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Iron Deficiency in Female Endurance Athletes: The Role of Hepcidin Regulation, Training Load, and Dietary Strategies in Optimizing Performance and Health

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1. Abstract

Purpose: Examine iron deficiency (ID) mechanisms in female endurance athletes, focusing on hepcidin dysregulation, training impacts, and dietary strategies.

Materials and Methods: Systematic review of 30 years of research on IL-6/hepcidin pathways, menstrual iron loss, supplementation (oral/IV), and dietary iron bioavailability. Data included hormonal studies, biomarker tracking (ferritin, CRP), and trials. **Basic Results:** Post-exercise hepcidin surges (peaking 6h) cut absorption 30-50%. Menstrual losses (0.5–2 mg/day) worsen depletion. Tapering cut hepcidin 35%; follicular-phase iron intake improved absorption. Oral iron (100mg/d) raised ferritin 20-30µg/L; IV iron boosted performance 8-12% in severe deficiency. Borderline cases (ferritin 30-50) had variable outcomes.

Conclusions: Integrated strategies: hepcidin-aware training, cycle-aligned nutrition (heme iron + vitamin C), ferritin monitoring (>30µg/L). Future research on progesterone's hepcidin

effects and improved iron formulations. Holistic ID management boosts performance/health.

Keywords: iron-deficiency, hepcidin, athletes, endurance, menstruation, inflammation, performance, ferritin

2. Introduction

Iron deficiency (ID) is a pervasive yet often overlooked challenge in female endurance athletes, with studies reporting prevalence rates as high as 35% depending on sport-specific demands and diagnostic criteria [1, 2]. This condition arises from a convergence of physiological and lifestyle factors: menstrual blood loss, exercise-induced iron sequestration, and diets inadequate in bioavailable iron [3, 4]. Even in its earliest stages, ID disrupts oxygen transport, impairs mitochondrial energy production, and weakens immune defenses, leading to fatigue, reduced aerobic performance, and increased infection risk [5, 6]. Precariously, many athletes and coaches misinterpret ID symptoms—such as declining race times or prolonged recovery—as overtraining, delaying critical interventions [7, 4].

At the heart of this issue lies hepcidin, a hormone first characterized in the early 2000s [8, 9]. It is a protein produced in the liver. Hepcidin is responsible for iron homeostasis. This happens due to the binding of hepcidin to ferroportin—the sole protein responsible for exporting iron from cells—and triggering degradation of ferroportin [8, 10]. Inhibition of ferroportin leads to reduced iron absorption and hinders the release of iron from cells. While this mechanism protects against systemic iron overload in sedentary populations, it becomes nonadaptive in athletes. Prolonged endurance exercise stimulates interleukin-6 (IL-6) release, which spikes hepcidin levels for hours post-exercise, effectively trapping iron in storage and limiting its availability for red blood cell production [11, 12]. For female athletes, this exercise-induced iron sequestration compounds menstrual iron losses, creating a perfect cause of deficiency that standard dietary approaches often fail to address [4, 13].

Despite growing awareness of hepcidin's role, critical gaps hinder effectiveness of operationalization in athletic populations. Current screening protocols frequently rely on hemoglobin thresholds, overlooking the nuanced iron dynamics revealed by ferritin and soluble transferrin receptor testing [7, 2]. Furthermore, the interplay between training load, menstrual cycle phase, and hepcidin activity remains poorly understood. Preliminary work by

Sim et al. [14] suggests estrogen fluctuations across the menstrual cycle may modulate hepcidin expression, but long-term data linking hormonal changes to iron absorption efficiency are lacking. Compounding these uncertainties, conflicting evidence surrounds the efficacy of iron supplementation: while deficient athletes show clear benefits [15, 16], those with borderline-low ferritin (30–50 μg/L) exhibit inconsistent performance improvements, suggesting individualized thresholds for intervention may be necessary [6, 17].

This review synthesizes three decades of research to bridge these gaps. First, it elucidates the interplay between exercise, hepcidin regulation, and menstrual physiology, drawing on foundational studies by Peeling [11, 12] and Nemeth [8, 10]. Second, it evaluates practical strategies to mitigate training-induced iron losses, including periodization models proposed by Sim et al. [14]. Finally, it establishes evidence-based guidelines for dietary and supplemental iron intake, informed by clinical trials [15, 16] and the International Olympic Committee's consensus on nutrient interactions [18]. By integrating these perspectives, the review aims to empower athletes, coaches, and clinicians with actionable strategies to optimize iron status, performance, and long-term health.

3. Mechanisms of Iron Regulation and Hepcidin

Iron homeostasis in female endurance athletes is a tightly regulated yet vulnerable system, governed by the hormone hepcidin- a basic factor in iron metabolism whose activity is profoundly influenced by exercise, inflammation, and menstrual physiology. Hepcidin, a 25-amino-acid peptide synthesized primarily in the liver, acts as the body's iron gatekeeper by binding to ferroportin, the sole iron exporter on the surface of enterocytes, macrophages, and hepatocytes [8, 9]. This binding triggers ferroportin's internalization and degradation, effectively trapping iron within cells and limiting its release into circulation [8, 17]. Under physiological conditions, this mechanism prevents iron overload during states of if its level is correct or infection. Nevertheless, in athletes, chronic exercise-induced inflammation and cyclical menstrual iron losses disrupt this equilibrium, creating a state of functional iron deficiency even when stored iron (ferritin) levels appear adequate [7, 4].

Hepcidin's Double Role in Exercise and Inflammation

Endurance exercise stimulates a transient inflammatory response characterized by elevated interleukin-6 (IL-6), a cytokine released by working skeletal muscles [10, 11]. IL-6 activates

the JAK2/STAT3 signaling pathway in hepatocytes, upregulating hepcidin transcription [10, 11]. For example, a 60-minute run at 75% VO₂max increases IL-6 concentrations by 10- to 100-fold within 3 hours post-exercise, driving hepcidin levels to peak at 6 hours and remain elevated for up to 24 hours [10, 13]. This acute hepcidin surge reduces intestinal iron absorption by 30–50% during the critical post-exercise recovery window, when iron is most needed for erythropoiesis and tissue repair [10]. Over time, repeated training sessions compound this effect, leading to chronic iron sequestration in storage areas (for example liver, macrophages) despite adequate or even elevated serum ferritin levels [7, 2].

The mechanical stress of high-impact sports, such as running, exacerbates iron loss through foot-strike hemolysis—a process where repetitive ground contact ruptures red blood cells in the capillaries of the feet, releasing hemoglobin into circulation [2]. While the liver's haptoglobin system recycles some hemoglobin-derived iron, chronic hemolysis overwhelms this system, leading to urinary and fecal iron excretion [3, 2]. For female athletes, this exercise-induced iron loss is compounded with menstrual blood loss, which averages 0.5–1 mg of iron daily but can exceed 2 mg/day in those with menorrhagia [4, 12]. The cumulative effect creates a cyclical drain on iron reserves, outpacing dietary intake even in athletes consuming iron-rich diets [3, 4].

Menstrual Cycle Dynamics and Hepcidin Modulation

Female athletes face unique challenges due to hormonal fluctuations across the menstrual cycle. Estrogen, which peaks during the follicular phase (days 1–14), appears to suppress hepcidin production, enhancing duodenal iron absorption efficiency by 15–20% [13]. Conversely, progesterone—dominant during the luteal phase (days 15–28)—has been hypothesized to upregulate hepcidin via STAT3 signaling, though direct evidence in athletes remains limited [28]. This cyclical variation creates a double-edged sword: while the follicular phase offers the posibility of enhanced iron absorption, intense training during this phase may counteract benefits by elevating IL-6 and reactivating hepcidin [13].

For example, an athlete training intensely during the follicular phase may experience a paradoxical decline in iron availability: estrogen-driven suppression of hepcidin is overridden by exercise-induced IL-6, negating potential absorption gains [13]. Conversely, training during the luteal phase—when hepcidin is already elevated—may exacerbate iron sequestration, particularly in athletes with heavy menstrual bleeding [4, 12]. Oral

contraceptives, used by many athletes to regulate cycles, further complicate this interplay. Monophasic contraceptives reduce menstrual blood loss by 30–50%, indirectly preserving iron stores [12, 28], but their impact on hepcidin regulation remains underexplored.

Macrophage Iron Recycling and Systemic Consequences

Except intestinal absorption, hepcidin critically impacts macrophage iron recycling—a process responsible for repurposing 90% of the body's daily iron needs [20, 17]. Macrophages phagocytize senescent red blood cells, extracting iron for release into circulation via ferroportin. However, exercise-induced hepcidin elevation degrades ferroportin, trapping iron within macrophages [8, 17]. This disruption starves erythropoiesis of recycled iron, forcing reliance on dietary absorption—a system already compromised by post-exercise hepcidin activity [10, 11]. The result is a self-perpetuating cycle: stored ferritin levels may appear normal or elevated due to inflammation, but functionally available iron plummets, impairing oxygen transport and energy production [7, 5].

The Vicious Cycle of Iron Sequestration

The interplay between hepcidin, exercise, and menstruation creates a vicious cycle in female athletes. Prolonged endurance training sustains low-grade inflammation, perpetuating hepcidin elevation and suppressing iron absorption [7, 11]. Menstrual blood loss further depletes reserves, while estrogen's transient suppression of hepcidin is often counteracted by IL-6 spikes from training [4, 13]. Over time, this cycle leads to progressive ferritin deficiency, manifesting as fatigue, reduction in aerobic capacity, and impaired recovery—symptoms frequently misattributed to overtraining rather than underlying iron deficiency [7, 4].

In summary, the regulation of iron in female endurance athletes is a delicate balance easily disrupted by the exercise, inflammation, and menstrual physiology. Hepcidin sits at the nexus of these problems, its dysregulation creating a biochemical paradox where iron exists in abundance yet remains functionally inaccessible. Addressing this conflict requires strategies that not only replenish iron stores but also modulate hepcidin activity through targeted training, diet, and hormonal balance.

4. Training Load and Iron Metabolism

Endurance training imposes a dual burden on female athletes: while it enhances aerobic

capacity and metabolic efficiency, it simultaneously disrupts iron homeostasis through an interplay of inflammatory, mechanical, and hormonal pathways. This phenomenon underscores the need for precise training strategies that balance adaptation with iron conservation—a challenge magnified by the unique physiological demands of female athletes.

Acute Exercise and Hepcidin Dynamics

The acute phase of endurance exercise triggers a cascade of inflammatory signals that directly interfere with iron metabolism. Prolonged aerobic activities, such as running or cycling, stimulate skeletal muscle to release interleukin-6 (IL-6), a cytokine that acts as both a myokine and a pro-inflammatory mediator [10, 11]. For example, a 60-minute running session with 75% maximum oxygen consumption achieved elevates circulating IL-6 concentrations by 10- to 100-fold within 3 hours post-exercise [10]. This IL-6 surge activates the JAK2/STAT3 signaling pathway in hepatocytes.This pathway drives the transcription of the HAMP gene, which encodes hepcidin [11]. Hepcidin levels peak 6 hours post-exercise and remain elevated for up to 24 hours, reducing intestinal iron absorption by 30–50% during this critical window [10, 13]. Athletes who engage in frequent high-intensity sessions—such as twice-daily training common in elite rowing or triathlon programs—face compounded risks.Repeated IL-6 pikes prolong hepcidin elevation, creating a chronic state of functional iron deficiency. This results in stored ferritin remains sequestered in macrophages and hepatocytes, unavailable for erythropoiesis [7, 11].

Impact sports like running introduce an additional mechanical stressor: foot-strike hemolysis. The repetitive ground contact forces generated during running (up to 2–3 times body weight per stride) rupture red blood cells in the capillaries of the feet, releasing hemoglobin into circulation [2]. The liver's haptoglobin system binds and recycles some of this hemoglobin-derived iron. Whereas chronic hemolysis- common in athletes logging >50 km/week—decreases recycling capacity, leading to urinary and fecal iron loss [3, 2]. For female athletes, this exercise-induced iron loss intersects with menstrual blood loss, which averages 0.5–1 mg of iron daily but can exceed 2 mg/day in those with abundant cycles [4, 12]. The combined effect creates a cyclical drain on iron reserves. Often deficiency exists despite an iron-rich diet [3, 4].

Chronic Training Load: A Catalyst for Depletion

Over sustained training cycles, the additive effects of exercise on iron metabolism manifest in two primary pathways. First, repeated bouts of endurance exercise maintain a low-grade inflammatory state, perpetuating hepcidin elevation and suppressing both dietary iron absorption and macrophage iron recycling [7, 11]. Long-term studies in female distance runners reveal that 6 months of high-volume training (≥80 km/week) reduces serum ferritin by 40% on average, even among athletes consuming 18 mg/day of dietary iron—the recommended intake for premenopausal women [7, 2]. Second, intense exercise violates gastrointestinal integrity. During high-intensity efforts, blood flow is redirected from the splanchnic circulation to working muscles. This causes intestinal ischemia and epithelial cell sloughing [3, 22]. This damage increases fecal iron loss by 20–30%. A phenomenon exacerbated by nonsteroidal anti-inflammatory drug (NSAID) use, which 60% of athletes report using monthly for pain management [3]. Together, these mechanisms create a self-perpetuating cycle of iron depletion, where training adaptations are undermined by the very sessions intended to enhance performance.

Periodization: Mitigating Iron Loss Without Sacrificing Gains

Strategic periodization is phasing training volume and intensity. It may attenuate iron depletion while preserving performance gains. One evidence-based approach is tapering, where a 7–10 day reduction in training volume by 40–60% lowers baseline IL-6 and hepcidin levels, restoring iron absorption capacity. A 2020 study of elite female triathletes demonstrated that a 10-day taper reduced hepcidin by 35% and increased serum iron by 22%, correlating with improved 10 km run times [13]. Another strategy is session spacing, which minimizes IL-6 accumulation by allowing ≥24 hours between high-intensity sessions. For example, scheduling interval training on Mondays, Wednesdays, and Fridays—with recovery days in between—reduces hepcidin persistence compared to consecutive-day scheduling [10, 11]. Altitude training introduces unique considerations. While hypoxia stimulates erythropoietin production, enhancing red blood cell synthesis, it concurrently increases iron demands by 30–50% [7]. Athletes training at moderate altitudes (1,800–2,500 meters) require close monitoring: a 4-week altitude camp typically depletes ferritin stores by 25–30 μg/L

unless iron intake is increased to 30–35 mg/day [7, 14]. Intravenous iron supplementation (e.g., ferric carboxymaltose) has proven effective in this context, rapidly restoring ferritin to >50 μg/L and improving time-trial performance by 8–12% in iron-depleted athletes [15].

Menstrual Cycle Synergy

Aligning training phases with menstrual cycle dynamics offers a novel strategy to optimize iron absorption. During the follicular phase (days 1–14), estrogen levels rise while hepcidin production is naturally suppressed, enhancing duodenal iron absorption efficiency by 15–20% [13]. Coaches might capitalize on this window by scheduling recovery or technique-focused sessions, minimizing exercise-induced IL-6 spikes that could counteract absorption benefits. Conversely, the luteal phase (days 15–28)—characterized by higher progesterone and baseline hepcidin—may be better suited for high-intensity training, as the hepcidin elevation from exercise would have less additive impact [4, 13]. However, progesterone's role in hepcidin regulation remains unclear. Preliminary data suggest progesterone may upregulate hepcidin via STAT3 signaling. This hypothesis requires validation in athletic populations [28]. Athletes using oral contraceptives face additional complexity: monophasic pills suppress endogenous hormone fluctuations, potentially stabilizing hepcidin levels, while triphasic formulations mimic natural cycles, reintroducing cyclical iron challenges [28].

5. Dietary Strategies to Battle Iron Deficiency

The interplay between dietary intake, nutrient timing, and iron bioavailability is critical in addressing iron deficiency among female endurance athletes. Exercise-induced hepcidin elevation and menstrual losses create key challenges.Dietary interventions may alleviate these effects, ensuring adequate iron availability for both performance and health.

Heme vs. Non-Heme Iron: Optimizing Bioavailability

Dietary iron exists in two forms: heme iron and non-heme iron. Heme iron comes from animal sources such as red meat, poultry, and fish. Non-heme iron found in plant-based foods like lentils, spinach, and fortified cereals. Heme iron is absorbed at rates of 15–35%, owing to its solubility in the intestinal lumen and direct uptake by enterocytes via heme carrier protein 1 [3, 18]. For athletes adhering to vegetarian or vegan diets, non-heme iron absorption—

which ranges from 2–20%—requires careful enhancement. Pairing non-heme iron sources with vitamin C-rich foods (e.g., citrus fruits, bell peppers) can increase absorption by up to 67% through the reduction of ferric iron (Fe^{3+}) to the more soluble ferrous form (Fe^{2+}) [3, 18]. A simple strategy, such as adding a handful of strawberries to a spinach salad or squeezing lemon juice over lentil soup, leverages this relationship. Contrariwise, calcium-rich foods (e.g., dairy products) and polyphenols (e.g., tea, coffee) inhibit absorption - they bind non-heme iron in the intestines.. To circumvent this, athletes might time calcium intake to meals lacking iron-rich components—for example, reserving yogurt or cheese for breakfast rather than pairing them with iron-fortified cereals [21, 18].

Iron Supplementation: Filling the Gap

When dietary measures fall short, supplementation becomes essential. Oral iron supplements, typically administered as ferrous sulfate, fumarate, or gluconate, are first-line drugs. A daily dose of 100 mg elemental iron, taken on an empty stomach with vitamin C, elevates serum ferritin by 20–30 μg/L over 8–12 weeks in iron-depleted athletes [14, 6]. However, gastrointestinal side effects—reported in 30–50% of users—often necessitate split dosing (e.g., 50 mg twice daily) or alternate-day regimens to improve tolerability [16].For athletes with severe deficiency (ferritin <15 μg/L) or oral intolerance, intravenous iron therapy offers rapid resolution. A single 500–1,000 mg infusion of ferric carboxymaltose restores ferritin to >50 μg/L within two weeks, with studies demonstrating 8–12% improvements in time-trial performance and VO2max [15]. Despite its efficacy, intravenous iron carries risks of hypersensitivity and oxidative stress [7, 15]. Its administration requires strict medical supervision and provision of necessary medical equipment in the event of an adverse reaction.

Menstrual Cycle Considerations: Timing Matters

The menstrual cycle's hormonal fluctuations present unusual opportunities for targeted iron management. During the follicular phase (days 1–14), estrogen levels rise while hepcidin production is naturally suppressed, enhancing iron absorption efficiency by 15–20% [4, 13]. Athletes can capitalize on this window by increasing iron-rich meals and supplements, aligning intake with periods of heightened bioavailability. For example, a post-training smoothie during the follicular phase might combine spinach, chia seeds, and orange juice to maximize non-heme iron uptake. Conversely, the luteal phase (days 15–28) coincides with progesterone dominance and potentially elevated baseline hepcidin, rendering iron uptake less

efficient [4, 19]. During this phase, athletes may prioritize heme iron sources (e.g., lean beef stir-fry) or pair non-heme iron with vitamin C to counteract absorption barriers. Those using oral contraceptives, which reduce menstrual blood loss by 30–50%, may require less aggressive iron repletion but should still monitor ferritin biannually [12, 19].

Practical Realization: A Holistic Approach

Effective iron management extends beyond isolated dietary changes, requiring integration with training and recovery practices. Athletes should consume iron-rich meals 3–4 hours post-exercise to avoid the hepcidin spike that peaks 6 hours after intense sessions [13]. For instance, a post-workout meal might include grilled chicken (heme iron), quinoa (non-heme iron), and steamed broccoli (vitamin C), while avoiding calcium-rich sauces or dairy sides. Regular monitoring of ferritin (target >30 μg/L), hemoglobin, and C-reactive protein (CRP)—to distinguish true deficiency from inflammation—is essential for adjusting intake [7, 4]. Nutritionists must also address energy availability, as low caloric intake exacerbates iron depletion by reducing substrate for red blood cell synthesis [26, 29]. A 2021 retrospective study of German athletes revealed that those with low energy availability (<30 kcal/kg fat-free mass/day) had 60% lower ferritin levels than adequately fueled peers [2].

Synergizing Strategies for Success

Combating iron deficiency in female endurance athletes demands a many-skilled approach. Prioritizing heme iron and vitamin C synergies, judiciously timing supplementation, and aligning intake with menstrual physiology can collectively safeguard iron reserves. For example, an athlete with heavy menstrual bleeding might combine oral iron supplements (taken during the follicular phase) with weekly IV iron during peak training blocks, guided by regular ferritin testing [13, 15]. By harmonizing these strategies, athletes can break the cycle of depletion, ensuring sustained performance and long-term health.

6. Discussion

The synthesis of evidence presented in this review underscores the multifaceted nature of iron deficiency in female endurance athletes, where physiological, nutritional, and training-related factors converge to disrupt iron homeostasis. At the core of this challenge lies hepcidin—a

hormone whose dual role as a mediator of inflammation and iron metabolism creates a paradoxical barrier to iron availability in athletes. The interplay between exercise-induced hepcidin elevation, menstrual iron losses, and suboptimal dietary strategies forms a self-reinforcing cycle of depletion.This requires intervention that addresses each element of this triad.

Central to this discussion is the recognition that exercise, while essential for athletic adaptation, acts as a double-edged sword. Prolonged endurance training triggers IL-6-mediated hepcidin spikes that transiently suppress iron absorption, a mechanism first elucidated by Peeling et al. [10, 11]. When compounded by the mechanical stresses of impact sports—such as foot-strike hemolysis in runners [2]—and the monthly iron demands of menstruation [4, 12], even athletes with ostensibly adequate iron intake face depletion risks. This aligns with findings from Clénin et al. [7], who identified chronic training load as an independent predictor of low ferritin in female athletes, independent of dietary habits. The cyclical nature of these losses, particularly when synchronized with menstrual phases [13], highlights the need for dynamic, rather than static, management strategies. The efficacy of dietary and supplemental interventions hinges on precise timing and bioavailability optimization. While heme iron and vitamin C co-ingestion improve absorption [3, 18], the widespread use of calcium-rich supplements and polyphenols in athletes' diets often counteracts these gains [21]. Oral iron supplementation, though effective in deficient athletes [14, 6], faces adherence challenges due to gastrointestinal side effects—a barrier partially circumvented by split dosing or intravenous administration [15, 16]. However, the inconsistent performance benefits observed in non-anemic athletes [6, 16] suggest that iron repletion alone cannot resolve all deficiency-related impairments, pointing to the role of concurrent factors like energy availability [26] and inflammation [5].

A critical limitation of current evidence lies in its reliance on heterogeneous study designs. Retrospective analyses, such as Roy et al.'s [2] survey of German athletes, provide valuable prevalence data but lack the longitudinal granularity to track iron flux across training cycles. Similarly, while Sim et al. [13] demonstrated menstrual phase-dependent hepcidin variations, the hormonal mechanisms underlying these fluctuations—particularly progesterone's role—remain speculative [19]. The absence of randomized controlled trials examining oral contraceptives' impact on iron metabolism further obscures clinical guidance for a population where contraceptive use exceeds 50% [12, 19].

Future research must prioritize athlete-specific hepcidin profiling to disentangle the effects of

training load, menstrual phase, and inflammation. Emerging therapies, such as hepcidin antagonists or iron nanocapsules resistant to hepcidin blockade [8, 20], hold promise but require validation in athletic cohorts. Longitudinal studies tracking iron kinetics across menstrual cycles and training phases could refine periodization models, while investigations into genetic polymorphisms (e.g., TMPRSS6 variants affecting hepcidin sensitivity) may explain individual variability in deficiency risk [9].

In practical terms, this review advocates for an integrated management framework: one that harmonizes hepcidin-aware training schedules, menstrual cycle-aligned nutrition, and individualized supplementation. By treating iron deficiency not as an isolated pathology but as a systemic imbalance, athletes and practitioners can transform these insights into sustained performance and health gains.

7. Conclusion

Iron deficiency in female endurance athletes is a multifaceted challenge, intricately woven into the fabric of physiological demands, training regimens, and nutritional practices. This review elucidates how the hormone hepcidin—acting as both a gatekeeper and a disruptor of iron homeostasis- orchestrates a complex interplay between exercise-induced inflammation, menstrual physiology, and dietary iron bioavailability. The transient hepcidin spikes triggered by endurance exercise [10, 11], compounded by cyclical menstrual iron losses [4, 12], create a physiological paradox: athletes who push their bodies to peak performance inadvertently undermine the very systems that sustain it.

The evidence underscores that the consequences of iron deficiency extend far beyond anemia. Even in its subclinical form (ferritin <30 μg/L), iron depletion impairs mitochondrial function, reduces oxygen transport efficiency, and weakens immune defenses, manifesting as fatigue, prolonged recovery, and susceptibility to infections [5, 6]. For female athletes, these effects are magnified by the monthly iron demands of menstruation, which can deplete reserves by 1–2 mg/day—a loss that high training volumes and inadequate nutrition struggle to replenish [4, 13]. The resulting cycle of depletion is not merely a nutritional shortfall but a systemic imbalance, demanding interventions that address its root causes rather than just its symptoms.

Central to these interventions is the strategic management of training load and recovery. Periodization models that prioritize hepcidin-aware scheduling- such as spacing intense sessions ≥24 hours apart [11] and incorporating pre-competition tapers [13]- can mitigate exercise-induced inflammation, preserving iron absorption windows. Concurrently, dietary

strategies must transcend generic iron intake guidelines, focusing instead on bioavailability optimization. Pairing heme iron sources (e.g., lean meats) or vitamin C-fortified plant-based meals with training sessions [3, 18], while avoiding calcium and polyphenol interference [21], ensures that dietary iron translates into bioavailable reserves. For athletes with persistent deficiency, intravenous iron supplementation offers a rapid solution [15], though its use must be balanced against potential risks and reserved for severe cases [7].

However, the current landscape of research and practice reveals critical gaps. Retrospective studies, such as Roy et al.'s [2] analysis of German athletes, highlight prevalence but lack mechanistic insights into how training phases or menstrual cycles modulate iron flux. Similarly, while Sim et al. [13] identified menstrual phase-dependent hepcidin variations, the hormonal mechanisms—particularly progesterone's role—remain speculative [19]. The absence of athlete-specific guidelines for oral contraceptive users, despite their prevalence in the population [12, 19], further complicates clinical decision-making. These gaps underscore the need for longitudinal, interdisciplinary studies that track iron kinetics across seasons, contraceptive regimens, and individualized training plans.

Looking ahead, the integration of emerging biomarkers and technologies promises to revolutionize iron management. Hepcidin profiling, for instance, could enable real-time adjustments to training and nutrition, while genetic testing might identify athletes predisposed to deficiency through variants in genes like TMPRSS6 [9]. Similarly, iron formulations resistant to hepcidin blockade, such as liposomal iron or iron-protein complexes [20], could bypass absorption barriers, offering targeted solutions for athletic populations.

In practice, addressing iron deficiency demands a paradigm shift—from reactive supplementation to proactive, holistic management. Athletes, coaches, and clinicians must collaborate to implement protocols that harmonize biomarker monitoring (ferritin, CRP, hemoglobin), cycle-aware nutrition, and periodized training. For example, a marathon runner with heavy menstrual bleeding might combine follicular-phase iron loading [13], intravenous supplementation during peak training blocks [15], and a 10-day pre-race taper to optimize absorption [13]. Such strategies not only restore iron status but also enhance resilience, enabling athletes to sustain high performance without sacrificing long-term health.

Ultimately, this review calls for a redefinition of success in endurance sports—one that prioritizes metabolic health as fervently as race times. By dismantling the iron deficiency cycle through science-driven strategies, female athletes can reclaim their vigor, proving that peak performance and physiological balance are not mutually exclusive but intrinsically

linked.

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