

**HormoneSynergy**  
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### Research and articles regarding testosterone pellet implants in men

- Brady BM, Waltoni M, Hollowi N, et al. Depot testosterone with etonogestrel implants result in induction of azoospermia in all men for long-term contraception. *Human Reproduction* 2004 19(11):2658–2667.
- Cantrill JA, Dewis P, Large DM, et al. Which testosterone replacement therapy? *Clin Endocrinol (Oxf)* 1984; 21:97-107.

*This study compared three different forms of testosterone replacement – intramuscular injection of mixed testosterone esters (250 mg), subcutaneous testosterone pellet implants (6 x 100 mg), and oral testosterone undecanoate (80 mg twice daily). In six men given oral testosterone, serum testosterone levels were markedly variable both between subjects, and within the same subject on different days. This is likely due to variability in absorption of oral testosterone undecanoate. In nine men given injected testosterone, serum testosterone levels rose to supraphysiological peak concentrations 24-48 hours after injection, followed by decline to baseline level after 2-3 weeks. In six men who received testosterone pellet implants, serum testosterone remained within the normal range for 4-5 months. Serum estradiol levels were within normal range in the oral and pellet implant group, but showed a supraphysiological peak 24-48 hours after injection. 5 alpha-dihydrotestosterone (DHT) levels paralleled those of testosterone, with DHT:T ratios highest for oral testosterone. The authors conclude that testosterone implants remain overall the most physiological form of replacement, and that pellets are well accepted with few side effects.*

- Conway A, Boylin L, Howe C, et al. Randomized clinical trial of testosterone replacement therapy in hypogonadal men. *Int J Andrology* 1988;11:247-264.

*15 men were given 3 treatment periods, each separated by a washout period. The treatments included IM injections of testosterone esters every 2 weeks, oral testosterone undecanoate, and subcutaneous testosterone pellets. Pellet implants produced the most prolonged, elevated total and free testosterone levels for up to 4 months. The authors concluded that pellet implants gave the closest approximation to steady-state, physiological delivery of the methods tested.*

- Dunning T, Ward G. Testosterone replacement therapy – perceptions of participants and partners. *Issues and Innovations in Nursing Practice* 2004:467-74.

*This study evaluated sense of well-being and sexual function in 10 men receiving testosterone pellet implants, 5 with partners and 5 without partners. Decreased testosterone levels had a statistically significantly different effect on libido at time zero between men with and without partners and on ability to sustain an erection, but the ability to achieve an erection persisted over the 6 months in both male groups.*

- Gooren L. New long-acting androgens. *World J Urol* 2003;21:306-10.

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*This article acknowledges the major goal of testosterone replacement therapy is to replace testosterone levels at as close to physiological concentrations as is possible. General agreements about such an androgen replacement therapy are (1) a delivery of the physiological amount of testosterone (3-10 mg/d); (2) consistent levels of testosterone, 5 $\alpha$ -dihydrotestosterone (DHT) and 17 $\beta$ -estradiol (E2) within normal physiological ranges; (3) a good safety profile without adverse effects on the prostate, serum lipids, liver or respiratory function; and (4) convenience in usage, patient-friendly, with a relative independence of medical services. The article discusses that pellets replicate the daily dosage of testosterone production in eugonadal men, with consistent levels for 4-6 months after implantation.*

- Gooren L, Bunk M. Androgen replacement therapy: present and future. *Drugs* 2004;64(17):1861-1891.
- Hair W, Wu F, Lincoln G. An investigation of the effectiveness of testosterone implants in combination with the prolactin inhibitor quinagolide in the suppression of spermatogenesis in men. *Human Reproduction* 2003;18(4):749-755.
- Handelsman DJ, Mackey MA, Howe C, et al. An analysis of testosterone implants for androgen replacement therapy. *Clin Endocrinol (Oxf)* 1997; 47: 311-6

*Review of 13 years of experience (220 men, 973 implant procedures) using testosterone pellets in order to identify pattern of usage, including continuation rates, and adverse events, including extrusion. Bleeding, infection, and fibrosis were rare; extrusion was related to work or procedure problems. Overall continuation rate with pellets increased with duration of use, 88% after the first implantation, 95% after the third.*

- Handelsman DJ, Conway AJ, Howe CJ, et al. Establishing the minimum effective dose and additive effects of depot progestin in suppression of human spermatogenesis by a testosterone depot. *J Clin Endocrinol Metab* 1996;81:4113-4121.
- Handelsman DJ, Conway AJ, Boylan LM. Suppression of human spermatogenesis by testosterone implants. *J Clin Endocrinol Metab* 1992;175:1326-1332.
- Handelsman DJ, Conway AJ, Boylan LM. Pharmacokinetics and pharmacodynamics of testosterone pellets in man. *J Clin Endocrinol Metab* 1990;71:216-222.

*Pharmacokinetics and pharmacodynamics of subcutaneous testosterone pellets were compared in this prospective, cross-over clinical trial. Plasma, free and total testosterone, SHBG, LH, and FSH were measured before and at monthly intervals for at least 6 months after 111 implantations in 43 men. Total and free testosterone levels were shown to peak at month one, and were maintained for 4-6 months depending on dosage. The authors conclude that testosterone pellets provide "very satisfactory depot androgen replacement exhibiting many desirable features for androgen replacement."*

- Jockenhovel F, Blum W, Vogel E, et al. Testosterone substitution normalizes elevated serum leptin levels in hypogonadal men. *J Clin Endocrinol Metab* 1997;82:2510-2513.

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- Jockenhovel F, Vogel E, Kreutzer M, et al. Pharmacokinetics and pharmacodynamics of subcutaneous testosterone implants in hypogonadal men. *Clin Endocrinol (Oxf)* 1996;45:61-71.

*50 men received testosterone implants for a total of 112 implantations. The only side effect noted was extrusion of pellets in 3 men. When given the choice, all patients except one preferred testosterone pellets to previous testosterone replacement methods. The authors conclude that "testosterone pellets are the androgen formulation with the longest biological action and strongest pharmacodynamic efficacy in terms of gonadotrophin suppression. The pharmacokinetic features are advantageous compared to other testosterone preparations and patient acceptance is high."*

- Kelleher S, Howe C, Conway A, Handelsman. Testosterone release rate and duration of action of testosterone pellet implants. *Clin Endocrinol* 2004;60:420-428.
- Kelleher S, Conway A, Handelsman D. A randomized controlled clinical trial of antibiotic impregnation of testosterone pellet implants to reduce extrusion rate. *European J Endocrinol* 2002;146:513-518.
- Kelleher S, Conway A, Handelsman D. Influence of implantation site and track geometry on the extrusion rate and pharmacology of testosterone implants. *Clin Endocrinol* 2001;55:531-536.
- Kinniburgh D, Zhu H, Cheng L, et al. Oral desogestrel with testosterone pellets induces consistent suppression of spermatogenesis to azoospermia in both Caucasian and Chinese men. *Human Reproduction* 2002;17:1490-1501.
- Leichtnam M, Rolland H, Wuthrich P, et al. Testosterone hormone replacement therapy: state-of-the-art and emerging technologies. *Pharmaceutical Research* 2006;23:1117-1132.
- Nieschlag E, Behre H, Bouchard P, et al. Testosterone replacement therapy: current trends and future directions. *Human Reproduction Update* 2004;10:409-419.
- Oettel M. The endocrine pharmacology of testosterone therapy in men. *Naturwissenschaften* 2004;91:66-76.
- Sader M, McCredie R, Griffiths K, et al. Oestradiol improves arterial endothelial function in healthy men receiving testosterone. *Clin Endocrinol* 2001;54:175-81.
- Schubert M, Bullmann C, Minnemann T, et al. Osteoporosis in male hypogonadism: responses to androgen stimulation differ among men with primary and secondary hypogonadism. *Hormone Research* 2003;60:21-28.
- Vest S, Howard J. Clinical Experiments with Androgens. *JAMA* 1939;113(21):1869-1872.

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*This article was published in 1939 discussing the use of testosterone pellet implants and case studies of two hypogonadal males.*

- Wang C, Swerdloff R. Male contraception. *Best Practice and Research Clinical Obstetrics and Gynaecology* 2002;16(2):193-202.
- Zacharin M, Pua J, Kanumakala S. Bone mineral density outcomes following long-term treatments with subcutaneous testosterone pellet implants in male hypogonadism. *Clin Endocrin* 2003;58:691-95.

*37 men with primary or secondary hypogonadism received long-term (mean 6.6 yrs) subcutaneous testosterone pellet implants. Bone density for treated men was the same as age-matched men not needing treatment. The authors conclude that subcutaneous testosterone pellet implants are safe and acceptable to the patient, and result in adequate bone mass and maintenance of normal bone mineral density. They also surmise that sustained physiological levels of testosterone via pellets may contribute to increased androgen effect at the receptor level.*

- Zacharin MR, Warne GL. Treatment of hypogonadal adolescent boys with long acting subcutaneous testosterone pellets. *Arch Dis Child* 1997; 76: 495-9.
- Zitzmann M, Nieschlag E. Hormone substitution in male hypogonadism. *Molecular and Cellular Endocrinology* 2000;161:73-88.