

David Serfaty

International Consortium for Male Contraception (ICMC) (www.ic-mc.info) 9 Rue de Villersexel, 75 007 Paris-France

## WHY MALE MODERN CONTRACEPTION?

The Food and Drug administration (FDA) approved the contraceptive pill for women on June 23, 1960, a milestone that may be considered the second most important landmark in the life of women in the 20th century (following the recognition of voting rights). Today, almost 60 years on, men who wish to control their fertility must rely on female compliance with contraceptives or use a condom, withdrawal, vasectomy or periodic abstinence. Is it conceivable, in 2019, that the condom should still be the only method of male reversible contraception that exists? Regardless of the advances made with regard to condom use (such as the diversity of types available and the recent introduction of reimbursement of prescription-bought condoms by the French National Health Service), this method interferes with each act of intercourse and may decrease sexual pleasure. In addition, it must be correctly used to be fully effective. Yet, numerous surveys indicate a strong interest in male contraception and numerous studies have shown efficacy of male hormonal contraceptives under development. However, over the past 15 years, the pharmaceutical industry has jettisoned most of its investment virtually ceased investing in the field of male contraception, leaving only non-profit organizations and public entities pursuing male contraception research.<sup>[1]</sup>

### ***Why should we fight for male contraception?***

Involving women's partners in family planning services may be one avenue to reduce rates of unplanned pregnancy. But reducing unwanted pregnancies (and voluntary abortions) is not the only objective behind efforts to involve men in contraceptive use. Another important goal is to promote gender equality and enable men to take responsibility for their sexual and reproductive behavior.

### ***Research in male contraception: what is on the horizon?***<sup>[2-6]</sup>

A drug called RISUG<sup>®</sup> (reversible inhibition of sperm under guidance) marketed as Vasalgel<sup>®</sup>, which the Parsemus Foundation likens to a reversible vasectomy, is certainly on the near horizon. This method entails injecting, into the vasa deferentia, a device composed of a high molecular weight polymer. This device remains in a soft gel-like state that allows water-soluble molecules to pass but not sperm. When men decide they no longer want to avoid pregnancy they receive a second injection

(sodium bicarbonate) to dissolve the polymer. This method provided effective reversible contraception in rabbits and apparently in rhesus monkeys. The first clinical trial of Vasalgel<sup>®</sup> was announced in 2018.

### ***Hormonal male contraception***

A high intratesticular testosterone (T) concentration is required to support spermatogenesis. Administration of exogenous steroids (androgens alone or in combination with a progestin) suppresses testicular T production. Below a threshold amount of testicular T, sperm production does not take place.<sup>[2]</sup>

The following two hormonal male contraceptive methods under development appear to be the most promising:

1. The combined nesterone-testosterone gel for men. A phase IIB study (Efficacy and Safety Multicenter Study), approved by FDA, was launched in November 2018 by the National Institute of Child Health and Human Development (NICHD) and the Population Council <https://www.popcouncil.org/news/first-trial-launches-to-test-effectiveness-of-male-contraceptive-gel>
2. A male contraceptive pill using a progestogenic androgen, dimethandrolone 17 $\beta$ -undecanoate (DMAU), may be available in the next decade, or one using 11 $\beta$ -methyl- nortestosterone-dodecylcarbonate (11 $\beta$ -MNTDC) also seems very promising<sup>[2]</sup>.

### ***Non-hormonal approaches to male contraception***

Several non-hormonal approaches to male contraception are also under development<sup>[2,7]</sup>: inhibitors of retinoic acid (essential for initiation of meiosis in spermatogenesis), BRDT (the bromodomain protein family is critical for chromatin remodeling during spermatogenesis), EPPIN (epididymal protease inhibitor added to the sperm surface), and gamendazole or Adjudin<sup>®</sup> (indazole carboxylic acid derivatives) may enter the clinical testing stage within a few years and become available about 10 years later.

In September 2013 an International Consortium dedicated to Male Contraception (ICMC) (www.ic-mc.info) was established in Paris. The ICMC is a network dedicated to all medical and socio-cultural aspects of male contraception, current and future, hormonal and non-hormonal, medical and surgical.

It currently has 114 members coming from 44 countries. Most of the leading researchers in male contraception worldwide are ICMC members.

The Consortium operates under the auspices of the European Society of Contraception, the European Society of Endocrinology, the Population Council, the Male Contraception Initiative, the Société Francophone de Contraception, the Association Française pour la Contraception, the European Society of Gynecology, and most recently, the European Academy of Andrology. The ICMC has organized two international congresses on male contraception (4 March 2016 and 7 May 2018), both held at the prestigious National Academy of Medicine in Paris. A «Paris Manifesto» was established after each congress. These manifestos were translated into several languages, including English, German French, Spanish, Portuguese, Chinese<sup>[7]</sup>, Hebrew and Arabic, and have been published in several medical journals. The programs of these past congresses as well as these «manifestos» are available on the ICMC website ([www.ic-mc.info](http://www.ic-mc.info)). The third International Congress on Male Contraception will take place on May 11, 2020, again at the National Academy of Medicine in Paris.

In addition, the ICMC has staged several scientific sessions on male contraception during European and other international congresses. Our aim is to continuously raise awareness about the field of male contraception and its progress.

Another important goal, as an advocacy group, is to prepare public, in particular medical, opinion for the much awaited advent of effective, reliable and well tolerated modern male contraceptives that may coexist harmoniously with the well-established modern forms of female contraception used worldwide.

I hope that the ICMC initiative, which highlights the state of the art in male contraception research, convening the international experts in this field at regular intervals, and addressing an area of family planning sidelined until now, will be successful in achieving its goals.

In any case, the time has come to address men's willingness to limit their family size and control their own fertility.

## References

1. Dorman E, Perry B, Polis CB, et al. Modeling the impact of novel male contraceptive methods on reductions in unintended pregnancies in Nigeria, South Africa, and the United States. *Contraception*. 2018; 97:62–9.
2. Bliithe D. Pipeline for contraceptive development. *Fertil Steril*. 2016; 106:1295–302.
3. Sitruk-Ware R. Emerging science and scientific opportunities for research in contraception. *Référence en gynécologie obstétrique*. 2016; 17:8–11.
4. Page ST, Amory JK, Bremner WJ. Advances in male contraception. *Endocr Rev*. 2008; 29:465–93.
5. Ayoub R, Page ST, Swerdloff RS, et al. Comparison of the single dose pharmacokinetics, pharmacodynamics, and safety of the two novel oral formulations of dimethandrolone undecanoate (DMAU) : a potential oral, male contraceptive. *Andrology*. 2017; 5:278–85.
6. O'Rand MG, Silva EJ, Hamil KG. Non-hormonal male contraception: a review and development of an Eppin based contraceptive. *Pharmacol Ther*. 2016; 157:105–11.
7. Wang C, Sitruk-Ware, Serfaty D. It is time for new male contraceptives! *Andrology*. 2016; 4:773–5.

**Acknowledgements** *The author would like to thank Dr Regine Sitruk-Ware for her support in establishing the ICMC, and Dr Marie Mayer as its General Secretary.*