

mesenchymal, multipotent progenitor cells into the myogenic lineage and inhibit their differentiation into the adipogenic lineage. Testosterone binding to AR promotes the association of liganded AR with β -catenin and its translocation into the nucleus where it binds TCF-4 and activates Wnt-target genes, including follistatin, which blocks signaling through the transforming growth factor β pathway, thereby promoting myogenic differentiation of muscle progenitor cells. Testosterone may have additional effects on satellite cell replication and polyamine pathway, which may contribute to an increase in skeletal muscle mass.

Other indications for androgen therapy are in selected patients with anemia due to bone marrow failure (an indication largely supplanted by erythropoietin) or for hereditary angioedema.

Male Hormonal Contraception Based on Combined Administration of Testosterone and Gonadotropin Inhibitors

Supraphysiologic doses of testosterone (200 mg testosterone enanthate weekly) suppress LH and FSH secretion and induce azoospermia in 50% of Caucasian men and >95% of Chinese men. The WHO-supported multicenter efficacy trials have demonstrated that suppression of spermatogenesis to azoospermia or severe oligozoospermia (<3 million/mL) by administration of supraphysiologic doses of testosterone enanthate to men results in highly effective contraception. Because of concern about long-term adverse effects of supraphysiologic testosterone doses, regimens that combine other gonadotropin inhibitors, such as GnRH antagonists and progestins, with replacement doses of testosterone have been investigated. Regimens containing an androgen plus a progestin such as depo-medroxyprogesterone acetate, etonogestrel, or norethisterone enanthate have been highly effective in inducing azoospermia or severe oligozoospermia (sperm density <1 million/mL) in nearly 99% of treated men over a 1-year period. The combined regimens of testosterone plus a progestin have been associated with weight gain, acne, mood changes including depressed mood, libido changes, and decreased plasma high-density lipoprotein (HDL) cholesterol, and their long-term safety has not been demonstrated. One such trial of a combined regimen of testosterone undecanoate plus norethisterone