorrheic; the other 50% had regular cycles. Obviously the relationship between body composition and menstrual irregularity is less than perfect.

The hypothesized mechanism by which body fat might affect the menstrual cycle is related to the role of fat cells in the aromatization of androgens to estrone. According to Frisch et al. (1981), adipose tissue is
an important extragonadal source of estrogen. They suggest that the loss
of this source in lean athletes may alter the feedback mechanisms in the
hypothalamic-pituitary-ovarian axis. To date no one has examined the
gonadotropin and steroid patterns before and after weight changes with
accompanying changes in menstrual function. A report by Fishman
(1980) that peripheral aromatization of androgens to estrone does not
decrease when obese women lose weight indicates the complexity of the
relationship. Presently it appears that neither low body fat or a marked
decrease in body weight entirely explains the incidence of oligo/amenor-
rea in female athletes. It is more likely that body composition interacts
with other factors involved in strenuous exercise or with individual
characteristics of some women athletes.

Investigation into the neuroendocrine response to exercise as it
relates to the menstrual cycle is still in a development stage. Numerous
problems relating to protocol, technique, adherence, and expense make
it very difficult to undertake these studies in the comprehensive manner
required to test the hypothesis that hormonal changes with exercise are
responsible for athletic oligo/amenorrhea. Generally the studies can be
divided into two categories: evaluating the chronic effects of exercise by
measuring basal levels of hormones, or studying acute effects by deter-
mining differences in hormone levels before and after exercise. A basic
problem is interpreting the concentration levels once they are deter-
mined. For example, an increase in serum estradiol may represent in-
creased secretion, decreased clearance, or failure to account for hemo-
concentration following exercise. Keizer, Kuipers, Verstapper, and
Janssen (1982) are quite emphatic in asserting that concentration per se
does not reflect biological activity and ignores the changes in steroid
binding dynamics resulting from increase in blood temperature and com-
petition between testosterone and estradiol for binding sites. However,
present attempts to relate exercise-induced changes in gonadotropins and
steroids to menstrual regularity rely on concentrations.

The chronic effects of exercise on the hormonal patterns of oligo/
amenorrheic athletes have been inferred from single samples of plasma
or serum obtained at intervals which vary from study to study. To date,
there are no published reports of patterns established by daily sampling
of blood from amenorrheic athletes throughout a time period equivalent
to a normal cycle (26-30 days). Dale et al. (1979) drew weekly samples
from runners, joggers, and nonrunning controls and reported anovulat-
ing women in each group, ranging from 17% in the control group to 50%
for the runners. Hormone patterns for all anovulating women were non-
cyclic. Unfortunately, the data were not reported for cyclic and noncyclic
women by activity group. Because LH and FSH were consistently low in
the anovulatory women, the authors concluded that the source of the
problem was in the hypothalamus and/or pituitary area.
The only two studies to use a daily sampling technique involved eumenorrheic rather than amenorrheic athletes, but the results were intriguing (Bonen et al., 1981; Shangold et al., 1979). In both cases, the hormone profiles departed from the norm even though the subjects were cycling regularly. A shortened luteal phase was observed in both studies with low levels of progesterone during the luteal phase. Bonen et al. (1981) conjecture that an imbalance of the gonadotropins during the follicular phase result in an immature corpus luteum which is unable to produce normal amounts of progesterone in the luteal phase. This hypothesis will require further confirmation since Shangold et al. (1979) found no difference in FSH levels between a normal cycle and one with a shortened luteal phase.

It is unfortunate but understandable that there is not more data on the effects of chronic exercise on the hormonal profiles of oligo/amenorrheic athletes across time. Not only are the hormonal analyses expensive, but the investigator must also recruit a large number of women, amenorrheic and eumenorrheic, who are willing to submit to daily venapunctures for 30 days. Nevertheless, this is the only way to identify differences in daily fluctuations of gonadotropins and ovarian hormones between these two groups.

A number of investigators have examined the acute hormonal response to a single exercise bout, but none have included oligo/amenorrheic athletes. Apparently the primary purpose of these investigations was to determine if the response of the gonadotropins and steroids to activity might conceivably affect the functioning of the hypothalamic-pituitary-ovarian axis and lead to menstrual dysfunction. Three of the studies (Bonen et al., 1979; Jurkowski et al., 1978; Shangold et al., 1981) used a similar duration and intensity of exercise, and illustrate the changes in concentration that follow 30-40 minutes of exercise at ~ 70% \( \text{VO}_{2\text{max}} \). All three reported a significant increase in progesterone during the luteal phase; Bonen et al. (1979) and Shangold et al. (1981) also noted an increase in the follicular phase. Estradiol was also elevated during the luteal phase in two of the studies (Bonen et al., 1979; Jurkowski et al., 1978), but there was no change in the follicular phase. There were mixed results also with FSH. Only Jurkowski et al. (1978) reported a significant rise in the follicular phase; no one observed a change during the luteal phase. LH was reported as unchanged by exercise in both phases of the cycle in all three studies.

Swimmers, runners, and weight lifters have all increased their testosterone levels following exercise, but the concentrations are still within the normal range for women and well below the values for men (Fahey, Rolph, Moungmee, Nagel, & Mortara, 1976; Shangold et al., 1981; Sutton, Coleman, Casey, & Lazarus, 1973). Because women with hyperprolactinemia are also amenorrheic, some investigators have measured...
prolactin levels before and after exercise and have found significant increases (Brisson, Volle, DeCarufel, Desharnais, & Tanaka, 1980; Noel, Dimond, Earl, & Frantz, 1972; Shangold et al., 1981).

Whether the increased concentration of gonadal hormones is related to an increase in secretion or a decrease in clearance cannot be determined from these studies. Keizer, Poortman, and Bunnik (1980) have shown a decrease in metabolic clearance rate of estradiol following 10 minutes of exercise at 70% $\dot{V}O_{2\text{max}}$, and most of the authors cited above suggest decreased degradation rather than increased production as the explanation for their observations. Nevertheless, the concentration is increased and may remain high for a considerable period of time in endurance athletes who train for an hour or more once or twice a day. Yet to be determined is whether the increase is of physiologic significance; that is, are the concentrations at a level capable of influencing events along the hypothalamic-pituitary-ovarian axis?

Evidence to support the psychological theory of athletic amenorrhea is lacking. Yet this would seem to be a productive area for research because it is a common observation that mental stress, such as a sudden change in lifestyle, a death in the family, or other distressing personal experience, may cause the menses to cease (Prior, 1982). Baker (1981) suggests that the stress associated with competition and arduous training schedules may have a direct effect on the hypothalamus via the neurotransmitters. However, in the only study to employ psychological tests to discriminate between amenorrheic and eumenorrheic runners, no significant differences occurred between groups in any psychological variable (Schwartz et al., 1981). Until researchers can provide more tangible evidence of a link between mental stress and athletic amenorrhea, this theory will remain untested.

The etiology of athletic oligo/amenorrhea may be of interest to the scientist, but the long-term consequences of the condition are the primary concern for the athlete. Her concerns revolve around three main issues: Is the oligo/amenorrhea a benign and reversible condition? Are there any problems associated with the failure of the ovarian hormones to cycle regularly once a month? And will there be any lasting effect on reproductive functions?

Shangold (1982) makes an important point regarding the first question. Amenorrheic athletes should not assume the amenorrhea was induced by exercise. A number of pathological conditions are marked by cessation of menses, and the female athlete is not immune to problems that afflict women in general. Shangold (1982) recommends that oligo/amenorrheic athletes consult their physician if the condition has existed longer than a year, did not coincide with the initiation of strenuous exercise, or if regular cycles do not resume when training ceases. If the oligo/amenorrhea is related solely to activity habits, the prognosis is
good. Many studies (Abraham et al., 1982; Erdelyi, 1962; Shangold et al., 1979; Warren, 1980) report a resumption of menses when training intensity decreases or the activity is discontinued.

In regard to the second question, it should be noted that not all oligo/amenorrheic athletes are hypoestrogenic. Some women have normal levels of estrogen but simply fail to ovulate. Since normal luteal levels of progesterone are not present, menses will not occur. In these cases the physician may prescribe progesterone therapy to avoid problems associated with endometrial hyperplasia (Prior, 1982; Shangold, 1982). Although the long-term effects of low estrogen levels are still speculative at the present time, the amenorrheic athlete should be aware of potential problems. A recent report at the Endocrine Society Annual Meeting in 1982 received wide media attention when the investigators suggested that amenorrheic athletes are at risk for developing osteoporosis (Gonzales, 1982), a condition associated with decreased estrogen production in postmenopausal women. Obviously this study must be replicated before the concept of premature osteoporosis in young amenorrheic athletes is accepted as fact. Among other possible effects of estrogen deficiency are vaginal atrophy, hypertension, and cardiovascular problems (Prior, 1982; Shangold, 1982), none of which have been documented.

The evidence regarding reproductive function is largely anecdotal and retrospective. It is encouraging to hear about former amenorrheic athletes giving birth to normal healthy children, but there is no data to document the circumstances surrounding these events. Most investigators in the field emphasize the need for controlled prospective studies to explore all the effects of the hormonal changes that occur during the strenuous training of women athletes. In the meantime no one is suggesting that women make any change in their active lifestyle. The beneficial effects of vigorous activity are well documented and women should share in these benefits while the investigation into exercise-associated amenorrhea continues.

REFERENCES


