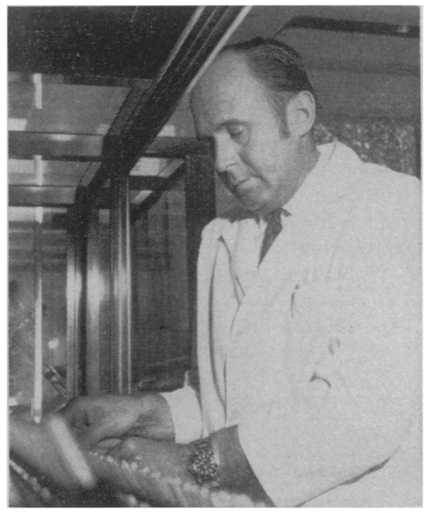
Toward birth control by peptides



Tulane Univ.

Schally: First in hormone synthesis.

Brain hormone synthesis offers sweeping new approaches to birth control

The ultimate control button in the elaborate reproductive hormone network—a hormone found in the brain's hypothalamus—has now been purified, characterized and synthesized, with the synthetic compound identical to the natural one in both structure and behavior. Credit for this long-sought-after achievement goes to a research team at New Orleans' Veterans Administration Hospital and Tulane University School of Medicine headed by Dr. Andrew Schally. Dr. Schally reported the structure and synthesis at the annual meeting of the American Endocrine Society in San Francisco.

The hormone contains 10 amino acids and has the unbelievable name of luteinizing hormone-releasing hormone/follicle-stimulating hormone-releasing hormone. For sanity's sake, it is called LH-RH/FSH-RH. What the hormone does is control the release as well as the synthesis of two pituitary hormones—LH and FSH, the luteinizing and follicle-stimulating hormones. These protein hormones then act on the ovaries and testes, causing, among other things, the secretion of various steroid sex hormones.

A synthetic LH-RH/FSH-RH opens the way to clinical studies into the hormone's potential as a new kind of female birth control method; before only preliminary studies could be done, using the natural hormone (which requires hormone extraction from 20,000 pigs' hypothalami for testing on one female patient). Now Dr. Schally is being bombarded with letters from physicians all over the world asking to assist in clinical studies of the synthetic hypothalamic hormone.

The work bring about the possibility of a contraceptive composed of a peptide—a compound of two or more amino acids. Birth control pills now commercially available are made of synthetic steroids—estrogen and progesterone. About the only other chemicals being tried clinically as contraceptives are the prostaglandins, hormone-like substances that work on immediate organ targets (SN: 10/10/70, p. 306). Under natural conditions they come into play toward the end of pregnancy. The prostaglandins are being intraveneously injected into a select group of women in Uganda as a post-coital contraceptive, or immediate abortive agent.

In all, a synthetic LH-RH/FSH-RH could have substantial impact on birth control research, a specialist on steroids and prostaglandins at a large American pharmaceutical company believes. Another drug company, manufacturer of one of the more popular steroid birth control pills, has refused to comment on the potential of a peptide "pill." Drug company watchers interpret their "no comment" in two ways. Either the company feels its interests are threatened, or it is out to get a share of the peptide research action.

Moreover a synthetic LH-RH/FSH-RH might be used for at least four different methods of birth control, Dr. Schally believes. One possibility would be to disrupt the normal events that occur during the menstrual cycle, in hopes, say, that ovulation will not occur. Dr. Akira Arimura of the New Orleans team will try this approach clinically in Japan, in September. Analogues, which resemble the natural hormone in structure, might be synthesized and used to inhibit the pituitary gland from releasing LH and FSH, thereby preventing ovulation. Yet another option would be to create a compound to neutralize LH-RH/FSH-RH that then might be used to immunize women against ovulation for several months at a time.

Finally, of interest to many Roman Catholics, would be an LH-RH/FSH-RH hormone that might be given around the middle of the menstrual cycle to induce ovulation and hence clear the way for intercourse during the rest of the cycle without fear of pregnancy. The steroid pills, by suppressing ovulation, do not have this potential.

The proof that LH-RH and FSH-RH activities are carried by the same substance comes as somewhat of a disappointment, however, for it lessens the chances for a male contraceptive. In men, follicle-stimulating hormone is needed for spermatogenesis; luteinizing hormone is needed for testosterone production. Blocking both with an FSH and LH antagonist would be a sort of temporary castration.

Ironically, about the time Dr. Schally's group reported LH-RH/FSH-RH synthesis, another group, headed by Dr. Karl Folkers, professor of chemistry at the University of Texas, and Dr. Cyril Bowers, professor of medicine at Tulane University Medical School, reported synthesis of a tetrapeptide (a four amino-acid compound) that acts similarly to LH-RH in an experimental rat model, yet is much smaller than the natural LH-RH in structure. Drs. Schally, Folkers and Bowers were colleagues at one time, before a rift occurred.

Drs. Folkers and Bowers say that in addition to being simpler and less expensive to produce than the natural hormone, the synthetic tetrapeptide may have some hormonal advantages over the natural LH-RH because its effect in the body may be more limited. The activities of natural peptide hormones often overlap those of other hormones because of their similarities in chemical structure. Dr. Folkers says he foresees the synthetic tetrapeptide more immediately assisting in the correction of sterility than as a birth control method.

But Dr. Schally sees little use in Drs. Folkers' and Bowers' mini LH-RH. The tetrapeptide, he says, "is half-a-million times weaker than ours." □