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Immunocontraceptive Vaccines: An Ethical Analysis

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The desire for safe and effective birth control has been a subject of intense interest since the earliest days of recorded history. In ancient Egypt, women mixed honey, dates, and acacia as a suppository they believed had spermicidal effects.[1] The Bible mentions *coitus interruptus*, perhaps the earliest form of contraception, in Genesis 38 when Onan refused Judah's command to impregnate his deceased brother's wife, but had a sexual relationship with her. Condoms were made from fish bladders and other materials that date back to as early as 3000 B.C.[2]

In 1960, the Food and Drug Administration approved the first oral contraceptive, not only for menstrual regulation but also to prevent pregnancy. The research, originally funded by Margret Sanger, was based on clinical trials with women in Puerto Rico, which, unlike in parts of the United States, did not prohibit birth control at that time.[3] Since that era, the use of contraceptives has become commonplace. The Centers for Disease Control and Prevention reported in 2019 that 12.6% of women of reproductive age used the pill, 10.3% used an intrauterine device or contraceptive implant, 18.6% underwent surgical sterilization, and in 5.9% of cases their partners underwent male sterilization.[4] Although contraception in the United States is widespread, it is much less available in developing countries, and women in the U.S. and abroad continue to look for more effective contraception with fewer side effects. According to a recent United Nations report:

> In 2015, 64 percent of married or in-union women of reproductive age worldwide were using some form of contraception. However, contraceptive use was much lower in the least developed countries (40 percent) and was particularly low in Africa (33 percent).[5]

A review from the Guttmacher Institute in 2016 claimed that 225 million women in developing countries have an "unmet need" for contraception, defining that phrase as follows: "Women are considered to have an unmet need if they are sexually active and want to avoid becoming pregnant but are not using contraception."[6]

This strong continued drive for access to safe and effective birth control is more muted in richer countries given the general availability and affordability of contraceptives. However, less developed countries have expressed concerns over their growing populations and the effect this may have on economic vitality, access to resources, and quality of life. One striking example of this trend is the government of India, which has long encouraged its population to

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reduce family size. These pressures led to coercive government policies that particularly targeted the poor, and, according to one review, have become "emblematic of everything that can go wrong in a program premised on 'population control' rather than on reproductive rights and health."[7]

A complete discussion of population pressures as an incentive for government birth control measures is beyond the scope of this paper. However, these forces, primarily in India, paved the way for a new type of birth control: immunocontraception, which has the potential to be effective, yet inexpensive and reversible. The most promising among such vaccines immunizes women against human chorionic gonadotropin (hCG). This paper will address its method of action and its ethical implications.

Clinical Background

In the normal reproductive process, at about six days after fertilization, a developing human embryo implants into the endometrial lining (innermost layer of the uterus). Back in the ovaries, the cellular "shell" left over after ovulation, called the corpus luteum, releases two major hormones: progesterone and estrogen, which help maintain a rich blood supply to the endometrium for successful implantation. Normally, if pregnancy had not occurred, the corpus luteum would degenerate after 12–14 days. Loss of the corpus luteum would deprive the endometrium of progesterone, and the inner layer of the endometrium would be destroyed and would slough away. These events would create the menstrual flow, and a new cycle would begin.

However, if implantation is successful, the developing embryo produces a hormone called human chorionic gonadotropin (hCG). This hormone stimulates the corpus luteum to continue its secretion of estrogen and progesterone. This so-called "rescue" of the corpus luteum maintains the endometrium, and the pregnancy can continue.[8]

The hormone hCG is attractive as a target for contraceptive strategies because it is unique to the developing embryo. It is not present before fertilization, and only appears in the bloodstream after implantation. Inducing a woman's immune system to produce antibodies to hCG would destroy the hormone immediately after its production. Without hCG, the corpus luteum loses its hormonal support and degenerates. Lacking a corpus luteum to release progesterone would, in turn, cause a loss of blood supply to the endometrium, and a normal menstrual period would ensue, eliminating a pregnancy that has just begun. A vaccinated woman would be unaware of her early pregnancy since hCG in the urine is what yields a positive pregnancy test.[9] This creates an ethical dilemma for those who identify the human embryo as a unique person, since, on that view, this mechanism of action is equivalent to that of an early medical abortion.

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Other Possible Vaccine Targets

While the most promising type of contraceptive vaccine targets hCG, it is not the only possibility. Vaccine research has considered three target mechanisms: gamete production, gamete function, and gamete outcome.[10] Vaccines that target gamete production, such as those against luteinizing hormone (LH), gonadotropin-releasing hormone (GnRH), or follicle-stimulating hormone (FSH), inhibit these hormones and ova do not develop within their ovarian follicles. These efforts have not been restricted to women only. A pilot study of FSH vaccines in men took place in Bangalore, India. The study results were inconclusive: "No significant changes in the levels of LH, FSH, and testosterone were observed in the immunized men."[11]

Various experiments in other mammals have led to disappointing results. Studies that targeted gamete production by inhibiting the hypothalamus delayed sexual maturity in both male and female adolescent animals and caused gonadal atrophy in adult animals.[12] Vaccines that target specific gamete components, such as sperm antigens or the zona pellucida (outer shell) of the oocyte, are not unique to gametes and are shared with somatic cells. This outcome means, for example, that zona pellucida vaccines are highly effective, but may cause ovarian inflammation. In spite of these other studies, hCG remains the most promising target for vaccine research, and has undergone Phase I and Phase II clinical trials in human subjects.[13]

Current Research on hCG Vaccines

Although the hCG vaccine has shown the most promise, it is far from becoming a commonplace contraceptive option. In a 2005 study, only one pregnancy occurred in 1,224 cycles and the induced infertility was reversible.[14] In a Phase II trial, women of proven fertility with regular ovulation cycles and who were sexually active consented to three intramuscular injections of the vaccine each month. Laboratory testing was done throughout the month, and if antibody titers were less than 50 ng/ml, the women received a booster injection. When antibody titers remained above 50 ng/ml, the vaccine was effective in blocking fertility. However, effective titers were present in only 60–80% of women, and one woman with a high titer became pregnant.[15] If this were a vaccine against an infectious disease, such a degree of efficacy would be considered very successful. However, a truly acceptable birth control vaccine would have to be effective in 90–95% of recipients.[16] Contrast this with oral contraceptives, which are at least that effective when used properly.[17] Therefore, targeting hCG with vaccines will require much more research to become a realistic

alternative to established birth control methods.

Ethical Considerations

Even though the hCG vaccine is not yet fully effective, this era of widespread interest in cheap and effective birth control, coupled with a concern for overpopulation, may well drive further research initiatives. These pressures may cloud ethical concerns that should receive more scrutiny.

Concerns about overpopulation are related to its effects on poverty, lawlessness, a lack of jobs, and a lack of resources. Proponents of an hCG vaccine claim that it would increase the overall availability of birth control, thus empowering women and increasing their economic freedom.[18] As a utilitarian side benefit, an hCG vaccine might reduce the need for elective abortion as a component of family planning. Furthermore, the vaccine does not have the same hormonal side effects of many contraceptive pills, making it theoretically a more favorable option.

There are, however, legitimate ethical concerns over hCG vaccines as a form of contraception. For those who hold that protectable human life begins at conception, it is not a vaccine that prevents pregnancy, but one that ends it. The vaccine works to attack the hormone that sustains a pregnancy after conception has already occurred. Therefore, many who approach ethics from a religious perspective, especially conservative Roman Catholics and Protestant evangelicals, would declare this method of contraception an abortifacient, making it immoral.[19]

Furthermore, hCG vaccines are unlike any other vaccine. In the usual scheme of things, a vaccine creates antibodies against an infectious pathogen to protect the body from disease. An hCG vaccine essentially treats pregnancy as a pathogen to be eradicated, i.e., a disease the body must be trained to attack. Ethical conservatives will not agree with the characterization of pregnancy as a disease, and its mechanism does not actually decrease the number of abortions; it is simply a different method.

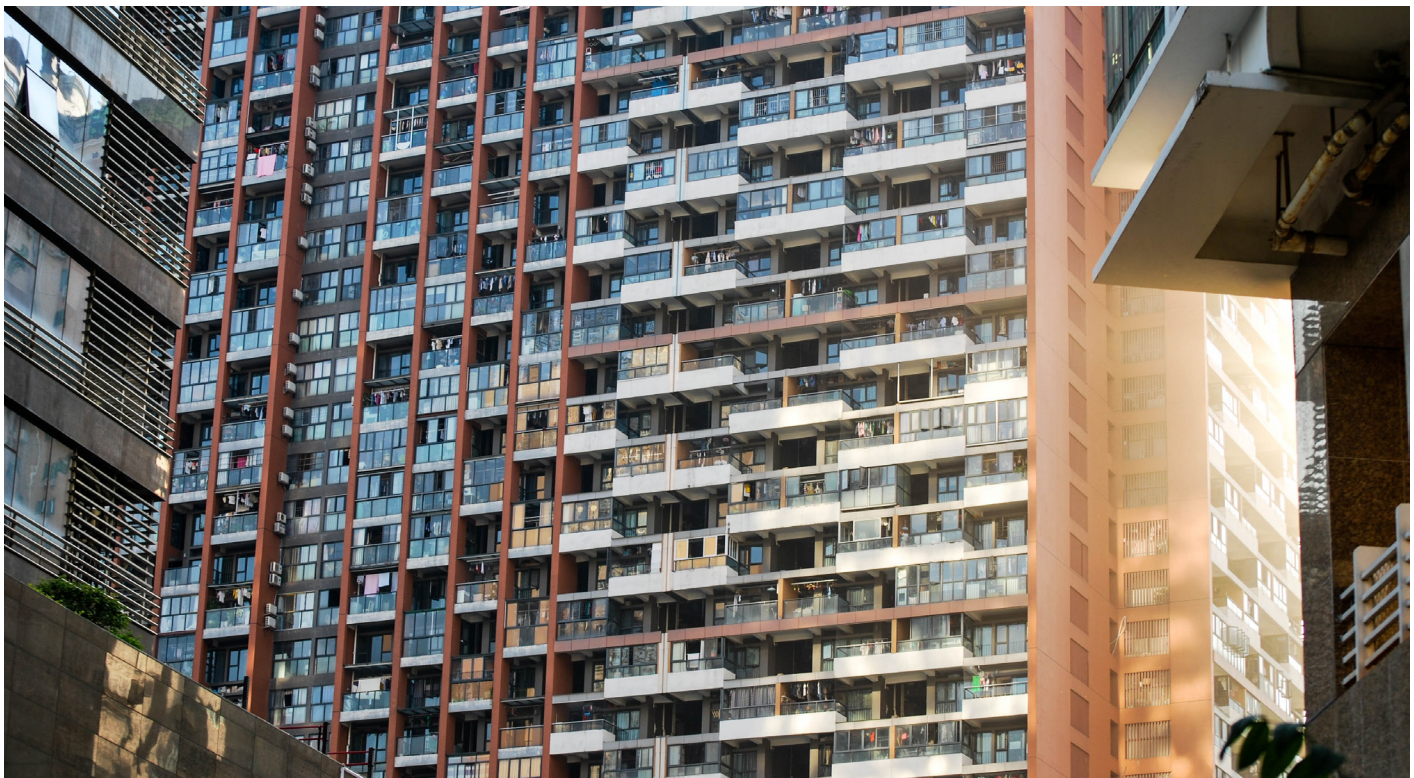
Though harder to predict from a utilitarian perspective, there may be subtle and undesirable effects on the fabric of society if an hCG vaccine becomes commonplace. While advocates of this method promise sexual freedom and economic opportunity, there is a risk that the mechanism of action may not be fully explained or understood by its users, which may therefore conflict with their personal moral values. Thus, hCG vaccines have the potential to actually limit the freedom and agency of women rather than to empower them.

Wider Social Policy Concerns

Widespread government-run programs to limit population have a questionable history of delivering the economic prosperity they promise. Unnatural policies that limit individual choice for family size have always yielded negative results and often open the door for terrible abuses. There are many examples of this.

In the 1970s in India, the prime minister's son Sanjay Gandhi led a campaign to sterilize poor men. In just one year, 6.2 million men underwent the procedure.[20] Mass sterilizations are still taking place in India. During the two-year period of 2013–2014, there were almost four million sterilizations, most of them in women. This happened even though over 700 had died of complications from 2009 to 2012.[21]

In China, since the institution of the One-Child policy in 1980, over a million "orphan parent" families have been created, where the loss of the one child has impoverished the parents, leaving them without any means of support. Even though this policy has now been officially rescinded, China's economic prosperity has been seriously affected. GDP will "likely decline from 7.2 percent in 2013 to around 6.1 percent by 2020."[22]



Also in China, the nation's preference for male children has skewed the sex-ratio so much that many single men are not able to find a wife. As a result, in 2016 there were 33.59 million more men than women.[23]

In the United States, a 1976 study by the U.S. General Accounting Office (GAO) revealed that four of the twelve Indian Health Service regions in the U.S. sterilized 3,406 American Indian women without their consent in the preceding three years.[24]

Surprisingly, few Americans today are aware of the dark history of eugenics in the U.S., based on outdated and scientifically discredited ideas of creating a better society by controlling human reproduction. During that era, which formally ended in 1939 with the closure of the Eugenics Record Office, over 60,000 Americans underwent sterilization against their will.[25]

In summary, broad government programs to promote population control have a disturbing history, and there is no evidence that such efforts have fared any better today. It is therefore not unreasonable to have grave concerns about how the government of India or that of any other society may employ an experimental vaccine to limit pregnancies in women.

Conclusion

Safe, effective, and affordable birth control is readily available in the United States and other developed countries. In India, however, concerns over a growing population and its possible related economic consequences has fueled initiatives for newer contraceptive methodologies. This paper has focused on the mechanism and ethics of immunocontraception using a vaccine against human chorionic gonadotropin (hCG).

Current research on hCG vaccines raises significant ethical concerns, primarily because the mechanism of action is abortifacient. It is likely that many Indian women will not receive adequate information to fully understand this mechanism, which they might not agree to if they were better informed. Furthermore, there are wider concerns over government programs to promote population control, which historically have led to disturbing abuses.

Advocates for increased access to birth control claim that contraceptives empower women, increase their economic and personal opportunities, and improve their lives. There is little evidence that current research initiatives into immunocontraceptive vaccines will help to accomplish these goals.

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