## The Male Contraceptive Pill

While women have hormonal contraceptive options that include pills, patches, rings, injections, implants, and intrauterine devices, development of a contraceptive option for men has been elusive. Theoretically, the hormonal methods work similarly in women or men – a high dose of a progestin suppresses the production of the egg or sperm. In men, high levels of intratesticular testosterone (~50 fold higher than normal range serum levels) are required to support sperm production. Men require a much lower amount of testosterone to circulate in their blood to maintain other normal functions (libido, ejaculation, maintenance of muscle mass). If men are given a progestin, intratesticular testosterone drops below the spermatogenic threshold and sperm production stops. However, serum testosterone must remain at a level that is sufficient to support other functions. There lies the challenge for an oral regimen. Natural testosterone (T), taken orally, is cleared very quickly from the body, requiring men with low testosterone to take a pill multiple times a day to maintain an adequate serum levels. Chemical modifications to T can cause an oral drug to last longer, but some synthetic testosterone drugs have caused liver toxicity, rendering them unacceptable. The development of the once-a-day "Pill" form of T remains challenging. New Selective Androgen Receptor Modulators (SARMs) have been developed with sufficient bioavailability that a single daily oral dose can maintain androgen-dependent functions other than spermatogenesis. The SARM drugs also have progestin receptor activity and can suppress gonadotropin secretion and reduce intratesticular testosterone production, resulting in suppression of sperm production. Early studies have demonstrated that repeat daily dosing of the new drugs appears to be well-tolerated and suppresses serum gonadotropin levels. One or more of these new SARMs may be able to control sperm production from a once-a-day oral dose regimen.

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## **Author:**

Diana Blithe NICHD, National Institutes of Health United States