Nature Reviews Urology **10**, 616 (2013); published online 8 October 2013; doi:10.1038/nrurol.2013.223

ANDROLOGY

Unique insight into the physiological functions of testosterone

A landmark study published in the *New England Journal of Medicine* details how researchers have teased out the physiological functions of different levels of testosterone in men. Moreover, the investigators found that some symptoms often attributed to testosterone deficiency are actually caused by a lack of oestrogen.

Joel Finkelstein and colleagues, from Massachusetts General Hospital, Boston, USA, report that testosterone levels regulate lean body mass, muscle size and strength, whereas oestrogen levels regulate fat accumulation. Both hormones contribute to sexual function, which encompasses both sexual desire and erectile function.

As men reach middle age, they often experience changes in body composition, energy levels, strength and sexual function that are commonly attributed to a decrease in testosterone. However, no-one has previously assessed the exact relationship between these symptoms and testosterone levels. Finkelstein *et al.* devised a study to artificially induce testosterone deficiency and oestrogen deficiency in healthy men, and analysed the hormone levels at which physiological dysfunction occurred.

Two groups of healthy men aged 20–50 years with normal serum testosterone levels were recruited for the study, and patients in both groups were treated with goserelin acetate to suppress the production of all reproductive hormones. Men in group 1 ($n = 198$) were randomly assigned to receive 1% testosterone gel at doses of 1.25 g, 2.5 g, 5 g or 10 g, or placebo gel (0 g) daily for 16 weeks. Men in group 2 ($n = 202$) were randomized in the same way, but all patients also received an aromatase inhibitor to suppress the conversion of testosterone to oestrogen.

Every 4 weeks, gonadal steroid levels were measured and questionnaires were administered for the evaluation of overall health and sexual function. Body fat and lean mass, thigh muscle area and lower-extremity strength were assessed at baseline and at the end of the study period.

Men without oestrogen deficiency (group 1) experienced a significant increase in body fat at low levels of testosterone (those who received 0 g, 1.25 g or 2.5 g) compared with men who received 5 g of testosterone. At very low doses of testosterone (0 g or 1.25 g), men also experienced a decrease in lean body mass and a reduction in thigh muscle area. Significantly reduced leg strength was observed in men who received placebo, compared with men receiving 2.5 g, 5 g or 10 g of testosterone daily. Decreased sexual desire was reported with each drop in testosterone level, whereas erectile dysfuntion did not occur until testosterone levels were very low (in men receiving 0 g).

Contrasting effects were reported by men in whom oestrogen production was blocked (group 2). These men experienced an accumulation of body fat at all testosterone levels; however, no effects additional to those caused by testosterone deficiency were observed on lean body mass, muscle size or leg strength. Sexual desire was significantly lower for men who received placebo than for men in the three highest dose groups, and erectile function was impaired in men who received placebo compared with all other groups.

This innovative study not only provides new information regarding the levels of testosterone needed for different functions, but also suggests that oestrogen deficiency is responsible for some of the symptoms of hypogonadism. The authors hope their data will prove useful for deciding when to use testosterone replacement therapy. However, they are careful to point out that the true nature of testosterone deficiency probably follows a continuum rather than threshold values, and the ultimate decision to treat each patient lies with the clinician.

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Original article Finkelstein, J. S. *et al.* Gonadal steroids and body composition, strength, and sexual function in men. *N. Engl. J. Med.* **369**, 1011–1022 (2013)