

## Relative energy deficiency in sport (RED-S)

### WHAT IS RED-S?

Relative energy deficiency in sport (RED-S) is a condition of low energy availability that has serious long-term consequences on health and sporting performance.<sup>1</sup> Whether intentional or unintentional, the impact of chronic low energy availability was previously described as the 'female athlete triad': low energy availability, amenorrhoea, and low bone density. Oestrogen plays an important role in calcium absorption, hence the link between amenorrhoea and low bone density. However, in 2014, the term RED-S was introduced by the International Olympic Committee (IOC) to reflect research that found much wider consequences across bodily systems, and that the condition affects both male and female athletes. In fact, exercisers of any activity, age group, or level of competition are susceptible to RED-S.

Personal experience of this condition can be harrowing. Bobby Clay is an example of a promising young athlete left with osteoporotic fractures aged 19.<sup>2,3</sup> Given that GPs will often be the first medical professional involved in these athletes/dancers' care, and many sports physicians have a general practice background, it is imperative to raise awareness of RED-S in primary care.

### COMMON PRESENTATIONS

#### Case 1

Athlete A presents with frequent coughs and colds, and persistent fatigue. He is applying for a scholarship to an international ballet school. He was told he would need to lose 2–3 kg. His mother reports that he has lost 7 kg so far, has become obsessive about his calorific intake, and has excluded both wheat and dairy from his diet. He has recently suffered increasing anxiety if he cannot attend ballet practice.

#### Case 2

Athlete B recently started university, having been a good club-level athlete at school.

She has increased her training volume, is cooking her own meals for the first time, and cycles 4 miles to and from each training session. She presents to the GP with a foot injury that has been causing her pain for 3 months and reports it has been very difficult to concentrate when revising for her exams. She has not had a period for 7 months but reports 'this is normal for an athlete'.

### WHAT ARE THE RISK FACTORS FOR DEVELOPING RED-S?

RED-S is most common in sports/dance activities where there is a perceived performance advantage in being light or where there is an aesthetic focus. While weight loss may initially benefit performance, a chronic low energy state prevents the body's adaptation to training, and performance will inevitably plateau or decline. For some athletes, as in Case 1, the pressure to lose weight can become overwhelming — the prevalence of eating disorders among male and female athletes is 20% higher than in non-athletes.<sup>4</sup> A lack of awareness about adequate fuel consumption can cause unintentional underfueling, as in Case 2, which can be precipitated by a change in circumstances. Any athlete who has increased their training load recently, reduced their rest periods, frequently exercises in the fasted state, or who is following an exclusionary diet will also be at increased risk of RED-S.

### HOW CAN RED-S BE IDENTIFIED?

Despite damaging myths that persist in sporting culture, it is not normal for females to lose their menstrual cycle (primary or secondary amenorrhoea) or suffer oligomenorrhoea regardless of their level of exercise. This is a clear red flag warranting urgent secondary care referral, as would loss of morning erections in male athletes (hypogonadotropic hypogonadism), delayed puberty, stunted growth, positive eating disorder screening,

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**Table 1. Common differential diagnoses for RED-S**

	Male RED-S	Female RED-S	PCOS	Prolactinoma	Ovarian insufficiency	Primary male hypogonadism (for example, Klinefelter)	Pregnancy
Oestradiol	N/A	↓ or ↔	↔	↓ or ↔ female	↓	↑	↑
LH	↓ or ↔	↓ or ↔	↔	↓ or ↔	↑	↑	↓
FSH	N/A	↓ or ↔	↔	↓ or ↔	↑	↑	↓
Testosterone	↓ or ↔	↓ or ↔	↔ or ↑	↓ or ↔ male	↓ or ↔	↓ or ↔	Variable according to trimester
TSH	↓ or ↔	↓ or ↔	↔	↓ or ↔	↔	↔	Variable according to trimester
T4	↓ or ↔	↓ or ↔	↔	↓ or ↔	↔	↔	Variable according to trimester
Prolactin	↔ or ↑ (<1000 mU/L)	↔ or ↑ (<1000 mU/L)	↔ or ↑ (<1000 mU/L)	↑ (>1000 mU/L)	↔	↔	↑
9 am cortisol	↑ (<1000 nmol/L)	↑ (<1000 nmol/L)	↔	↓ or ↔	↔	↔	Variable according to trimester
b-HCG	Negative	Negative	Negative	Negative	Negative	Negative	Positive
Hb/ferritin	↓ or ↔	↓ or ↔	↔	↔	↔	↔	Variable according to trimester

*b-HCG = beta-human chorionic gonadotropin. FSH = follicle-stimulating hormone. Hb = haemoglobin. LH = luteinising hormone. N/A = not applicable. PCOS = polycystic ovary syndrome. RED-S = relative energy deficiency in sport. TSH = thyroid-stimulating hormone. T4 = thyroxine. ↑ = high. ↓ = low. ↔ = within normal range.*

headaches (pituitary tumour), or markedly raised prolactin levels (Table 1).

It can be difficult to recognise RED-S given the vague symptoms that it can present with, particularly in male athletes. A thorough review of systems may elicit additional symptoms, including sleep disturbance, gastrointestinal disturbances, lack of concentration, depressed mood, increased anxiety, fatigue, increased frequency of minor illnesses, increased frequency of injuries, hormonal disturbances, and slowing of growth in paediatric patients. RED-S is also difficult to identify in the absence of weight loss, but does occur in athletes with a normal body mass index.<sup>5</sup> In both male and female athletes, weight can be maintained by the body's compensatory mechanisms — the body adapts to chronic low energy availability by prioritising movement over 'unnecessary' bodily functions.

**WHEN ARE INVESTIGATIONS WARRANTED?**

The combination of risk factors and symptoms present in the clinical history should raise clinical suspicion and trigger further investigation.

**WHAT INVESTIGATIONS ARE MOST USEFUL AND WHY?**

The following biochemical investigations are essential to exclude other causes of

endocrine disturbance and identify which part of the hormonal axis is disrupted:

- *female*: follicle-stimulating hormone (FSH), luteinising hormone (LH), oestradiol, testosterone, pregnancy test;
- *male*: testosterone, LH; and
- *all athletes*: full blood count (FBC), thyroid function tests, ferritin, vitamin B12, vitamin D, 9 am cortisol, prolactin.

The GP should also consider a coeliac screen/faecal calprotectin if there are persistent digestive disturbances in keeping with a possible history of coeliac disease/inflammatory bowel disease. A bone density scan (DEXA) should also be considered in athletes at high risk of poor bone health, for example, someone who is amenorrhoeic or who has had two or more stress fractures.

RED-S will commonly cause hormone levels to be in the low end of normal range, and to be outwith the normal range in more severe cases (Table 1). A pregnancy test is required in all amenorrhoeic women (in paediatric patients, this should be guided by sexual and pubertal history). Testosterone levels are important to distinguish between polycystic ovary syndrome and the functional hypothalamic amenorrhoea associated with RED-S in females. In males, testosterone helps to determine if hypogonadism is responsible for the

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patient's symptoms and, if it is, LH helps to determine primary (raised LH, testicular pathology) or secondary hypogonadism (reduced LH, pituitary-hypothalamic pathology). Patients with low energy availability often have dietary deficiencies and are in a state of high stress that may cause elevated cortisol levels (Table 1).

Abnormal results can serve an important psychoeducation role, convincing an athlete that there is a problem, motivating an urgent change in behaviour, and measuring improvement. However, it is important to note that normal results do not exclude RED-S. For female athletes, taking the combined oral contraceptive pill (COCP) may falsely normalise hormone levels. Table 1 shows the results of male/female patients with RED-S and how they compare to common differential diagnoses. Unfortunately, it is beyond the scope of this article to provide an exhaustive list.

## HOW CAN GPs ASSESS SEVERITY OF RED-S?

The IOC has published clear guidance on risk assessment and management of RED-S including a validated risk assessment tool, RED-S CAT,<sup>6</sup> which stratifies an athlete's risk with guidance on return to exercise appropriately.

## HOW CAN GPs MANAGE RED-S IN PRIMARY CARE?

GPs have an important role to play in educating patients about RED-S, initiating management, avoiding common pharmacological pitfalls, and signposting athletes to further resources, such as the Health 4 Performance Working Group (<https://health4performance.basem.co.uk>) and Project RED-S (<https://red-s.com>). Management should focus on the underlying energy availability by modifying fuelling strategy and training load. Particular attention should be paid to encouraging adequate carbohydrate intake before and after exercise, as evidence suggests within-day deficits can contribute to RED-S despite sufficient overall calorie intake.<sup>7</sup>

## WHAT ARE THE COMMON PITFALLS IN PHARMACOLOGICAL MANAGEMENT?

Many women are prescribed the COCP to 'stimulate' or 'control' their cycle. This has serious consequences in the context of RED-S: first, the withdrawal bleed can be mistaken for a regular period, masking oligo/amenorrhoea. Second, evidence suggests that the oral contraceptive pill can worsen bone health and the metabolic consequences of RED-S. Short-term

hormone replacement therapy (HRT), prescribed by secondary care, is a more appropriate treatment until the underlying energy deficiency is reversed.<sup>8</sup>

In male athletes, testosterone replacement is not indicated if blood tests are in keeping with functional suppression of the hypothalamic pituitary axis as levels will rise when energy availability is restored. GPs should be aware that testosterone is on the World Anti-Doping Agency (WADA) prohibited-substance list.

It is not necessary to prescribe thyroxine in cases of borderline/low thyroid function. Prescribing thyroxine replacement will not solve the underlying low energy availability that has led to the hormonal axis shutting down and may cause the athlete to become fixated on this as the cause of the problem. GPs should be aware of athletes who demand thyroxine in the belief that it has performance-enhancing effects.

## WHEN AND TO WHOM SHOULD GPs REFER?

Dietician support can help an athlete to address their low energy availability. Patients who have any red-flag features, or who show a lack of improvement or resistance to behavioural change, should be referred to endocrinology or paediatric endocrinology. Additional investigations may include karyotyping, DEXA scan, and a pelvic ultrasound scan for amenorrhoeic female patients. For athletes with prolonged and complex recovery, such as those with an eating disorder, the help of a wider multidisciplinary team is required: clinical psychologist, specialist dietician, sports medicine physician, and psychiatrist.

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