SOUTHWESTERN NEWS

June 26, 1992

PROSCAR, FUTURE PROSTATE DRUGS BASED ON UT SOUTHWESTERN STUDIES

DALLAS -- Research on a rare genetic disorder, done at The University of Texas Southwestern Medical Center at Dallas in the early '70s, laid the theoretical foundation for the development of a drug to shrink benign enlargement of the prostate gland. Finasteride (manufactured by Merck Sharp & Dohme as Proscar) was approved by the U.S. Food and Drug Administration on June 19.

In 1974, Dr. Jean D. Wilson, professor of internal medicine, holder of the Charles Cameron Sprague Distinguished Chair in Biomedical Science and one of the world's leading authorities on sexual endocrinology, published the first description of a rare genetic disorder. Noting that men with a deficiency of the enzyme 5-alpha reductase did not develop normal prostates or prostatic enlargement, he wondered if there might be a way to reproduce this condition artificially as an aid to the treatment of enlarged prostates.

In the late 1970s and early 1980s Wilson studied the active site of the 5-alpha reductase molecule, which controls the uptake of testosterone and its conversion to dihydrotestosterone--the male hormone most closely associated with enlargement of the prostate. He began devising compounds that would bind to it in order to block testosterone from doing so. Nothing worked, however, and Wilson abandoned the effort.

A Merck scientist pursued the project and eventually developed

(More)

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Proscar, which was shepherded through clinical trials spanning several years at UT Southwestern and several other sites.

Extensive testing has shown that Proscar may bring significant relief from symptoms for between 30 and 40 percent of BPH patients.

The UT Southwestern arm of the trials was conducted by Dr. John D. McConnell, associate professor of urology and chairman of a panel appointed by the U.S. Dept. of Health and Human Services' Agency for Health Care Policy and Research to develop BPH treatment guidelines.

The prostate is a walnut-sized gland just beneath the bladder that secretes one of the primary constituents of seminal fluid. Somewhere in middle to late-middle age, about eight in 10 men experience some degree of non-cancerous prostatic enlargement, a condition termed benign prostatic hyperplasia (BPH). Of these, about one in 10 eventually undergoes surgery.

Researchers have yet to determine what triggers the process leading to BPH. Once under way, however, it follows a fairly predictable course. First, the bladder becomes more muscular in response to the resistance created by the enlarged prostate, causing frequency and urgency of urination--early symptoms of BPH. Over time, the bladder becomes less able to compensate as the prostate continues to enlarge. Then symptoms of actual obstruction begin to occur.

Symptoms include impairment in the urine stream, decreased force of urination, nocturia (nighttime urination) and incomplete bladder emptying. Eventually, the blockage can reach a point at which a man becomes incapable of urination--the condition known as urinary retention. Advanced BPH also can cause bleeding, infection, renal insufficiency and kidney failure.

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NOTE: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences, Southwestern Allied Health Sciences School, affiliated teaching hospitals and outpatient clinics.