

## ENDOCRINE/MENSTRUAL FACTORS

The female athlete responds to a programme of regular exercise in a similar fashion to the male. Women show improvements in aerobic capacity, strength, and “speed” to the same qualitative degree as men. However, due to differences associated with in-utero hormonal effects on myocyte stem cell number, as well as those induced by estrogen vs. androgen, women have a smaller skeleton, less muscle mass, lower hemoglobin levels, and a higher proportion of body fat. Thus, women’s world records are 7–10% lower than those of men. Female athletes generally show training-induced structural changes of lower body fat and a higher percent of muscle than untrained women.

### A. Endocrine Function

The changes in body composition and energy metabolism associated with intense exercise may be responsible for a number of changes in endocrine function, particularly those related to the reproductive cycle.

#### 1. Menarche

A number of studies have suggested that an exercise programme begun early in life may delay the onset of menarche. This has not been confirmed, but women who have not begun menarche by age 16 in the northern hemisphere (and perhaps earlier in other populations) should have an endocrine evaluation.

#### 2. Exercise-Related Changes in the Menstrual Cycle

Exercise and its energy demands, if not compensated by adequate nutrition, may affect several cerebral neuro-transmitters and, subsequently, the hormones of the hypothalamic-pituitary-ovarian axis. These hormonal changes may be reflected in various ways: luteal phase deficiency, anovulatory cycles, and exercise-associated amenorrhea (EAA). About 2–5% of the untrained female population has one of these abnormalities; among distance runners and some athletes in other events the incidence ranges from 5–65%.

##### a. Luteal Phase Deficiency

In this condition, the menstrual cycle length is unchanged, but the luteal phase is shortened. Progesterone secretion is deficient, probably associated with a defective mid-cycle LH surge. The subject usually does not notice any changes, and therefore does not seek evaluation unless complications occur. These include infertility, endometrial hyperplasia, and a reduced bone mass (with stress fractures). Studies show an absence of the basal body temperature (BBT) rise (due to the lack of the LH surge), low plasma progesterone, and an abnormal endometrial biopsy. This may represent a precursor to the development of anovulation or amenorrhea. Although menstrual cycles may be within normal limits, it is uncertain whether estrogen therapy may be necessary to prevent bone mineral loss.

### b. Anovulation

Anovulatory cycles may be short (less than 21 days between menses) or very long (35 to 150 days). Affected women may produce adequate estrogen, but do not have an LH pulse, and have low progesterone levels. The unopposed estrogen causes proliferative endometrial growth and may lead to irregular, heavy bleeding. This can cause iron deficiency and anemia. Management may include monthly progestin therapy during days 14–25, or oral contraceptives for sexually active women. Clomiphene may be used to induce ovulation if pregnancy is desired. However, in these cases there may not be adequate estrogen to protect bone mineral competence, and estrogen replacement or an oral contraceptive should be considered. Athletes and physicians should always be aware that clomiphene is included in the list of prohibited substances.

### c. Exercise-Associated Amenorrhea (EAA)

This is the commonest type of menstrual change noted in athletes, and occurs in one of two forms:

- i. Primary amenorrhea. Primary amenorrhea is the absence of menses by age 16. This is probably due to multiple factors, including intense training from an early age, plus dietary inadequacy leading to an energy drain. Risks include a low bone density, scoliosis, and stress fractures. Amenorrhea beyond age 16 should be fully evaluated.
- ii. Secondary amenorrhea. This is defined as the absence of 3 to 12 consecutive menses. The lack of a uniform definition makes the incidence difficult to determine. About 2% to 5% of “normal” women are amenorrheic at some time. The incidence in athletes ranges from 5% to 65%, depending upon the sport and event. This condition is most common among distance runners.

The causes of amenorrhea are not well-defined, but are probably multi-factorial. Intensive training demands in the face of inadequate caloric and nutritional replacement leads to an “energy drain” that affects cerebral neuro-transmitters and the hypothalamic-pituitary-ovarian hormone system.

EAA is a type of hypothalamic amenorrhea. The gonadotrophin-releasing hormone (GnRH) pulse generator is suppressed. Many hormones that affect the GnRH pulse generator are altered by exercise. These include the endorphins, prostaglandins, catecholestrogens, serotonin, catecholamines, dopamine, cortisol, etc. These hormones in turn affect the release of LH and FSH, and thus estrogen and progesterone. A combination of the above factors, which results in an energy drain, is likely responsible for this reversible suppression of the GnRH pulse generator. The long-term consequences include infertility, a reduced bone density, stress fractures, and increased injuries.

## 3. Medical Assessment

Changes in the menstrual cycle associated with exercise are probably caused by a variety of complex, interrelated factors that are still under study. Menstrual

Table 13-1. Differential diagnosis of secondary amenorrhea.

Source	Abnormal Findings
<i>Uterine</i> Pregnancy Asherman's Syndrome	Positive pregnancy test Uterine scarring
<i>Pituitary</i> Prolactin-secreting adenoma Tumours Pituitary failure	Elevated prolactin Abnormal sella X-ray/CT Low FSH, LH, TSH
<i>Ovary</i> Ovarian failure Ovarian tumours Polycystic ovary syndrome (PCO)	Elevated LH, FSH Palpable mass LH/FSH = 3/1, elevated testosterone, DHEA-S
<i>Hypothalamus</i> Anorexia nervosa Tumour Exercise-induced amenorrhea	Distorted body image Abnormal sella X-ray/CT History
<i>Adrenal</i> Cushing's disease/syndrome Congenital adrenal hyperplasia	Elevated cortisol Elevated androgens, 17-OH progesterone
<i>Other Endocrine</i> Hyperthyroid Hypothyroid	Suppressed TSH Elevated TSH
<i>Medications</i> Oral contraceptives Anabolic steroids/testosterone	

changes should not automatically be attributed to the exercise programme, and other causes must be considered (Table 13-1).

EAA should be considered part of the Female Athlete Triad of disordered eating, amenorrhea, and a low estrogen state leading to decreased bone mineral content and eventually osteoporosis. Evaluation requires a physical examination and careful medical history, including the timing of menarche and changes in the menstrual cycle in relation to the initiation and intensity of training. Weight fluctuations and nutrition habits should also be correlated with menstrual changes. Concerns about body image, ideal weight, and methods of weight control must be noted. Many distance runners have adopted the "be thin to win" myth and develop a distorted perception of their body image. They acquire disordered eating patterns, including bulimia and anorexia. These behaviors may be difficult to elicit initially, so the examiner must be persistent. Athletes at risk of disordered eating should be evaluated and appropriate referrals made (Figure 13-1).



Figure 13-1. Disordered eating decision tree.

Team physicians should also be alert to other gynecologic disorders, sexual activity, sexually transmitted diseases, contraceptive practices, thyroid disorders, and other medical illnesses. Symptoms and signs of androgen excess, such as male pattern hair growth and acne (endogenous or exogenous androgens), visual changes (pituitary mass), and galactorrhea (prolactin-secreting adenoma) should also be evaluated.

#### 4. Testing

A step-wise protocol should begin with a pregnancy test, thyroid stimulating hormone (TSH) and a prolactin level (see Figure 13-2). Androgens (testosterone, DHEA-S and androstenedione) can be measured if virilisation or hirsutism are noted. If the pregnancy test is negative, a progesterone challenge test may be started. Progesterone can be administered orally in doses of 5–10 mg daily for 7–10 days, or in a single intramuscular dose of 100–200 mg of progesterone in oil. Progesterone converts an estrogen-stimulated proliferative endometrium into a secretory one, which is shed when the progestin is stopped. Bleeding suggests anovulation rather than hypothalamic amenorrhea. The pregnancy test should precede the progesterone challenge because this hormone is teratogenic.

If the progesterone test is positive, search for causes of unopposed estrogen, including androgen excess syndromes. If there is no response, causes of inadequate estrogen must be sought, including pituitary or ovarian failure. Measure LH and FSH, which are elevated in primary ovarian failure and low in hypothalamic-pituitary disorders such as anorexia nervosa and EAA.

#### 5. Risks of Altered Menstrual Function

Abnormal menstruation or amenorrhea are often regarded by athletes as favorable, because they believe that performance is affected by the menstrual cycle and that amenorrhea is indicative of “leanness” and fitness. Recent studies have shown, however, that serious consequences result from prolonged amenorrhea, or even a short luteal phase. This hypoestrogenic state results in an uncoupling of bone formation and resorption, with increased resorption resulting in an approximate 4% loss of trabecular bone for each year of amenorrhea. This results in a higher incidence of stress fractures, and also eventual osteoporosis. Mineralisation is only partially restored with estrogen therapy and cannot be restored with calcium administration alone. Therefore, intervention should take place within 3 to 6 months of the onset of amenorrhea.

Further, the low estrogen state also affects the vascular endothelium and may be a factor in the development of premature atherosclerosis. Also, athletes must be cautioned that EAA should not be considered a form of contraception, as ovulation may occur before menses resume.

#### 6. Management

EAA should be regarded as a form of “energy drain,” symptomatic of several possible stresses upon the athlete. Adequate nutrition must be emphasised, with stress placed upon a balanced, high-carbohydrate diet (see Chapter 6, *Nutrition*, section C.3). There should be a calcium intake of 1500–2000 mg daily, to provide a substrate for bone mineralisation. Physical and psychological stresses should be minimised. It will be difficult if not impossible for the athlete to accept a reduced training load unless there is clear evidence of overtraining. A bone mineral density examination (DEXA scan) may be needed to demonstrate to the athlete the presence of osteopenia and the need for nutritional changes and further therapy.

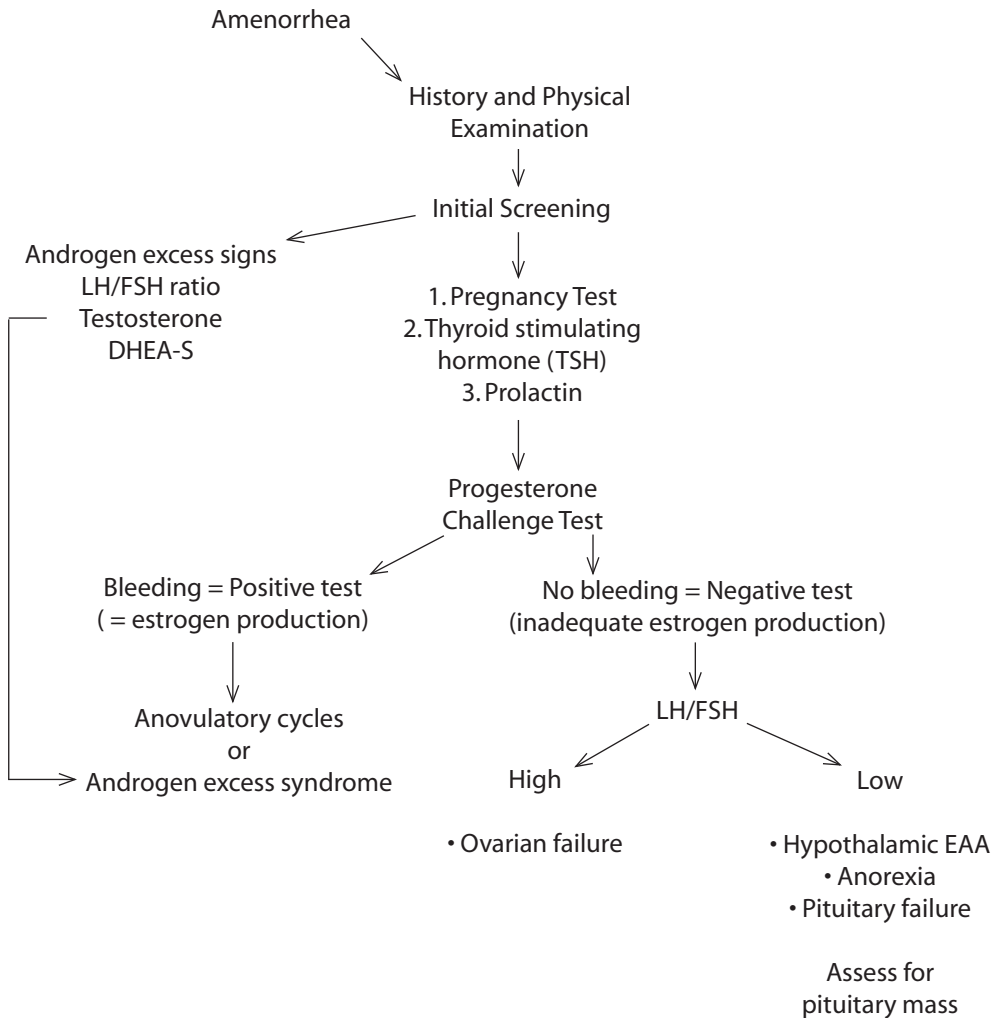


Figure 13-2. Flow chart for assessing amenorrhea.

Estrogen replacement is essential if other measures do not alleviate the condition within a few months. Estrogen therapy is best accomplished by the use of low-dose oral contraceptive pills. Although athletes may be concerned about adverse effects on performance, this is a minor problem with modern formulations and can be alleviated by trying different preparations. Recent studies show estrogen therapy has no effect on aerobic capacity, reaction time, speed, or strength. Unless there is a change in lifestyle, medications should be continued. Discontinuance may be tried, but hormonal therapy should be resumed if there is no menses in 3 to 6 months.

### B. Dysmenorrhea

Pre-menstrual symptoms of bloating, weight gain, depression, and abdominal cramping affect the athlete's sense of well being and ability to perform. Exercise is helpful in reducing some of these effects, but it does not totally alleviate the

problems. Simple analgesics may be sufficient in mild cases, but non-steroidal anti-inflammatory drugs are more effective as prostaglandin inhibitors, especially if begun just prior to the anticipated onset of symptoms.

More complete control can be obtained by suppressing ovulation with hormones, such as oral contraceptives. These can be used to regulate the timing of the menstrual cycle to avoid major competitions as well as to control symptoms. Use of these agents has been shown to produce minimal if any weight gain and no changes in performance-related factors.

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# GENDER VERIFICATION AND SEX REASSIGNMENT POLICY

## A. History

Gender verification has been required of all female athletes since the early 1960s, when allegations surfaced that men and perhaps “hermaphrodites” were participating in women’s sports events. Although there was no strong evidence to support these claims, the IOC and other international sports governing bodies initiated gender verification procedures.

At first, athletes were physically examined by a panel of female physicians. Because this caused considerable embarrassment, athletes and officials quickly embraced the buccal smear (Barr body) method, which can separate XX (genetic female) from XY (genetic male) individuals. However, geneticists have shown that a number of genetic defects in hormone synthesis or recognition can render an XY individual anatomically and physiologically female. Labeling these women as “male” has caused irreparable harm.

In 1991, the IAAF abandoned the X-chromatin (buccal smear) test and adopted the recommendation that female and male athletes undergo a general physical examination by their team physician as part of a general “health check” prior to international competition. Thus, questions concerning sexual identity could be resolved in the athlete’s own country. This procedure, however, was nearly impossible to standardise or verify at the international level.

## B. Current IAAF Policy

In 1992, the Medical Committee recommended and the Council adopted the current policy on gender verification, which states:

1. The general “health check” is strongly recommended, but no longer required.
2. Visual examination of the genitalia during the delivery of a urine specimen in the women’s doping control station is a sufficient method of determining whether the athlete is male or female. The risk of a male being discovered during the doping control procedure is sufficient deterrent to prevent males from attempting to compete as females.
3. The Medical Delegate at international competitions has the authority to initiate additional examinations if there is a question or ambiguity concerning an athlete’s gender.

There is currently concern among some athletes and officials that genitalia are not being examined adequately in doping control stations, due to lack of training of station personnel, and perhaps due to cultural constraints as well. Hence, further clarification or changes may be forthcoming. (See also Appendix 13, *Process for the Management of Gender-Related Issues*.)

### **C. Sex Reassignment—IOC Consensus Statement**

The IAAF Medical /Anti-Doping Commission has adopted the IOC Medical Commission’s statement on sports participation for athletes who have undergone sex reassignment.

#### **1. Before Puberty**

“Individuals undergoing sex reassignment of male to female before puberty should be regarded as girls and women.” Similarly, this also applies to female to male reassignment, and they should be regarded as boys or men.

#### **2. After Puberty**

Individuals undergoing sex reassignment from male to female, or the reverse, after puberty are eligible to participate in their reassigned gender under the following conditions:

- a. Surgical anatomic changes have been completed, including external genitalia changes and gonadectomy.
- b. Legal recognition of their assigned sex has been conferred by the appropriate official authorities.
- c. Hormonal therapy appropriate for the assigned sex has been administered in a verifiable manner and for sufficient length of time to minimise gender-related advantages in sport competitions.

Further guidelines:

- a. Eligibility should begin no sooner than two years after gonadectomy.
- b. A confidential case-by-case evaluation will occur.
- c. In the event that the gender of a competing athlete is questioned, the medical delegate (or equivalent) of the relevant sporting body shall have the authority to take all appropriate measures for the determination of the gender of a competitor.

### **Reference**

1. International Olympic Committee. IOC Medical Commission. Statement of the Stockholm consensus on sex reassignment in sports. 28 October, 2003.