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The Menstrual Cycle and Sport Performance

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The female reproductive life cycle is one of the most important biological rhythms. From prepuberty through to menarche, conception, pregnancy, the postpartum period, menopause, and beyond, the female athlete is exposed to a constantly shifting kaleidoscope of endogenous sex steroid hormones. Although estrogen and progesterone are the most important in terms of their actions on the various body systems, more recent research has explored the effects of other hormones, such as testosterone, relaxin, and leptin, to name just a few. Oral contraceptives and hormone replacement therapy further introduce exogenous synthetic hormones (in varying proportions) to the equation.

Female athletes, coaches, medical professionals, and researchers have long been fascinated with potential menstrual cycle fluctuations in athletic performance, secondary to the differential effects of sex steroid hormones. Studies have shown that estrogen can influence the cardiovascular system (including blood pressure, heart rate and rhythm, and vascular flow), substrate metabolism, and even the brain itself. Progesterone and other progestins, on the other hand, appear to mainly affect thermoregulation, ventilation, and, to a lesser extent, the choice and usage of fuel for energy needs. The end results can be additive or synergistic, interactive or even antagonistic. Changing relative proportions of hormones throughout a "regular" ovulatory menstrual cycle can potentially alter many

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important facets of athletic performance, itself a complex phenomenon. Components of sports performance that may be affected by the menstrual rhythm are listed in Box 1. Menstrual cycle variation in aerobic and anaerobic capacity, aerobic endurance, and muscle strength has been investigated to some extent. Maximal physical performance requires an array of mental and physical functions acting in optimal concert. The female hormones can affect many of these factors; hence the cycling of estrogen and progesterone levels can influence performance in many ways. The relatively common occurrence in athletes of menstrual dys-

Box 1. Components of sports performance that may be affected by the menstrual rhythm

- Brain function
  - Mood
  - Arousal
  - Cognition
- Cardiovascular
  - Heart rate and rhythm
  - Stroke volume
  - Blood pressure
  - Body fluid volume
  - Coagulation
  - Vascular function
  - Sympathetic activity
- Respiratory
  - Ventilation
  - Asthma
- Metabolic
  - Core body temperature
  - Thermoregulation
  - Resting oxygen consumption
  - Substrate availability and metabolism
  - Acid-base balance
- Strength
- Aerobic capacity (VO_2 max)
- Anaerobic capacity
- Response to ergogenic aids
  - Glucose
  - Caffeine
- Orthopedic
  - Injury rate
  - Ligament laxity
  - Low back pain

function (such as amenorrhea, oligomenorrhea, anovulation, and short luteal phase) further complicates the picture. This dysfunction may be more prevalent in certain sports particularly at the elite level, which is coincidentally made up of athletes who have the greatest vested interest in performance enhancement. Unfortunately, most previously published research is limited by methodological problems, preventing undisputed conclusions. Previous reviews have described earlier studies in detail [1–3], so this article primarily focuses on more contemporary work.

The menstrual cycle

The menstrual cycle is perhaps the second most important biological rhythm, next to the circadian one. It is created by the interplay between hypothalamic, hypophyseal, and ovarian hormones, bringing about various changes not only in the female reproductive tract but also in many other tissues of the body. It is traditionally divided into two phases (follicular and luteal) or three phases (follicular, ovulatory, and luteal), based on ovarian function. The follicular phase begins on the first day of menses, lasts an average of 9 days, and is the period when follicles are grown under the influence of the hypophyseal follicle-stimulating hormone (FSH). Estrogen levels, secreted from the cells surrounding this follicle, slowly increase, inducing the secretion of the hypophyseal luteinizing hormone (LH). As estrogen levels increase further, a surge of LH is secreted, and about 1 day later ovulation occurs. This marks the beginning of the ovulatory phase, which lasts about 5 days. During these phases, endometrial thickness increases in preparation for receiving the embryo. A few days after the follicle has released the ovum, it is transformed into the progesterone-secreting corpus luteum, bringing about the luteal phase, which normally lasts 14 days. Progesterone acts to support the endometrium until the embryo can create the placenta, which will take over this function. At the end of the luteal phase, progesterone secretion from the corpus luteum ceases, the endometrium is no longer supported and it sloughs off as menstrual bleeding. As estrogen levels decrease in these days, FSH secretion enhances and begins the cycle again. The three phases of the cycle are therefore differentiated from one another by the estrogen and progesterone level ratios: (1) low estrogen and low progesterone levels are present during the follicular phase, (2) high estrogen and low progesterone levels are present during the ovulatory phase, and (3) high estrogen and high progesterone levels are present during the luteal phase.

Methodological considerations

Proper study design and methodology are necessary for any meaningful research into the relationship between the menstrual cycle and athletic perfor-

mance. Case reports or clinical series (with or without historical controls) and cross-sectional studies do not offer much helpful information and cannot be generalized for a larger population. Case-control (retrospective) studies are notoriously prone to subjective recall and other types of bias. Prospective and historical cohorts can be followed for a few cycles, but only randomized clinical trials provide the best evidence of alterations in athletic performance attributable to either endogenous or exogenous hormonal variations. Many technical issues arise when attempting to construct a consensus regarding menstrual cycle and exercise performance. These include cycle phase definitions and verification, timing of hormone measurements, exercise testing, and injury documentation and their associations [4].

Two different approaches are used to divide the menstrual cycle. A somewhat older one compares the premenstrual and menstrual days with the rest of the cycle. These days consist of psychologic and physical discomfort, fluid retention, headaches, bloating, breast tenderness and, of course, bleeding. These factors may easily combine to reduce performance. The second approach divides the cycle by hormone levels, into two (follicular/luteal phases), three (follicular/ovarian/luteal phases), or five (early follicular/late follicular/ovarian/early luteal/late luteal phases) stages. Comparison of studies using these methods is difficult, as the premenstrual and menstrual days span luteal and follicular phases, each with very different hormone levels. Also, many female athletes (depending on their sport and other risk factors) may have luteal phase deficiency or anovulation. Therefore, estimation of cycle phase without measuring hormone levels may be inappropriate.

All studies require adequate documentation of menstrual cycle phase, as natural variability in cycle-phase length precludes simple numbering of the days of the cycle. Numerous reference methods are used to monitor ovulation and, by extension, menstrual cycle phase [5]. Calendar calculation, measuring the increase in basal body temperature (BBT) after ovulation, and examining changes in cervical appearance and its mucus are simple and inexpensive methods, but are inaccurate. Definitive determination of follicular, ovulatory, and luteal phases of the menstrual cycle requires the assessment of serum estradiol and progesterone levels. Concentrations of these hormones in the saliva or urine appear to correlate with serum levels, and therefore collection of these fluids may be used as non-invasive methods. However, using urine samples to detect the midcycle LH surge can be less accurate.

Another confounding factor is the possible time lag between changes in hormone levels and any impact on performance. For example, one study employing hormone level measurement on a daily basis found a 4-day time-phase delay between the hormonal changes and their effect on knee laxity changes [6]. The hypothesis that similar time-shifts exist with other components of performance still needs to be examined.

Other factors, such as the time of day or ‘‘ultradian rhythm’’ [4], ambient temperature and humidity, nutrition and hydration, fitness level, and training status must also be standardized in any exercise study.

There is also a the high variability among subjects, which can impede conclusions from being drawn from studies involving a small number of subjects or when applying study results to a single athlete.

Finally, it is important to distinguish between statistically significant and biologically or functionally significant differences, as most races or events are not won by a statistically significant margin.

Biological effects of the sex steroid hormones

Estrogen in its various forms is responsible for the development of secondary sexual characteristics and the typical female pattern of fat deposition in the breasts, buttocks, and thighs. Progesterone can, in many ways, have antiestrogenic and androgenic actions. Circulating estrogen and progesterone levels cause variation in many cardiovascular, respiratory, and metabolic parameters, with subsequent implications for strength and aerobic and anaerobic performance. Much less is known about the effects of the various androgens in female athletes, which were found to be elevated in some athletes with menstrual dysfunction [7,8]. The progestins currently used in oral contraceptives (and injectable forms of birth control) have varying estrogenic, progestogenic, and androgenic actions. Many other hormones, such as growth hormone and cortisol, are also impacted, which further confuses the understanding of experimental findings.

Cardiovascular system

The relationship between the female reproductive hormones and the cardiovascular system is complex and related to myriad sites and mechanisms of action [9]. Some issues relevant to sport performance are that estrogen can enhance endothelium-dependent vasodilatation [10], and there also appears to be a difference in cardiac excitability possibly caused by calcium antagonism or inhibition of angiotensin-converting enzyme. Estrogen and progestin stimulate the renin–angiotensin system, a suggested mechanism of end-luteal phase (ie, premenstrual) fluid retention. Administration of exogenous forms of these hormones found in oral contraceptives or hormone replacement therapy (HRT) may have similar consequences. Other hormones (such as vasopressin and corticotropin) that influence fluid balance and vascular tone also appear to be affected by menstrual cycle phase [11].

Cardiovascular responses to stress (eg, myocardial ischemia) are more easily elicited when estrogen concentrations are low (ie, during the follicular phase); conversely, in women with premenopausal coronary artery disease, the best treadmill performance occurred at midcycle or ovulation (ie, phases characterized by high blood-estrogen levels) [12]. A recent Doppler echocardiographic study of left ventricular structure and function during the midfollicular and midluteal phases did not document any significant differences, but the time of maximal estrogen concentration (ie, immediately before ovulation) was not captured [13].

Progesterone may increase cardiac excitability by its opposing effects on estrogen. Increased cardiovascular strain (ie, higher heart rate) has been documented for the same level of work during the luteal as in the follicular phase [14], but the associated luteal-phase increase in body mass and body temperature makes it difficult to interpret this information.

Respiration and ventilation

The sex steroid hormones are involved in the central neural control of breathing, affecting central neurotransmitters, peripheral chemoreceptors, and perhaps the lung and airways [15,16]. Endogenous progesterone leads to a greater minute ventilation and maximal exercise response during the luteal phase of the menstrual cycle and during pregnancy, whereas synthetic medroxyprogesterone acetate can induce similar respiratory responses in male subjects and in postmenopausal women. Estradiol increases the number and sensitivity of progesterone receptors, so combination hormonal therapy could theoretically have an even greater influence. In addition, the overall sensitivity of the respiratory drive appears to be enhanced by a lowering of the threshold and an increase in excitability of the medullary respiratory center. This action can potentially be detrimental to endurance-trained athletes, who normally benefit from decreased hypoxic and hypercapneic respiratory drives at rest and during exercise. However, this has only been significant in untrained athletes [17].

Increased ventilation leads to a partially compensated respiratory alkalosis, but the concurrent left shift in the pH curve caused by increased temperature during the luteal phase may mean no net consequences in terms of oxygen delivery from the red blood cells to the tissues [18]. No correlation has been found between ventilation and progesterone levels, but this might be caused by a time-phase delay in the effect of the hormone, circulating levels of bound progesterone, or interaction with other hormones such as estradiol. Other reproductive hormones (eg, LH, FSH, prolactin), catecholamines (eg, epinephrine, norepinephrine), thyroid and adrenocortical hormones, dopamine, leptin, and serotonin, just to name a few, also appear to be involved in the complex control of breathing. Environmental factors, such as exposure to high altitude, also have additional potential to alter ventilation during the menstrual cycle [19].

Premenstrual and perimenstrual aggravation of asthma (as measured by peak expiratory flow rate) can be seen in up to 30% to 40% of asthmatic women, even though they may not be aware of it. Cyclically increased visits to emergency departments for asthma have been documented [20]. Most studies, however, have been performed in nonathletic populations without hormonal verification of cycle phase. The clinical possibilities are numerous. For example, the late luteal phase drop in plasma levels of progesterone (a known smooth muscle relaxant) might lead to bronchoconstriction through withdrawal of its effect on bronchial smooth muscle. In addition, estradiol is associated with increases in acetylcholine concentration, mucus secretion, and prostaglandin production. Furthermore, ventilation at rest is controlled by central and peripheral chemoreceptors, whereas

neurogenic factors predominate during exercise. And lastly, acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs (NSAIDs), frequently taken for dysmenorrhea, may affect airway resistance through prostaglandin inhibition [21]. In the subgroup of female asthmatics who have menstrual-linked asthma or perimenstrual asthma, there may be a future role for ''respiratory endocrinology'' and hormonal manipulation with medications such as progesterone or danazol, oral contraceptives, or GnRH agonists and analogs. Current knowledge regarding asthma and the sex hormones is well reviewed in recent publications [22,23], but there is an obvious need for further well-designed studies of sufficient sample size to build evidence in this area.

Thermoregulation

Progesterone and the synthetic progestins have a central thermogenic effect, modulated at the level of the preoptic/anterior hypothalamus. This is responsible for the increase in BBT (0.3°C to 0.5°C) during pregnancy and the luteal phase of the cycle, and the smaller core temperature changes seen with oral and injectable forms of contraception. Altered skin blood flow [24] and an increased threshold for cutaneous vasodilatation and onset of sweating are thought to be the major mechanisms of this action, as presented in Fig. 1.

A higher core body temperature may reduce the safe margin for heat accumulation when exercising or even working in a hot environment, decreasing the time to fatigue [25]. During the luteal phase, and especially under conditions of extreme heat and humidity, female athletes may be at a thermoregulatory disadvantage for training and competing [26,27]. There may also be indirect and

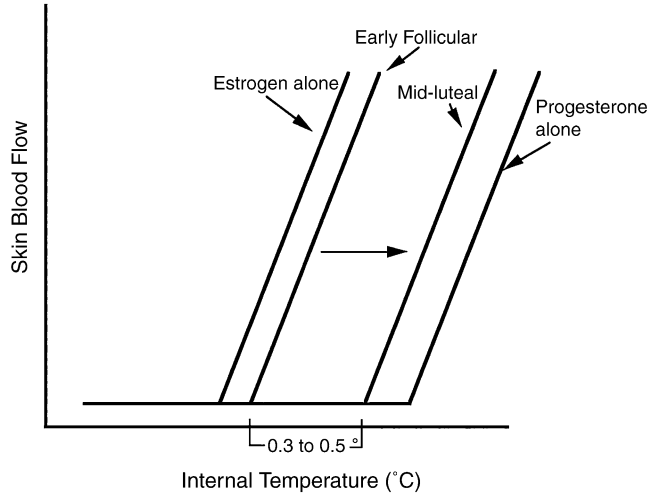

Fig. 1. Relationship of skin blood flow and internal temperature, depending on cycle state or the presence of estrogen. (*From* Charkoudian N, Johnson JM. Female reproductive hormones and thermoregulatory control of skin blood flow. Exerc Sport Sci Rev 2000;28(3):108–12; with permission.)

independent effects from the higher heart rate and greater sense of exertion during this phase. Interestingly, thermo-sensitivity to cold-water immersion does not seem to be affected by menstrual cycle phase [28].

Substrate metabolism

The known gender differences in energy metabolism are largely caused by the differential actions of the sex steroid hormones [29]. Research in animals [30] and humans has shown that estrogen promotes glycogen uptake and storage in liver and muscle through increased lipid synthesis and enhanced lipolysis in muscle. Higher levels of estrogen (and progesterone to a lesser extent) tend to spare glycogen stores by shifting metabolism more toward free fatty acids [31]. This metabolic hormonal action may contribute to women's enhanced capability for ultra-endurance exercise, as compared with men. This greater dependence on fat stores for energy is primarily seen at certain (low to moderate) exercise intensities, whereas greater relative efforts depend increasingly on blood glucose and muscle glycogen as substrates [32].

Overall, progesterone likely also shifts substrate metabolism toward a greater dependence on fat, through antagonism of the lipolytic effects of estrogen, but accentuation of its carbohydrate-sparing effects (constraint of peripheral blood-glucose uptake, decreased hepatic glycogenolysis). There is debate as to which hormone has the predominant function and at which time in the menstrual cycle this is most manifest: around the time of ovulation, implying that it is primarily an estrogen effect [33], or during the luteal phase when both hormones are high (and muscle biopsies have documented higher muscle glycogen stores) [34]. Changing absolute and relative proportions of estradiol and progesterone make it extremely difficult to ascertain the individual hormonal effects in human studies. Additionally, the ovarian hormones may have indirect effects on substrate metabolism through interactions with other hormones, such as the catecholamines, especially during exercise [35]. Endocrine and intracellular factors play critical roles in determining substrate balance during sustained exercise. However, glucose ingestion can improve performance regardless of menstrual phase (Fig. 2).

Estrogen is believed to improve carbohydrate tolerance through actions on lipolytic enzymes and glucoregulatory hormones such as growth hormone, catecholamines, and insulin, an effect opposite to that of progestins. A recent review [36] describes the complex interactions of these hormones and energy metabolism. Deterioration of carbohydrate metabolism and relative glucose intolerance during the luteal phase has also been attributed to progesterone, through its contra-insulin effects on extrahepatic tissues and increase in insulin resistance. In rats, progesterone decreases glucose transporter protein (GLUT-4) content in skeletal muscle and adipose tissue. In humans, the insulin resistance of pregnancy is at least partially caused by the actions of progesterone, and may also contribute to the onset of gestational diabetes mellitus. The synthetic progestins that are currently used in oral contraceptives have varying effects, depending on their androgenicity, with norgestrel and levonorgestrel being the most potent in

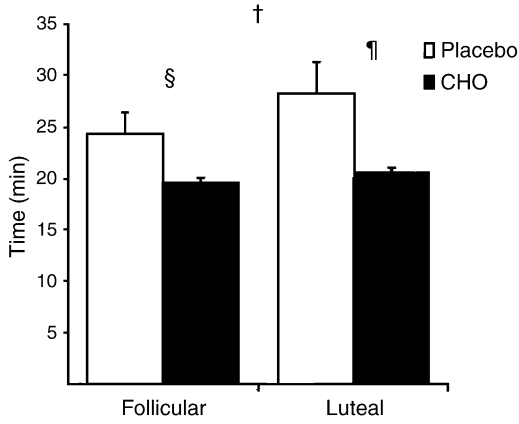

Fig. 2. Time to complete a cycle ergometer test during follicular and luteal phases, with or without carbohydrate ingestion. Note better performance in the follicular phase compared with the luteal phase ($P < .05$), and that performance with glucose ingestion was similar in both phases. CHO, carbohydrate. (*From* Campbell SE, Angus DJ, Febbraio MA. Glucose kinetics and exercise performance during phases of the menstrual cycle: effect of glucose ingestion. Am J Physiol Endocrinol Metab 2001;281:E817–25; with permission.)

this regard, and norethindrone having the least impact. There are obvious clinical implications for the choice of medications in patients who have diabetes mellitus or glucose intolerance. In this population, there may also be minor variations in glucose control during an ovulatory menstrual cycle or postmenopause, but there are many other confounding variables to factor in. As muscle contraction is a far more potent stimulus for glucose uptake than insulin, exercise studies at different menstrual cycle phases are needed to look at the effect of female sex steroids on glucose uptake during exercise.

Psychological factors: estrogen and the brain

In the behavioral literature, there is some evidence that estrogen may potentially mediate different aspects of cognition, alertness, and cognitive performance [37]. Beneficial effects on cognitive function and verbal memory are believed to be secondary to changes in the availability of neurotransmitters such as serotonin in the brain. Estrogen and testosterone have demonstrated opposite influences on modulation of spatial cognition [38], whereas progesterone may have negative, even sedative, effects [39]. Higher levels of estradiol during the luteal phase are postulated to cause poorer performance on tasks of spatial ability [40,41]. However, few early studies on cognitive functions and the menstrual cycle use anything more than calendar estimation of cycle phase, so most are little more than conjecture. More recently, advanced imaging techniques, such as functional MRI studies, in conjunction with measurement of sex steroid hormone levels are being used to better delineate neuropsychologic parameters associated with menstrual cycle phases and HRT. Although this field is still in its infancy, its

potential importance should not be ignored, because at least some of these mental functions are required in certain sporting activities.

The menstrual cycle and physical performance

Several factors related to the menstrual cycle, including psychologic and physical, affect athletic performance. Key physical factors are strength, and aerobic and anaerobic capacity.

Menstrual cycle and strength

Muscular strength (eg, handgrip strength, isokinetic and isotonic knee flexion and extension, leg and bench press) does not appear to fluctuate significantly during an ovulatory menstrual cycle. Although more recent studies contain hormonal documentation of cycle phase [14,42], the numbers are still small. In addition to the athletic arena, there can be important implications for the workplace and industry. One study looked at manual handling performance (eg, isometric and 10-minute dynamic lifting performance) at five distinct times in the cycle: menses, midfollicular, ovulation, midluteal, and premenses (72 hours before menses) [42]. Neither maximal isometric lifting strength (MILS) nor endurance time at 45% of MILS at two standardized heights were affected by menstrual cycle phase. A luteal phase increase in the heart rate response to exercise (of 7 beats/min) suggested increased cardiovascular strain, possibly related to either alterations in blood flow or thermoregulation.

Some investigators have reported an inotropic effect of estrogen on muscle [43], peaking just before ovulation, of a 10% to 11% magnitude [44], and postulated a switching of muscle cross-bridges from low- to high-force generation. There was an associated slowing of relaxation and increase in fatigability at midcycle, but because of the lack of hormonal verification of cycle phase these findings are somewhat suspect. However, another study that did monitor LH, estradiol, and progesterone levels concluded that maximal voluntary muscle contraction was significantly higher in the ovulatory phase, perhaps related to intrinsic contractile properties [45]. A contemporary study eliminated many of the methodological problems found in the previous literature [46] by using electrical stimulation to ensure maximal neural activation and muscle contraction. In this study, the investigators found no significant changes in quadriceps muscle strength, fatigability, or electrically stimulated contractile properties in 19 women over three phases of the menstrual cycle, and no significant correlations of any of the strength indices with female reproductive hormone concentrations.

Most recently, researchers studied ten moderately active subjects over two consecutive menstrual cycles during hormonally verified times: early follicular phase, ovulation, and midluteal phase. Tests included handgrip strength, one-leg hop test, isokinetic muscle strength, and muscle endurance [47]. This stronger

repeated-measures design confirmed the earlier and more current research results [48,49] showing a lack of systematic menstrual cycle variation in strength parameters. Other studies continue to report a circamensal effect, possibly caused by peripheral rather than central mechanisms [50]. Some have even suggested periodization of training programs for female athletes to take advantage of any optimal hormonal fluctuations [51]. This concept is not so far-fetched, as estradiol, in addition to exercise itself, is known to modify growth hormone (GH) secretion and metabolism [52]. The anabolic effects of this hormone may promote maximal muscle gain at certain times during the natural menstrual cycle or hormonally controlled cycles in women taking oral contraceptives [53]. Similarly, a separate body of literature is emerging on the potential clinical use of estrogen replacement therapy in postmenopausal women to preserve muscle strength [54].

Menstrual cycle and aerobic capacity

For the most part, it does not appear as if maximal oxygen capacity and submaximal exercise responses are significantly different during any phase of the menstrual cycle. Previous studies have been reviewed in detail elsewhere [1,2,4]. Some responses do suggest a possible slight decrement in aerobic capacity [48] or exercise efficiency during the luteal phase [55]. This decrement can be seen in Fig. 2, along with an increase in oxygen consumption and metabolic rate. Running economy (the rate of oxygen consumption during a given submaximal steady-state running speed) has been examined at five hormonally distinct times in the cycle, with concomitant hormonal verification. A lower running economy was found at 80%, but not 55%, of maximal aerobic capacity during the luteal phase, with associated changes in ventilatory drives and fluctuations in mood state [56]. Ventilatory changes may be more significant under conditions of diminished oxygen availability. In a relatively large group of sedentary high-altitude native women exercising at 3600 m, maximal work output was approximately 5% higher during the luteal phase, with higher submaximal minute ventilation and ventilatory equivalents, but no overall effect on VO_2max [57]. A separate study of lowlanders, using a hypobaric chamber to simulate altitude, did not document any significant differences in either ventilation or physical performance [19]. The corollary of such findings for athletes training and competing at sea level is unclear. Another group tested eight moderately active women during three separate hormonally verified cycle phases: early follicular (low estrogen and progesterone), midfollicular (elevated estrogen and low progesterone), and midluteal (elevated estrogen and progesterone [58]. No significant differences in lactate threshold, VO_2max, or any other measures of cardiorespiratory fitness were detected. Menstrual cycle effects on various aspects of athletic performance likely vary greatly between individuals, making it essential for each woman to monitor her own response and document the times at which she trains and performs her best.

Menstrual cycle and aerobic endurance

Although the combined effects of the female sex steroid hormones on substrate metabolism could theoretically affect aerobic endurance, evidence to date is contradictory. An improvement has been reported during the luteal phase, in association with increased muscle glycogen [33,34] or diminished blood lactate (the balance of lactate produced by working muscles, against what is cleared or metabolized) [59]. The magnitude of such change may be greater with an adequate antecedent diet than with the hormones alone. For example, an 8% greater luteal phase endurance and muscle glycogen storage was demonstrated on a high-carbohydrate diet compared with a moderate-carbohydrate diet [60]. A wide variety of different protocols have been used, including incremental versus steady-state exercise, differing percentages of aerobic capacity, and cycle ergometer versus treadmill testing. Standardization of other variables, such as the time of day, nutritional status, or psychological motivation of the subjects, has been inconsistent. The impact of menstrual cycle phase and oral contraceptive use (with the addition of thermal stress) has been studied with more complicated protocols, such as intermittent high-intensity shuttle running in a hot environment [61]. As can be imagined, the amount of data generated in such studies is staggering, and interpretation of the results can be confusing.

After vigorous sustained exercise, there is a necessary repayment of oxygen debt, which can be quantified as excess postexercise oxygen consumption (EPOC). The EPOC and resting metabolic rate have been shown to be significantly higher and the postexercise respiratory exchange ratio (RER) (an indirect measure of fat oxidation) significantly lower during the luteal phase compared with the follicular phase, suggesting greater use of fat for fuel [62]. In contrast, other investigators have reported no menstrual cycle phase changes in the effects of carbohydrate supplementation on performance or in plasma levels of related substrates during prolonged exercise at 70% VO_2max [63]. It is likely that baseline nutritional status and glycogen stores and adequate carbohydrate replenishment during exercise contribute as much or more to enhancement of performance than menstrual cycle phase, as seen in Fig. 2 [55].

Nevertheless, subtle differences have been noted in blood glucose responses to moderate and short-term high-intensity exercise across menstrual cycle phase. These appear to be relatively resilient to diurnal rhythms of cortisol [64]. With the development of isotopic tracers of glucose and glycerol has come the ability to monitor substrate turnover during exercise in more accurate detail during exercise, using the dual catheter technique. Although such studies should help to clarify previous conflicting results, they actually add to the confusion. Some have measured a lower glucose flux during exercise in the midluteal versus early follicular phases at intensities of 90% of lactate threshold (LT), but not at 70% LT [65]. Another investigation of women exercising 50% of VO_2peak at altitude did not find any significant differences [66]. Other studies have shown no alteration in whole-body exercise nutrient oxidation (protein, fat, and carbohydrate) in response to moderate-intensity long-duration exercise between early follicular,

late follicular (high estradiol), and luteal phases [67]. Neither were overall plasma glucose kinetics significantly altered across these cycle phases, despite a greater increase in glucose and insulin concentrations during exercise in the luteal phase. These investigators correctly point out that some of the discrepancies from earlier work could have resulted from grouping early follicular (low hormone) and late follicular (ie, time of ovulation) phases together. In addition, the method of choosing and determining exercise intensity differs between studies. For example, in some it is relative to the subject's VO_2max, in others a percentage of LT. Work in this area is further complicated by the training status of the subjects, in that the more physically fit women may have different patterns of glucose use and, by extension, demands on endogenous glucose.

Many believe that these effects on glucose kinetics are largely caused by estradiol, and have attempted to study this hormone in isolation. Administration of transdermal estrogen to amenorrheic women decreased glucose flux at rest and during moderate intensity exercise, but did not cause any significant change in the relative contribution of glucose and glycogen to total body carbohydrate use [68]. The postulated mechanisms included decreased gluconeogenesis, epinephrine secretion, or glucose transport. Similarly, when men were given a higher relative dose of estrogen in the form of oral estradiol, they demonstrated decreased glucose flux without any effect on substrate oxidation during exercise [69]. However, the underlying hormonal milieu in these two subject populations is not representative of the changes that take place over the course of an ovulatory menstrual cycle, where estrogen and progesterone likely interact to affect exercise glucose metabolism. Recently, some excellent work in one laboratory confirmed no significant menstrual phase effect on glucose flux, and the investigators attempted to put it all in perspective:

> The results are interpreted to mean that in women fed several hours before the study, 1) glucose flux is directly related to exercise intensity, 2) menstrual cycle phase does not alter glucose flux during rest and exercise and 3) the subtle effects of endogenous ovarian hormones on glucose kinetics are subordinate to the much larger effects of exercise and recent carbohydrate nutrition [70].

Because of the complexity of these diverse hormonal interactions, it is strongly suggested that variations in sex steroids be controlled for in metabolic studies using female subjects.

Menstrual cycle and anaerobic capacity

Anaerobic capacity reflects rapid use of the phosphagen (creatine phosphate) and ATP stores in the local muscles, with type II fibers providing the largest contribution. Anaerobic endurance or anaerobic glycolysis can be estimated using numerous laboratory and field tests. In the anaerobic speed test, subjects do a maximal timed run to fatigue on a treadmill at a speed of 8 mph and a 20% grade [48]. Anaerobic capacity also involves measures such as mean power output and peak power output. A recent study of seven eumenorrheic women during

menstruation, midfollicular phase, and midluteal phases, and ten women taking monophasic oral contraceptives, examined force-velocity (maximal cycling power on a cycle ergometer), multi-jump (maximal jump power), and squatting jump tests (maximal jump height) [71]. There were no significant differences between phases or in the oral contraceptive group in any measure of anaerobic performance. However, it was suggested that the presence or absence of premenstrual or menstrual syndrome symptoms might have an effect, possibly through the stretch-shortening cycle of tendons and ligaments. Other studies have found either no difference in anaerobic power output between cycle phases, or greater anaerobic capacity and peak power during the luteal phase [72,73]. Newer exciting technologies, such as nuclear magnetic resonance spectroscopy, make it possible to instantaneously and objectively assess muscle phosphate dynamics at the cellular level. Such techniques will offer a fascinating window into muscle metabolism during the menstrual cycle.

The menstrual cycle and performance in different sports

Peak athletic performance is composed of anatomic, physiologic, metabolic, biomechanical, and psychologic elements. The relative contribution of each of these elements varies, depending on the type of sport. Therefore, the diverse effects on performance will not necessarily result in any significant changes in actual achievements. The ventilatory effects of hormones may be more relevant to an aerobic sport, as thermoregulation may be more relevant on a hot day; hormone levels on one day may not be the same on the next; a current cycle may be anovulatory; and external factors, even an argument with a boyfriend or coach, may interact with the psychologic influence of one specific cycle phase, but not another. Therefore, it is not surprising that most of the early literature on athletic performance was based on subjective feelings alone, disregarding specific menstrual cycle phase [74]. Data are inconsistent; many athletes in these studies reported a decrease in performance during the premenstrual and menstrual phase, whereas others reported performance enhancement during their menstrual phase, winning gold medals and breaking world records. In a recent study from Greece [75], over half of 373 athletes from six different disciplines complained of abdominal/thoracolumbar discomfort, fatigue, or nervousness during menstruation, yet over two thirds of the subjects did not feel these complaints impacted their performance. Gold medals have been won throughout the female cycle, emphasizing that menstrual phase effects are not so dramatic.

Few studies have intentionally addressed menstrual cycle and performance in specific sports. Brooks-Gunn et al [74] tested swimming times of adolescent swimmers over a 12-week period. They found that swimming was fastest during menstruation and slowest during the premenstrual period. However, there were only six subjects in this study, menstrual cycle was assessed by BBT changes, and only half of the swimmers had a clear biphasic temperature.

One study of cross country skiers found that performance was better in the early luteal and late follicular phases [76]. Again, cycle phase was determined by BBT with the addition of cervical mucus examination. A study conducted among 16 female runners (only eight were eumenorrheic) found no effect of cycle phase on aerobic parameters or perceived exertion [77]. Here, cycle phase was determined by plasma and urine hormone levels.

In summary, few studies have examined the end result of menstrual cycle influence on performance in the actual sport type. Additional studies using athletes from different sport disciplines are needed to help answer the question of whether the menstrual cycle significantly impacts on performance. Negative results may suggest that, in general, menstrual cycle phase should not be considered a major determinant. However, data should still be collected to assist those individual athletes who feel (or are proven to be) detrimentally affected by a certain cycle phase.

Menstrual cycle, injuries, and ligament laxity

Women have a higher injury rate in sports than men, sometimes by a factor of almost ten [78]. These data have been accumulated from activities such as ball games, running, and military training. Suggested mechanisms that may be affected by the female hormones include anatomic and biomechanical factors, neuromuscular control, and ligament laxity. Interestingly, females also have higher injury rates in sport types that do not include the more common running, jumping, and landing activities. In a recent study on mountain biking injuries, women exhibited almost twice the injury rate compared with men [79]. The investigators postulated that lower body and bone mass may increase the risks of falls and fractures. Still, most studies focus on knee injuries and the laxity of the anterior cruciate ligament (ACL).

In the past 4 decades, several studies have reported on the incidence of ACL injury related to the menstrual cycle phase [80–84], with the more recent ones using measurements of hormone levels rather than relying solely on self-report. Wojtys and colleagues [85] described a clustering of injuries in the ovulatory phase (ie, days 10 through 14) of the menstrual cycle. A lower-than-expected rate of events occurred in the luteal phase. Menstrual cycle was determined by questionnaire and urinary hormone levels, but only fair agreement was found between the two methods. Hence, one should use caution regarding studies using self-report, as verification of the phase of a biological rhythm can be difficult. In another study, two thirds of ACL injuries were sustained during the follicular phase, with a small cluster also found within the first 2 days of menses [83]. Here, menstrual cycle phase was determined by questionnaire, and saliva and plasma hormone levels, with a good correlation reported between these methods.

These studies suggest a potentially higher incidence of ACL injury during the ovulatory phase, and a lower one during the luteal phase. It is unclear whether the follicular phase harbors increased risk. Additional studies have been

performed using questionnaires among professional athletes which have yielded conflicting results, perhaps as a result of methodological issues discussed earlier.

Injury mechanism

There are several suggested mechanisms for the higher rate of ACL injury in females, although the neuromuscular factor seems to be the most important [86,87]. As estrogen, progesterone, and relaxin may affect neuromuscular function, changes in hormone levels throughout the menstrual cycle can be a cause for injury dispersion along the cycle. Muscle strength has been found to increase around the time of ovulation, but so has muscular fatigability, a possible reason for increased injury rate at this time [88]. As mentioned earlier, this issue is not undebated.

It has been found that PMS affects injury risk in some women compared with those who do not experience symptoms [84]. In a study examining balance and kinesthesia as related to the menstrual cycle, it was found that women who had PMS had poorer balance and motion perception compared with women who did not have symptoms [47]. As plasma hormone levels (eg, FSH, LH, estrogen, progesterone) did not differ between groups, another mechanism may explain these findings, such as other hormones or psychologic factors that were not measured.

The anterior cruciate ligament

Much attention is also directed toward cellular effects of female hormones on ACL laxity, which is a controversial issue. Although several studies do show increased ACL laxity in the luteal phase, others do not. Heitz et al [89] measured ACL laxity among 11 female subjects while assessing cycle phase by plasma levels. Increased laxity was seen in the luteal phase, compared with the follicular. Deie et al [90] measured ACL laxity every 3 to 4 days among 20 females, along with plasma hormones. Larger knee laxity was observed in the ovulatory and luteal phases, compared with the follicular phase. Shultz et al [6] used much more complex methods, measuring knee laxity and plasma levels of estrogen, progesterone, and testosterone on a daily basis. Knee laxity increases were associated with higher levels of estrogen, progesterone, testosterone, and all three hormones together. Increases in knee laxity that were associated with all three hormones may be seen in the luteal phase. A time lag of 3 to 4 days was found between hormone level changes and laxity changes. Other studies, however, did not find an association between menstrual cycle phase and knee laxity. Karageanes et al [91] measured knee laxity in 26 adolescent females while cycle phase was determined by self-report. No statistically significant difference was found in ACL laxity between the phases of the menstrual cycle. Belanger et al [92] measured knee laxity before and after exercise along three phases of the cycle in 18 athletes. Cycle phase was determined by BBT and menstruation reports. ACL laxity was not affected by either exercise or menstrual cycle phase.

Van Lunen et al [93] used an arthrometer and plain films among 12 females, measuring ACL laxity at the early follicular, ovulatory, and midluteal phases, as assessed by hormone levels in plasma and urine. No statistically significant change in ACL laxity was found, as determined by either the arthrometer or the radiograph studies.

The reasons for the apparent discrepancies among these studies are, as always, methodological. Studies differed in the subject population (athletes or non-athletes), the exact period of the menstrual cycle examined, the method of cycle verification, the method of laxity assessment, and the applied forces. Therefore, a meta-analysis is necessary to combine the data from these studies and draw appropriate conclusions.

The mechanism of the possible change in laxity throughout the cycle may include a direct action of estrogen on the ligament. Estrogen receptors exist in human ACL [94], and an inhibitory effect of estrogen on fibroblast proliferation and collagen production in human ACL has been demonstrated [95]. Progesterone was found to be protective in this matter, which may partially explain the reduced injury rate observed in the luteal phase of the menstrual cycle. Other potential hormones affecting ligament laxity are relaxin, estrone, and testosterone. One study found no effect of relaxin on knee laxity among female athletes [96]. In another study, estrone was found to correlate negatively with ligament laxity [97]. Testosterone levels also change over the menstrual cycle, but this has only been rarely addressed in studies on knee laxity, despite the fact that testosterone has been found to have an even greater effect than progesterone [6]. Future studies on the effects of hormones or their combinations on ligament laxity are needed.

Hence, it is unclear whether the increase in knee injuries is related to changes in hormone levels. Table 1 presents studies using hormonal verification of men-

Table 1
Effect of menstrual cycle on injury rate and anterior cruciate ligament laxity in studies using hormonal verification of cycle phase

Study	Method of cycle assessment	Injury rate in follicular phase	Injury rate in ovulatory phase	Injury rate in luteal phase
Wojtys, et al [85]	Urine hormones	↔	↑	↓
Slauterbeck, et al [83]	Saliva hormones	↑[a]	↑	↓
		Knee laxity in follicular phase	Knee laxity in ovulatory phase	Knee laxity in luteal phase
Heinz, et al [89]	Plasma hormones	Reference value	↑	↑
Deie, et al [90]	Plasma hormones	Reference value	↑	↑
Van Lunen, et al [93]	Plasma hormones	Reference value	↔	↔
Shultz, et al [6]	Plasma hormones	Reference value	↑	↑

↑, increase; ↓, decrease; ↔, no change.
[a] Especially on days 1 to 2 of menses.

strual cycle phases on injury rate and ACL laxity. It seems that although there is an increase in injury rate during the ovulatory phase and a decrease during the luteal phase, knee laxity increases during both. It is uncertain whether a relationship between these small changes in laxity and injury rates exists. Does increased laxity lead to increased injury (the knee may ''give'' more), as may be seen in the ovulatory phase, or is it protective (a lax ligament may tear less easily), as seen in the luteal phase? Additional mechanisms must therefore play a role in knee injuries.

Injury prevention

Most researchers raise the question of whether oral contraceptive pill (OCP) use affects injury rate distribution along the various stages of the menstrual cycle [82–85], yet sample sizes have been too small for detailed statistical comparisons with nonusers. Moller-Nielsen and Hammar [84] did find a decreased risk for traumatic lower extremity injuries in the premenstrual and menstrual periods among OCP-using soccer players, yet several methodological considerations, such as the smaller number of athletes using OCPs or their older age, remain possible confounders. A recent study found decreased knee laxity among OCP users compared with nonusers [98]. However, the inclusion of monophasic and triphasic pills in the same group, the disregarding of menstrual cycle phase in both groups, and the cross-sectional design prohibit any conclusion regarding hormonal effects. In her review, Ireland [86] reports on a consensus conference held in 1999, stressing that there is no justification for sex-specific hormonal manipulation to prevent ACL injuries. One more recent study has shown that a prevention training program consisting of running, jumping, and balance exercises enabled some reduction in injury rate among female handball players [99]. Hewett [87] designed another training program, and the American Academy of Orthopaedic Surgeons [100] also published an official guide for ACL injury prevention. Such programs are extremely important, regardless of menstruation effects. The prevention of ACL injuries and optimal treatment are critical, and their importance further underscored by the high incidence of osteoarthritis and functional limitations found as much as 12 years after acute ACL injury among female soccer players [101].

Therapeutic considerations

The question of *how* to alter the menstrual cycle to improve performance must only be asked following the question *whether* the menstrual cycle should be altered. Most of the literature indicates that regularly menstruating female athletes do not need to adjust their menstrual cycle to maximize performance, unless possibly competing in endurance events under hot and humid conditions. Also,

the pattern of the hormonal changes during the menstrual cycle and any physiologic and psychologic effects differ greatly from one woman to another. Therefore, even if there is a consensus on a particular effect, that effect does not necessarily apply to the individual athlete.

Still, although premenstrual and menstrual symptoms are less frequent and severe in athletes, they can be disabling and should be treated if they interfere with training and competition. OCPs, other than being a reliable contraception method, have several additional benefits. For one, they can postpone menses until after a competition or, alternatively, induce menses before it. They can also reduce PMS, dysmenorrhea, menorrhagia, and dysfunctional uterine bleeding, thereby decreasing the risk of iron deficiency so prevalent in female athletes [102,103]. And, not exclusive to athletes, they can reduce functional ovarian cysts, benign breast lesions, and endometrial and ovarian cancers, and, of course, prevent unwanted pregnancies. Whatever the intention, this type of intervention should be limited to only mature, elite athletes, whose performance is undoubtedly affected by their menstrual cycle, and it should be used only for critical competitions and not for training or minor events.

Education

The attitude toward the menstrual cycle in general, and its negative effect on performance in particular, is often influenced by social and cultural beliefs, which may result in self-fulfilling prophecies [104].

In earlier years, a fair number of women, including Olympic athletes, did not train during their menses; a practice which fortunately is no longer common.

Athletes and coaches should receive information about the pathophysiology of the normal menstrual cycle and its relationship to physical activity and performance. They should understand that despite possible minor physiologic disadvantages in some areas of performance, a positive psychologic attitude can be helpful. World records have been broken during menstruation, and Olympic gold medals have been won throughout the cycle.

Premenstrual syndrome

Over 100 different somatic and psychologic qualities and changes have been described as part of PMS. Though symptoms are minor in most cases, they may sometimes prevent the athlete from reaching her full capability. In addition, the increased injury rate and poorer balance and motion perception occurring in women who have PMS may even pose a risk [47,84]. To those athletes who are severely affected, shifting the time of PMS away from a competition or prohibiting menses (thus preventing PMS) by continuous OCP use may prove helpful. Additional therapeutic options include psychologic interventions, dietary modifications (eg, salt restriction, increased carbohydrate intake), or pharma-

cologic measures (eg, pyridoxine 50 to 150 mg/d, spironolactone 100 mg/d, or progesterone 50 to 400 mg/d).

Dysmenorrhea

Dysmenorrhea affects 47% to 80% of the general population [105]. In athletes, the incidence and severity is decreased as a result of lower prostaglandins or higher pain threshold. In most of the cases the symptoms, which include lower abdominal pain often radiating to the lower back or legs; headache; nausea; and vomiting, are mild. Because the pain is caused by increased prostaglandin secretion from the endometrium, NSAIDs are very effective in reducing symptoms. Treatment is effective if instituted at the sign of first bleeding and usually requires 2 to 3 days. OCP use also tends to reduce symptoms of dysmenorrhea.

Training program

In the former Soviet Union, coaches used to plan the training sessions according to the menstrual cycle [106]. They theorized that the menstrual cycle could be divided into five stages, and that high-intensity loading should be done only postovulation and postmenstruation. Because of weight changes and physical and psychologic stress, training should be lighter during ovulation, premenstruation, and menstruation. Each athlete kept a log of her menses and the length of each stage, and trained accordingly. This idea of individualization of the training routine makes sense, especially at the elite level; however, the various stages were not supported by hormone measurements. There is currently no scientific explanation or support for the concept of avoiding high-intensity training during most of the menstrual cycle.

Hormonal modification of the menstrual cycle

The menstrual cycle can be easily controlled and manipulated by hormonal therapies. However, therapeutic usage of hormones merely for menstrual manipulation should be saved only for mature, elite athletes whose performance is negatively affected, as the health implications of continuous shifting of the menstrual cycle are not yet known.

Progesterone

An athlete who has a regular menstrual cycle and who cannot or does not want to take HRT or OCPs but wants to avoid menstruation during the time of competition can take 10 mg of hydroxyl progesterone for five consecutive days from day 15 of the cycle. Withdrawal bleeding will then occur within about 2 days, thus advancing the menstrual cycle by a week.

Estrogen & progesterone

Athletes who are not sexually active and who desire shifting in the timing of their menstrual cycle can take a combination of estrogen and progesterone, such as Kliogest or Activelle (Novo Nordisk, Denmark). The amount of estrogen in these tablets is minimal (2 mg and 1 mg estradiol, respectively), which lessens the chance of weight gain or breast discomfort.

To date, there are no studies concerning the effect of these hormones on performance.

Oral contraceptive pills

An increasing number of athletes at the recreational and elite levels use oral contraceptives for cycle control or contraceptive purposes. In addition, these medications are used for management of premenstrual symptoms, dysmenorrhea, and time-shifting of the menstrual cycle. Therapeutically, physicians frequently prescribe them for women who have prolonged menstrual dysfunction, such as amenorrhea and oligomenorrhea. OCPs may have potential osteogenic actions, and perhaps also provide protection against stress fractures and other soft tissue injuries, but the current evidence is somewhat contradictory [107]. Other possible benefits include protective effects against heart disease through actions on endothelial function and lipoproteins, among others.

Although the OCP has been touted as ''a revolution for sportswomen'' [107], concern still remains about any potential detrimental effect on performance. Monophasic combination pills consist of an estrogenic and progestogenic component in fixed doses, whereas biphasic and triphasic preparations attempt to more closely mimic the conditions of a natural menstrual cycle by varying the hormonal concentrations. Progestin-only ''minipills'' and injectable or implantable forms of progesterone are also effective for contraception. More recently, a monthly injectable combination of estradiol and progesterone was developed. Earlier pills contained much higher hormonal concentrations than contemporary formulations. Lower estrogen levels (30 μg and 20 μg of ethinyl estradiol, compared with the initial doses of 150 μg) and more selective progestogenic agents (eg, gestodene, desogestrel) have largely been successful in decreasing unwanted side effects and, more than likely, any putative associated effects on athletic performance. Given the widespread usage of these medications, studies are surprisingly scarce in this area.

Oral contraceptive pills and performance

Some studies have suggested a potential decline in aerobic performance (VO_2max) in response to oral contraceptive administration, ranging from 5% to 11% but reversible on discontinuation of therapy [2,3]. More recent publications have shown a slight decrease in maximal aerobic capacity [108,109] or no

significant effects [110], despite increases in blood lactate and ammonia responses to high-intensity intermittent exercise [111]. A study of five elite rowers taking a triphasic OCP found a lower anaerobic power and anaerobic capacity during the time of highest exogenous hormone administration [112]. Another group [71] found a 3% to 5.8% lower oxygen consumption for a given exercise intensity, and improved running economy on a monophasic OCP. Generalization of any of these findings is limited by the small subject numbers and the wide range of testing protocols and oral contraceptive formulations used.

Depending on the combination of hormones used, there are theoretical benefits for cardiac output (increased vascular volume and preload). There may also be effects on the peripheral circulation through the activity of nitric oxide [113]; however, it is difficult to dissociate cardiovascular functions from thermoregulatory effects. Depending largely on the progestin component, the biphasic body temperature response found in eumenorrheic women is somewhat attenuated in OCP users [114]. This has variously been found to cause a higher heart rate and reduced capacity [115,116] or to marginally improve performance compared with the pill-free days [61]. The magnitude of any thermoregulatory effect likely depends on the type of progestin and estrogenic components of OCPs and their interaction.

In terms of OCPs and substrate metabolism, some have suggested a trend toward carbohydrate sparing, with a shift toward free fatty acids for fuel [117]. A lower blood glucose response during exercise could result from a decrease in hepatic glucose output or enhanced glucose uptake in muscles, or could be caused by alteration of glucoregulatory hormones and insulin sensitivity [118,119]. However, OCPs can cause insulin resistance, rises in plasma insulin, and relative glucose intolerance [117]. It is difficult to draw meaningful conclusions when most study populations consist of less than ten women taking multiple OCPs. Much more research is needed, and substrate turnover studies would also be helpful in this area.

Strength may be impacted by a direct action of estradiol on muscle cross-bridges, or indirectly through stimulation of GH secretion. Possible androgenic actions of the progestins in OCPs have, in the past, also been thought to improve muscle strength, and OCPs containing norethindrone were even banned by the International Olympic Committee for a while. In a recent study on the effect of 10 months of OCP therapy on performance of female athletes [120], no change in isometric measurements (knee extension and hand grip) was demonstrated.

It has also been suggested that reduction of premenstrual symptoms, such as fatigue, fluid retention, weight gain, and dysmenorrhea, may also improve athletic performance. Decreased monthly blood loss and a lower incidence of iron deficiency anemia are likely beneficial to endurance athletes.

Finally, potential alterations in body composition with OCP administration have been considered. The largest and most comprehensive study to date compared 26 endurance athletes (13 who experienced regular menstruation and 13 who experienced oligo/amenorrhea) with 12 sedentary controls before and after 10 months of treatment with a low-dose, combined monophasic OCP con-

taining 30 μg ethinyl estradiol [120]. Although little impact on endurance performance was seen, there was a minimal decrease in performance on a multistage progressive shuttle-run test, the "beep test," in the oligo/amenorrheic athletes only, associated with an increase in fat mass. More comprehensive studies are necessary to further delineate any proposed effect of OCPs on body fat in athletes, especially given the lower hormonal concentrations in contemporary OCPs.

Prescribing oral contraceptive pills for menstrual cycle manipulation

In the absence of medical contraindications, such as thromboembolic disease, impaired liver function, and estrogen-dependent neoplasia, OCPs can be prescribed to athletes who are at least 2 years postmenarche, as administration at an earlier age might halt growth.

There is an extensive choice of OCPs, many with various types and amounts of estrogen and progesterone. Which OCP to prescribe is an individual decision and depends on what the specific needs of the woman are and what suits her. The estrogen component is usually ethinyl estradiol, and a dose of 20 to 30 μg is usually well-tolerated. The progesterones vary in terms of pharmacologic properties. Some have antiandrogenic or antimineralocorticoid activity, which can offer favorable effects in terms of skin, hair, and water retention.

The monophasic pills, in which the dose of both hormones is constant throughout the cycle, are easiest to use during competition and travel. Biphasic and triphasic pills, although better in terms of mimicking the natural cycle, are harder to manipulate.

With a careful yearly planning, it is possible to shorten the cycle over a few months by decreasing the number of pills in each cycle so that the major competition will occur when desired (usually athletes prefer to compete after bleeding has ceased, when levels of estrogen and progesterone are at their lowest). Another option is to stop the OCPs 10 days before the anticipated competition; bleeding usually occurs within 2 days and lasts for 5 to 7 days.

Those who do not mind competing while taking hormones can continue to take monophasic pills until after the competitions. The pills can be taken for a couple of months with no risk other than breakthrough bleeding (ie, spotting) [121]. Recently, a 3-month pill containing 30 μg ethinyl estradiol and 150 μg levonorgestrel (Seasonale, DuraMed Pharmaceuticals, Inc., New York) was introduced. This extended-cycle OCP is effective, safe, and well-tolerated and allows women the option of decreasing the number of withdrawal bleeding intervals from 13 to 4 per year [122]. Extended regimens of up to 126 days of OCPs containing 30 μg ethinylestradiol and 3 mg drospirenone have also been shown to offer positive effects that might be particularly advantageous to the athlete, such as a decrease in weight gain, breast tenderness, bloating, and some psychologic symptoms [123]. Other preparations have also been used in cycles of 2 to 3 months and more, significantly reducing the number of menstrual periods per year. This reduction is particularly advantageous for the female athlete, as it

Box 2. Possible advantages and disadvantages of oral contraceptive use relevant to sport performance

Advantages

Contraception
Control of menstruation
Reduction of
- PMS
- Dysmenorrhea
- Cramps
- Menstrual migraines
- Menorrhagia
- Iron deficiency
- Functional ovarian cysts
- Benign breast lesions
- Ectopic pregnancy
- Pelvic inflammatory disease
- Endometrial hyperplasia
- Endometrial and ovarian cancer
- Rheumatoid arthritis

Possible Advantages

Bone loss prevention (associated with oligomenorrhea and amenorrhea)
Increase in aerobic economy
Carbohydrate sparing
Increased ligament laxity[a]
Decreased injuries

Disadvantages

Headache
Fluid retention and weight gain
Nausea
Breast tenderness
Potential cardiovascular & thrombotic complications

Possible Disadvantages

Prolonged exercise in the heat
Decrease in peak exercise capacity (VO_2max)

Decrease in anaerobic performance
Increased insulin resistance (depending on the OCP composition)
Increased ligament laxity[a]

Unclear effect

Strength

[a] Increased ligament laxity may be beneficial or detrimental in different situations.

can decrease the iron loss that occurs during menstruation, which is a serious problem in athletic women. Box 2 lists the possible advantages and disadvantages of oral contraceptive use in sport performance, although for many of the sport-related factors, an unequivocal conclusion cannot yet be made.

The issue of weight gain, which is of great concern to athletes and coaches, particularly in low–body weight sports, should be discussed. Most of the studies do not indicate overall effect on body weight while taking OCPs, and the newer 20 μg-dosage pills claim to have the least effect.

Oral contraceptive pills and drug testing

In 1987, norethindrone (norethisterone), a progesterone found in many OCPs, was placed on the list of banned substances by the International Olympic Committee. Despite the lack of scientific evidence of any performance enhancement, this was done because of difficulties distinguishing between the metabolites of norethindrone and those of nandrolone, a common anabolic-androgenic steroid. This ban was overturned a few months later thanks to the efforts of Dr. Andrew Pipe from Canada and others, who claimed that a drug with a legitimate medical purpose and which is not performance-enhancing should not be banned simply because it confuses the drug-testing process [124]. However, because the cutoff level for women of nandrolone metabolites in the urine was reduced from 5 to 2 ng/mL, women on pills containing norethisterone will usually have a concentration over the new cutoff (but less than 5 ng/mL). Currently, World Anti-Doping Agency (WADA) laboratories are advised to check beta-hCG when a woman has a concentration above 2 ng/mL to see if she is pregnant or not, as pregnancy could explain the increased value. If the beta-hCG test is negative the laboratories will look for norethisterone in the sample, which would explain the increased value of the nandrolone metabolites. The decision, however, is ultimately made by the sport governing body that receives the

laboratory report, not the laboratory itself. The laboratories will report all values above 2 ng/mL and the additional tests for beta-hCG and norethisterone. To avoid this potential confusion, female athletes who are subject to drug testing should perhaps stay away from OCPs containing norethisterone, if possible (Bengt O. Eriksson, Professor Emeritus, personal communication, 2004).

Pregnancy

There have been anecdotal reports about women who conceived to increase performance. The suggested mechanism was through an increase in levels of beta-hCG, a hormone with some anabolic properties. Additional hormonal and biochemical changes occurring in pregnancy may also play a role. Nevertheless, this method seems out of place and extremely unethical, especially if an abortion is originally planned.

Summary

Over the course of an ovulatory menstrual cycle, there are predicable and measurable variations in the female sex steroids (eg, estradiol and progesterone) that have multiple and variable effects on different body systems. Although there are theoretical implications for physical and mental performance in sports, the workplace, and special populations such as the military, there is no conclusive evidence that significant menstrual cycle differences exist. An exception might be a potential adverse luteal-phase effect for endurance events taking place in extremely hot and humid conditions. The ability to generalize current findings is limited by significant methodological problems, and there is substantial inter- and intraindividual variability. In addition, the full spectrum of menstrual dysfunction that is frequently seen in female athletes further complicates investigation and management.

Athletes and coaches should be counseled regarding the menstrual cycle, its relation to performance, the great variability that exists among individuals, and the therapeutic possibilities. OCPs containing synthetic estrogens and progestins are the most commonly used drugs for controlling and manipulating the menstrual cycle, as they have several advantages for the female athlete in addition to being a good contraceptive method. However, although being prescribed for over 40 years, the effect of OCPs on performance and their potential health advantages and disadvantages, especially with the new extended regimens, are not clear. There is a great need for continuing research in this area by studying larger groups of subjects in carefully designed and controlled prospective randomized trials, although individual data collection and tailored therapy should be applied for elite athletes.

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