

What male contraceptives currently exist and what is the outlook for new male contraceptives?

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Vasectomy and condoms

Efficacious contraceptive options currently available to men are vasectomy and condoms, which together account for 20-30% of all current contraception in the US. Vasectomy is a safe, simple, outpatient surgery performed under local anesthesia in which the vas deferens is severed and the ends ligated and/or cauterized through a small scrotal incision. Vasectomies are highly effective with a failure rate of less than 1%. The “no scalpel” technique, in which a single puncture is made midline in the scrotal raphe with scissors, is probably superior to older techniques. Drawbacks to vasectomy include a delay in the onset of azoospermia of several months, pain and rare infections. While post-operative pain resolves quickly, some men will experience chronic scrotal discomfort. Vasectomy is most appropriate for men who no longer wish to father children, since surgical reversal does not always restore fertility.

Condoms made of animal intestine have been used as a means of male fertility control for several hundred years. Since 1920, most condoms have been made of latex rubber, which affords some protection against sexually transmitted diseases including HIV/AIDS. However, condoms have a marginal contraceptive efficacy with pregnancy rates approaching 10-15% per year. This is mainly due to improper or inconsistent usage, although condom breakage can occur. In addition, latex allergies can be a problem for some users. For these men, polyurethane condoms are a reasonable alternative.

Experimental male contraceptives

Efforts are ongoing to develop new methods of contraception for men. The approach that has been tested most extensively involves the administration of testosterone, which functions as a contraceptive by suppressing the secretion of luteinizing hormone and follicle-stimulating hormone from the pituitary (Chapter 8; Fig. 1). This deprives the testes of the signals required for spermatogenesis and results in markedly decreased spermatogenesis and effective contraception in most men. Male hormonal contraception is well tolerated, fully reversible, and appears to be free from serious adverse effects. Unfortunately, regimens in which testosterone is

used alone fail to completely suppress spermatogenesis in some men, meaning that the potential for fertility persists. Because of this, combinations of testosterone and progestins, which synergistically suppress gonadotropins, have been studied (see below).

Normally, sperm concentrations exceed 15 million/ml. The absence of sperm in the ejaculate, a condition called azoospermia, makes fertilization impossible. A sperm concentration below 1 million/ml., or “severe oligospermia,” is associated with a pregnancy risk of approximately 1% per year. Therefore, achieving severe oligospermia in all men is considered a reasonable goal of male contraceptive development. Because male hormonal contraceptives inhibit sperm production, 2-3 months elapse until the sperm concentration in most men is fully suppressed. In addition, for unknown reasons Asian men exhibit higher rates of azoospermia than non-Asian men.

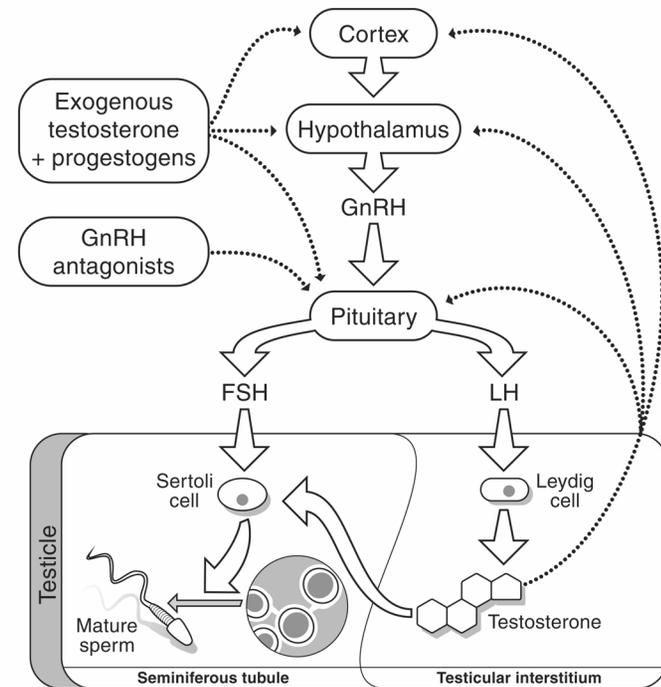


FIG. 1. Spermatogenesis and male hormonal contraception. Solid arrows, promotes spermatogenesis; dashed arrows, inhibits spermatogenesis. Abbreviations: FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone. Negative feedback of testosterone occurs at the level of the pituitary, the hypothalamus and the cortex.

The World Health Organization conducted two large, multicenter trials of injections of testosterone enanthate for male contraception. The first enrolled 271 subjects who were administered 200 mg testosterone enanthate by intramuscular injection weekly for six months. Sixty percent of the men in this study became azoospermic, and an additional 30% became severely oligospermic. The fertility of 119 of the azoospermic men was then tested in a 12-month efficacy phase. In these couples, only 1 pregnancy occurred, corresponding to a pregnancy rate of less than 1%.

The second study examined the fertility of men who became either azoospermic or oligospermic (variably defined in this study as less than 3-5 million sperm/ml. ejaculate) with injections of 200 mg of testosterone enanthate weekly. Of a total of 399 mostly Asian men, all but 8 (2%) became oligospermic or azoospermic. There were no pregnancies fathered by the men who became azoospermic, and fertility was reduced to 8.1 pregnancies per 100-person years in the men who suppressed to less than 3 million sperm/ml. Therefore, the overall failure rate was 3.4%, for an overall contraceptive efficacy of 96.6%. All subjects returned to normal after the testosterone injections were discontinued. These two studies demonstrated that testosterone is safe, reversible and highly effective in a majority of men. However, they also demonstrate that pregnancy is possible even at very low sperm concentrations.

Side effects in these trials included a 10-20% decrease in serum HDL-cholesterol, occasional acne and small, reversible reductions in testicular volume. Importantly, cognitive function, well-being, quality of life and sexual function were not adversely affected. The regimen was found to be better than expected by a majority of subjects; however, the requirement for weekly intramuscular injections led twelve percent of the subjects to discontinue participation.

As a result, recent research in male hormonal contraception has focused on formulations of testosterone that can be administered less frequently, such as testosterone undecanoate. Monthly injections of 500 mg of testosterone undecanoate were studied in 308 Chinese men, 299 of whom suppressed to sperm concentrations below 3 million sperm/ml. Two hundred and ninety six of these men went on to use the testosterone undecanoate injections as a sole means of contraception for one year. In these couples, only one pregnancy occurred, for an overall contraceptive efficacy of 97%. Testosterone undecanoate has also been combined with the progestin etonogestrel in an implant formulation in 350 subjects with greater than 90% suppression of spermatogenesis to less than 1 million sperm/ml.

Why some men fail to fully suppress their spermatogenesis despite profound suppression of gonadotropins is unknown. Since there are few

significant differences in the gonadotropin levels during treatment among men who suppress to azoospermia and those who do not, the degree of gonadotropin suppression itself is not the answer. Therefore, genetic, dietary or other factors likely play a role. Clearly, further studies of the control of spermatogenesis are needed.

Summary

Vasectomy and condoms are widely used, effective forms of male contraception. Experimental testosterone-progestin based male hormonal contraceptives reversibly suppress human spermatogenesis without severe side effects in most men; however, a uniformly effective regimen has remained elusive. Nevertheless, it is possible that improvements in this approach may soon result in the clinical introduction of a safe, reversible and effective form of male contraception.

Suggested reading

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