Male contraceptive in stomach salve

In the ongoing quest for contraceptives, a scientist at Johns Hopkins University in Baltimore is refining a hormone salve for men that suppresses sperm production. Last week, at the annual meeting of the Society for the Study of Reproduction (SSR) in Cleveland, Larry L. Ewing said he is in the process of applying to the Food and Drug Administration (FDA) for approval to conduct clinical tests on humans.

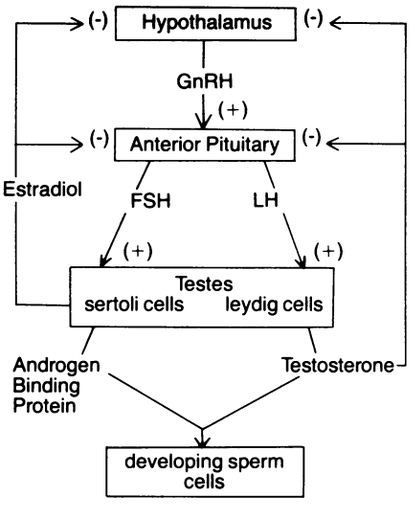
The salve, to be rubbed on the stomach, delivers testosterone, the primary male sex hormone, and estradiol, a form of estrogen, into the bloodstream. Operating on the same principle as oral contraceptives in women, this hormone combination patented by Ewing tricks the brain into halting production of gonadotropins, the hormones necessary for reproduction. As a result, the salve would inhibit sperm production without affecting libido or other secondary sex characteristics.

Scientists have been researching this method of sperm suppression for a long time, but have been slow to find an acceptable way to get the hormones into the bloodstream while avoiding the large doses required in an oral contraceptive. For the past 12 years, Ewing has used subcutaneous implants to deliver his hormone combination in tests on rats, rabbits and rhesus monkeys. In animal tests, Ewing says he "never had a contraceptive failure," and found "no hint" of health hazards associated with the hormones. "We don't know if this male contraceptive will be effective or safe for humans," he says. "But we've done all we can do in animals, and based on those results, we're ready to try it on humans."

Because the large size of implants would make them impractical for use in humans, Ewing will package the hormones, which readily permeate the skin, in the form of a salve. "It's an old principle with a new application," says Daryl Foreman, director of the SSR meeting.

According to this principle, the hypothalamus normally initiates the signal for sperm growth by sending gonadotropin-releasing hormone (GnRH) to the nearby pituitary, which responds by releasing gonadotropins — luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These travel via the bloodstream to the testes, where the hormones induce specialized cells to produce testosterone and androgen-binding protein (ABP). Together, ABP and testosterone aid in sperm production. The testes also make small amounts of estradiol, which, along with testosterone, circulates back to the brain, signaling it to lower the release of gonadotropins. Thus, the sex hormones regulate their own production.

Enter the salve. Under its influence, the brain, which cannot distinguish between hormones in the salve and those produced by the testes, slows production of gonadotropins, indirectly inhibiting the growth of the 500 million or so sperm a man makes every day.



A negative feedback loop controls hormones of the male reproductive system. Ewing's salve would switch off the brain's production of LH and FSH, thereby inhibiting sperm production by the testes. (+) indicates stimulation; (–) indicates inhibition.

If Ewing receives FDA approval, he will collaborate with the National Institutes of Health on tests to determine if the salve is safe and effective enough for humans. Carl Djerassi, of Stanford University in Stanford, Calif., who synthesized the first oral contraceptive, feels that the salve is an interesting approach, but not a practical one for worldwide use. He told SCIENCE NEWS, "It's extremely difficult to control dosage with a salve." —*S. Steinberg*

Insect resistance: A sticky issue

USDA

This newly hatched alfalfa weevil larva, magnified 100 times, will not live up to its reputation as one of the most destructive alfalfa pests. Glandular hairs on its host exude a sticky fluid that fatally traps young insects before they have a chance to feed or lay eggs. In an effort to capitalize on this biological method of pest control, Edgar L. Sorenson, a U.S. Department of Agriculture researcher in Manhattan, Kansas, crossed hay-type alfalfa of the genus Medicago *with wild and hairy species. He's now field testing the hybrids, which he hopes will resist bugs and produce a lot of hay.*

Mammals enhance gene activity

Turn them around, move them about, they still work to boost the activity of a gene several hundredfold. Such DNA segments, called enhancer elements, were first identified in animal viruses (SN: 2/26/83, p. 139). Now several research groups report evidence of enhancer elements among the genes of animal cells. These enhancers might regulate genes in development and malignancy.

The first example of enhancer sequences found in animal cells controls a gene in antibody production. Before the gene becomes active, DNA segments must be rearranged to form the mature gene. Recent experiments indicate that this rearrangement places an enhancer element in position to boost expression of the antibody gene. Similarly, chromosome rearrangements in a variety of cancers may put DNA sequences containing enhancers near cellular genes that have the potential for causing cancer.

The most extensive evidence for a cellular enhancer comes from work on the heavier of the two types of protein chains that make up antibody molecules. Experiments by Susumu Tonegawa of the Massachusetts Institute of Technology (MIT) in Cambridge and colleagues, and by Walter Schaffner and colleagues at the University of Zurich, Switzerland, are reported in the July CELL, and research by Kathryn Calame and co-workers at the University of California at Los Angeles is described in the Aug. 12 SCIENCE.

The heavy-chain enhancer was found in the DNA region, called an intron, between two coding segments of the mature heavy-chain gene. It is required for expression of that gene and will stimulate activity of other genes the scientists link to it. The enhancer element works independently of its orientation, or its position (within a stretch of a few thousand nucleotides, the elementary subunits of DNA). The enhancer contains two copies (and one copy in reverse orientation) of a short DNA segment that is similar to repeated sequences found in viral enhancer elements. In most cases, the enhancer only works in cells that normally make antibodies. The enhancer sequence may be an entry site for some component of the apparatus of gene expression.

The gene for the lighter protein chain of an antibody also has a control segment in its intron, but the evidence it is an enhancer is less clear, report Cary Queen of the National Cancer Institute in Bethesda, Md., and David Baltimore of MIT in the July CELL. Vernon Oi and Leonard Herzenberg of Stanford University in Stanford, Calif. and Sherie L. Morrison of Columbia University in New York also find this element does not stimulate activity of other genes they link to it. —*J. A. Miller*