

# BIRTH CONTROL IN THE BRAVE NEW WORLD

Brain hormone manipulation, immunization, and bioengineering  
loom as contraceptives of the future

by Joan Arehart-Treichel

*"And round her waist she wore a silver-mounted green morocco-surrogate cartridge belt, bulging . . . with the regulation supply of contraceptives."*

—Aldous Huxley, *Brave New World*

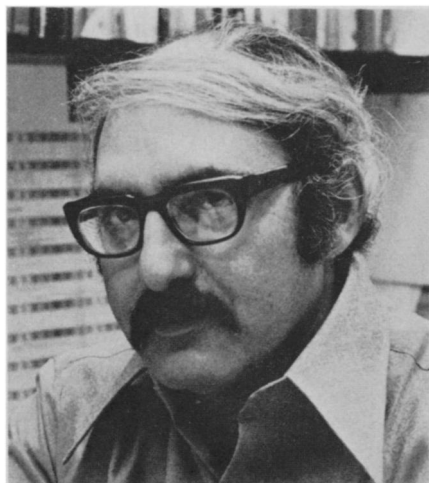
Huxley published his science fiction classic in 1932. It predicted that birth control would be a major need in the utopia of the future. But what kinds of contraceptives will scientific research really be able to serve up in the next several decades? Research efforts of the moment suggest that, in addition to contraceptives now on the market, there will be contraception by brain hormone manipulation, selective immunization against certain chemicals of the reproductive system, and bioengineering contraceptive devices for men as well as for women.

Brain hormone manipulation may be the most imminent. In women, luteinizing hormone, released by the pituitary gland in the brain, in turn releases the sex hormones estrogen and progesterone. When the sex hormones are secreted, they cause ovulation. Still another hormone, luteinizing hormone-releasing factor (LH-RH or LRF), is secreted by the hypothalamic region of the brain. LH-RH serves as a master switch over luteinizing hormone, the sex hormones and ovulation. A year-and-a-half ago, Andrew Schally of the Veterans Administration Hospital in New Orleans, and soon afterward Roger Guillemin of the Salk Institute in La Jolla, isolated, sequenced and synthesized LH-RH (SN: 7/17/71, p. 37). Since then they have headed up the two major American research teams that are looking into the hormone's contraceptive possibilities.

One of their goals is to make analogues of LH-RH. An analogue is a synthetic chemical that is structurally like, yet slightly different from, the natural chemical. Out of this hopper of analogues they hope to find one that, when injected into a woman, reacts with the

pituitary gland and thereby keeps the real LH-RH from doing so. If luteinizing hormone is jammed, the sex hormones estrogen and progesterone cannot be released, and ovulation cannot take place.

How close are the researchers to making this approach to contraception work? Schally says that while his group has been successful in correcting infertility in women by giving them injections of LH-RH, they have not found an ideal inhibitor out of the hundred or so analogues of LH-RH they have



Uldis Saule, Northwestern Univ.

*Goldberg seeks male contraceptive.*

examined. Still, he is convinced the approach "is more than feasible."

Guillemin's group appears to be having more success along these lines. They have found eight analogues that inhibit LH-RH action in animals. But Guillemin stresses that they will not be able to move into clinical trials on women until they get analogues that are more potent. Still, he believes they are on the right track; the analogues they have made in the past couple of months are more potent than those they made a year ago.

The other goal the Schally and

Guillemin teams are intensely pursuing is to use an injection of LH-RH to induce ovulation. Such induction might clear the way for intercourse without fear of pregnancy for the rest of a woman's monthly ovulatory-menstrual cycle. Ovulation-induction could give the rhythm method of birth control the certainty it now lacks.

A year ago the U.S. Food and Drug Administration granted Guillemin and Sam Yen of the University of California School of Medicine in La Jolla permission to try LH-RH induction of ovulation on female volunteers. They first scrutinized some 500 women for possibly adverse side effects. When they found the injections safe they attempted to see whether an injection, given about the time a woman is expected to ovulate, can make her ovulate. So far they have successfully induced ovulation in several dozen women over several ovulatory-menstrual cycles. "The initial attempt is promising," Yen says. "Over the next two or three years we should be in a much better position to say whether ovulation-induction is applicable to rhythm or not."

One of the major hurdles Guillemin and Yen still have to overcome is to prove that LH-RH can induce ovulation if taken by mouth. They are working on a pill form of the hormone. "I think it will be active," Yen says, "but we do not have enough information yet to say so for sure."

With luck, LH-RH inhibition or manipulation may become available to the public within a decade. Immunization as a means of contraception should become available in the 1980's, investigators in that field anticipate. Birth control by immunization is not a new idea. But sophisticated techniques of immunologic research have become available only in the past decade.

In the late 1960's, antibodies were detected in the bloodstreams of sterile

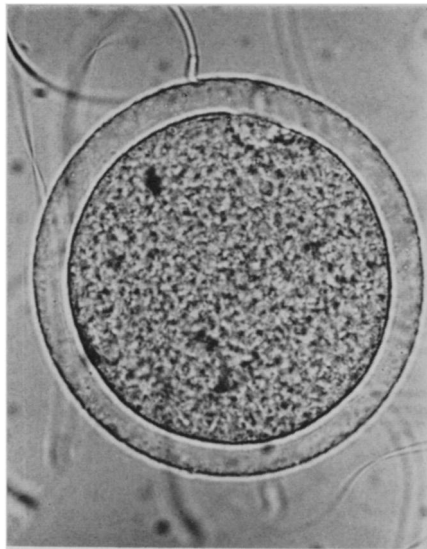
men and of some infertile women, suggesting that the antibodies might cause sterility and infertility. About this time some investigators also managed to deplete sperm production in male animals, or to impair fertility in female animals, by injecting them with extracts of sperm or testes. These accomplishments were stronger evidence that antibodies formed against foreign materials might impede reproduction. But researchers were still in the dark about how sperm, testes or other foreign-material injections might raise antibodies in the reproductive tissues. And antibodies to what, precisely? There was also the danger, as one investigator recalls, of undesired effects, because sperm and testes contain a number of different chemicals.

So the challenge was to identify specific antigens (proteins) in sperm, testes or ovaries that, when injected into male or female, trigger specific antibody reactions that inhibit specific reproductive activities. Only if they could identify and manipulate specific antigens, would they be able to come up with a narrow-acting and safe means of contraception for men or women.

During the past three years they have made progress in this direction. Allen Menge of the University of Michigan, for example, has found at least 12 different kinds of antigens in rabbit sperm. He has also found that when these antigens are injected into female rabbits, antibodies form in the uterus, perhaps also in the vagina, against the antigens. Menge is trying to purify some of these antigens to find which ones spark antibody responses that alter specific reproduction functions in the female.

Erwin Goldberg of Northwestern University and William Zinkham of Johns Hopkins University have identified, for what appears to be the first time, a specific substance in sperm and testes that is immunologically active against conception. The substance is a protein, an enzyme specifically, known as lactate dehydrogenase (LDH-X). They identified the enzyme in sperm and testes of various animals as well as of man and purified it in ample amounts. For the past few years they have used the purified material to explore the enzyme's contraceptive potential.

Goldberg injected the enzyme, taken from mice testes, into rabbits. The rabbits raised antibodies against it because their bodies considered it a foreign protein. The antibodies were taken from the rabbits and injected into female mice, thereby reducing incidents of conception. Zinkham is injecting the enzyme into female rabbits to see whether it inhibits their reproductive ability. He says he has no results yet. Both researchers hope that



*Sperm swim to an egg whose circumference is coated with antibodies.*



Photos: Shivers/Science  
*Sperm are not able to penetrate it.*



*Untreated egg was penetrated, fertilized (arrows show the changes).*

the enzyme, or antibodies made against it, might eventually provide a new means of birth control for women. Goldberg, in fact, is just getting primate studies under way, with the Population Council of Rockefeller University. They will be injecting LDH-X into monkeys to see whether it inhibits conception as it did in mice.

The Chicago and Baltimore scientists are particularly interested in exploring the potential of the enzyme as a male contraceptive, since there is no good contraceptive for men on the market yet. Zinkham has found that LDH-X does not appear in males until puberty. He is injecting the enzyme into immature animals to see whether the enzyme might be recognized by their bodies as a foreign protein and, by building up antibodies to the enzyme, impede sperm production. Goldberg is attempting to see whether antibodies to the enzyme might inhibit sperm production in adult male rabbits. "I do not have results that are ready to publish yet," he says, "but I do have an indication that fertility of the male is affected."

Goldberg is also trying to learn what role the enzyme normally plays in sperm or testes. Then he might find a way of interfering with the enzyme in the male, thereby impeding the male's reproductive capacity. David Bishop of the Medical College of Ohio has also identified an enzyme in the testes of various animals and man that, if knocked out of operation, jams sperm production. It is sorbitol dehydrogenase. "Why the enzyme is critical for the testes we don't know yet," he says. He too is interested in the possibility that blocking critical enzymes in the male reproductive system might provide a means of male contraception. "Such blockage, with a drug, say, may in the long run prove more valuable than immunizing a person against enzymes or proteins."

In the Dec. 15 *SCIENCE*, C. Alex Shivers of the University of Tennessee reported what appears to be the first known ovary antigen that can inhibit conception. Antibodies raised against specific antigens in the ovary of hamsters were put in a laboratory culture of hamster sperm and eggs. The antibodies kept the sperm from penetrating the outer layer of the eggs. Shivers told *SCIENCE NEWS* that he has also taken embryos out of animals, treated the embryos with the ovary-specific antibody, then put the treated embryos back into the animals. The antibody treatment kept the embryos from re-implanting in the uterus. He is now injecting the antibody into the reproductive tracts of hamsters to see whether the antibody prevents sperm from penetrating eggs and resulting in conception. If successful, he then plans


to introduce the antibodies into the general bloodstreams of the animals to determine whether the antibodies reach their reproductive tracts in high enough concentrations to keep sperm from penetrating eggs. The ovary-specific antigen has not yet been identified in man, but Shivers says there is no reason to believe it is not present.

How practical might these approaches be in people? Bishop voices his major concern and probably that of other scientists in the field: "A lot of people say, oh sure, immunization can be reversed. But we really haven't figured out yet how to do it. On the other hand, since our work is just beginning, there is reason for optimism. We may come up with something before long."

A bioengineering approach to birth control has been under way for two years or so, especially since the Government has made research money available. Some major work is taking place at the Illinois Institute of Technology Research Institute in Chicago. Marvin Burns, one of the researchers there, says he and his colleagues are having considerable success in fitting valves into the sperm ducts of dogs that block passage of sperm. The valves, made of silicon rubber, stainless steel and porous materials that encourage tissues to grow into them, can be opened or shut. Such reversibility may make the valves superior to vasectomy, where ducts are cut and cannot always be hooked up again. Burns says they hope to move into trials on men in a year or two.

Provided brain hormone manipulation and selective immunization pan out as the contraceptives of the future, what impact might they have on society? An LH-RH inhibitor might prove more convenient and safer than contraceptive pills now on the market. It could be taken once a month instead of daily. It might be safer than presently available contraceptives because it is more specific in its action. Inducing ovulation with LH-RH might have profound effects on population control in developing countries that are largely Roman Catholic. The only method of birth control now approved by the Church is the rhythm method, because it predicts rather than prevents ovulation. Guillemin anticipates that the Church would approve a pill by which women can induce ovulation in themselves each month because such a pill would time (predict) rather than suppress ovulation. Immunization against conception, if it can be made reversible, might provide the ideal male contraceptive.

Huxley once said, "It is only by means of the sciences of life that the quality of life can be radically changed." □



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