WOMEN AND SPORT
SCIENTIFIC REPORT SERIES
ISSUE 5.2 • YEAR 2014

MENSTRUAL DISORDERS IN FEMALE ATHLETES

Angelica Lindén Hirschberg

PUBLISHED BY SISU SPORT BOOKS IN COOPERATION WITH WORLD VILLAGE OF WOMAN SPORTS

MENSTRUAL DISORDERS IN FEMALE ATHLETES

Angelica Lindén Hirschberg

Angelica Lindén Hirschberg is Professor of Obstetrics and Gynecology at the Department of Women's and Children's Health at Karolinska Institutet in Stockholm, where her research centers on women, hormones and sport. She is the official gynecologist of the Swedish Olympic Committee (since 2001) and a member of the medical committee of the Swedish Anti-Doping Commission (since 2002). In addition, Angelica is the medical advisor for both the International Association of Athletics Federation (IAAF) and the International Olympic Committee (IOC), and is a member of the World Village of Women Sports (WVWS) Scientific Board.

SUMMARY

Physical activity is well known to promote physical and mental health for the majority of women engaged in competitive and recreational sports. Still, strenuous exercise in women may have significant negative effects on the reproductive system, which are often—but not always—related to insufficient energy intake. This text discusses the causes and consequences of menstrual disorders in female athletes.

Projektledning: SISU Idrottsböcker
Översättning: Leigh Findlay
Formgivning: Catharina Grahn, ProduGrafia
Omslagsfoto: Urszula Striner
ISBN: 978-91-87745-40-9

TAKE HOME MESSAGES:

- Amenorrhoea in athletes is most common in sports that emphasise leanness; chronic energy deficiency or eating disorders that lead to inhibition of the reproductive system are likely explanations.
- The medical consequences of longstanding amenorrhoea and oestrogen deficiency are loss of bone mass and increased risk of musculoskeletal injuries.
- The female athlete triad—amenorrhoea, eating disorders and osteoporosis—was regarded as the most serious medical problem in female elite sport in the 1990s, but now low bone mass seems rare among top elite athletes.
- Adequate nutrition is the first-line strategy in athletes with amenorrhoea and oestrogen deficiency. In some cases, oestrogen treatment with oral contraceptives may also be considered. Athletes with specific eating disorders need specialist attention.
- Polycystic ovary syndrome (PCOS), characterised by increased testosterone production in the ovaries, disturbed ovulation and polycystic ovaries, is an alternative cause of menstrual disorders in sportswomen.
- PCOS is associated with an anabolic (well-muscled) body composition and may confer an advantage for physical performance.
- In women with PCOS, oral contraceptives are used to regulate menstruation and to counteract symptoms of increased testosterone production such as acne and body hair growth.

ATHLETIC AMENORRHOEA

A higher prevalence of menstrual disorders in female athletes compared to the prevalence in the general female population was first reported in the late 1970s. This and subsequent findings gave rise to the term 'athletic amenorrhoea', that is, loss of menstruation due to intense physical training. Athletic amenorrhoea can be primary (spontaneous menstruation has never occurred) or secondary (at least three consecutive months of absent menstruation). The reported prevalence of athletic amenorrhoea ranges from 6% to 79% in various investigations, as opposed to the estimated prevalence of amenorrhoea in the general population of 2–4%. The large variations reported among athletes can be explained by the significantly different prevalence in various sports. Athletic amenorrhoea is most common in endurance and aesthetic sports and activities such as running, ballet and gymnastics, while rowers have the lowest frequency. The sports with highest frequencies are those in which a lean body composition is regarded as an advantage for physical performance (Figure 1). It is well known that low bodyweight and a low percentage of body fat are associated with amenorrhoea.

ENERGY DEFICIENCY AND EATING DISORDERS

Today we understand that the most common cause of amenorrhoea in female athletes is low energy availability. Numerous studies have shown that the calorie intake of many sportswomen is much too low in relation to their energy expenditure, which results in a negative energy balance. However, not only the *quantity* of food intake matters, but also its *quality*. Vegetarian and fat-restricted diets, which are common among sportswomen, are known to be associated with amenorrhoea. One reason for this association is that an intake of animal fat is important for its cholesterol content, because cholesterol is required to manufacture sex steroid hormones. Another possible mechanism is that a high-fibre diet might inhibit the re-uptake of steroid hormones from the intestine, thus increasing the elimination of sex hormones via the gut.

Figure 1. An endurance athlete with a very lean body form. These athletes have an increased risk of athletic amenorrhoea.

The reasons for the common discrepancy between energy intake and output include the difficulties involved in eating and digesting large portions of food when engaging in a large amount of exercise, and poor knowledge about nutritional requirements. Another problem for athletes is that the biological feedback mechanisms for energy status are unreliable. For instance, appetite does not dependably reflect the caloric deficit induced by an intense training session. A more frequent cause of energy deficiency, however, is an exaggerated pursuit of leanness, (i.e. a relatively low proportion of body fat mass in relation to muscle mass), which is a crucial component of athletic success in many disciplines. For instance, endurance athletes (e.g. long-distance runners or cycling athletes) and athletes participating in gravity-opposing events (e.g. high jump) typically benefit from having a low body mass to displace. In addition, athletes performing in events that involve weight classes need to strictly regulate their body fat content and bodyweight to remain within a given class.

Female athletes have an increased risk of developing eating disorders (see Part A of this chapter). Disturbed eating in athletes may be described on a continuous scale, ranging from restrictive behaviours to severe conditions meeting the diagnostic criteria for anorexia nervosa or bulimia nervosa. Symptoms of eating disorders in athletes that do not meet the criteria for such conditions are often termed ‘anorexia athletica’. The occurrence of clinical eating disorders in female athletes has been reported as between 1% and 30%, and as high as 70% in weight-class sports. These rates are very high compared to the prevalence of eating disorders in young women in the general population: less than 1% for anorexia nervosa and about 2% for bulimia nervosa. All types of eating disorders are associated with menstrual disorders, and amenorrhoea is one of the diagnostic criteria for anorexia nervosa.

HORMONAL DISTURBANCES

Amenorrhoea due to energy deficiency is attributed to hypothalamic dysfunction in the brain, which leads to suppression of the menstrual cycle (so-called hypothalamic amenorrhoea). The release of gonadotropin-releasing hormone (GnRH) from the hypothalamus appears to be disrupted in this condition. This in turn causes reduced secretion of luteinizing hormone (LH) and, to a lesser extent, follicle stimulating hormone (FSH) from the pituitary gland. These two hormones control the function of the ovaries. Therefore, reduced secretion of the ovarian sex hormones such as oestradiol occurs, resulting in no ovulation and subsequent amenorrhoea (Figure 2).

Several mechanisms are involved in the inhibition of reproductive function in female athletes. One possible mechanism is an exercise-induced release of stress hormones that inhibit the reproductive system. Numerous studies have shown that sportswomen with menstrual disorders and low body fat have elevated levels of stress hormones such as cortisol in the bloodstream. This hormone increases in situations of acute physical and psychological distress in order to mobilise glucose for energy production. In male athletes, however, cortisol levels normalise between training sessions, whereas the levels may remain increased in women athletes. This sex difference suggests a different sensitivity to the stress associated with participation in sports. Elevated cortisol levels in female athletes are associated with higher blood glucose levels, a low amount of body fat and longstanding amenorrhoea. The increased cortisol levels indicate catabolic metabolism (breakdown of muscle and energy stores) and adaptation to negative energy balance. Chronic elevation of cortisol levels in sportswomen is probably a sign of general activation of the stress response, which includes increased secretion of corticotrophin releasing hormone (CRH) in the hypothalamus (Figure 2). This stress hormone inhibits GnRH secretion in the hypothalamus.

There is also support for the involvement of endorphins[1] in disturbed reproductive function; β-endorphin is released acutely during physical activity and might inhibit GnRH secretion in the hypothalamus in concert with CRH.

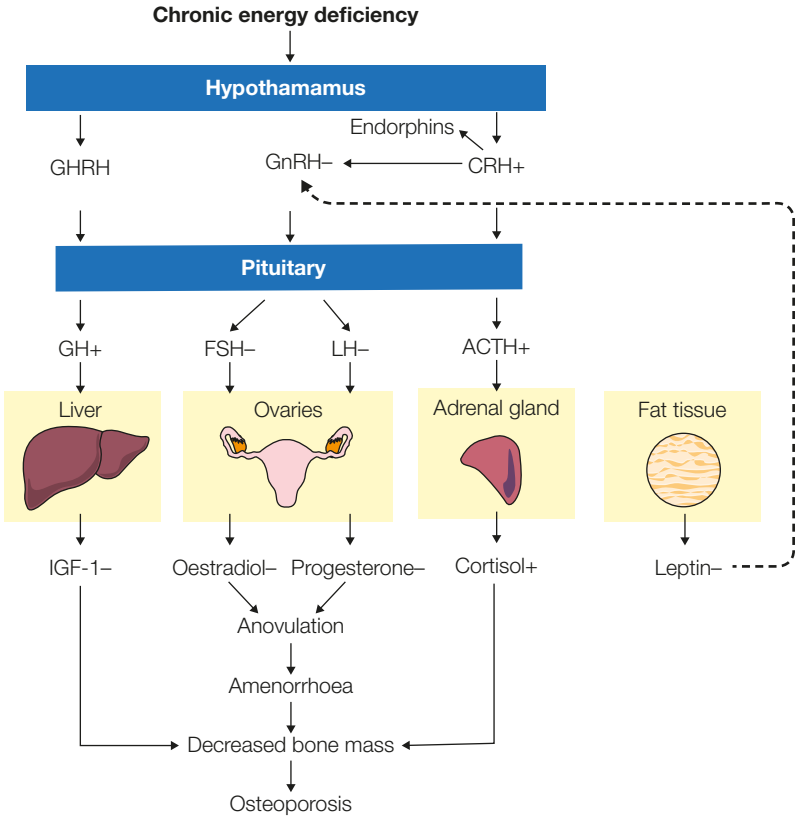

Figure 2. A summary of endocrine disturbances associated with athletic amenorrhoea. For explanations and abbreviations, see the accompanying text.

Secondary to chronic energy deficiency, circulating levels of insulin and insulin-like growth factor-I (IGF-I) are reduced, while growth hormone and IGF binding protein (IGFBP)-1 are increased. IGF-I, which is secreted from the liver, is an anabolic (body-building) hormone that is important for muscle and skeletal growth, and blood levels increase in conditions of good nutrition. IGF-I also stimulates the release of GnRH and LH, which could explain the decreased pulsatile release of LH in amenorrhoeic athletes.

Leptin is another marker of energy availability. This hormone, produced in the cells that store fat, is an independent regulator of metabolism, and levels are markedly reduced in amenorrhoeic athletes. Leptin is thought to be an important link between nutritional status and reproductive capacity. Leptin receptors on nerve cells in the hypothalamus indicate that the hormone is involved in the pulsatile secretion of GnRH. There are also leptin receptors in the ovary, which suggests a direct regulatory effect on oestrogen production.

In summary, amenorrhoea in athletes can be explained by central inhibition of the reproductive system by stress hormones and endorphins, and by reduced stimulation of GnRH due to low levels of IGF-I and leptin, the peripheral signals of energy deficiency.

1 *Endorphins* are chemicals released by the brain that are part of the body's inbuilt system for pain relief; they are also implicated in the phenomenon of the 'runner's high'

MEDICAL CONSEQUENCES OF AMENORRHOEA FOR BONE MASS AND THE CARDIOVASCULAR SYSTEM

Hypothalamic amenorrhoea in athletes has both short-term and long-term implications. One consequence of amenorrhoea is infertility. By definition, however, hypothalamic amenorrhoea is a functional disorder and does not involve any organic pathology. Such disorder can be normalised spontaneously, for example, by reducing training and improving nutrition. If pregnancy is desired, ovulation can be stimulated by hormone therapy. Fertility can thus be restored in most cases and is rarely a clinical problem. However, it is important to investigate all cases of menstrual disorders in exercising women.

In contrast, hypothalamic amenorrhoea can have far-reaching effects on the skeleton. Significant bone loss can occur after only one year of amenorrhoea. Because physical activity usually promotes a strong skeleton, it was initially considered paradoxical that elite athletes could develop reduced bone mass (i.e. osteopenia or even osteoporosis). However, numerous studies since support the conclusion that low bone mass in amenorrhoeic athletes is due to low energy availability and its endocrine (hormonal) consequences (Figure 2).

Oestrogen is important for bone cell metabolism and acts via specific receptors in bone tissue to prevent bone resorption. Consequently, longstanding amenorrhoea and the resultant oestrogen deficiency are associated with bone loss, in particular the bone in the spine and the pelvis. Chronic elevation of cortisol levels may also contribute to increased bone resorption. Furthermore, bone *formation* has been found to decrease in amenorrhoeic athletes, which is related to low energy availability. Low levels of anabolic factors such as IGF-I are probably also important in impaired bone formation. Thus, even though physical activity has the potential to increase bone mass, the overall result from energy deficiency and a catabolic hormone balance is decreased bone mass (Figure 3).

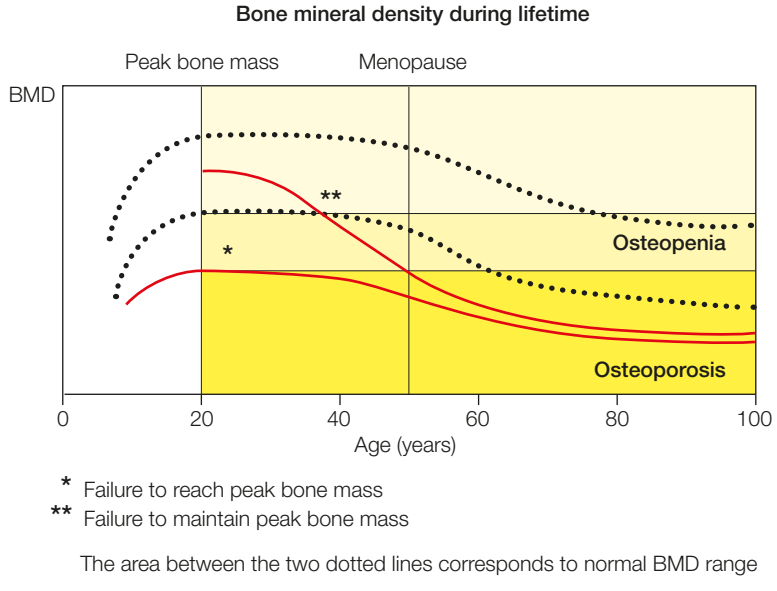

Figure 3. Changes in bone mass in women during the lifetime and the hypothetical consequences of low energy availability and oestrogen deficiency.

Amenorrhoeic athletes are also at increased risk of musculoskeletal injuries. Their risk of stress fractures is two to four times that of sportswomen with regular menstruation. Also, fractures sustained by these athletes in the pelvis, hip joint and spine may be more serious.

Oestrogen status has a significant impact on cardiovascular function in women. Similar to physical exercise, oestrogen has beneficial effects on endothelium-dependent[2] dilation of blood vessels and the serum lipid (fats and cholesterol) profile. An impaired endothelial function is an early risk marker for cardiovascular disease. Menopause, regardless of age, is associated with an increased risk of cardiovascular disease, indicating that oestrogen deficiency has a negative effect on the cardiovascular system. Likewise, amenorrhoea in female athletes is associated with impaired endothelial function and lipid profile, but oral contraceptives in these women normalise endothelial function. Thus, oestrogen deficiency counteracts the beneficial effects of exercise on the cardiovascular system. However, whether longstanding amenorrhoea implies an increased cardiovascular risk in older age is unknown. Nevertheless, studies in postmenopausal former elite athletes have shown that long-term endurance training benefits the cardiovascular system.

THE FEMALE ATHLETE TRIAD

In the 1990s, research focused on the relationship between amenorrhoea, eating disorders and low bone mass (osteoporosis). The 'female athlete triad' of these three associated conditions (Figure 4), was defined for the first time in 1992 at a consensus conference organised by The American College of Sports Medicine (ACSM) and was updated in 2007. The triad has been highlighted as the most serious medical problem in the female elite sport and is considered most common in sports that emphasise leanness. Since the concept was introduced, central sports organisations have made great efforts to alert the athletic community to these issues and to educate sports leaders and athletes in healthy training and eating habits.

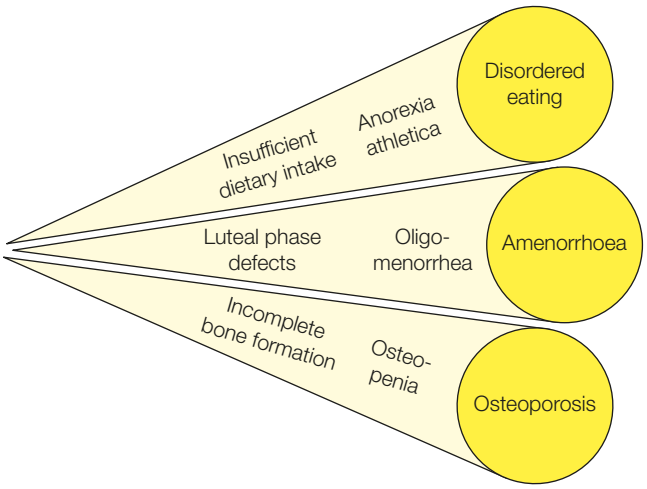

Figure 4. The three components of the female athlete triad.

However, later in the 2000s, the prevalence of the triad and the occurrence of osteoporosis were investigated among Norwegian elite athletes. None of the 186 sportswomen had osteoporosis, while two of the 145 inactive controls had this diagnosis. Although none of these female athletes fulfilled the triad, menstrual disorders and eating disorders were common. The World Health Organization defines osteoporosis as a bone mineral density (BMD) 2.5 standard deviations or more below the peak bone mass in young women. That

2 The *endothelium* is the name of the single layer of cells that lines the blood vessels.

is, a large deviation from what is normal in a young individual is required for a diagnosis of osteoporosis; however, this degree of bone loss may be normal in older women (Figure 3). A recent study of 90 Swedish Olympic sportswomen confirmed that low bone mass is rare among top elite athletes. In general, BMD was very high in the Olympic athletes and none had osteopenia (BMD 1 or more standard deviations below average) or osteoporosis.

These emerging results have made the prevalence of the triad, and especially the prevalence of osteoporosis, in elite athletes questionable, although researchers in the United States maintain its importance. Whether the prevalence of the triad has declined in recent years is unclear, and its occurrence may differ between countries.

POLYCYSTIC OVARY SYNDROME AND HYPERANDROGENISM

As already discussed, the most common reason for amenorrhoea among sportswomen is chronic energy deficiency leading to inhibition of the reproductive system and hypothalamic amenorrhoea. This condition is acquired and should be reversible by optimal nutrition in relation to the amount of exercise performed. However, not all sportswomen with menstrual disorders have catabolic metabolism (negative energy balance). Recent research shows that polycystic ovary syndrome (PCOS) is an alternative mechanism behind menstrual disorders in sportswomen, particularly in those with oligomenorrhoea (irregular periods at intervals of more than 6 weeks).

PCOS is one of the most common endocrine disorders in women of fertile age, affecting 5–10% of the female population. The syndrome is characterised by increased ovarian production of testosterone, which leads to disturbed ovulation and menstrual disorders, increased body hair and ultrasound findings of polycystic ovaries (Figure 5). Further, PCOS is associated with insulin resistance and abdominal obesity, although this is not seen in female athletes. What causes PCOS is largely unknown, but there is strong evidence for a genetic predisposition, although environmental factors also play a part.

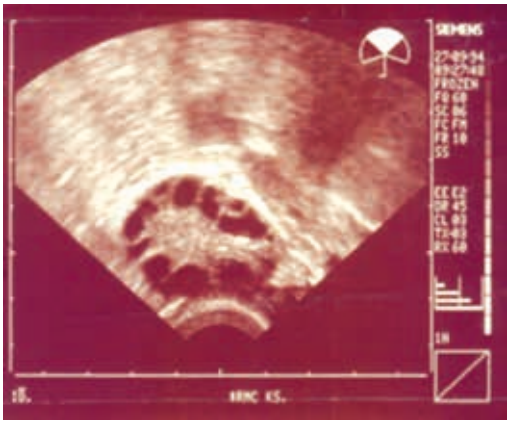

Figure 5. Ultrasound picture of a typical enlarged polycystic ovary. The ovary shows an increased number of small follicles (the dark areas on the edge of the ovary).

PCOS is a hormonal condition that has anabolic (body-building) effects on metabolism and body composition. Many women with PCOS have well-developed muscle mass and high BMD, but also have an accumulation of abdominal fat. Hyperandrogenism (increased 'male' hormones) and insulin resistance explain the anabolic body composition in PCOS.

Testosterone is one of the most potent anabolic hormones in the body and has direct stimulatory effects on muscle mass and bone tissue. Research has shown that testosterone levels in premenopausal women correlate positively with both muscle mass and bone mass. Furthermore, there are well-known associations between muscle mass, muscle strength and BMD. Muscles exert a mechanical action on bone that stimulates the formation of bone tissue—the more muscle mass, the more stimulation. Testosterone also stimulates the immune system and the formation of new blood cells. Considered together, these effects of testosterone improve physical performance.

Indeed, some studies suggest that PCOS is favourable to physical performance; endurance athletes with PCOS have higher maximal oxygen uptake and their performance is better than that of athletes without PCOS, presumably because of their increased testosterone levels (Figure 6). Therefore, some have suggested that PCOS could play a role in the recruitment of women to sports activities. Furthermore, PCOS appears to provide protection from the metabolic consequences of oestrogen deficiency, such as bone loss. Recent research showed that PCOS was the most common cause of menstrual disorders in Swedish Olympic sportswomen; the highest occurrence of polycystic ovaries was found among athletes in power disciplines.

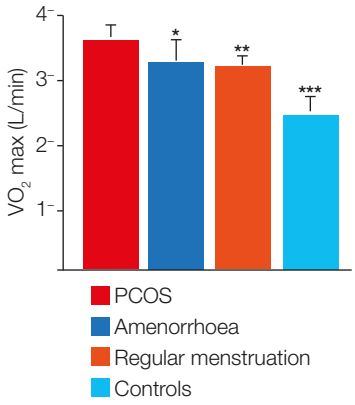

Figure 6. Maximal oxygen uptake in groups of athletes with polycystic ovary syndrome (PCOS), hypothalamic amenorrhoea and regular menstruation, and in a sedentary control group. Athletes with PCOS had the highest maximal oxygen uptake, which may confer a performance benefit.

Although PCOS may seem advantageous to physical performance, it is important to stress that women with this disorder seldom have pathologically increased testosterone levels; rather, they have levels within the upper range of normal. In addition, the overall hormonal profile in PCOS is different from that seen with intake of anabolic steroids. Thus, the hormonal profile of PCOS cannot be mistaken for the profiles seen with doping.

In almost all sports, men's performance is superior to that of women, and therefore sports are divided into female and male competitions. The mechanical advantage of the male body is explained, in most part, by the fact that the concentration of testosterone in the blood of men is about 10 times that of women. Usually, there is no overlap between testosterone levels in women and men. However, some rare conditions in women, for example, disorders of sexual development, may cause a greatly increased production of male hormones (androgens) that extends into the male range. These increased androgen levels may cause masculinisation of the body. Cases of extreme hyperandrogenism among sportswomen have attracted great attention in recent years and the issue has been discussed in relation to 'fairness in sport'. Recently, the International Olympic Committee (IOC) and the International

Association of Athletics Federations (IAAF) finalised guidelines for the management of severe hyperandrogenism in female athletes. The aims were to establish rules for identifying, diagnosing and ensuring adequate medical care and treatment for such women in order to determine eligibility for participation in women's competitions.

MANAGEMENT OF MENSTRUAL DISORDERS

Menstrual disturbances are symptoms of hormonal imbalance and should always be investigated by means of gynaecological examination and endocrine evaluation. Amenorrhoea in a woman with low bodyweight is often caused by chronic energy deficiency or eating disorders that lead to hypothalamic suppression of the reproductive axis, while irregular periods of long intervals (oligomenorrhoea) in a woman with anabolic body composition may be due to PCOS. Each condition requires specific care and treatment.

In the former case, hypothalamic amenorrhoea is an acquired condition that can be normalised once the balance between energy intake and energy expenditure has been improved. A careful review of eating habits in relation to training, and counselling by a dietitian, is recommended. For eating disorders, the individual must be referred to a specialist clinic. Laboratory tests should include measuring blood levels of hormones and nutritional factors. The most typical hormonal pattern of hypothalamic amenorrhoea includes suppressed levels of LH, FSH, oestradiol and IGF-I; however, cortisol levels are increased.

Longstanding amenorrhoea in athletes is related to low bone mass, endothelial dysfunction and unfavourable lipid profile. Bone mass is preferably measured by dual energy X-ray absorptiometry (DXA) at a hospital or a large specialist clinic. Supplementation of calcium and vitamin D may be beneficial for low bone mass. Adequate nutrition should always be the first-line strategy, but oestrogen treatment with, for example, oral contraceptives may also be considered because they can counteract the negative effects of amenorrhoea in athletes. Despite concerns, no evidence exists that oral contraceptives adversely affect physical performance, although minor changes in body composition may occur.

The hormonal profile of PCOS is completely different from that of hypothalamic amenorrhoea (Figure 7); women with PCOS have increased levels of LH and testosterone. PCOS, which has a genetic component, is managed according to symptoms. Treating menstrual disorders in these women is recommended because longstanding anovulation is considered to increase the risk of endometrial cancer. The mechanism is attributed to the continuous stimulation of the endometrium by oestrogen (due to the absence of ovulation), without the concomitant counteracting effect of progesterone. Treatment with oral contraceptives or cyclic progestins abolishes this risk and is used to regulate the menstrual cycle. Oral contraceptives also inhibit the effects of androgens and counteract acne and increased growth of body hair. Women who wish to become pregnant may need hormonal stimulation of ovulation or, ultimately, in vitro fertilisation. Because women with PCOS tend to accumulate abdominal fat and become overweight, continued exercise is recommended beyond their sports career.

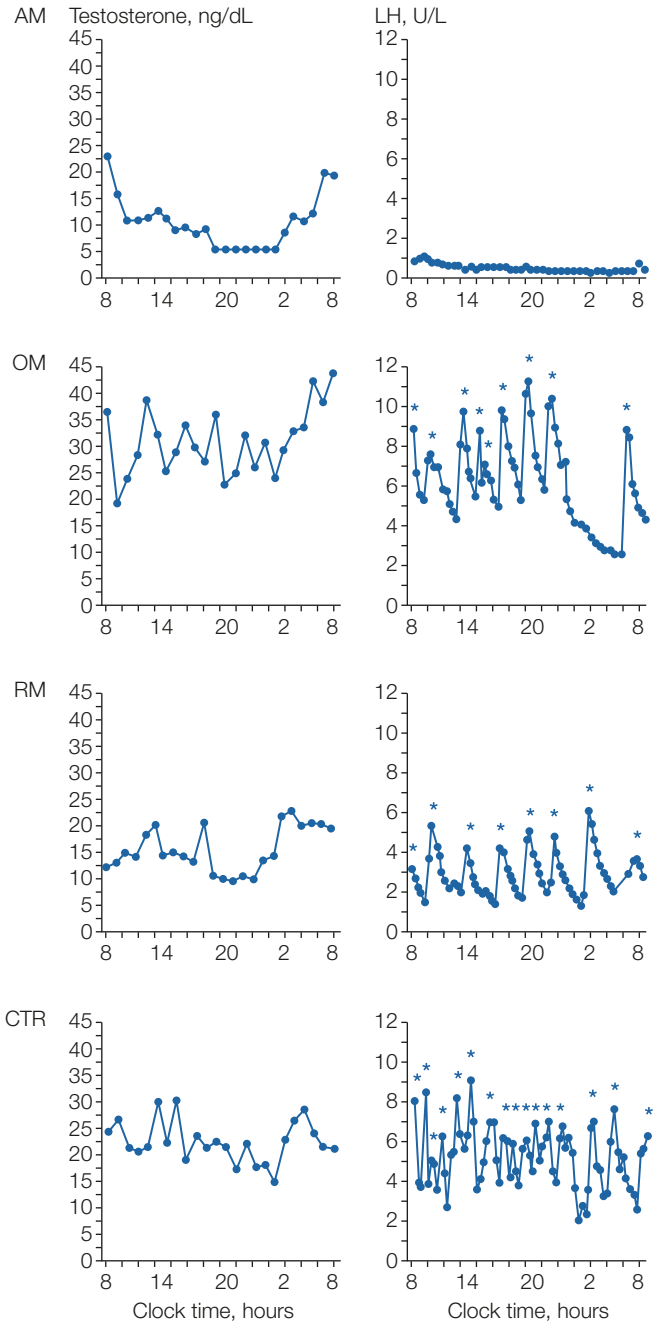

Figure 7. Typical 24-hour hormonal profiles in individual female athletes and a sedentary control woman. AM = athlete with hypothalamic amenorrhoea, OM = athlete with oligomenorrhoea and polycystic ovary syndrome (PCOS), RM = athlete with regular menstruation, CTR = sedentary control.

SELECTED REFERENCES

Coste, O., Paris, F., Galtier, F., Letois, F., Maimoun, L., & Sultan, C. (2011). Polycystic ovary-like syndrome in adolescent competitive swimmers. *Fertility and Sterility*, *96*, 1037–1042.

Feingold, D., & Hame, S. L. (2006). Female athlete triad and stress fractures. *The Orthopedic Clinics of North America*, *37*, 575–583.

Goodman, L. R., & Warren, M. P. (2005). The female athlete and menstrual function. *Current Opinion in Obstetrics and Gynecology*, *17*, 466–470.

Hagmar, M., Berglund, B., Brismar, K., & Hirschberg, A. L. (2009). Hyperandrogenism may explain reproductive dysfunction in female Olympic athletes. *Medicine & Science in Sports & Exercise*, *41*, 1241–1248.

Hagmar, M., Hirschberg, A. L., Berglund, L., & Berglund, B. (2008). Special attention to the weight-control strategies employed by Olympic athletes striving for leanness is required. *Clinical Journal of Sports Medicine*, *18*, 5–9.

Hagmar, M., Hirschberg A. L., Lindholm, C., Schenck-Gustafsson, K., & Eriksson, M. J. (2005). Athlete's heart in postmenopausal former elite endurance female athletes. *Clinical Journal of Sports Medicine*, *15*, 255–260.

Lambrinoudaki, I., & Papadimitriou, D. (2010). Pathophysiology of bone loss in the female athlete. *Annals of the New York Academy of Science*, *1205*, 45–50.

Nattiv, A., Loucks, A. B., Manore, M. M., Sanborn, C. F., Sundgot-Borgen, J., & Warren, M. P. (2007). American College of Sports Medicine position stand. The female athlete triad. *Medicine & Science in Sports & Exercise*, *39*, 1867–1882.

Redman, L. M., & Loucks, A. B. (2005). Menstrual disorders in athletes. *Sports Medicine*, *35*, 747–755.

Rickenlund, A., Carlström, K., Ekblom, B., Brismar, T., von Schoultz, B., & Hirschberg, A. L. (2003). Hyperandrogenicity is an alternative mechanism underlying oligomenorrhea and amenorrhea in female athletes and may improve physical performance. *Fertility and Sterility*, *79*, 947–955.

Rickenlund, A., Carlström, K., Ekblom, B., Brismar, T., von Schoultz, B., & Hirschberg, A. L. (2004). Effects of oral contraceptives on body composition and physical performance in female athletes. *Journal of Clinical Endocrinology and Metabolism, 89*, 4363–4370.

Rickenlund, A., Eriksson, M., Schenck-Gustafsson, K., & Hirschberg, A. L. (2005). Amenorrhea in female athletes is associated with endothelial dysfunction and unfavorable lipid profile. *The Journal of Clinical Endocrinology and Metabolism*, *90*, 1354–1359.

Rickenlund, A., Thorén, M., Carlström, K., von Schoultz, B., & Hirschberg, A. L. (2004). Diurnal profiles of testosterone and pituitary hormones suggest different mechanisms for menstrual disturbances in endurance athletes. *Journal of Clinical Endocrinology and Metabolism*, *89*, 702–707.

Sundgot-Borgen, J., & Torstveit, M. K. (2010). Aspects of disordered eating continuum in elite high-intensity sports. *Scandinavian Journal of Medicine & Science in Sports, 20*(suppl. 2), 112–121.

Torstveit, M. K., & Sundgot-Borgen, J. (2005). Low bone mineral density is two to three times more prevalent in non-athletic premenopausal women than in elite athletes: A comprehensive controlled study. *British Journal of Sports Medicine*, *39*, 282–287.