

# **Beyond Johnny and the Snip: Investigating the Male Contraceptive Pill**

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In the UK, the dominant form of contraception is “the pill”; at 28% usage rate being more popular than condoms (24%), sterilisation (10%) or other forms of contraception. The pill is particularly popular among younger age groups, being taken by two-thirds of 20-34 year old women. (Office for National Statistics 2008). There are various types of pill, though all have essentially the same mechanism and effects, and are collectively known as “the pill”. The pill contains hormones which prevent fertility by a variety of methods, and is reported to be over 99% effective.

The success of the female pill might surely beg the question: why is there no male equivalent? Currently, contraceptive options for males are condoms, vasectomy, and abstinence. Condoms therefore are the only contraceptive technique for men which do not incorporate an unrealistic level of co-operation (abstinence) or a drastic and irreversible procedure (vasectomy). However, even condoms have their drawbacks, and a male contraceptive pill would be a well-embraced – and lucrative – invention. This article will investigate the male pill, its development and future.

Male (and female) reproduction depends on hormonal control. Testosterone is the most important androgen (male hormone), made in the Leydig cells of the testes. This hormone is essential for production of sperm, as well as secondary sexual characteristics, such as body hair etc. Testosterone levels are controlled by luteinising hormone (LH) produced in the pituitary. LH itself is controlled by gonadotrophin-releasing hormone (GnRH) produced by the hypothalamus. This sequence allows testosterone to have negative feedback control: increased levels result in reduced GnRH levels, suppressing further testosterone production. Males also require oestrogen – classically thought of

as a “female” sex hormone. Oestrogen has been shown to be important in fertility, sex drive, behaviour and general health (Simpson *et al* 2005).

These hormones provide a seemingly solid basis for a male pill. Increasing testosterone in men should lead to a negative feedback process beginning with reduced GnRH levels, subsequently lowered LH and follicle stimulating hormone (FSH) levels. These would result in a lack of mature male sperm, and hence, infertility (McLachlan *et al* 2002).

Natural testosterone given by a pill or injection is degraded quickly in the body. However testosterone ethanate (a synthetic ester of testosterone) has been shown to be effective by use of a skin patch. In addition, although the testosterone level produced by the testes would drop, the contraceptive dose maintains body levels high enough so as not to affect sex drive and sexual ability (Crust *et al* 1989).

Unfortunately, in clinical trials with testosterone ethanate, although it did suppress production of sperm, it did not result in azoospermia (immeasurable sperm levels). Only around 50% of men reached this level, a failure rate obviously unacceptable to be a useful birth control method (Anderson *et al* 1996).

Another approach has been to give testosterone with another hormone that prevents sperm production: the combination lowering the failure rate to acceptable levels. In one trial, an antagonist of GnRH was used with testosterone: this method actually proved to be effective. However, this technique was not feasible as a widely available method, since the antagonist is very expensive, and needs to be given as a weekly intramuscular injection, which would have low compliance rates.

A further study used testosterone patches with desogestrel (a hormone used in female contraceptives): the testosterone patches again used to combat reduced naturally produced testosterone (Morton Hair *et al* 2001). As before, the study showed that success rates were far too low to be a suitable

contraceptive, with only 7 of 17 patients becoming azoospermic and a 57% success rate at the highest dose given. However, in a study by Kinniburgh *et al* (2002), all Caucasian men in the trial achieved azoospermia with desogestrel pills and testosterone pellets (though the success rate was lower in the Chinese members of the study group).

Hormonal implants have also been tested: a study trialled an implant releasing a progesteron from a rod under the skin (in the arm). Again, this was an effective method, but resulted in lowered testosterone levels. This was an unacceptable side-effect for many of the men in the study, as reduced testosterone levels can lead to loss of male characteristics such as facial hair, and even breast development. To combat the effects of a reduced level of testosterone, they were given injections of the hormone every 4-6 weeks. This method was effective, but does not have an acceptable level of ease for the patient. Therefore it does not appear to have the potential of the female pill, which is essentially very straightforward and safe to use (Brady *et al* 2006).

Any method utilising increased androgens will have certain problems. It takes about 3 months for the treatment to start being effective, and another 3-4 months after stopping treatment to restore fertility levels. The studies mentioned also demonstrate that effectiveness of hormonal treatments is widely variable, with the practicalities of treatment being problematic (Aitken *et al* 2008). Therefore non-hormonal methods have been investigated.

One such approach is to use an immune response to attack the sperm, egg or zygote. For example, there is a calcium channel found in sperm tails – and only in sperm tails – which is vital in allowing the tail to beat strongly and the sperm to swim. This channel was disrupted in mice (by genetic engineering), who were infertile, though otherwise healthy (Clapham *et al* 2007). Because genetically engineering men to lack this gene is a little unfeasible (!), there are approaches to try and develop antibodies which specifically target the protein comprising this channel. Though in theory this might work, it is not yet known how quickly this treatment would take to reach effective therapeutic levels, and how long it would take to restore fertility after cessation of treatment.

In 2006, it was reported that a new male contraceptive had been discovered. This pill is designed to be taken shortly before sex, as –not containing hormones - the effects last just a few hours. It works by preventing ejaculation – though supposedly does not adversely affect the male’s sexual ability or desire. This pill then, has arguably the ideal characteristics of a contraceptive pill (short-lived effects, does not adversely affect sexual functioning, and does not need to be taken on a daily basis). The research, at King’s College London, is yet to be published but has been picked up by newspapers. It will be interesting to see whether this or other new developments have the potential to become a major new contraceptive method.

Finn (2007) describes some other possible methods. “Reversible inhibition of sperm under guidance” (RISUG) involves an injection of styrene maleic anhydride into the vas deferens – a tube which the sperm moves along in preparation for ejaculation. This leads to sterility, until a second injection restores fertility. This method is currently in Phase III testing (on human subjects). Vas-occlusive contraception involves the temporary blockage of the vas deferens. Once the blockages are removed, fertility is regained.

The scrotum is located outside the body so that the testes are at a temperature lower than body temperature. One contraceptive method involves short term heating of the testicles to a high temperature to prevent sperm formation (Male Contraceptives, 2009). This method has not been completely investigated, and one wonders how attractive such a method might be to men.

It should be added that there is some uncertainty over what the effect of a male contraceptive pill might have on sexually transmitted infections. This is not necessarily a direct effect, but results from a change in condom usage. The condom, unlike the female pill and presumably a male pill, is effective in reducing transmission of these diseases. If a male pill were to become available and widespread, there might then be implications and a risk of rises in STIs, as condom use declines. Whilst a subjective view, with the rise in STIs over the last decade or so this is surely an important issue.

The male system constantly produces sperm, whereas the female system only releases one egg a month: it is relatively easy to block this short period of fertility each month in females, but harder to combat males' continual fertility. Despite some concerns about male reliability of taking such a pill, Glasier *et al* (2000) showed that 98% of women would trust their partners in taking the pill, with an average 87% of women thinking the male pill would be a good idea. Whilst this might not indicate actual reliability, it surely emphasises the potential for the market.

A contraceptive pill should have short term effects (yet also allow a dose to be missed without having effectiveness compromised); have no serious side-effects, and be highly effective (over 99%). The female pill has all these characteristics, but a male pill possessing these seems some way off. Numerous methods are being investigated, with varying degrees of success. Further results from on-going studies should be interesting to see. If successful, there will probably be a considerable amount of time before such a product is widely available and publicised. Change might well be coming, but for the moment, it seems the pressure of contraception is still largely on women.

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