

Relative Energy Deficiency in Sport (RED-S) – a Narrative Review and Perspectives from the UK

Relativer Energiemangel im Sport (RED-S) – ein narratives Review und Perspektiven aus dem Vereinigten Königreich

Summary

- › **Relative Energy Deficiency in Sport (RED-S)** is a clinical syndrome comprising low energy availability (LEA) as a result of over-training and a negative calorific balance. This syndrome has a wide range of biological, physiological and psychological effects on athletes. These include hormonal changes, low bone density and depression. Diagnosis of RED-S is challenging, as often initial signs are subtle and not widely recognized by general physicians, and access to imaging can be difficult.
- › **In this narrative review** we discuss the consequences of RED-S, risk factors for the condition and management. Emergence of educational resources such as the BASEM (British Association of Sports and Exercise Medicine) Health and Performance website and the RED-S Clinical Assessment Tool (CAT) is improving understanding of this condition.
- › **We highlight a literature gap** which is leading to difficulty identifying and managing athletes with health consequences subsequent to low energy availability. Notably, there is a dearth of research in para-athletes, minority group athletes and adolescents.
- › **Thus, we propose** an increase in implementation of previous research and further funding for large scale studies to define the long-term health and performance consequences of LEA, which will in turn educate and lead to better outcomes for patients.

KEY WORDS:

Female Athlete, Low Energy Availability, Clinical Syndrome, Athletes

Zusammenfassung

- › **Relativer Energiemangel im Sport (RED-S)** ist ein klinisches Syndrom, das aus einer niedrigen Energieverfügbarkeit (low energy availability; LEA) als Folge von Übertraining und einer negativen Kalorienbilanz entsteht. Es resultieren weitreichende physiologische und psychologische Auswirkungen auf betroffene Athleten, einschliesslich hormoneller Veränderungen, niedriger Knochendichte und Depressionen. Die Diagnose von RED-S ist eine Herausforderung, da die ersten Anzeichen oft subtil sind, generell wenig bekannt sind und der Zugang zu bildgebenden Verfahren schwierig sein kann.
- › **In diesem narrativen Überblick** diskutieren wir die Folgen von RED-S, Risikofaktoren für die Erkrankung und die Behandlung, Entstehung und Weiterentwicklung pädagogischer Ressourcen, wie die Website für Gesundheit und Leistung der BASEM (British Association of Sports and Exercise Medicine) und das RED-S Clinical Assessment Tool (CAT) verbessern das Wissen um diese Erkrankung.
- › **Wir weisen auf eine Literaturlücke hin**, welche die Identifikation und das Management von betroffenen Athleten einschränkt. Insbesondere besteht ein Bedarf an weiterer umfassender Forschung über RED-S bei Parasportlern, Randsportarten und Jugendlichen.
- › **Wir betonen die klinische Implementation** früherer Forschungsarbeiten sowie die Wichtigkeit groß angelegter Studien zu langfristigen LEA-bedingten Folgen auf die Gesundheit und Leistungsfähigkeit ganz im Sinne von verbesserter Aufklärung und Behandlung von Patienten.

SCHLÜSSELWÖRTER:

Sportlerin, Niedrige Energieverfügbarkeit, klinisches Syndrom, Athleten

What is Relative Energy Deficiency in Sport (RED-S)?

Relative Energy Deficiency in Sport (RED-S) is a complex syndrome associated with 'impaired physiological functioning caused by relative energy deficiency and includes, but is not limited to, impairments of metabolic rate, menstrual function, bone health, immunity, protein synthesis and cardiovascular health' (12). This definition describes a much more systemic syndrome compared to previous

descriptions of "female athlete triad" which is described as amenorrhoea, disordered eating and reduced bone mineral density (4). In the female athlete triad model, there is a parallel syndrome in undernourished male athletes, where low energy availability may lead to hypogonadotropic hypogonadism and impairment of bone health, which is now addressed in RED-S (19). RED-S is the more recently

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preferred term as it is applicable to both physically active men and women and encompasses the effects of low energy availability on physiological function, health and athletic performance (14). RED-S also encompasses disabled athletes, and implications on different races are included. Health consequences may include immunological, cardiovascular, psychological and endocrine disorders, in addition to menstruation and bone health concerns. The health implications as a result of RED-S may affect performance by increasing the risk of injury, reducing coordination, decreasing muscle strength and decreasing concentration. RED-S has also been associated with the onset of depression (14).

The aetiological factor underpinning RED-S is low energy availability (LEA). LEA is a mismatch between an athlete's energy intake from their diet and the energy expended during exercise, which results in inadequate energy to support the physiological functions needed by the body to maintain optimal health and performance (12).

Energy Availability (EA) = Energy Intake (EI) – Exercise Energy Expenditure (EEE) relative to fat-free mass (FFM)

This has been calculated to be approximately 45kcal/kg/FFM/day when an athlete does not have any physiological impairment. LEA may subsequently lead to impairments in physiological functioning and performance. However, diagnosing RED-S can be challenging as symptoms are often subtle and vague, therefore, a high index of suspicion is required in at risk athletes (12).

RED-S can have serious consequences for many body systems including the cardiovascular, gastrointestinal, endocrine, reproductive, skeletal, renal and central nervous systems, leading to short-term and long-term complications (11, 18). Athletes who experience long-term low energy availability have the potential to develop nutritional deficiencies (including anaemia), chronic fatigue, as well as being at an increased risk of infections and illnesses (15). RED-S also has a negative effect on bone health, leading to an increased risk of stress fractures and osteoporosis (2).

RED-S is not just a Female Specific Syndrome!

Prior to the emergence of RED-S, LEA in female athletes has been referred to as the 'Female Athlete Triad', suggestive that only females can be affected by low energy availability. It is now known that anyone who expends more energy than they have available, open themselves to a risk of low energy availability (LEA). Certain populations are more at risk of having a negative energy balance, for example athletes and recreationally active sports men and women. If more energy is expended via exercise than is consumed in a diet, a state of LEA occurs, which increases the risk of an athlete developing RED-S (12, 16, 17). Some sports or activities come with a greater risk of RED-S than other sports, such as sports in which a low body mass index (BMI) is ideal. Athletes who aim to maintain a low body weight may potentially increase their exercise levels, which may exceed their energy intake levels (10). They may alternatively, or additionally, reduce calorific intake whilst continuing with high levels of exercise training. These sports include weigh-in sports where athletes aim to compete at a desired weight (such as rowing and combat sports), as well as sports that benefit from an aesthetic advantage. It is important to recognise that LEA can also arise inadvertently from high volumes of exercise accompanied by insufficient fuelling, where the athlete may not necessarily be trying to maintain or lose body weight(6).

Male athletes are also affected by RED-S (6, 8). Male athletes in a variety of sports have been identified with disordered eating, eating disorders, and compulsive exercise disorders, subsequently leading to LEA (6). A potential consequence of LEA in males is reduced levels of testosterone. A recent study has identified that after 5 days of severe energy deficit and six months of endurance training, reduced testosterone levels have been reported in male athletes (6, 20). This has been associated with an increased risk of bone health disorders, as testosterone stimulates bone turnover and calcium absorption. In male ultra-endurance cyclists, testosterone, insulin-like growth factor 1 (IGF-1) and leptin have been reported to be considerably suppressed after 54 hours of extreme exercise. Additionally, lowered tri-iodothyronine (T3) and insulin and increased cortisol and cholesterol levels have been reported amongst exercising athletes exposed to LEA. In addition to the likely performance degradation, the suppression of these metabolic hormones secondary to prolonged LEA is associated with other adverse health consequences (20). Decreased immunological function, lower sex hormones, impaired bone health and reproductive function have been demonstrated in males with LEA. The sports or activities with the highest risk are endurance and light-weight sports (9). Male endurance cyclists in particular have been shown to have low energy availability (5).

As well as encompassing male athletes, RED-S is also inclusive of the para-athlete population, regardless of sex or sport type (1). Para-athletes, particularly those with limited weight bearing, may have lower bone mineral density and therefore at greater risk of atypical fractures. 50% of bone stress injuries in para-athletes were sustained in athletes with low bone mineral density (3). However, the consequences of LEA in para-athlete populations are poorly understood and awareness of RED-S in para-athletes is low.

RED-S Diagnosis

Screening for RED-S should be considered as part of an annual health or pre-participation examination, especially in endurance athletes or sports emphasising aesthetics or a lean physique (17). Screening should also be considered when an athlete presents with disordered eating, an eating disorder, weight loss, lack of normal growth and development, endocrine dysfunction, recurrent injuries and illnesses, decreased performance, performance variability or mood changes (13). Early detection of RED-S is paramount, and a high level of suspicion is warranted in endurance and lean body sports. It is important to be aware of potential symptoms and clinical features of RED-S (13, 17). A general physical examination may include assessment of height, weight, orthostatics (blood pressure and pulse) and body fat percentage, in addition to identification and examination of the clinical features shown in table 1.

Additional blood test analysis may be necessary depending on the athlete's clinical presentation, such as significant fatigue/poor performance, prior bone stress injury, severe hypogonadotropic hypogonadism or functional hypothalamic amenorrhoea (FHA). Further investigations should include analysis of gonadotropins, thyroid hormones, vitamin D levels, prolactin, magnesium, coeliac serology and a pregnancy test in women. In men, both free and total testosterone levels should be measured. When there are signs and symptoms suggestive of polycystic ovarian syndrome (PCOS) in females, it may also be useful to measure LH (LH: FSH ratio) and testosterone. An athlete with primary amenorrhoea, or who is suspected of having PCOS, should also have an ultrasound scan.

Table 1

Summarising the clinical features of RED-S (adapted from 13, 17).

EXAMINATION	SIGNS
General physical signs and symptoms of disordered eating or LEA	Parotid gland enlargement, hypercarotenaemia, lanugo, Russel's sign, acne, male pattern hirsutism, dry mucous membranes
Cardiac tests	Arrhythmias, prolonged QT intervals, bradycardia
Biochemical tests	Hypokalaemia, hypophosphatemia, hypomagnesaemia, hypoalbuminemia, Anaemia
Imaging	Dual-energy X-ray Absorptiometry (DEXA) may show low mineral density

FHA occurs when there is a reduction in the release of gonadotropin-releasing hormone from the hypothalamus, which is caused by stress and low levels of energy availability. This leads to a reduction in luteinising hormone (LH), resulting in changes the menstrual cycle. Subtle changes may also occur, such as mid-cycle spotting or light bleeding.

The long-term reproduction effects on males and females with prolonged sex hormone dysfunction is not yet known, but it is clear that bone health is affected, and any factor that contributes to sex hormone dysfunction can have an influence. Endogenous oestrogens and androgens have effects in both men and women on the absorption of calcium into the blood and deposition into bone is facilitated by oestrogen, and the balance between progesterone and oestrogen is important in assisting this action. Bone turnover and calcium absorption is stimulated by testosterone. Soft tissue composition (lean vs. fat mass), lifestyle factors (alcohol consumption or smoking), physical activity and medication are all modifiable determinants of BMD (18, 20).

RED-S Clinical Assessment Tool (RED-S CAT)

In 2014, the IOC introduced the first RED-S Clinical Assessment Tool (RED-S CAT). The tool uses a spotlight methodology to determine risk state of athletes suffering with RED-S and activity recommendations. As described in the IOC consensus statement, the RED-S tool uses three levels of risk, identified as “High risk: no start red light,” “moderate risk: caution yellow light,” and “low risk: green light”. Each risk category resembles an athlete eligibility pronouncement. Red light is “restricted from play,” yellow light is “provisionally cleared,” and green light is “fully cleared.” Red Light requires a diagnosis of anorexia nervosa or another serious eating disorder, LEA related serious medical conditions, or life-threatening conditions due to weight loss techniques. In cases where an athlete scores ≥3 in the yellow light, moderate risk criteria, red light status can also be attained. Several risk factors detailed in the IOC guidelines as “yellow light” criteria include, prolonged LEA, health consequences secondary to low EA, reduction of expected development and growth, eating disorder behaviour negatively affecting other team members, and non-compliance or lack of progress in treatment (7,13).

The RED-S clinical assessment tool uses specific category descriptions such as substantial weight loss, which is defined as 5-10% body mass in one month. Menstrual cycle dysfunction is defined as primary amenorrhoea when there is failure to achieve menarche by age 15, and secondary amenorrhoea (FHA) lasting >3 months. A history of stress fractures with hormonal/menstrual dysfunction and/or LEA is also noted (see figure 2). Reduced bone mineral density is documented by comparing previous DXA or having a Z-score <-1 standard deviation (A Z-score compares bone density to the average values for a

person of the same age and gender). Having bone mineral density measured by DXA can make screening unaffordable in some populations, due to the cost of these scans (13).

Although LEA is a key element in RED-S, there is no standardised protocol for undertaking an assessment of energy availability in recreational athletes. Energy availability may be monitored by tools to monitor energy availability developed by some sports nutrition specialists and these may use these to screen for problems or guide dietary counselling. However, there is currently not a universally approved protocol to measure energy availability that is reliable, sensitive, time-efficient and cost-effective.

How is RED-S treated?

RED-S management relies on a multidisciplinary approach to educate and support the athlete with the primary aim to correct and maintain energy balance. Athletes should receive medical assessment and treatment if they are characterised in the red light and yellow light zones. The treatment of RED-S should ideally comprise of an MDT comprising of many healthcare professionals such as a dietician, physician, physiotherapist or athletic trainer, exercise physiologist and psychological support. The treatment programme for RED-S should focus on reversing the underlying cause, which is LEA. The treatment must focus on increasing the caloric intake to match the caloric expenditure (and potentially decreasing the training demands) to correct the energy balance. It is critical that athletes also receive education on RED-S, as many athletes believe it is normal to experience menstrual dysfunction, fatigue, low appetite, recurrent injuries and mood swings. Education is also essential in order to gain trust from the athlete, family, coaches and teammates. Psychological strategies, such as encouraging ‘eating to perform’, can be helpful to change an athlete’s relationship with food (13, 14). Increasing body weight, while ensuring an adequate intake of protein and carbohydrate, is the best management strategy for menstrual dysfunction. The use of the oral contraceptive pill for the treatment of RED-S is not generally advised, as it may mask clinical signs of RED-S, such as amenorrhoea, thus increasing the risk to miss an ongoing loss of bone mineral density due to RED-S. If an athlete is suffering with osteopenia or osteoporosis, a diet with adequate intake of vitamin D and calcium and supplementation may be necessary. Bone mineral density should be re-assessed at intervals of 6-12 months. Other medical therapies (such as the use of bisphosphonates) might be used judiciously in high-risk cases, but in the absence of metabolic bone disease remain secondary to measures to optimise nutrition and lifestyle factors for long term health.

Finally, and crucially, a treatment plan for any psychological sequelae is critical to athlete recovery from RED-S and health. The psychological effects of removing an athlete from competition for a time period due to any injury are well-known. ➤

In the case of athletes unable to compete due to RED-S related pathology, psychological effects may be more profound given that the athlete may have an underlying mental health issue. Any eating disorders or disordered eating behaviours also require psychological and medical support. This may include psychotherapy or medical therapy, in the inpatient or outpatient setting, depending on the clinical scenario. Given the nature of the condition, and the involvement of a multidisciplinary team, it is essential that patient confidentiality is maintained. The use of an athlete and health professional contract is also recommended (13,14).

RED-S – Prevention

The IOC consensus group have made four recommendations to prevent RED-S (16):

1. Education using reputable sources of information, involving athletes, their families, coaches, medical providers and sports organisations. The education should cover healthy eating and nutrition, the concept of EA and the risks of LEA on performance and health associated.
2. Policies should be utilised by coaches on the development of healthy weight and body composition goals for athletes. The importance on weight and body composition to enhance performance should not be encouraged and the focus should be on nutrition.
3. The concept that good performance does not necessarily mean good health should be promoted. Education should be given on prolonged poor health and the inevitable impact on performance.
4. Multidisciplinary health support teams well educated in the detection and treatment of RED-S and the use of risk assessment and return to play models should be created.
What research needs to be done in the future?

As a relatively new sports and exercise medicine concept, there is a clear scarcity of literature on identifying and managing athletes with LEA. Further research is needed to better understand assessment and management strategies and the potential long-term health consequences to effectively serve athletes with suspected RED-S signs.

Male Athletes

At present, repercussions of LEA among male athletes are poorly understood and should therefore form the basis of future research. It is likely to result it will have similar manifestations akin to men who have low testosterone and therefore lead to mental health issues such as depression, physical symptoms such as low libido and erectile dysfunction, although currently little is published in the literature. The male athlete triad is not yet an official entity, but a team of experts are creating a consensus statement to be published in the near future (13).

Race and Ethnicity

Published research is greatly lacking on RED-S in African-American athletes and it still unknown as to whether race plays a role in the incidence and underlying aetiology of RED-S. Whether the prevalence of menstrual disorders varies among racially diverse athletic groups remains speculative. The risk of disordered eating in African-American compared to Caucasian

females has been found to be reduced, and stress fractures in African-American military recruits have also been found to be lower than in Caucasian recruits (8). As studies are limited, it has been identified that there is a need to include more diverse athlete populations in RED-S research and to integrate race and ethnicity in the prevention and treatment of RED-S (14).

Junior Athletes

Other directions for future exploration include junior and developmental athletes, and the prevalence and long-term risks of LEA. The development of standardised tools to diagnose LEA in this population have the potential to improve athlete specificity and develop management approaches to reduce the risk of long-term health consequences. By furthering in knowledge on LEA in junior athletes this will support development effective prevention, early detection and management strategies in various athlete populations (16).

Para Athletes

As mentioned previously, factors associated with the RED-S are present in an elite para athlete population, regardless of sex or sport type. However, awareness of RED-S in para athletes is low and the consequences of LEA in para athlete populations are poorly understood. The high prevalence of factors observed in para athletes suggests value in advancing screening tools and education efforts to optimise health and management of RED-S in this population (1).

Conclusion

Though awareness of RED-S is recently increasing, further research is needed to better understand athlete specific risk factors, screening tools, assessment and management strategies and effectiveness of education and prevention programmes in athletes with LEA. Thus, we propose an increase in large scale research defining the long-term health and performance consequences of LEA, which will in turn educate and lead to better outcomes for patients. For further information on the symptoms and potential outcomes of RED-S, what to look out for, management and what to do in each of the sections tailored according to the nature of involvement in exercise, the British Association of Sports and Exercise Medicine (BASEM) 'Health for Performance' web page proves a reputable resource to start. As knowledge and understanding of RED-S develops through research and clinical practice, this website will be updated to provide the most current information on the identification, clinical risk assessment and management of RED-S and return-to-play guidelines. ■

Conflict of Interest

The authors have no conflict of interest.

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