

**Emerging Male Contraception**

Product	Phase	Studies	Country	Description	Organization	Researchers	Availability
<b>HORMONAL</b>				Male hormonal contraceptives attempt to block or severely reduce the production of sperm. They accomplish this by stopping the secretion of a man's reproductive hormones in the brain and testes. When levels of testosterone in the testes are low, sperm production slows or halts. Typical MHC formulations provide replacement testosterone to the man's bloodstream to maintain male characteristics like muscle mass and facial hair.	Schering, Organon, World Health Organization, CONRAD, Population Council, Chinese National Research Institute for Family Planning, & over a dozen universities around the world	Amory, JK, ST Page, BD Anawalt, AD Coviello, AM Matsumoto and WJ Bremner, Liu, PY, RS Swerdloff, PD Christenson, DJ Handelsman, C Wang	
<b>Combined Androgen and Progestin Formulations</b>							
Testosterone undecanoate depot injection + etonogestrel implants	Phase 2		Europe		Schering, Organon		
Testosterone undecanoate + norethisterone enethate combined depot injection	Phase2		10 countries		WHO, CONRAD		
Nestorone gel + testosterone gel	Phase 1	Under study for gonadotropin suppression	US		Contraception and Reproductive Health Branch-NICHD		
Nestorone gel + testosterone gel	Phase 1 trials starting soon	Under study for spermatogenesis inhibition	US		Contraception and Reproductive Health Branch-NICHD		
<b>Androgenic Steroids (oral and injectible)</b>							
CDB-4730 [11(beta)-methyl-19-nortestosterone 17(beta)-dodecylcarbonate]	Possible clinical trials	Pending toxicology studies			Contraception and Reproductive Health Branch-NICHD		
CDB-4521 [Dimethandrolone undecanoate]	Possible clinical trials	Pending toxicology studies			Contraception and Reproductive Health Branch-NICHD		
<b>Progestin (injectible)</b>							
CDB-1830 (Levonorgestrel butanoate)	Pre-clinical testing	Identified as a potential compound			Contraception and Reproductive Health Branch-NICHD		
<b>GnRH antoagonist (oral and injectible)</b>							
Acylene (CDB-3883)	Pre-clinical testing	Identified as a potential compound			Contraception and Reproductive Health Branch-NICHD		
<b>NONHORMONAL</b>							
<b>Nonhormonal antispermatogenic agents</b>							
Idenopyridine (CDB-4022)	Possible clinical trials	Pending toxicology studies			Contraception and Reproductive Health Branch-NICHD		

Lonidamine analog (CDB-4776)	Pre-clinical testing	Identified as a potential compound			Contraception and Reproductive Health Branch-NICHD		
<b>Molecular Methods</b>							
Adjudin	Pre-clinical testing	Toxicity and teratogenicity tests complete, concept proven in murine models, researchers are streamlining the manufacturing process		Adjudin provides contraception by disrupting the process of sperm maturation in the testes. It changes the way Sertoli cells – which divide to produce new sperm cells and then nurse the immature sperm – interact with sperm. The prematurely released sperm are molecularly incomplete and never become capable of fertilizing an egg	Population Council	Mruk, D, CH Wong, B Silvestrini and CY Cheng	
Sperm-surface enzyme blocker	Basic research stages.	Enzymes involved in sperm-egg binding are still being identified, and drugs which will bind to each of them being sought		A man taking this drug would produce sperm in the normal quantity, and the sperm would appear normal when viewed under a microscope, but they would not bind to an egg. The drug would not interfere with a man's hormones or libido.	Norfolk State University	Joseph Hall, Tubbs, CE, JC Hall, RO Scott, VP Clark, TL Hermon and C Bazemore-Walker	
CatSper	Basic research stages.	Genes for sperm-specific calcium ion exchange channels identified, drugs which block their action being sought		CatSper disables the protein that enables sperm to swim forward. In mice, the sperm not only don't swim forcefully, but they can't tunnel through the outer coating of an egg.	Hydra Biosciences at Harvard University	Carlson, Fliesler, Cromie	
SFEC1	Basic research stages.	Newly identified sperm tail energy carrier protein (SFEC1) involved in glycolysis which may be a good target for a small-molecule drug		Inhibit sperm motility	University of Virginia		
(Ca-s)	Basic research stages.	Novel sperm tail protein (Ca-s) identified, drugs sought to block its action		Inhibit sperm motility	University of Massachusetts Medical Center and Spermatech		
Dry Orgasm Pill	Basic research stages.	Not yet tested in vivo in any animal model.		Drug candidates identified which may block the contractions of the vas deferens.	Kings College London		
Nifedipine	Basic research stages.	Nifedipine has not been tested in men with normal or low blood pressure for contraceptive use. Due to the lack of industry interest, Dr. Benoff is pursuing other funding options and has a patent on the use of several different CCBs as male contraceptives until 2016		Calcium Channel Blocker (CCB) and established treatment for hypertension. CCB's also partially block the calcium channels within the cell membranes of sperm. This affects sperm function rather than production. A man taking nifedipine produces a normal amount of sperm, and the sperm appear functional when viewed through a microscope. But <i>in vitro</i> tests show that these sperm cannot fertilize an egg.	New York University's North Shore Hospital	Susan Benoff, Opie, LH, S Yusuf and W Kubler	

Tripterygium wilfordii (lei gong teng)	No clinical trials in humans.	Lab extract studies show potent antifertility effect. Rodent studies show little to no side effects.		Traditional Chinese medicine used to treat inflammatory conditions. Doses 1/3 or less than the dose used for immune suppression show reversible infertility. These doses produce significantly lowered sperm density, with the remaining sperm incapable of swimming effectively. One study suggests that, like nifedipine, T. wilfordii derivatives may act as calcium channel blockers. Much current research is focused on establishing the mechanism by which the plant affects fertility and investigating potential toxicity and side effects		Qian, Waites, Zhen, Shi, Bai, Wang, Lue	Available in pill form (lei gong teng pian)
Zavesca	Phase 3 as treatment of Gaucher disease; no clinical trials for contraceptive use.	Disappointing results for contraception in rodent studies. Further mechanism of action research needed.		Low doses interfere with sperm development and the effects are reducable. Impairs sperms' ability to swim. Removes sperms' ability to fertilize an egg. Does not effect the genetic integrity of the sperm.	NIH, NICHD	Actelion Ltd	Available as a Gaucher disease treatment.

<b>Immunocontraception</b>							
Sperm surface protein immunocontraception	No clinical trials in humans.			Recombinant DE proteint (sperm epididymal surface protein for gamete fusion) is able to both elicit a specific immune response and inhibit male and female fertility, supporting the use of this sperm epididymal protein for the development of immunocontraceptive approach.	Instituto de Biologia y Medicina Experimental (Institute of Biology and Experimental Medicine) in Argentina; WHO	Diego Ellerman, Dolores Busso, Julieta Maladera, Patricia Cuasnicu	
Eppin immunocontraception	No clinical trials in humans.	An eppin immunocontraceptive has been tested in monkeys			University of North Carolina at Chapel Hill		
LDH-C4 immunocontraception	No clinical trials in humans.	An LDH-C4 immunocontraceptive has been tested in mice			Northwestern University, various research institutes in China		
<b>Devices/ Barriers</b>							
RISUG	Phase 3 clinical trials in 4 centers in India	Awaiting results from two studies: 1) follow-up of Phase II; 2) reversibility studies in humans-reversibility proven in primates but not in men	India	RISUG is an injectable compound that partially blocks the vasa deferentia (tubes that carry sperm), providing effective contraception for up to 10 years per dose. It is effective immediately, has few side effects, and has proven to be reversible in primate studies.	Indian Council for Medical Research	Chaudhury, Guha, Barone, Lohiya, Manivannan, Mishra	Limited availability in India possible in 3 years; U.S. partner assessing bringing RISUG through FDA's NDA process
Intra Vas Device (IVD)	Phase 2	Collecting long-term use safety and efficacy data	China	Nylon mesh plug core that allows vasal fluid to pass through the vasa deferentia but blocks sperm	Chinese National Research Institute for Family Planning; Foshan Medical Company		
Intra Vas Device (IVD)	Phase 1	Reversibility has been tested in primates but not in men	US	Dual flexible silicone plugs that block sperm in the vasa deferentia	Shepherd Medical Company		FDA device approval process is less onerous; could come to market relatively quickly

Suspensories/Internal Heat		Concept proven in small-scale human studies, researchers investigating safety of long-term use		The testes are located outside the body cavity and are usually 1-2° C cooler than body temperature. Warming the testes by a few degrees has a significant negative impact on spermatogenesis. Suspensories do just that: a custom brief holds the testes close to the body, warming the testes to body temperature. Researchers have reported resultant decreases in both the rate of spermatogenesis and the quality of the sperm produced. Men who wore one suspensory design with a rubber ring to hold the testes in the inguinal canals had 100% effective contraception. All trial participants achieved very low motile sperm counts, between 0 and 1.6 million sperm per milliliter. There was one pregnancy during this trial, but the man subsequently admitted that he had stopped wearing the suspensory for 7 weeks. Consistent daily usage is critical for the effectiveness of this method.	Centre d'Etudes et de Conservation des Oeufs et du Sperme humain (CECOS) Midi-Pyrenees in Toulouse, France; WHO	Mieusset & Bujan, Kandeel & Swerdloff	
External heat	No clinical trials in humans.	Concept proven in large-scale but informal human studies in India during the 1950s		Optimal sperm production (spermatogenesis) requires temperatures several degrees Celsius below average body temperature. The testes are located outside the body in the scrotum, which has several mechanisms to keep the testes cooler than the rest of the body. Warming the testes to or above body temperature temporarily disrupts spermatogenesis.		Voegli, Corea, Giwercman, Muller, Skakkebock	
Injected plugs	No clinical trials in humans.	Last studies done in China in the late 1990s - results haven't been released ( Zhao, Lian, Chen)		Developed in China as a potential alternative to vasectomy. The concept is similar to the Intra Vas Device, except instead of implanting pre-formed plugs, the plugs are injected into the vasa deferentia in liquid form. The plugs then harden in place and block the flow of sperm. Two different types of injected plugs have been tested: medical-grade polyurethane (MPU) and medical-grade silicone rubber (MSR).			
Polyester Underwear	No clinical trials in humans.			Polyester underwear creates a greater "electrostatic potential" than either cotton or half cotton underwear. Based on this, its developer concluded that the zero sperm counts obtained with polyester suspensories might be the result of both heat and static electricity across the testes. Many researchers reject this theory.	UCLA, USAID, WHO, NIH, Contraceptive Research and Development Program	Shafik, Ibrahim, & el-Sayed, Wang.	