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Quest for Male 'Pill' Is Gaining Momentum

By LESLIE BERGER

Scientists have suspected since the 1960's, when they invented the birth control pill for women, that manipulating hormones could also suppress the production of sperm.

By giving a synthetic androgen, or male hormone — whether in a pill, an implant or a shot — it is possible to trick the body into halting production of its own testosterone and, in turn, sperm cells.

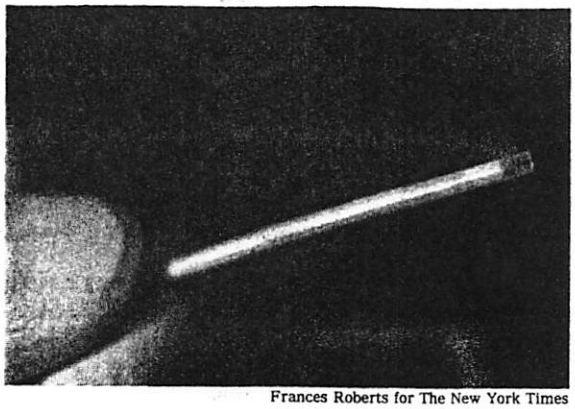
But finding the lowest effective dose and limiting the side effects have been other matters, ones that have been delayed by skepticism that men will use a hormonal contraceptive and by the reluctance of companies to invest in the research.

Now, recent studies in Britain have shown that a male pill will indeed find a market, mainly among men in monogamous relationships. Moreover, there has been a sharp rise in information, much of it developed through fertility research, about how low sperm levels need to be for a man to be infertile.

A male pill is 5 to 10 years away and is more likely to take the form of an implant or a shot since the most common testosterone taken orally can damage the liver, several experts said. But efforts to develop a male contraceptive are finally gaining momentum, with several clinical trials under way or about to begin.

In the largest study, sponsored by the World Health Organization and the Chinese government, a total of 1,000 men in 10 locations are receiving monthly testosterone injections. Once their sperm counts drop low enough, the participants begin having unprotected sex with their partners.

The short-term side effects of testosterone shots can include acne and weight gain (not in fat but in muscle, like the extra bulk seen in athletes using steroids). But its long-term effects are still largely unknown, so the study's two-year duration is important, said Dr. Christina Wang, a Harbor-U.C.L.A. Medical Center professor and head of the World Health Organization committee overseeing male contraceptive research.



Frances Roberts for The New York Times

MENT, developed as a breast cancer treatment in the 60's, is being studied as a male contraceptive.

The World Health Organization is negotiating with Schering AG, the German pharmaceutical company, to start another study, this one involving 400 men in Asia, Europe, Australia and the United States. Every two months the men would receive shots of testosterone along with progestin, the female hormone used in birth control pills and other contraceptives. Progestin seems to lower the dose of testosterone and, in turn, temper its effects on the prostate gland, possibly preventing disease, Dr. Wang said.

The sperm count question: how low do you go?

Another drug company, Organon, is conducting a study combining testosterone shots with progestin implants. "We are seeing which are the best combinations to use," Dr. Wang said.

In smaller studies, the Population Council, an independent research organization, is starting to gauge the effects of an androgen derivative called MENT, an acronym for its chemical formula, developed in the 1960's by the Upjohn Company as an estrogen-suppressing treatment for breast cancer. But it holds more promise as a male contraceptive because it is 10 times as active as testosterone without over-stimulating the prostate, Dr. Kalyan Sundaram, a senior scientist at the council, said.

MENT is delivered into the man's body through an implant. It was recently tested in 36 men in Germany, Chile and the Dominican Republic, and now is being studied in 72 men in Germany, Chile and Los Angeles, Dr. Sundaram said. The new study combines MENT with progestin.

Schering AG is also experimenting with MENT in a gel form as a possible hormone therapy for men with abnormally low levels of testosterone.

The hormone replacement therapy could be on the market in five years, said Dr. Elof D. B. Johansson, the Population Council's vice president. But a MENT contraceptive is at least 10 years away, he said.

"Male physiology conspires against an easy solution," Dr. Nancy J. Alexander, medical services director for Organon USA, wrote in a 1999 article in Scientific American. While fertile women produce a single egg a month on a predictable cycle, men produce tens of millions of sperm every day in the testes. Since it takes about 75 days for sperm cells to mature and become capable of fertilizing an egg, any contraceptive aimed at sperm production needs at least two and a half months to work.

Chinese scientists thought they had found an answer in the 1970's with gossypol, the active ingredient derived from cottonseed oil, after they realized that poor rural families who cooked with it had lower birth rates. A yellow compound whose effects were greatest when its color was brightest, gossypol pills suppressed fertility by damaging the testes. But it caused unacceptably low potassium levels and irreversible infertility in some men, Dr. Alexander said.

Researchers then tried gossypol in a vaginal cream. That proved an effective contraceptive, she said, but marketing efforts ended because the compound's intense and essential color stained bed sheets.