

# Nutrition-Based Interventions and Menstrual Cycle

Subjects: Nutrition & Dietetics

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Despite the steady increase in female participation in sport over the last two decades, comprehensive research on interventions attenuating the influence of female menstrual physiology on performance remains scarce. Studies involving eumenorrheic women often only test in one menstrual phase to limit sex hormone variance, which may restrict the application of these findings to the rest of the menstrual cycle. The impacts of nutrition-based interventions on athletic performance throughout the menstrual cycle have not been fully elucidated. We addressed this gap by conducting a focused critical review of clinical studies that reported athletic outcomes as well as menstrual status for healthy eumenorrheic female participants. In total, 1443 articles were identified, and 23 articles were included.

Keywords: menstrual cycle ; female athlete ; exercise performance ; rehydration ; electrolytes ; vitamins ; minerals ; phytochemicals

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## 1. Introduction

Female participation in sport, as a mode of recreation and profession, has been increasing in the United States and worldwide throughout the last two decades. After London won the 2012 Olympic Games bid in 2005, England saw an increase of one million women participating in sport and physical activity <sup>[1]</sup>. From 2011 to 2012, female participation in soccer increased by 43% in Australia <sup>[1]</sup>. In the United States, more than three million girls participate in high school athletics, and 46% of athletic collegiate scholarships are awarded to female recipients <sup>[1]</sup>. The 2016 Olympic Games had a historic 5059 female athletes, equaling 45% of the participants <sup>[2]</sup>.

Despite this increasing exercise involvement, research supporting the optimization of female athletes and their performance is comparatively sparse. The menstrual cycle has been reported to influence athletic performance <sup>[3][4]</sup> and exercise metabolism <sup>[5]</sup>. Menstrual hormones also impact hydration mechanisms <sup>[6]</sup>, which may have implications for female athletes and recreational exercisers. For eumenorrheic women, the menstrual cycle is an average of 28 days, characterized as two stages—follicular and luteal. The follicular phase begins on the first day of menses and ends at ovulation. The luteal phase begins after ovulation and ends on the first day of menses. These two stages can be characterized by reproductive hormone fluctuations <sup>[7]</sup>. Throughout the rise and fall of reproductive hormone concentrations within the menstrual cycle, the early follicular stage has a lower concentration of estrogen, which increases halfway through the phase and peaks prior to ovulation <sup>[7]</sup>. Estrogen and progesterone are both elevated in the luteal stage <sup>[7][8]</sup>. In a 28-day cycle, the early follicular phase is days 1–9, the late follicular phase is days 10–14, the early luteal phase is days 15–17, the mid-luteal phase is days 18–23, and the late luteal phase is days 24–28. Due to these hormone fluctuations, women are often tested in exercise science research during the early follicular phase to reduce hormone variance <sup>[8]</sup>.

The historic lack of inclusion of women in sport and exercise research trials because of hormonal variability makes it difficult to accurately determine the implications of the cyclical menstrual cycle on performance <sup>[8]</sup>. Studies that do include women often test during the follicular phase of menstruation <sup>[8]</sup>, when endocrine hormones are the least variable. Although testing exclusively in the follicular phase may reduce variability among research outcomes, the application of these findings for eumenorrheic athletes and recreational exercisers is inherently limited. By only having performance recommendations based upon one phase of the menstrual cycle, women are consequently left blinded to the optimization of training or performing during the rest of their menstrual cycle. Nearly 40% of surveyed women who engage regularly in exercise reported a belief that their menstrual cycle negatively impacted exercise training and performance <sup>[8]</sup>, thus creating the necessity to expand exercise performance investigations on mechanisms impacted by intra-cycle fluctuations.

Menstrual hormones are speculated to impact thermoregulation <sup>[9]</sup>, fluid balance <sup>[6]</sup>, blood plasma volume <sup>[10]</sup>, and water and electrolyte regulation <sup>[11]</sup>. Blood plasma volume and fluid balance have a direct relationship with exercise performance. A decrease in body mass of 2% due to dehydration can impede athletic performance <sup>[12]</sup>, and hypohydration at the start of exercise has been shown to reduce sport-specific performance <sup>[13]</sup>. This is further exacerbated by the fact

that sweat rate is modulated by the menstrual cycle, and is increased during the luteal compared to the follicular phase [14]. Given the relationship between menstruation and fluid balance, rehydration-based strategies should consider the menstrual phase during which a female athlete or recreational exerciser is rehydrating.

Analogous to hydration levels and rehydration therapies, iron status and subsequent supplementation impact athletic performance. Iron status varies throughout the menstrual cycle, and biochemical markers (i.e., serum iron and transferrin saturation) are significantly associated with the menstrual cycle: the values are lowest during menses [15]. In a representative sample of eumenorrheic women, the diagnosis of iron deficiency was more likely during menses than the luteal phase, indicating a significant reduction in serum ferritin or mean corpuscular volume [15]. Even without clinical iron deficiency, iron supplementation has been shown to improve distance running performance by reducing perceived fatigue and mood disturbances [16]. Iron stores also play a role in energy levels, and studies have shown that iron supplementation for non-anemic women can reduce unexplained fatigue [17], which could improve performance because mental fatigue is associated with poor physical performance [18]. Iron metabolism plays a role in both endurance performance and recovery from resistance training [19]; however, studies linking the female endocrine hormone fluctuation to performance outcomes concerning iron stores are nascent.

Athletic performance additionally relies on adequate calcium stores for the maintenance of bone health, which has become increasingly associated with energy availability in female athletes. A reduction of 15 kcal per kilogram of lean body mass has been shown to decrease bone formation [20], increasing the risk of stress fracture injuries. A better understanding of calcium supplementation throughout the menstrual cycle could offer an enhancement of training programs to maximize bone metabolism while minimizing the risk of stress fracture injury due to fluctuations in female endocrine hormones.

## **2. Hydration Interventions**

Among the studies examining hydration interventions, we identified the role of carbohydrate–electrolyte solutions (CESs) in improving time-trial performance [21] and increasing exercise time to exhaustion [22] in the follicular phase. Of note, the effectiveness of the CES interventions was only tested in the follicular phase for both studies. The CES beverages included 6% carbohydrate content, totaling 24 calories per 100 mL [21][22]. Glucose is known to delay gastric emptying due to its caloric content and osmolality [23]. Electrolytes similarly contribute to the osmotic gradient between plasma and the large intestine, increasing net water movement into the intestine [24]. By reducing the rate of water loss while also changing the osmotic concentrations, and promoting water absorption, CES therapies mechanistically promote euhydration throughout bouts of exercise. Fluid retention during exercise supports aerobic performance by preventing a decline in stroke volume and cardiac output, ultimately mitigating cardiovascular drift [25].

The application of CES to improve aerobic performance in the luteal phase is less clear. Studies measuring gastric emptying rates along with sex hormone concentration have reported inconsistent findings between the luteal and follicular phases [26]. The influence of sex hormones on gut permeability has not been extensively studied. However, progesterone has been reported to decrease gut permeability by increasing trans-epithelial electrical resistance [27]. With a reduction in large intestine mucosa permeability, the luteal phase may hinder the success of CES rehydration therapies.

Sex hormone variability does not seem to influence fluid and electrolyte restoration after dehydration [28], or absolute stroke volume during a graded exercise test [29]. Despite a comparable absolute stroke volume between the luteal and follicular phase, stroke volume had a larger negative relative change in the luteal phase [29]. Considering the reduction in aerobic performance in the luteal phase [3][4] and the influence of progesterone on intestinal permeability [27], intra-exercise rehydration should further be evaluated in the luteal phase. Interventions accounting for differences in luteal phase gastric emptying or gut permeability may mitigate the greater decrement in stroke volume percent change when compared to the follicular phase.

## **3. Micronutrient Interventions**

Of the studies assessing micronutrient interventions, we identified the role of iron in improving endurance [30]. In the aerobic trial, non-anemic women received 30 mg of elemental iron [30]. Iron recommendations for treating iron deficiency (ID) and iron deficiency anemia (IDA) range between 80 and 200 mg elemental iron [31]. The recommended iron dosage for premenopausal women is 18 mg per day [32]. Despite supplementing with a dosage below the recommended amount for treating iron deficiency, the study still reported an improvement in iron stores with the 30 mg supplementation [30].

In animal models, dietary iron deficiency reduces the ability of skeletal muscle tissue to consume oxygen and produce adenosine triphosphate (ATP) due to decreased mitochondrial dehydrogenase activity [33]. The reduction in mitochondrial enzymatic activity limited endurance capacity in iron-depleted rats; however, with iron repletion, endurance capacity improved after five days of supplementation [33]. In the same study, oxygen uptake improved only three days after iron repletion, likely due to the rapid recovery in hematocrit and hemoglobin levels [33]. Iron status is closely correlated to skeletal muscle mitochondrial function and oxygen-carrying capacity, thus influencing aerobic athletic performance.

Regular menstrual blood loss has not been reported to influence hemoglobin mass; however, oral contraceptives increase serum iron levels, potentially contributing to increased oxygen-carrying capacity [34]. Given the relationship between oral contraceptives and serum iron levels, the need for or dosage of iron supplementation may vary for female athletes, depending on their contraceptive use. Future studies should evaluate what amount of iron supplementation is necessary to promote a comparable oxygen-carrying capacity for women not taking oral contraceptives.

We also identified the role of calcium in favorably modulating exercise-induced bone resorption by reducing parathyroid hormone (PTH) immediately after exercise and 40 min after exercise [35]. The intervention was provided as a single pre-exercise calcium-rich meal with approximately 1352 mg of calcium, which is 135% of the daily recommended intake for premenopausal women [36]. In mice, a single bout of exercise can increase circulating PTH [37], which has been reported to stimulate a reduction in osteoblasts and proliferation of osteoclasts in cellular models [38]. PTH secretion is also stimulated by a reduction in serum calcium concentrations. In animal models, induced hypocalcemia increased PTH levels 10- to 12-fold to restore serum calcium homeostasis [39]. Previous studies suggest that bone resorption (as measured by serum deoxypyridinoline) increases in the follicular phase due to reduced progesterone and relative estrogen concentration [40]. The calcium-based meal, however, was given to groups balanced between follicular and luteal phases, suggesting a positive influence over bone resorption, independent of sex hormone variation [35].

## **4. Omega-3-Fatty Acids and Phytochemical-Based Dietary Supplement Interventions**

Among the studies assessing phytochemical-based dietary supplement interventions, we identified the role of 3 mg of caffeine per kg body weight in improving anaerobic power generation [41], mean peak strength velocity [42], and the perception of muscle power and endurance during exercise [43]. Muscular contraction relies on extracellular calcium concentration, and in skeletal muscle, calcium ions enter the cytosol from the sarcoplasmic reticulum [44]. Caffeine has been shown to increase the release of calcium ions from the sarcoplasmic reticulum of frog muscles [45] while also increasing muscular contraction force through increased calcium sensitivity in mice [46]. Caffeine intake has been suggested to impact plasma concentrations of female sex hormones and increase testosterone levels [47]. However, due to methodological inconsistencies, conflicting results exist in the literature on the impact of female sex hormones and skeletal muscle contraction. The power and velocity improvements measured throughout the menstrual cycle, however, suggest that caffeine enhances anaerobic performance regardless of female sex hormone concentration.

Anthocyanin-rich supplementation had differential effects on performance outcomes, whereby blackcurrants had little influence on oxygen uptake despite increased fat oxidation [48][49], and beetroot juice had little impact on sprint performance [50]. Despite reporting similar results, the two trials with blackcurrant supplementation provided differing doses of anthocyanin: 67 mg [49] and 105 mg [48], suggesting a plateau in the dose–response relationship of blackcurrant supplementation.

In animal models, anthocyanins have been reported to up-regulate lipid metabolism by enhancing the expression of fatty acid synthase, glycerol-3-phosphate acyltransferase, 3-phosphate dehydrogenase, hormone sensitive lipase, and perilipin gene expression [51]. This interaction between adipocytes and anthocyanins may explain the increases in fat oxidation during exercise when supplemented with blackcurrants [48][49]. Future studies should evaluate time to exhaustion in females to assess the impact of increased fat oxidation on submaximal athletic performance. In animal models, organic nitrates induced vasodilation by stimulating cyclic guanosine monophosphate (cGMP) accumulation and relaxing vascular smooth muscle [52]. Clinical applications of vasodilators have reported increases in cardiac output due to reduced peripheral resistance [53], and the menstrual cycle has been reported to impact flow mediated vasodilation [54]. High estradiol levels increase flow-mediated diameter [54]; therefore, the impact of high-dose dietary nitrate supplementation should also be assessed during the follicular phase to determine any auxiliary effect.

Fish oil supplementation increased soreness across menstrual phases [55]. The supplementation provided 2.4 g of eicosapentaenoic acid (EPA) and 1.8 g of docosahexaenoic acid (DHA), which are 960% and 720% of daily recommended values (0.25 g each), respectively [56]. Studies assessing fish oil have reported inconsistent results

concerning muscle soreness <sup>[55]</sup>, and some data suggest that despite the modulation of exercise-induced damage by fish oil, soreness is not reduced <sup>[57]</sup>. Estrogen has an inverse relationship with creatine kinase, a marker of mechanical muscle damage, suggesting protection against muscle soreness <sup>[58]</sup>. However, our findings do not support this relationship, because women supplementing fish oil still reported a high perception of soreness, despite increased serum estradiol levels <sup>[55]</sup>. Reduced oxidative stress may not directly correlate to reduced soreness <sup>[57]</sup>; therefore, the role of fish oil in modulating muscle soreness for female athletes throughout the menstrual cycle needs future attention.

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