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New Approaches to Male Contraception

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The world population, currently estimated to be over seven billion, is expected to double in less than four decades. A recent survey shows that the majority of today's young men in many countries are willing to take full control of their fertility [1]. However, the contraceptive options available to them that primarily involve male physiology have not changed in the past century. Ever since the approval of the birth control pill for women in the 1960s, scientists have been hoping for a male equivalent. It has however been a difficult road, in part, because of the science of the male reproductive system [2]. It is relatively easier to control a monthly event of ovulation in women than to regulate the production of millions of fertile spermatozoa every single day in post-pubertal men. Thus, the contraceptive options available to men are still limited to the traditional approaches of abstinence and timely withdrawal (*coitus interruptus),* the barrier method of the use of condoms [3,4] or the surgical method of vas occlusion or vasectomy [5,6].

If not defective and used correctly, condoms can protect from unwanted pregnancies as well as sexually transmitted diseases [3,4]. However, condoms and the two traditional approaches mentioned above, have relatively high typical use failure rates, whereas vasectomy is largely irreversible [5,6] and not suitable for younger men. Thus, providing a safe, effective, reversible and affordable contraceptive for men has remained an elusive goal. In this editorial, I will briefly describe new hormonal and non-hormonal approaches that are at various stages of research and development and may one day be used to regulate male fertility. I will describe a male oral pill that is currently available to men in Indonesia. My intention is also to describe three intra-vas approaches that will soon be available to men in multiple countries to regulate their fertility. The intra-vas approaches will be effective, affordable and reversible. Finally, I will mention, "sperm-switch", the latest invention designed to allow men to turn the switch on/off and decide when to ejaculate spermatozoa during coitus.

When the question of new contraceptives for men is discussed, many wonder how many men will use them. Accumulated data suggest that approximately 33% of men use currently available contraceptives [7] which are not very effective. Thus, it is reasonable to argue that the availability of safe, effective, reversible and user friendly male contraceptives will encourage many more men to use them, and take full control of their fertility.

Progress in male reproductive technology is a crucial part of controlling population growth. This will require a serious commitment and resources from governments of all nations, and resources from both small and large pharmaceutical companies to invest generously in the research and development of the male contraceptive field to meet the growing needs of men. Since any failure in male contraception has a personal consequence for women, serious concerns and uncertainties remain whether women who are not in a stable relationship will trust a man who claims to be using a male contraceptive. These concerns have prevented many drug companies from generously providing funds for the research and development of new contraceptives for men. Many drug companies are also reluctant to invest in male contraceptive products intended for healthy men who may use them for several decades, raising the possibility of unintended side effects on their health. The pharmaceutical companies may need incentives from the government to assure their full participation in the field of male contraception. This type of collaboration from various groups is expected to hasten the process of providing men of all ages with new and improved contraceptives.

The purpose of any male contraceptive is to either prevent sperm from reaching the egg or prevent sperm-egg interactions that lead to the formation of a zygote and pregnancy [8]. The male contraceptives can be achieved by: I) preventing/suppressing sperm formation and development (spermatogenesis) in the testes [9,10]; II) blocking their maturation in the epididymides [11]; III) interfering with the sperm capacitation in the female genital tract [12]; IV) preventing sperm from reaching the *in vivo* site of fertilization; and V) interfering with sperm functions necessary for normal fertilization [13,14]. The contraceptive options currently available to men are all based on approaches that prevent sperm from reaching the egg, using either device-free traditional approaches of abstinence or withdrawal [15] or barrier approaches of the use of condoms [3,4] and vasectomy [5,6]. No new male contraceptives have been introduced in the past century.

Based on the current knowledge of spermatogenesis [9,10], investigators are working on hormonal and non-hormonal approaches to prevent/suppress spermatogenesis and develop new and readily available contraceptives to control male fertility. Two hormonal approaches that have been tried on men include using a combination of progestin and androgen or a high dose of testosterone [16]. The progestin is supplemented with androgen because if administered alone, it can cause the loss of libido due to its effect on testosterone deprivation [17]. Though the hormonal approach is within our reach, two major hurdles remain. First, the approach shows ethnic differences between Chinese men (>90 responsive) compared to Caucasian men (<60% of Europeans, Americans and Australian men are responsive). Second, the cost effectiveness of the hormonal approach. These are serious hurdles which make it difficult to predict the future of hormonal-based contraceptives for men.

Non-hormonal approaches include some natural [18-21] and synthetic compounds [22,23] that have ability to either inhibit/suppress spermatogenesis or interfere with the sperm function(s) necessary for normal fertilization. These agents have been described in an earlier article [24]. Research on these compounds is still at the basic science stage; many more years of basic and clinical work is needed before these compounds can be approved as safe and effective agents to control male fertility.

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An orally effective contraceptive pill has been approved in Indonesia for use by men. The pill, when taken by men 30-40 minutes before coitus, prevents pregnancy by inhibiting multiple enzymes on the sperm head. The inhibition prevents spermatozoa from penetrating the egg's extra cellular coat, the zona pellucida, and fertilizing the egg [24]. The pill contains a purified agent from the leaves of the plant Gandarusa. There are no published reports on the biologically active agent of the pill; however, according to Indonesian government sources, the purified compounds, when used by men in the form of a pill, prevent pregnancies. The pill became available to Indonesian men by prescription in 2014. I am hopeful that world-wide collaboration will soon begin so the pill can be available around the world. Additional details about the pill can be found by searching "Indonesian male pill" using Google or another comparable internet search engine.

Two vas-based male contraceptive approaches have undergone advanced clinical trials and are either approved or will soon be approved for use by men in multiple countries. These are: I) the reversible inhibition of sperm under guidance (RISUG) approach is being tried in India and uses the non-toxic chemical maleic anhydride dissolved in dimethyl sulfoxide (DMSO). Within minutes after the solution is injected into the lumen of the vas deferens tubes, the chemical polymerizes and anchors to the inner walls of the vas tubes, partially or fully closing them and preventing spermatozoa from going through the tubes [25]. The poly-electrolytic nature of the chemical kills sperm cells when they come in contact with the chemical [26]. The approach can be safely reversed by the injection of DMSO or sodium bicarbonate (baking soda) that solubilizes the chemical and flushes it out of the vas tubes. The approach has undergone advanced clinical trials under the supervision of the government of India and has either been approved or will soon be approved for use by Indian men.

An intra-vas device (IVD), introduced by Chinese researchers, blocks the flow of sperm through the vas tubes. The new generation of IVD uses tiny preformed polyurethane implants filled with a medical grade nylon mesh (sieve) to capture spermatozoa in the vas tubes [27]. The flow of sperm can be restored by removing the implants. The approach has undergone multi-center clinical trials in China with good efficiency and proven reversibility. The approach is expected to be approved for use by Chinese men in 2016.

Finally, the RISUG approach described above is gathering interest beyond India. In 2010, Parsemus, a not-for-profit organization in the USA, bought the international rights to the RISUG technology. The approach has been renamed as Vasalgel, a multi-year male contraceptive. As in the RISUG approach, a maleic anhydride solution is injected into the vas tubes. The chemical polymerizes and becomes gel which anchors to the inner walls of the vas. The gel allows fluid from semen to pass through the vas tubes but retains spermatozoa. If a man wishes to restore his fertility, the gel is flushed out of the vas tubes as in the RISUG approach. The Vasalgel approach has completed basic research and toxicology testing in the USA, and is expected to be approved by the Food and Drug Administration (FDA) for use as a safe and reversible contraceptive for men by 2017.

The latest addition to male contraceptive approaches is to install a valve on the spermatic duct. The so-called "sperm-switch" can be turned on/off to control the flow of sperm and male fertility. This is a new invention, and when approved could change men's reproductive future. Interested readers can find more details about this approach by searching the internet with Google or a comparable internet search engine.

In summary, I have attempted to write an overview of the current status of research and development on many promising possibilities for the regulation of male fertility. I believe that intra-vas approaches described in the editorial will provide safe, efficient, reversible and affordable contraception for men within the next two years. The availability of these contraceptives will allow many men to take full control of their fertility.

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References

1. Heinemann K, Saad F, Wiesemes M, White S, Heinemann L (2005) Attitudes toward male fertility control: results of a multinational survey on four continents. Human Reprod 20: 549-556.
2. Tulsiani DRP, Abou-Haila A (2008) Male contraception: an overview of the potential target events. Endocr Metab Imm Disorder-Drug Targets 8: 122-133.
3. Steiner MJ, Cates W Jr (2006) Condoms and sexually transmitted infections. N Eng J Med 354: 2642-2643.
4. Winer RL, Hughes JP, Peng O, O'Reilly S, Kiviat NB, et al. (2006) Condom use and the risk of genital human papillovirus infection in young women. N Eng J Med 354: 2645-2654.
5. Sharlip ID (2003) What is the best pregnancy rate that may be expected after vasectomy reversal? J Urol 149: 1469-1471.
6. Li S, Goldstein M, Huber D (1991) The no-scalpel vasectomy. J Urol 115: 341-344.
7. Mosher WD, Martinez A, Chandra A, Abma JC, Wilson SJ (2002) Use of contraception and use of family planning services in the United States 1982-2002 (10 edtn). US Department of Health and Human Services- Center for Disease Control and Prevention, National center for health services Division of Vital Statistics.
8. Yanagimachi Y (1994) In: Mammalian Fertilization; Physiology of Reproduction; Knobil E Neil JD Eds Raven Press New York 189-317.
9. Kiesenbaum AL (1994) Mammalian spermatogenesis in vivo and in vitro: A partnership of spermatogenic and somatic cell linkages. Endocrinol Rev 15: 116-134.
10. Abou-Haila A, Tulsiani DRP (2000) Mammalian sperm acrosome: formation, contents and function. Arch Biochem Biophys 379: 173-182.
11. Young CH, Barfield JP, Cooper TG (2006) Physiological volume regulation by spermatozoa. Mol Cell Endocrinol 250: 98-105.
12. Abou-Haila A, Tulsiani DRP (2009) Signal transduction pathways that regulate sperm capacitation and the acrosome reaction. Arch Biochem Biophys 485: 72-81.
13. Mandal A, Naaby-Hansen S, Wolkowick MJ, Klotz K, Shelty J, et al. (1999) FS p95-Kilodalton fibrous sheath antigen that undergo tyrosine phosphorylation in capacitated human spermatozoa. Biol Reprod 61: 1184-1197.
14. Li YF, He W, Jha KN, Klotz K, Kim YH, et al. (2007) FSCB, a novel protein kinase A-phosphorylated calcium-binding protein, is a CABYR-binding partner involved in late steps of fibrous sheath biogenesis. J Biol Chem 282: 34104-34119.
15. Tulsiani DRP, Abou-Haila A (2014) Importance of male fertility control in family planning. Endocrinol Metab Imm disorder-Drug Targets 14: 134-144.
16. Anawalt BD, Bebb RA, Bremmer WJ, Matsumoto AM (1999) A lower dosage of levonogesterel and testosterone combination effectively suppresses spermatogenesis and circulating gonadotropin levels with fewer metabolic effects than higher dosage combination. J. Androl 20: 407-414.
17. Wu FC (2006) Hormonal approaches to male contraception: approaching reality. Mol Cell Endocrinol 250: 2-7.
18. Zhen QS, Ye X, Wei ZJ (1995) Recent progress in research on Tripterygium: a male fertility plant. Contraception 51: 121-129.
19. Lue Y, Hikim APS, Wang C, Leung A, Baravarian S, et al. (1998) Triptolide: a male fertility plant. J Androl 19: 479-486.

20. Lohiya NK, Manivanan B, Mishra PK, Pathak N, Sriram B, et al. (2002) Chlorofrom extract of carcia papaya seeds induces long-term reversible azoospermia in Langoor monkey. Asian J Andrology 4: 17-26.

21. Pathak N, Mishra PK, Mannivanan B, Lohiya NK (2000) Sterility due to inhibition of sperm motility by oral administration of benzene chromatographic fraction of the seeds of carcia papaya in rat. Phytomedicine 7: 325-333.

22. Cheng CY, Mruk D, Silverstini B, Bonanomi M, Wong CH, (2005) AF-2364 [1-(2,4-dichlorobenzyl)1H-indazol-3-carbohydrazide] is a potent male contraceptive: a review of recent data. Contraception 72: 251-261.

23. Van der Spoel AC, JeyaKumar M, Bulters TD, Charlton HM, Moore HD, et al. (2002) Reversible infertility in male mice after oral administration of alkylated imino sugars: a non-hormonal approach to male contraception. Proc Natl Acad Sci USA 99: 17173-17178.

24. Tulsiani DRP, Abou-Haila (2015) Biology of male fertility control: an overview of various male contraceptive approaches. Minerva Ginecol 67: 169-183.

25. Guha SK, Singh G, Ansari S, Kumar S, Srivastava A (1997) Phase II clinical trials of a vas deferens injectable contraceptive for the male. Contraception 56: 245-250.

26. Chaudhary K, Bhatacharya AK, Guha SK (2004) Studies on the membrane integrity of human sperm treated with a new injectable contraceptive. Human Reprod 19: 1826-1830.

27. Lu WH, Liang XW, Gu Y, Wu WX, Bo LW, et al. (2014) A randomized controlled multi-center contraceptive efficacy clinical trials of the intra-vas device: a non-occlusive surgical male sterilization. Asian J Androl 16: 1-5.