Case Report

# EXTREMELY LOW TESTOSTERONE DUE TO RELATIVE ENERGY DEFICIENCY IN SPORT: A CASE REPORT

*Ana Narla, MD[1,2]; Kimberly Kaiser, MD, MPH[3]; Lisa R. Tannock, MD[1,2]*

## ABSTRACT

***Objective:*** Recognize extremely low testosterone due to hypothalamic dysfunction from overtraining syndrome in a male athlete with relative energy deficiency in sport (RED-S).

***Methods:*** Clinical and laboratory information are described.

***Results:*** A 20-year-old male division I collegiate swimmer was found to have strikingly low total, free, and bioavailable testosterone levels with normal sex hormone–binding globulin and inappropriately normal follicle-stimulating hormone and luteinizing hormone. Lab testing ruled out hyperprolactinemia and hypothyroidism as etiologies, and pituitary imaging was normal. A diagnosis of RED-S was made, and the patient worked with the sports medicine team to increase nutrition and modify physical activity. His repeat testosterone levels improved after minor weight gain and decreased training regimen and eventually returned to normal.

***Conclusion:*** Secondary hypogonadism with extremely low testosterone can be seen in male athletes with suspected RED-S. **(AACE Clinical Case Rep. 2019;5:e129-e131)**

Submitted for publication July 11, 2018
Accepted for publication September 24, 2018
From the [1]Department of Internal Medicine, [2]Barnstable Brown Diabetes Center, and [3]Department of Orthopaedic Surgery and Sports Medicine, University of Kentucky, Lexington, Kentucky.
Address correspondence to Dr. Lisa R. Tannock, Division of Endocrinology, Department of Internal Medicine, Barnstable Brown Diabetes Center, 553 Wethington Building, 900 South Limestone, University of Kentucky, Lexington, KY 40536-0200.
E-mail: Lisa.tannock@uky.edu.
DOI: 10.4158/ACCR-2018-0345


**Abbreviation:**
**RED-S** = relative energy deficiency in sport

## INTRODUCTION

The female athlete triad consisting of disordered eating, amenorrhea, and osteoporosis is a well-documented and recognized disorder of female athletes (1,2). The International Olympic Committee (IOC) updated their position statement on the female athlete triad in 2014 with the new term ‘Relative Energy Deficiency in Sport’ (RED-S) (3). RED-S is a syndrome of impaired physiologic function due to a deficiency in the balance between energy intake and expenditure. The new terminology facilitates recognition that male athletes can be affected by relative energy deficiency; however, it can be more difficult to identify this condition in males, as they do not have the menstrual abnormalities that are seen in female athletes.

## CASE REPORT

A 20-year-old division I collegiate swimmer reported performance concerns. His initial weight at college entry was 201 pounds with 17.3% body fat; after 1 year of training, his weight was 189 pounds with body fat of 15.3%. Performance issues became obvious when his weight was 183 pounds with a body fat of 11.2%. At this time, his evaluation was significant only for mild normocytic anemia (hemoglobin of 12.7 g/dL [normal, 13.7 to 17.5 g/dL], mean corpuscular volume, 96 fL [normal, 79 to 98 fL]). He had a positive fecal occult blood test and underwent an upper and lower endoscopy, which were normal. He then had a bone marrow biopsy, which showed normal male chromosome analysis, normal fluorescence in situ hybridization analysis, normocellular marrow with orderly trilineage hematopoiesis, and no evidence of infection or infiltrative process. Infection screens were negative, and computed tomography scans chest, abdomen, and pelvis were unremarkable. Total testosterone was very low on two measures: 20 ng/dL drawn at 12 PM, and repeat level of 36 ng/dL at 8 AM (normal range, 160 to 726 ng/dL).

The patient denied any change in facial hair, shaving frequency, erectile function, or academic performance. He used supplements including multivitamins, probiotics, creatinine, and Osteo Bi-flex closely monitored by the team dietician. He specifically denied using anabolic steroids. He stated he spent up to 6 hours a day in the pool or lifting weights. In addition, he attended class and tutoring sessions, leading to sleeping less than 6 hours a night. Review of energy balance showed he was expending over 4,000 calories per day and eating less than 2,000 calories per day. This was in part intentional and guided with the goal of decreasing from 201 pounds at the start of his collegiate career to a goal weight of 190 pounds, as determined by the team coaches and sports physician.

On examination, he was a healthy young man, well-virilized and fit but without excessive muscle development. Blood pressure was 109/64 mm Hg, and heart rate was 46 beats per minute. His height was 6 feet 1.5 inches, and his weight was 182 pounds (body mass index [BMI], 23.71 kg/m$^2$). Testicular examination revealed normal testes of 15 to 20 mL bilaterally, normal phallus, and no abnormalities. The rest of his examination was normal.

Repeat tests sent out to a reference laboratory were drawn at 8 AM and confirmed low total testosterone of 30 ng/dL (normal range, 348 to 1,197 ng/dL), low free testosterone of 3.6 pg/mL (normal range, 52 to 280 pg/mL), low bioavailable testosterone of 10 ng/dL (normal range, 128 to 430 ng/dL), and normal sex hormone–binding globulin of 34.8 nmol/L (normal range, 16.5 to 55.9 nmol/L). Luteinizing hormone (LH) was low at 0.5 mIU/mL (normal range, 1.7 to 8.6 mIU/mL), and follicle-stimulating hormone was low normal at 1.5 mIU/mL (normal range, 1.5 to 12.4 mIU/mL), indicating secondary hypogonadism. Prolactin, thyroid-stimulating hormone, and free thyroxine were all normal. Gonadotropin-releasing hormone (GnRH) was appropriately elevated at 13.3 pg/mL (normal range, 4.0 to 8.0 pg/mL), and a pituitary-directed magnetic resonance imaging was normal. At this point, a diagnosis of presumptive RED-S was made.

In discussion with the team physician and coach, he was advised to decrease physical activity and work with a nutritionist. At this point, his energy availability was estimated at −1.3 kcal/kg fat free mass/day. He was not permitted to swim, weight train, or pursue extra exercise on his own for 1 month until he was able to regain weight to at least 190 pounds. After patient had regained this minimum weight, he was gradually re-introduced to his physical activity. He signed a behavioral health contract stating that if he fell below 190 pounds (goal determined by his sports physician based on his personal weight history and predicted by adequate energy availability), he would be pulled from activity.

After only 13 days, his weight increased from 183.1 pounds to 190.4 pounds. A repeat testosterone level was 136 ng/dL (normal range, 160 to 726 ng/dL). Nutritional therapy was continued as the patient gradually increased his activity, with a recommended calorie intake goal of 4,700 calories/day (energy availability estimated at 42 calories/kg fat free mass/day). Repeated early morning testing over the next few months while his weight was stable (197 pounds, body fat 14%) showed total testosterone levels of 269 ng/dL, 302 ng/dL, and 244 ng/dL, all in the normal range.

## DISCUSSION

RED-S is a syndrome caused by low energy availability in which dietary intake is insufficient to support energy expenditure for activities such as daily living, as well as basic health and functioning after the cost of exercise and sporting activities are taken into account (4). Note, RED-S can occur without decreased body weight or low BMI, as the main driver is the limited energy availability. RED-S can impact a variety of health functions, leading to impairment in cardiovascular health, bone health, menstrual function, immunity, protein synthesis, growth and development, and metabolism. RED-S can affect sport performance by leading to decreased muscle strength, decreased glycogen stores, depression, irritability, decreased concentration, decreased coordination, impaired judgment, decreased training response, increased injury risk, and decreased endurance performance.

Historically, literature on low energy availability has focused on female athletes with the original 2005 IOC consensus statement focusing on the "Female Athlete Triad." Recognition of the female athlete with energy deficiency is easier given the ability to use menstrual cycles as a gauge of energy status. A reduction in energy availability affects GnRH output, thereby disrupting LH pulsatility, which then alters the menstrual cycle. This is also known as functional hypothalamic amenorrhea. Current literature now recognizes that low energy availability can be seen in male athletes as well and occurs in the same at risk "weight-sensitive" sports as for female athletes (5). However, to date, the majority of literature evaluating RED-S in males has focused on cyclists, runners, rowers, and jockeys (6,7). While the underlying etiology and endocrine outcome of low energy availability and RED-S do not differ between male and female athletes, the prevalence in male athletes is likely underestimated, in part due to a more subtle presentation and in part due to decreased awareness of the existence of the condition in males (6). There is a growing awareness in the literature of RED-S overall and in males (8).

Male hypogonadism may be caused by congenital, structural, or destructive disorders, resulting in permanent hypothalamic, pituitary, or testicular dysfunction, or it can be functional, usually reversible, caused by conditions that suppress gonadotropin and testosterone concentrations (5). Our patient had strikingly low testosterone levels (measured by tandem mass spectrometry) for an otherwise healthy 20 year old. The 2018 Endocrine Society guidelines state a reference range for total testosterone in healthy, nonobese young males aged 19 to 39 years of 264 to 916 ng/dL (using the 2.5th and 97.5th percentiles) or 303 to 852 ng/dL (using the 5th and 95th percentiles). This patient's testosterone level was strikingly low. RED-S should be considered in the differential diagnosis of hypogonadism in an at-risk individual (male athlete in a sport that emphasizes leanness) such as this patient. We point out that competitive swimming is an at-risk sport, in addition to what has been found in a majority of other reports which focus on runners and cyclists (9).

Overtraining, which is an accumulation of stress due to training and additional life stressors that results in long-term performance loss that can be accompanied by psychological and physiologic signs and symptoms, is a well-recognized phenomenon in elite-level athletes. In this case, the energy expenditure from training exceeded the energy intake from diet, leading to RED-S. Our patient met with a sports dietician and team physician routinely and with a decreased swimming schedule and increased caloric intake and was able to regain weight, which resulted in improvement in testosterone levels.

Anemia and hematologic abnormalities are common symptoms of RED-S (termed "sports anemia"), albeit predominantly studied in endurance and ultra-endurance athletes, primarily runners (10). The anemia is multifactorial, with etiology including hemodilution, oxidative stress, iron deficiency, hematuria, and hemolysis from compressive action of muscles on capillaries. Prolonged levels of endurance exercise can cause intestinal hypoperfusion, ischemia, and loss of gastrointestinal barrier integrity, leading to positive fecal occult blood tests (11). Endoscopic evaluation is generally recommended to exclude other etiologies, but it is often unremarkable, as in this case. His anemia and positive fecal occult blood test were consistent with sports anemia, but to our knowledge, this has not been previously reported in endurance swimmers.

## CONCLUSION

Secondary hypogonadism with very low testosterone levels due to hypothalamic dysfunction from energy deficiency can be seen in male athletes with suspected RED-S due to overtraining syndrome and can be reversed with adequate energy availability, rest, and recovery. All athletes, regardless of sport, are at a risk for RED-S, not just those in weight-sensitive sports. There should be a high index of suspicion in all athletes with symptomatology including performance issues, regardless of sport and/or weight or body habitus.

## DISCLOSURE

The authors have no multiplicity of interest to disclose.

### REFERENCES


1. **Javed A, Tebben PJ, Fischer PR, Lteif AN.** Female athlete triad and its components: toward improved screening and management. *Mayo Clin Proc*. 2013;88:996-1009.
2. **West RV.** The female athlete. The triad of disordered eating, amenorrhoea and osteoporosis. *Sports Med*. 1998;26:63-71.
3. **Mountjoy M, Sundgot-Borgen J, Burke L, et al.** The IOC consensus statement: beyond the female athlete triad--relative energy deficiency in sport (RED-S). *Br J Sports Med*. 2014;48: 491-497.
4. **Mountjoy M, Sundgot-Borgen J, Burke L, et al.** RED-S CAT. Relative energy deficiency in sport (RED-S) clinical assessment tool (CAT). *Br J Sports Med*. 2015;49:421-423.
5. **Bhasin S, Brito JP, Cunningham GR, et al.** Testosterone therapy in men with hypogonadism: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2018;103:1715-1744.
6. **Burke LM, Close GL, Lundy B, Mooses M, Morton JP, Tenforde AS.** Relative energy deficiency in sport in male athletes: a commentary on its presentation among selected groups of male athletes. *Int J Sport Nutr Exerc Metab*. 2018;28:364-374.
7. **Mountjoy M, Sundgot-Borgen JK, Burke LM, et al.** IOC consensus statement on relative energy deficiency in sport (RED-S): 2018 update. *Br J Sports Med*. 2018;52:687-697.
8. **Mountjoy M, Sundgot-Borgen J, Burke L, Stellingwerff T.** Special issue: relative energy deficiency in sport (RED-S). In: *Metabolism*. IJoSNaE, ed. Vol. 282018.
9. **Tenforde AS, Barrack MT, Nattiv A, Fredericson M.** Parallels with the female athlete triad in male athletes. *Sports Med*. 2016;46:171-182.
10. **Cronin O, Molloy MG, Shanahan F.** Exercise, fitness, and the gut. *Curr Opin Gastroenterol*. 2016;32:67-73.
11. **Chiu YH, Lai JI, Wang SH, How CK, Li LH, Kao WF, Yang CC, Chen RJ.** Early changes of the anemia phenomenon in male 100-km ultramarathoners. *J Chin Med Assoc*. 2015;78:108-113.