# Male contraception

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Although female contraceptives are very effective at preventing unintended pregnancy, some women can not use them because of health conditions or side-effects, leaving some couples without effective contraceptive options. In addition, many men wish to take active responsibility for family planning. Thus, there is a great need for male contraceptives to prevent unintended pregnancies, of which 80–90 million occur annually. At present, effective male contraceptive options are condoms and vasectomy, which are not ideal for all men. Therefore, efforts are under way to develop novel male contraceptives. This paper briefly reviews the advantages and disadvantages of condoms and vasectomies and then discusses the research directed toward development of novel methods of male contraception. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)

**Key Words:** Spermatogenesis, testes, condoms, vasectomy, unintended pregnancy, spermatozoa, novel male contraceptives

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## OVERVIEW OF MALE REPRODUCTIVE PHYSIOLOGY

Production of mature sperm in the human testes takes ~72 days (1). After puberty, sperm production is continuous and occurs in four distinct phases: 1) a mitotic phase in which the stem cells, the spermatogonia, give rise to diploid spermatocytes; 2) a meiotic phase in which spermatocytes double their chromosome complement and undergo two cycles of cell division resulting in haploid spermatids; 3) spermiogenesis, which involves spermatid nuclear condensation and flagellum formation; and 4) spermiation, which involves release of the spermatozoa into the tubular lumen (2). Storage and further maturation of sperm take place in the epididymis. Sperm aspirated from the cauda epididymis are capable of fertilizing an egg in vitro (3). The testes also synthesize testosterone, a steroid hormone. Testosterone is necessary for sperm production and maintains sexual function as well as muscle and bone mass (4). Testosterone is produced by Leydig cells in the interstitium of the testes when stimulated by LH. Sperm production occurs in the seminiferous tubules, where the sperm are nurtured by Sertoli cells stimulated by FSH and high concentrations of intratesticular testosterone (Fig. 1A) (5). Given the physiology of sperm production, a male contraceptive can work in one of several ways:

1. By preventing sperm from reaching the egg by physical barriers (condoms, vasectomy, and experimental vas occlusion methods).
2. By preventing sperm production (experimental hormonal and nonhormonal methods).
3. By killing or inhibiting the function of sperm or the sperm's ability to bind the egg after ejaculation (spermicides, experimental antimotility agents).

This last category of contraceptives, such as spermicides, are usually intended to be used intravaginally by the female and are therefore more properly considered female contraceptives, so they will not be discussed further in this review. Instead, the present article will describe the efficacy of existing methods of male contraception and then discuss the research directed toward development of novel methods of male contraception that function either by inhibiting sperm production or by preventing sperm from reaching the female reproductive tract.

## CURRENTLY AVAILABLE MALE CONTRACEPTIVE METHODS

### Vasectomy

Vasectomy is a simple outpatient surgery performed under local anesthesia, in which the vas deferens is surgically interrupted bilaterally through a small scrotal incision. There are ~500,000 vasectomies performed in the United States yearly and worldwide >50 million men have undergone the procedure (6), although there are significant cultural differences in the acceptability of this procedure in different settings. Vasectomies are highly effective, with a failure rate <1% and a low rate of complications (Table 1) (7, 8). The "no-scalpel technique," developed in China (9) that relies on a single midline puncture in the scrotal raphe with the use of scissors, had been widely adopted (10, 11). Drawbacks to

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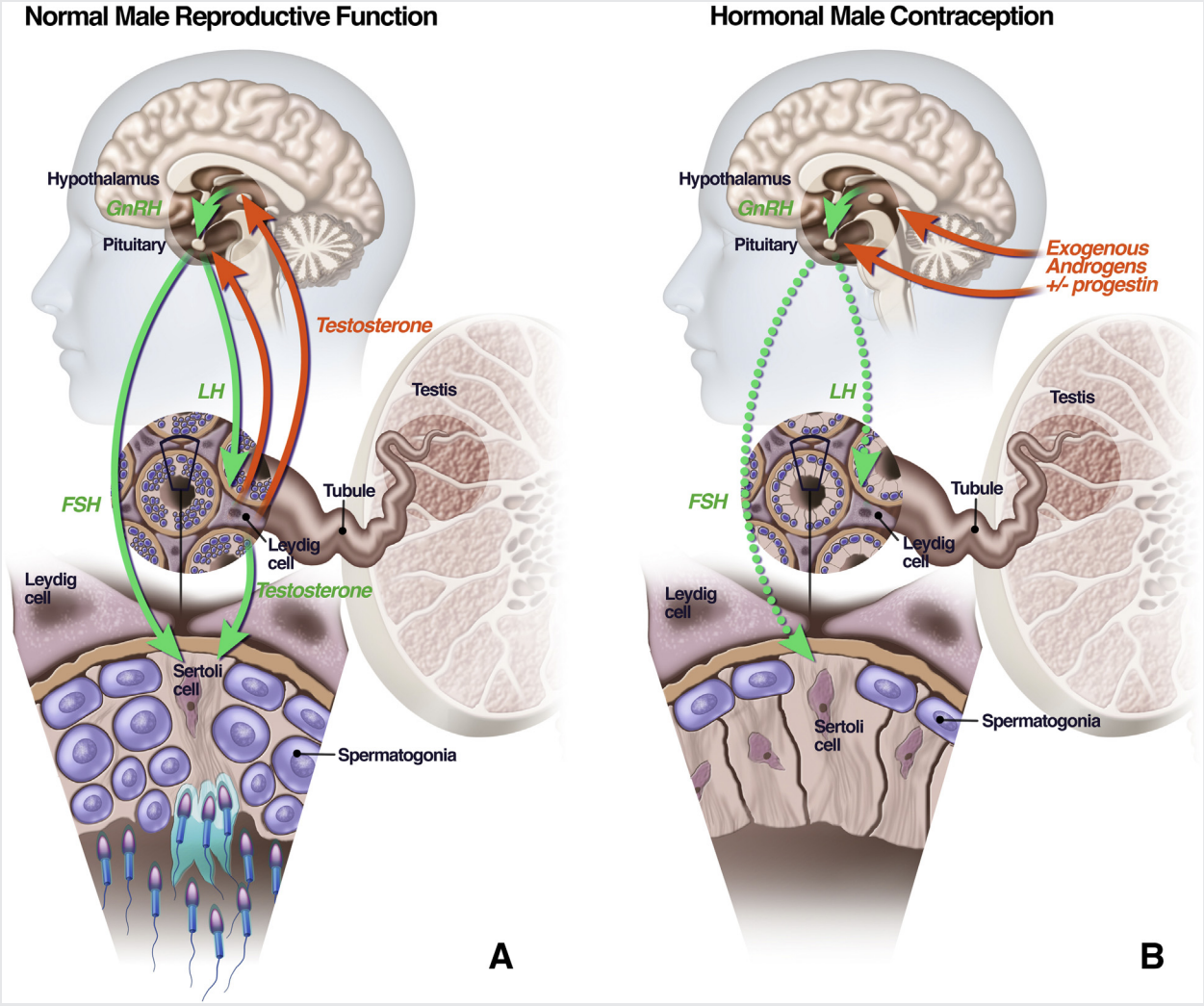
**FIGURE 1**




(**A**) Normal function of the hypothalamic-pituitary-testicular axis, with FSH and LH stimulating the testes to produce sperm and testosterone, and testosterone providing feedback regulation of FSH and LH production in the pituitary. (**B**) Suppression of FSH and LH production by exogenously administered androgens and progestins, which lowers FSH and LH concentrations, depriving the testes of the signals required for sperm production and leading to contraception.

*Amory. Male contraception. Fertil Steril 2016.*

vasectomy include a delay in the onset of azoospermia of 3–4 months, postoperative pain, and rare infections. Although most postoperative pain resolves quickly, 10%–15% of men experience chronic testicular discomfort (12). In one study of such men, 27 out of 33 had relief of their discomfort after reversal of the vasectomy (13).

Vasectomies are most appropriate for men who do not desire any future fertility. However, 3%–5% of men with vasectomies do eventually request reversal, usually because of remarriage (14). For this reason, some urologists recommend freezing a semen sample before the procedure. Vasectomy reversal, or vasovasostomy, restores fertility in most cases; however, rates of pregnancy vary from 50% to 75% depending on the length of time between the vasectomy and the vasovasostomy for two reasons. First, in some men vasovasostomy is unable to restore patency of the vas, especially if >8 years have elapsed since the original vasectomy (15). Second, 20%–30% of men remain infertile despite restored patency of the vas, as documented by imaging techniques, probably because of the presence of antisperm antibodies (16). For these reasons, vasectomy can not be recommended as a truly reversible method of contraception. Vasectomy is safe in terms of overall male health. Reports of associations between vasectomy and cardiovascular disease and prostate cancer first reported in the 1980s have proven to be incorrect (17, 18). In summary, vasectomy is highly effective and very safe. The major drawbacks are chronic testicular discomfort in some men and the inability of vasovasostomy to reliably restore fertility in all cases when desired.