

# Testosterone Administration During Energy Deficit Suppresses Hepcidin Concentrations and Increases Iron Utilization in Healthy Males (OR15-08-19)

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**Objectives:** Military personnel are exposed to periods of energy deficit and stress, which is typically accompanied by reductions in testosterone concentrations and declines in iron status. Exogenous testosterone administration may increase erythropoiesis and iron availability.

The objective of this study was to determine the effects of exogenous testosterone on iron homeostasis in healthy young males during energy deficit.

**Methods:** Fifty males ( $24.8 \pm 5.0$  y,  $78.6 \pm 12.2$  kg) completed this randomized, double-blind, placebo-controlled trial. Participants were provided a eucaloric diet during a 2-week free-living phase (day 1–14). Following the free-living phase, participants completed a 4-week live-in phase (day 15–42). During the live-in phase participants were randomized to 200 mg testosterone enanthate/week ( $n = 24$ ) or 1 mL sesame oil/week (placebo,  $n = 26$ ) and were in an energy- and exercise-induced energy deficit equal to  $53 \pm 4\%$ . Blood was collected on days

14 and 42 to determine concentrations of testosterone, hemoglobin, hematocrit, ferritin, hepcidin, and erythroferrone. Data are reported as change scores (mean  $\pm$  SD).

**Results:** Total testosterone concentrations increased with testosterone and declined with placebo ( $569 \pm 271$  nmol/L and  $-83 \pm 142$  nmol/L,  $P < 0.0001$ ). Testosterone attenuated the decline in hemoglobin ( $-0.04 \pm 0.7$  g/L and  $-0.6 \pm 0.8$  g/dL,  $P < 0.01$ ) and hematocrit ( $0.6 \pm 2.2\%$  and  $-1.3 \pm 2.1\%$ ,  $P < 0.01$ ) that occurred with placebo. Hepcidin ( $-3.7 \pm 5.0$  ng/mL and  $2.1 \pm 5.0$  ng/mL,  $P < 0.001$ ) and ferritin ( $-32.5 \pm 38.6$  ng/mL and  $15.4 \pm 41.2$  ng/mL,  $P < 0.0001$ ) were reduced with testosterone as compared to placebo. Erythroferrone ( $-0.5 \pm 2.1$  ng/mL and  $0.5 \pm 2.0$  ng/mL,  $P = 0.11$ ) did not differ when comparing testosterone to placebo.

**Conclusions:** Testosterone administration during energy deficit suppressed hepcidin concentrations and increased iron utilization in healthy young males. The reduction in hepcidin with testosterone administration appears to occur through an erythroferrone-independent mechanism.

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