Major male sex hormone unraveled

Among the handful of executive hormones secreted by the pituitary gland are two master sex hormones—luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Unknown to many people, these two hormones are secreted in both men and women. Their actions differ, however. In women, both LH and FSH contribute to the development of eggs, the inducement of ovulation and the regulation of the female sex hormones—the estrogens—that are secreted by the ovaries. In men, FSH is concerned exclusively with the production of sperm cells; LH is concerned exclusively with the regulation of the male sex hormones—the androgens—that are secreted by the testes.

The chemical structure of human LH was unraveled a year ago by Albert F. Parlow and Basudev Shome of Harbor General Hospital in Torrance, Calif., and of the University of California at Los Angeles. It has since been confirmed by C. H. Li at the University of California at San Francisco. Parlow and Shome now report in the July JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM that they have determined the chemical structure of human FSH. The unraveling has vital clinical potential. It may be possible to use FSH as a male contraceptive and as a means to correct infertility in men and women where infertility results from inadequate production of the hormone.

FSH, like LH, is a glycoprotein. The protein part of each hormone has an alpha and beta subunit. The alpha subunits of LH and FSH are identical, Parlow and Shome have found, but the beta subunit of FSH differs somewhat from that of LH. "What was interesting and surprising to us," Parlow told SCIENCE NEWS, "is that the beta subunit of FSH is closer to that of TSH than of LH." TSH is thyroid-stimulating hormone. It is a third glycoprotein secreted by the pituitary gland and controls the release of thyroid hormone. Parlow and Shome were also the unravelers of the chemistry of TSH. The alpha subunit of TSH is identical to that of LH and FSH.

The California endocrinologists are now exploring the value of FSH as a male contraceptive. Since they have worked out the techniques for determining the chemistry of human FSH, they will use the same methodology to unravel the chemistry of sheep FSH. They will then take the beta subunit of the FSH and vaccinate rodents, rabbits and primates with it. The sheep FSH should raise antibodies in the rodents, rabbits and primates. These antibodies should cross-react with the FSH naturally produced in the rodents, rabbits and primates. If this is the case, then natural FSH production should be turned off in the animals, and sperm production along with it. If things go as planned, Parlow and Shome hope to start clinical trials within three to five years. They would use the beta subunit of sheep FSH to vaccinate men against sperm production.

They don't anticipate any side effects from the vaccine, but they do worry whether the vaccine will be permanent or temporary and wonder how often it would have to be given. They hope that these questions will be answered in their animal experiments.

The reason FSH cannot be used to vaccinate women against ovulation, Parlow explains, is that not just ovulation but also estrogen production would be switched off, since FSH controls both. "This would be bad," Parlow says, "because females, in the absence of their sex hormones, lose their soft smoothness and roundness and become wrinkled. If one selectively disrupts FSH production in the male, however, he won't produce sperm, but he will still have normal production of sex hormones by the testes. So he can engage in the usual male behavior, still have hair on his face and be happy, except that he'll be sterile."

Although Parlow and Shome do not intend to work on the synthesis of FSH, they anticipate that chemists who specialize in the synthesis of protein hormones will. But synthesizing protein hormones is a formidable challenge. And even when a protein hormone is synthesized, there is no guarantee that it will be easy to synthesize on a large scale. For instance, the protein hormone insulin was synthesized 20 years ago, but even now there is no widespread synthesis of insulin. Diabetics must depend on natural insulin obtained from the pancreas glands of cattle, and the cost of this source of insulin is rising along with beef prices. Since FSH is a much larger protein than insulin, it will probably be some time before it is synthesized, and even longer before its synthesis can be conducted for widescale clinical use.

When that time comes, though, synthetic FSH will probably be used to treat both men and women who are infertile because their pituitary glands do not produce enough FSH. Men need especially large quantities of FSH. Natural sources of FSH are now exceedingly limited—human pituitary glands obtained at autopsy and the urine of postmenopausal women. □

Chocolate, cheese and migraines

John Fothergill, a British physician long since over his worldly headaches, published in 1784 the first medical research linking migraine headaches with consumption of certain types of food. He found that many of his patients suffered attacks after eating cheese.

It wasn't until 1967 that another British physician, Edda Hanington of the Wellcome Trust in London, determined that tyramine in cheese was the headache initiator. Three years later, Hanington published evidence that the most common "dietary trigger" is chocolate. The obvious question was, then, what chemical do these two foods have in common? It turned out to be phenylethylamine, which chocolate has in large amounts, and which is common to many, but not all, cheeses.

A new study of migraine and food ingestion by Hanington, M. G. H. Youdim of Oxford's Radcliffe Infirmary and M. Sandler of Queen Charlotte's Maternity Hospital in London is reported in the July 26 NATURE. They studied a group of migraine sufferers, administering placebos and capsules containing phenylethylamine. Thirty of the 36 had no migraine reaction from the sugar capsules, while 18 of the 36 suffered a migraine attack after the phenylethylamine. "This," they state, "seems to be a *prima facie* case for the existence of a cause and effect relationship" between ingesting the amine and the onset of migraine in some patients.

One unusual fact associated with this phenomenon is a delay of from three to twelve hours in headache onset after amine ingestion. In their paper, the team puts forth and tests a hypothesis concerning this. The delay seemed to rule out a simple trigger action by phenylethylamine itself, so they suspected that it might somehow cause the release of vasoactive agents (chemicals that cause vein and artery constriction). Phenylethylamine is known to be inactivated by the enzyme monoamine oxidase (MAO), and the team suspects a form of MAO in migraine-prone individuals may function defectively, allowing the buildup of the amine. If a certain critical level is reached, an "all-or-none response" occurs, and the high amine levels trigger the release of a vasoconstrictor which acts on the vessels in the brain to cause a migraine attack.

They took blood samples from migrainous and nonmigrainous volunteers, and tested the platelets to determine how effectively the MAO was breaking down various amines. There was a "highly significant decrease" in the ability to break down these products in the migrainous individuals, they say, and the MAO pathway is very likely at the roots of the migraine problem. □