

Hormone-blockers may yield male 'Pill'

A troubling side effect has long stymied the search for a male contraceptive drug. Shutting off testosterone, the male hormone that spurs sperm production, can shut down a man's love life as well, because men lacking the hormone often can't get or keep an erection. Now, a research team may have overcome this hurdle. By combining a novel hormone-blocker with testosterone, they completely — and reversibly — thwarted sperm production in a small group of volunteers, without robbing the men of their sex lives.

The researchers, led by Laurie Tom at the Harbor-UCLA Medical Center in Torrance, Calif., targeted gonadotropin-releasing hormone (GnRH), a master-control hormone secreted by the brain's hypothalamus. GnRH initiates the sex-hormone production cascade in both men and women.

In men, GnRH turns on two pituitary hormones — follicle-stimulating hormone and luteinizing hormone — responsible for priming sperm-producing cells in the testes and stimulating testosterone, which initiates sperm production.

Tom and her colleagues gave daily injections of a modified, inactive form of GnRH to eight healthy men over a period of 16 weeks. The modified GnRH "antagonist" was designed to block the men's own GnRH from binding to its receptors, thus preventing the sperm production. The

researchers also gave the men testosterone injections every two weeks, which allowed them to get erections.

After 10 weeks, seven of the eight men had no sperm in their ejaculate, although their sexual abilities were otherwise normal. Tom's group reported last week in Washington, D.C., at the annual meeting of the Endocrine Society. Two weeks after the men stopped taking the shots, sperm reappeared in their ejaculate, reaching normal levels after 10 to 14 weeks. The eighth man quit the study because he developed welts at the injection sites.

Tom says her group's study shows that GnRH antagonists could lead to an effective male contraceptive drug. But, she acknowledges, "what needs to be done is to develop a long-acting form," so the drug could be taken less often or orally.

"GnRH antagonists will be the male contraceptive within the next 10 years," predicts Spyros Pavlou, an endocrinologist at Vanderbilt University in Nashville. Several years ago, Pavlou tested a larger dose of the same GnRH antagonist used by Tom's group, together with a smaller dose of testosterone, but the combination did not halt sperm production in his volunteers.

Pavlou reported to the Endocrine Society that a different GnRH antagonist alone suppressed levels of the follicle-stimulating and luteinizing hormones in all of 16 men, none of whom dropped out of the study because of side effects. He plans next to test the compound on a larger number of men to demonstrate whether the suppressed hormone levels block sperm production. — C. Ezzell

Cyclic weight gain may harm the heart

It may be worse to have lost pounds and regained them than never to have dieted at all — from a life-expectancy standpoint, at least. That's the message from a new analysis of the effects of weight fluctuation on nearly 3,200 men and women in the Framingham (Mass.) Heart Study.

The Framingham study has monitored participants' health at two-year intervals since 1948. All volunteers were healthy at the outset, their ages ranging from 30 to 62. An international research team has now conducted three different analyses of data spanning 32 years, looking for statistical associations between volunteers' weight variability and each of the following: deaths from all causes; deaths from coronary artery disease; nonlethal coronary artery disease; and cancer risk.

The investigators, led by Lauren Lissner in Göteborg, Sweden, and Kelly D. Brownell of Yale University, found no link with cancer but a significantly elevated risk of premature deaths in general and an even stronger association with heart disease. "Persons whose body weight fluctuates often or greatly have a higher risk of coronary heart disease and death than do persons with relatively stable body weights," they write in the June 27 *NEW ENGLAND JOURNAL OF MEDICINE*.

Overall, weight variations increased an individual's chances of premature death in general and the threat of lethal or nonlethal coronary disease by 30 to 100 percent, and the increases "tended to be higher for men than for women," the researchers report. Moreover, the heart risk proved independent of obesity and smoking — and was equal to the risk of being overweight, they assert. The strongest links between weight change and health appeared in men and women under age 45.

In an accompanying editorial, Claude Bouchard of Laval University in Ste. Foy, Quebec, observes that "this study has considerable strengths," including its large size and its statistical accounting for potentially confounding variables. However, he adds, the finding that variable weight "may have negative consequences for health that are independent of obesity and the rate of [weight] change... is likely to be controversial" — especially when animal data have yet to suggest a possible mechanism.

An estimated 25 to 50 percent of U.S. and Canadian adults are attempting to lose weight — and most will not keep their shed pounds from returning. Lissner's team concludes that the new data "suggest that overweight persons should be taught skills to maintain weight loss and that the prevention of relapse should become a more central focus of weight-loss programs." — J. Raloff

Glitches bump ROSAT off the fast track

ROSAT, the German-U.S.-British research satellite launched last June, has already produced X-ray and ultraviolet images of the universe with unprecedented clarity and wavelength range (see story, p. 408). The satellite's two telescopes depend on three gyroscopes to point them toward their celestial targets, but on May 12 one of these critical devices went awry. This has forced research teams to drastically revise their observing plans, at least for most of the summer. No longer able to move rapidly from target to target, the telescopes are now making fewer observations and spending much more time on each.

Joachim Trümper, director of ROSAT research at the Max Planck Institute for Extraterrestrial Physics in Garching, Germany, says the satellite currently observes one target per day instead of the 10 to 15 planned. He notes that software experts in Germany plan to reprogram the satellite in August so that its sun sensors and magnetometers can take the place of the ailing pointer.

Tinkering with software also seems critical for correcting another problem plaguing the satellite. It's no mean feat to convert the raw data from ROSAT's two telescopes into usable images. And ROSAT programmers still have not ironed out all the bugs in a software program designed to create such images from a wide variety of telescope data. For this reason, most scientists who have conducted ROSAT observations since February have yet to receive their processed images.

"The data are sitting on the ground on magnetic tapes," says David N. Burrows of Penn State University in University Park, who has received some but not all of his images. "The problem is that the programs that read those magnetic tapes and generate useful information for scientists to look at isn't working right yet. It's very frustrating."

This week, Trümper told *SCIENCE NEWS* that the software has been refined and that ROSAT researchers should begin receiving their data in July.

— R. Cowen