

Sperm and eggs on the go

Executive sex hormones can make or break reproduction,
a leading European endocrine team is finding

by Joan Arehart-Treichel

The target sex hormones—estrogen, progesterone, testosterone, and androgen—are generally well understood, artificially synthesized and easy to give to people who are deficient in them. But scientists are discovering more and more that sex hormone actions and deficiencies may not lie at the level of the target sex hormone at all, but high up in the hormone executive switchboard. The switchboard consists of the small disk-like pituitary gland. The pituitary, in turn, is controlled by the nearby, elusive hypothalamus of the brain.

Last summer, Andrew Schally's group at the Veterans Administration Hospital in New Orleans elucidated and synthesized the hypothalamic sex releasing factors—luteinizing hormone-releasing hormone (LH-RH) and follicle-stimulating hormone-releasing hormone (FSH-RH) (SN: 7/17/71, p. 37). Now a team of internists, chemists and radiobiologists at the Institute of Medicine in Liège, Belgium, headed by Paul Franchimont, is shedding considerable light on the pituitary sex hormones—luteinizing hormone (LH) and follicle-stimulating hormone (FSH)—and their role in male and female fertility. Their research also helps clarify how the birth control pill works. They are laying the groundwork for clinical diagnosis of male and female sterility problems at the pituitary level. And most crucial, as far as population control is concerned, they are able to pinpoint ovulation in women within 24 to 48 hours. The group's success is largely due to the radioimmunoassay techniques they are using, since such assays are excellent for detecting elusive protein hormones. The Liège team, in fact, is one of the most progressive radioimmunoassay hormone research groups in Europe.

Franchimont and his co-director, Jean Jacques Legros, explained their work in an interview with SCIENCE NEWS at the Institute of Medicine.

Many persons are unaware that there is a fine line between the male and female sexes as far as hormones are concerned. Both men and women have the same hypothalamic sex factors and the same pituitary sex hormones; only their target sex hormones differ. Women have

estrogen and progesterone, and men have testosterone and androgen. How the pituitary sex hormones LH and FSH are implicated in sperm production in the male has been largely a mystery. Now Franchimont and his group have clearly demonstrated that there is a feedback mechanism between both LH and FSH and testosterone, the target sex hormone involved in sexual characteristics. This means that testosterone levels are monitored by the quantities of LH and FSH found in the pituitary gland. Furthermore, there is a feedback mechanism between sperm maturation and FSH via an undefined substance. Indeed, Franchimont's team has shown that men who do not produce sperm in the usual amounts—40 million to 80 million sperm per ejaculation—or who are altogether infertile, may have something go wrong during one of the several stages of sperm maturation. At this critical stage, a substance, probably a steroid, is produced; it modifies FSH levels. As a result, FSH levels remain higher than normal. The team has also shown that when this stage of sperm maturation is not arrested, FSH levels remain normal. This work was published in the June JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM.

Concerning female fertility and infertility, the Liège investigators were

the first to show that FSH peaks at a woman's mid-cycle—halfway between menstrual periods—or at the supposed time of egg production. This was in 1966. They have since found, along with several other research groups, that the FSH peaks induce the formation of the corpus luteum. The corpus luteum is made in the ovary to prepare the uterus to receive the fertilized egg.

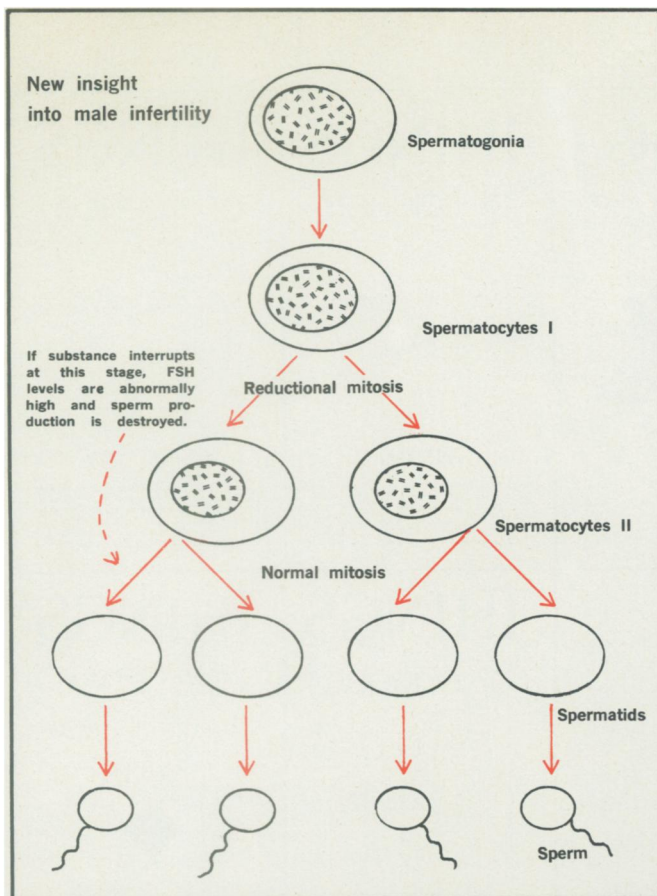
In 1969 and 1970 the Belgian team, with some others, showed that the estrogen peak during the preovulatory phase of a woman's cycle precedes the LH peak at the mid-cycle. Thus, the team reasoned, estrogens probably cause LH to rise at mid-cycle. To find out if this really happens, they injected estrogen into non-menstruating women, and the injections indeed caused an LH burst, confirming their theory. In addition they have shown that the chemical structure of estrogen is what causes LH to peak. Franchimont says: "The radical 17β hydroxy of the estrogens is of the first importance in the feedback between LH and the estrogens." These most recent findings are in press in HORMONE AND METABOLISM RESEARCH.

Obviously, then, the target sex hormone, estrogen, works closely with LH, and one would assume also with FSH, in releasing an egg at mid-cycle, and in preparing the uterus in the event the

*Franchimont
(second from r.)
discusses with
staff how
LH-RH affects
LH and FSH,
and in turn
male and female
fertility.*

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Male infertility may be caused by a steroid interfering with FSH, and in turn with sperm maturation.

Paul Franchimont,
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egg is fertilized. Again, these interactions were anticipated. But experimental confirmation of such speculations holds profound clinical importance.

For example, distinction between estrogen action on LH and estrogen action on FSH helps explain how the birth control pills work. The pills are mostly estrogen. Radioimmunoassays show that 50 micrograms of an estrogen pill is enough to suppress both LH and FSH action, whereas 20 micrograms is sufficient only for suppressing FSH action. "Although clinicians have previously estimated 50 micrograms to be the right amount for best contraceptive protection, we now have experimentally confirmed the estimate," Franchimont reports.

The Belgians' work also provides strong guidelines for correcting male infertility. If FSH levels are measured and found higher than normal, obviously the patient suffers a problem in the critical stage of sperm maturation, and neither FSH injections nor testosterone injections will alleviate the problem. On the other hand, if FSH levels are found to be normal, FSH or testosterone injections might prove beneficial.

Although Franchimont's team has now found that FSH peaks and LH peaks indicate a woman will ovulate within 48 hours, they cannot get the results of their assays back before six days. Obviously such an assay wouldn't help a woman who wants to know on the mo-

ment whether she is susceptible to becoming pregnant. But the correlation with ovulation should eventually lead to some practical home assay for detecting the hours of ovulation. Once available, a woman might then take a mini-pill, to suppress the crucial sex hormones only during the critical ovulation hours. Or she might simply abstain from intercourse during those hours, until the dangers of conception is past. A convenient home ovulation detector might become the answer to world population control, since present contraceptive devices are laden with drawbacks.

Considerably more work will be required before these clinical potentials are brought to fruition and become clinically widespread. But the vigorous new science of endocrinology has come far in the past decade. It will probably not be too much longer before the Liège research leads to clinical applications. Franchimont's group is now just starting to test some of Andrew Schally's synthetic LH-RH, to see exactly what clinical effects the synthetic peptide might have on LH and FSH, and in turn on the target sex hormones. Once such insights are provided, the correction of infertility and fertility control might be exerted on the hypothalamic rather than pituitary or target-hormone levels. Such manipulation of precision chemicals at the executive hormone switchboard might even be more effective. □

films OF THE WEEK

IF A BOY CAN'T LEARN. 16mm, color, sound, 28 min. A 17-year-old boy with learning disability is now a senior in high school. A nonreader, he was "passed along" through school, and entered high school without graduating from elementary. He has been a disciplinary problem and a teaching challenge. His teacher persuades school administration and the boy's parents to pay for diagnostic work-up and evaluation at the Learning Disabilities Center of Pacific Medical Center, San Francisco. Following testing, a specialist from the center is seen in conference with the boy's parents. They devise ways for using his learning strengths to compensate for his weaknesses. Result: a dramatic change in attitude on the part of the boy, his teachers and school administration. Audience: teachers and student teachers, physicians, parents, counselors, psychologists. Purchase \$295 or rental \$20 from Lawren Productions, Dept. SN, P.O. Box 1542, Burlingame, Calif. 94010.

TAKE TWO FROM THE SEA. 16mm, color, sound, 28 min. Depicts the adventures of two young hopefuls who are surprised to learn that their "big break" as Hollywood film makers is to make a documentary on oysters and clams—about which they know nothing. As they travel to the West, Gulf and East Coasts oyster-clam shellfishing sites, the audience sees methods of harvesting, aquaculture, processing, cooking and serving shellfish. Audience: general. Purchase about \$75 or free loan from Motion Picture Service, Dept. SN, NOAA, 1815 N. Fort Myer Dr., Arlington, Va. 22209.

THE UNCONQUERED PLAGUE: SCHISTOSOMIASIS. 16mm, color, sound, 30 min. Schistosomiasis is the almost unavoidable disease of 200 million people in poor agricultural regions of the Far and Middle East, Africa, eastern South America, and the Caribbean. One form of the parasite lives in freshwater and can enter the body through the skin. Its eggs are carried in the bloodstream and lodge in various organs, progressively destroying them as the infection builds. The common snail is a carrier of the disease, and the film details efforts in the Island of St. Lucia to control and eradicate the disease through various means. Audience: high school, college. Purchase \$385 or rental \$31 from McGraw-Hill Films, Dept. SN, 1221 Avenue of the Americas, New York, N.Y. 10020.

UNDERSTANDING AGGRESSION. 16mm, color, sound, 29 min. Psychologist Roger Ulrich presents significant research findings and discusses a problem especially relevant today—the possible destruction of mankind by means of man's own aggressive tendencies. Utilizing a freeze-frame technique, images of man's aggressive behavior as depicted by artists throughout the ages are presented. Actual footage of the Chicago riots and other illustrative examples of filmed violence are shown. In a laboratory setting, Dr. Ulrich demonstrates some of his own findings with animal experiments. Explanations of research findings and theories throughout the film serve to make the various points clear. Some of the avoidable causes of aggression are identified, such as aversive environment, pain, necessary-adaptive reactions, glorification of war and punishment of aggressors. The film suggests possibilities for prediction and control: stop glorifying violence, stop using violence to control others, stop using aggressive means, and improve aversive environments. Audience: boards of education, police, PTA's, youth and church groups, parents, etc. Purchase \$350 or rental \$45 (prices tentative) from Appleton-Century-Crofts, Dept. SN, 440 Park Ave. S., New York, N.Y. 10016.

Listing is for readers' information of new 16mm and 8mm films on science, engineering, medicine and agriculture for professional, student and general audiences. For further information on purchase, rental or free loan, write to distributor.