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Relative Energy Deficiency in Sport (RED-S): A Systematic Overview of Mechanisms, Effects, and Clinical Implications

Milena Fortuna
5th Military Clinical Hospital in Krakow
Wrocławska 1/3, 30-901 Kraków, Poland
milenafortuna1@gmail.com
ORCID: 0009-0009-5670-1926

Paulina Hetnar
Medical Centre in Piekary Slaskie, Limited Liability Company
Piekarskie Centrum Medyczne Sp. z o.o.
Szpitalna 11, Piekary Śląskie, Poland
phetnar3@gmail.com
ORCID: 0009-0005-2920-2575

Sebastian Kiper
5th Military Clinical Hospital in Krakow
Wrocławska 1/3, 30-901 Kraków, Poland
sebastiankiper02@gmail.com
ORCID: 0009-0006-4708-2121

Sławomir Toczek
105th Borderland Military Hospital with a Clinic, Independent Public Health Care Facility in Zary
Domańskiego 2, 68-200 Żary, Poland
slawektoczek@interia.pl
ORCID: 0009-0000-3936-7115

Magdalena Tomala
Military Institute of Aviation Medicine
Zygmunta Krasińskiego 54/56, 01-755 Warszawa, Poland
magda.tomala99@gmail.com
ORCID: 0009-0000-4236-4943

Katarzyna Jastrowicz-Chęć
5th Military Clinical Hospital in Krakow
Wrocławska 1/3, 30-901 Kraków, Poland
katarzyna.jastrowiczchec@gmail.com
ORCID: 0009-0001-4820-0373

Klaudia Koryszko
1st Military Clinical Hospital in Lublin
1 Wojskowy Szpital Kliniczny z Poliklinikąą SPZOZ, Lublin
al. Racławickie 23, 20-049 Lublin, Poland
klaudia.koryszko@wp.eu
https://orcid.org/0009-0005-6294-8694

Natalia Pokrywka
Medical University in Lublin
Al. Racławickie 1, 20-059 Lublin, Poland
pokrywkan@gmail.com
ORCID: 0009-0004-1593-8760

Dawid Suwała
Medical University in Lublin
Al. Racławickie 1, 20-059 Lublin, Poland
dawid.suwala22@gmail.com
ORCID: 0009-0004-7606-7065

Marcelina Polak
Medical University in Lublin
Al. Racławickie 1, 20-059 Lublin, Poland
marcelina0polak@gmail.com
ORCID: 0009-0008-5987-4948

Abstract

Relative Energy Deficiency in Sport (RED-S) is a multifactorial condition resulting from low energy availability (LEA), where energy intake is insufficient to support physiological functions after accounting for exercise expenditure. Initially derived from the Female Athlete Triad, RED-S now encompasses a broader spectrum of health and performance consequences in both female and male athletes. LEA negatively impacts metabolic rate, menstrual and reproductive function, bone health, immunity, and cardiovascular and psychological well-being. Hormonal disruptions, including reduced levels of leptin, estrogen, testosterone, and thyroid hormones, contribute to impaired physiological adaptation and increased injury risk.

Diagnosing RED-S requires a comprehensive assessment of medical history, nutrition, training, and psychological factors, often supported by tools like the RED-S Clinical Assessment Tool and DXA scanning (Dual-energy X-ray Absorptiometry). Treatment focuses on restoring energy balance through increased caloric intake, modified training, and psychological support. A multidisciplinary approach is essential for recovery, emphasizing education, early detection, and individualized care. Successful management leads not only to restored physical health but also to improved mental well-being and a healthier approach to sport.

Key words: Relative Energy Deficiency in Sport, RED-S, low energy availability, Female Athlete Triad

Introduction

Relative Energy Deficiency in Sport (RED-S) is a condition that extends beyond the original concept of the Female Athlete Triad, first introduced in 1993 [1]. The American College of Sports Medicine (ACSM) initially defined the syndrome as comprising three distinct yet interconnected conditions: disordered eating (DE), amenorrhea, and osteoporosis. In 2007, the definition was updated to describe the triad as the interrelationship between low energy availability (LEA), rather than disordered eating, menstrual function, rather than amenorrhea, and bone health, rather than osteoporosis. There was a greater understanding, LEA can occur with or without the presence of a clinical eating disorder and that each component, energy availability, menstrual function, and bone health, were on an interrelated spectrum rather than each an isolated clinical finding [2]. Although some studies suggest that male athletes are at a lower risk of developing eating disorders [3], evidence still supports a link between LEA and reduced bone mineral density (BMD) in male populations [4].

In 2014, the International Olympic Committee (IOC) broadened the framework by introducing the concept of RED-S, recognizing that energy deficiency impacts not only female athletes, but also males, and that the consequences extend beyond reproductive and skeletal health [5]. Evidence firmly supports the hypothesis that it is the presence of LEA that increases the risk of developing the remaining components of the triad. The etiology of RED-S lies in an imbalance between energy intake and energy expenditure, required for optimal physiological processes, leading to impairments in metabolic rate, menstrual function, bone health, immunity, protein synthesis, and homeostasis [5, 6].

The latest IOC consensus statement on RED-S aimed to improve upon earlier versions by addressing their limitations and incorporating recent developments in research. Key updates included a broader spectrum of symptoms, acknowledgment that not all instances of low energy availability result in negative health or performance effects, and the inclusion of various differential diagnoses. The statement introduced the concept of “adaptable” LEA, where physiological systems adjust without significant harm, versus “problematic” LEA, which results in clinical symptoms. However, the statement lacks reference to primary research or objective criteria to clearly distinguish between adaptable and problematic LEA, apart from waiting for symptoms to appear. This presents a significant limitation, as most of the research supporting the RED-S model has focused on adaptable rather than problematic LEA. Furthermore, the updated framework accepts that additional "moderating factors", such as psychological stress or sleep disturbances, may influence RED-S development independently of energy availability [7].

Low Energy Availability

Medical complications in RED-S are primarily associated to low energy availability, where energy availability (EA) is calculated as dietary energy intake (EI) minus exercise energy expenditure (EEE) divided by fat-free mass (FFM). Energy Availability can be understood as the amount of energy left after exercise to support essential physiological functions such as thermoregulation, cellular growth, maintenance, and reproduction and is optimized at greater than or equal to 45 kcal/kg FFM/day in female athletes. It looks like:
energy availability (kcal kg FFM day−1) = [energy intake (kcal day−1) − exercise energy expenditure (kcal day−1)] / FFM [5,8]. Figure 1.

$$EA = \frac{\text{Energy Intake} - \text{Exercise Energy Expenditure}}{\text{Fat Free Mass (FFM)}}$$

Figure 1. Equation defining the energy available

Numerous researchers have tried to define the threshold beyond which LEA triggers metabolic changes. However, due to the high interpersonal variability, it can only be estimated that when energy availability drops < 30kcal/kg of free fat mass/day, the body is likely to adapt by prioritizing vital physiological functions [8,9]. Such exact cutpoints for exercising men have not yet been established definitively, since there has been less research on this topic focusing on the male population. However, some studies have applied thresholds derived from female data to male athletes [10]. Athletes in individual sports are at a significantly higher risk of LEA compared to those participating in team sports [11]. Additionally, LEA is commonly observed among athletes in weight-sensitive sports and dance, because of their desire for leanness to enhance both performance and appearance, while simultaneously coping with the high energy demands of their training routine [12,13]. Recreationally active individuals who deliberately limit their energy intake or perform excessive exercise entailing high energy expenditure, may also be at risk of developing LEA [14]. Although many adolescent athletes are at risk of experiencing low energy availability and its associated health effects, overall awareness of the condition remains poor. In a survey involving 712 young runners, dancers, and figure skaters, only 12% had ever heard of the female athlete triad, and just 7% could correctly identify two out of the triad's three components. There are also widespread misunderstandings about menstrual health, between 28% and 56% of female adolescent athletes mistakenly believe that missing periods is a normal consequence of intense athletic training [15].

Reproductive dysfunction, and other hormonal disturbances

A normal menstrual cycle depends on an intact hypothalamic-pituitary-ovarian axis [16]. Endocrine dysregulation in females secondary to LEA is well-documented in the literature. In response to energy deficiency, the body conserves energy by suppressing the reproductive system and prioritizing essential physiological functions [17]. Exercise affects the hypothalamic-pituitary-ovarian axis by increasing the activity of the hypothalamic-pituitary-adrenal (HPA) axis and inhibiting gonadotropins release, which affects ovulation [18]. Menstrual disturbances related to exercise can range from a shortened luteal phase to anovulation, oligomenorrhea, and in more severe cases, secondary amenorrhea that may persist for years. In athletes who have not yet reached menarche, it can also lead to delayed puberty and primary amenorrhea [19, 20]. Functional hypothalamic amenorrhea, commonly seen in athletes with LEA, refers to the absence of regular menstrual cycles without any underlying organic cause. It results from a disruption in the pulsatile release of gonadotropin-releasing hormone (GnRH), leading to reduced or borderline-normal levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), while the body's ability to respond to GnRH stimulation remains intact [16, 21, 22]. This leads to changes in folliculogenesis and ovulatory function, resulting in lower estradiol and progesterone levels [19]. Functional hypothalamic amenorrhea is thought to result from multiple pathways triggered by LEA, which negatively impact GnRH secretion, including elevated cortisol levels [16] and corticotropin-releasing hormone (CRH) in response to stress and decreased leptin, with impact directly GnRH [24]. While inadequate body fat stores, exercise stress, and abnormal hormone levels may contribute to menstrual dysfunction in athletes, LEA has demonstrated impairments in female reproductive function in both short-term and long-term exposures [25].

Changes in nutritional intake and weight loss can affect the activity of leptin, an appetite-regulating hormone produced by adipose tissue that also plays a role in reproduction. To better understand the effects of energy availability and exercise stress on leptin’s daily rhythm, the findings of Hilton and Loucks [26] showed that LEA reduced both the 24-hour average and amplitude of leptin’s diurnal rhythm, whereas exercise stress had no such effect. Although highly trained eumenorrheic athletes had lower leptin levels compared to sedentary individuals, complete suppression of leptin’s 24-hour rhythm—along with decreased plasma glucose and insulin—was observed only in amenorrheic athletes, which negatively impacted gonadotropin-releasing hormone secretion [27].

Ghrelin, an orexigenic hormone, increases in response to weight loss and energy deficiency, such as that induced by a three-month diet and exercise intervention, potentially acting as a mechanism to restore energy balance [28]. Elevated ghrelin levels have also been observed in adult individuals who over-exercise, as well as in normal-weight adolescent athletes with amenorrhea, compared to their eumenorrheic and non-athlete counterparts of similar age and body mass index [29]. Notably, ghrelin has been found to inhibit the secretion of luteinizing hormone and follicle-stimulating hormone in women [30].

Beyond reproductive hormones, LEA also affects the hypothalamic-pituitary-thyroid axis, leading to metabolic adaptations that prioritize survival over performance. The suppression of thyroid-stimulating hormone (TSH) results in lower levels of triiodothyronine (T3) and thyroxine (T4), reducing metabolic rate and impairing thermoregulation [31, 32].

Immunological and hematological effects

Studies in mice have shown that energy deficiency, primarily through reduced leptin levels, can disrupt immune function by altering the Th1/Th2 cytokine balance, increasing proinflammatory cytokines such as IL-6 and TNF-α, and elevating cortisol levels. These changes associated with low energy availability may heighten susceptibility to certain infections [33]. Both the 2018 and 2023 IOC consensus statements emphasized the potential for LEA to compromise immune function [7, 8]. This is supported by observational findings, including higher rates of upper respiratory and gastrointestinal infections in amenorrheic elite female distance runners and in Olympic athletes identified as being at risk of LEA [34].

In an observational study involving judo athletes, weight loss resulting from reduced energy intake was linked to compromised cell-mediated immunity, evidenced by a decline in specific monocyte and T-cell subset counts, alongside an increased vulnerability to symptoms of upper respiratory tract infections [35]. Similarly, case-control studies conducted on amateur wrestlers and judo athletes found that intentional weight reduction led to diminished cytokine production, such as interferon-gamma, impaired T-cell proliferation, and reduced neutrophil phagocytic function [36]. Moreover, evidence from a randomized controlled trial indicated that when calorie restriction was combined with high-intensity exercise, it resulted in elevated inflammatory markers such as IL-6 and TNF-α, along with notable changes in lymphocyte, leukocyte, and neutrophil counts [37].

Low energy availability has been linked to reduced iron stores and lower ferritin concentrations, potentially contributing to the development of iron deficiency anemia, a condition frequently observed in young female athletes [38]. The 2018 updated IOC consensus statement on RED-S identified iron deficiency as a relevant hematological issue within this syndrome and suggested it could play a role in triggering other related health complications [8].

Bone Health

Both the Female Athlete Triad and RED-S models highlight low energy availability as a key factor negatively impacting bone health. While there is evidence supporting the link between LEA and impaired skeletal outcomes, this relationship may not be as strong or straightforward as often assumed. This is partly due to the challenges in accurately measuring energy availability, assessing bone health in athletic populations, and disentangling the specific effects of LEA from other influencing factors such as training load, nutritional intake, sleep patterns, illness, and psychological stress. Moreover, the long-term impact of short-term

LEA episodes on skeletal health is still not fully understood [39]. While some data come from studies on individuals with eating disorders, extrapolating those findings to athletes can be problematic, as their energy demands, physical activity types, and nutrient profiles often differ significantly [40]. In athletes, LEA typically occurs alongside high exercise energy expenditure, which can influence bone outcomes in ways that differ from the general population. Another complication in evaluating LEA's effects on bone is the difficulty in distinguishing between low overall energy availability and specific nutrient deficiencies [41].

LEA adversely affects bone metabolism by disrupting hormonal balances, notably reducing estrogen and testosterone levels, which are critical for bone maintenance. This hormonal disruption leads to decreased bone formation and increased bone resorption, culminating in reduced bone mineral density and heightened fracture risk [42]. Research has shown that adolescent athletes with menstrual disturbances, which often signal LEA, tend to have weaker bone microarchitecture compared to their eumenorrheic peers. This underscores how even early signs of energy deficiency can affect bone health and may have lasting consequences if not addressed [43].

Performance and Injury Implications

Prolonged periods of LEA can lead to various physiological consequences that negatively affect athletic performance. These consequences can manifest in several ways, such as a higher risk of injury and illness, compromised cardiovascular health, decreased neuromuscular function, and reduced ability to adapt to training. Low energy availability is considered a major predictor of injury risk in athletes. Athletes experiencing oligomenorrhea or functional hypothalamic amenorrhea tend to report higher rates of serious musculoskeletal injuries, which often lead to longer periods of time away from their sport [8]. One study found that bone injuries were 4.5 times more common in athletes, both female and male, who exhibited signs of hormonal disruption. Specifically, females with FHA and males with low testosterone levels missed over four times as many training sessions compared to their hormonally healthy peers [44]. These findings reinforce the idea that hormonal health is closely tied to training consistency and injury prevention. As such, LEA doesn't just threaten long-term health, it has immediate implications for performance and recovery.

Diagnosis

A thorough clinical evaluation is crucial when diagnosing Relative Energy Deficiency in Sport. This assessment should include a detailed medical history, along with an evaluation of the athlete's nutritional habits, training load, and psychological status. Key indicators of RED-S may involve unexplained fatigue, recurrent injuries, menstrual irregularities, and signs of hormonal imbalances. However, these symptoms are often nonspecific and can overlap with other conditions, making the diagnosis challenging. Therefore, a comprehensive approach that considers the athlete's overall health status is necessary [45]. That's why a holistic approach, considering both physical and mental health, is essential.

To support the clinical evaluation, practitioners often use diagnostic tools. One of the most recognized is the RED-S Clinical Assessment Tool (RED-S CAT). This tool helps identify athletes at risk by focusing on factors like menstrual health, bone status, and psychological well-being. In addition to clinical assessment, hormonal testing, including estrogen, testosterone, and thyroid hormone levels, can offer deeper insight, as these hormones are often affected by energy deficits [46].

Another important tool in the diagnostic process is the measurement of bone mineral density using dual-energy X-ray absorptiometry (DXA). This scan can help detect the skeletal effects of low energy availability and is particularly useful in identifying early signs of compromised bone health [47].

Prevention - Treatment Recommendations

Due to the complex and multifactorial nature of the Female Athlete Triad, which is influenced by factors such as stress, weight loss, excessive exercise, and inadequate nutrition, a comprehensive, multidisciplinary approach is crucial for effective management and treatment. Physicians should regularly assess athletes during health check-ups to detect early signs of overtraining syndrome and evaluate the risk of RED-S. One of the key roles of the doctor is to diagnose RED-S and use the RED-S Clinical Assessment Tool (CAT) to guide athletes safely back into their sport, minimizing the risk of additional injuries or illnesses [48].

Recognizing and treating underlying psychological factors, such as disordered eating behaviors or body image concerns, are critical for effective treatment. Psychological interventions, including cognitive-behavioral therapy (CBT), can be particularly beneficial in modifying harmful behaviors and promoting a healthier relationship with food and exercise.

Treatment strategies should focus on reversing the energy imbalance at the core of the syndrome. This may involve increasing caloric intake, reducing exercise intensity or volume, or a combination of both. A multidisciplinary team, including physicians, sports dietitians, mental health professionals, and athletic trainers, should work collaboratively to develop and monitor individualized care plans. In more severe cases involving disordered eating or psychological distress, referral to a therapist experienced in eating disorders is necessary. Hormonal treatments, such as oral contraceptives, are not recommended as first-line options, as they may mask symptoms without addressing the root cause, namely, low energy availability. Although non-pharmacological strategies are primary, certain cases may benefit from medical treatments. For instance, vitamin D and calcium supplementation can be useful for supporting bone health. However, hormonal therapies, including oral contraceptives, should be approached cautiously, as they may hide symptoms without solving the underlying issue of energy deficiency [43].

The administration of medications such as bisphosphonates, denosumab, testosterone, or leptin is not advised for adolescents, as there is insufficient evidence regarding their safety and efficacy. In adult women, recombinant parathyroid hormone might be considered for cases of significantly delayed fracture healing or extremely low bone mineral density. However, this treatment should be avoided in adolescents and young adults who still have open growth plates, due to potential risks [49].

Long-term follow-up is essential, as recovery of menstrual function and bone density can be gradual, often taking months or years. The authors emphasize that success is measured not only by the return of menses or improvements in bone health, but also by the restoration of psychological well-being and healthy attitudes toward training and nutrition [45].

Conclusions

Relative Energy Deficiency in Sport is a multifaceted condition that affects a wide range of body systems and can have serious health and performance consequences for athletes. At the core of RED-S is low energy availability, which can lead to hormonal imbalances, menstrual disturbances, decreased bone density, and increased injury risk. While the condition is often associated with female athletes, it is now clear that male athletes are also affected. Effective prevention and treatment rely on early recognition and a holistic, individualized approach. This includes nutritional rehabilitation, possible adjustments to training load, and support from a multidisciplinary team including physicians, dietitians, mental health professionals, and coaches. Psychological support is especially important in cases where disordered eating patterns or body image concerns are present. Education and regular screening play a key role, particularly in younger athletes, who may not fully understand the long-term risks of energy deficiency. Recovery is often a gradual process that requires patience and continuous follow-up, but with the right interventions, athletes can return to full health and performance while building a healthier relationship with their sport.

Author's contributions:

Conceptualization: Milena Fortuna, Paulina Hetnar, Sebastian Kiper; Methodology: Sławomir Toczek; Software: Katarzyna Jastrowicz-Chęć; Check: Magdalena Tomala, Klaudia Koryszko, Natalia Pokrywka; Formal analysis: Dawid Suwała; Investigation: Marcelina Polak; Resources: Sebastian Kiper; Data Curation: Dawid Suwała, Marcelina Polak; Writing- rough preparation: Milena Fortuna; Writing - review and editing: Paulina Hetnar, Katarzyna Jastrowicz-Chęć, Klaudia Koryszko; Visualization: Sławomir Toczek; Supervision: Milena Fortuna; Project administration: Natalia Pokrywka; Receiving funding, not applicable.

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