Can Male Hormones Really Help Women?

M. J. Friedrich

BOSTON—Androgens, which are vital for proper development and maintenance of the male reproductive system, also play important physiological roles in women, some of which are only beginning to be understood. Because of the importance of these hormones to human health, researchers suspect that a decline in androgen levels, which occurs with age, may have adverse effects on women's health.

Unraveling the impact of androgen deficiency in women is a goal of Susan R. Davis, MBBS, PhD, of the Jean Hailes Foundation, an Australian not-for-profit organization in Clayton, Victoria, involved in education about, research into, and treatment of women's health care issues. Davis and colleagues have been studying why androgens are biologically important for women and how the replacement of testosterone may alleviate some symptoms that seem to be associated with androgen deficiency.

Androgens appear to have an important effect on women's energy and well-being, said Davis at the American Society of Andrology meeting here last month. She shared her results, soon to be published, from an Australian clinical trial of a transdermal testosterone patch developed specifically for women. Davis said postmenopausal women using the active preparation had an improvement in well-being as measured by the Psychological General Well-Being Index, particularly in relation to depression. Improvements in libido also were reported.

Assessment of patient well-being is a sort of touchy-feely aspect of endocrinology, Davis said, but an important one. Lack of energy is one of the factors that most negatively affect the quality of life for many menopausal and postmenopausal women, she said, and women who receive testosterone therapy claim the biggest boost is to their energy level. "They have more energy to do things, and I think that is what ultimately affects libido," she said.

DEFINING A DEFICIENCY

Davis acknowledged that there is no accepted biochemical or clinical definition of androgen deficiency in women. (According to *Dorland's Medical Dictionary*, the reference range for testosterone plasma levels in women is 0.8-2.6 nmol/L [23-75 ng/dL].) "There are studies showing that replacement shows improvements, but there's been no deficiency state documented or explanation of how this might relate to clinical symptomatology," she noted.

"I would consider treating a woman with a level of free testosterone below the midpoint of the normal range for the available assay," said Davis. "Units differ among countries and assays differ, but that is what I find useful." Davis proposes that a symptom triad of low libido, blunted motivation, and persistent background fatigue be used as a clinical definition of androgen deficiency in randomized trials of testosterone therapy.

Davis said the concept of androgen deficiency has been most readily accepted in the case of women who have had bilateral oophorectomy, since the ovaries are a main source of circulating testosterone. However, because testosterone levels decline with age, women in their later reproductive years also may have lower levels of testosterone than younger premenopausal women and may experience such symptoms as loss of libido, she said.

By the time a woman has gone through menopause, said Davis, her testosterone levels may be further depleted, especially if she is taking estrogen replacement therapy. Because estrogen replacement therapy can significantly reduce bioavailable testosterone in postmenopausal women, "this can add insult to injury." Davis said oral contraceptives also can reduce greatly levels of bioavailable testosterone in younger women, which may be the reason that some women on the pill report a loss of libido.

Because symptoms of androgen deficiency can be caused by a number of factors, Davis said that before making this diagnosis, other possible causes of fatigue and low libido such as depression or iron deficiency should be ruled out. Many of the patients Davis sees are referred by sex therapists and psychiatrists "who feel they have nothing to offer their patients because they aren't clinically depressed or don't seem to have underlying sexual relationship problems," she said.

A "NASTY" HORMONE?

There is a tendency, said Davis, to think of testosterone as a "nasty" steroid in terms of cardiovascular risk. "Common wisdom has it that women are protected [from cardiovascular disease] because they have estradiol and men are at increased risk because they have high levels of testosterone throughout their lives." Yet the picture may not be so simple. Recently, estradiol's cardiovascular protective effect was called into question by results from the Women's Health Initiative study of hormone replacement therapy, in which women on active therapy had a 1% rise in risk of cardiovascular disease and stroke. Davis suggested that as more is learned about testosterone, assumptions about its negative effects may be found to be overstated. "In our studies," she said, "testosterone has some benefits and doesn't appear to have risks."

The increased risk reported in some studies may relate to oral vs parenteral dosing. For example, there have been reports that oral administration of testosterone can reduce levels of high-density lipoprotein cholesterol and apolipoprotein A-I, but Davis said to her knowledge, this has not been seen with parenteral administration.

Another concern about testosterone therapy is the risk of breast cancer. Epidemiological studies have shown both

positive and negative associations between endogenous androgen levels and breast cancer risk, she said, and more research is needed to clarify this question, said Davis.

While adverse effects of testosterone in women, such as masculinization and fluid retention, are possible, Davis said these effects are unusual when therapeutic hormone levels are maintained within normal physiological levels.

"This is cutting edge work," said Erol Onel, MD, chief of andrology at Tufts University School of Medicine, commenting on Davis' presentation. The potential risks associated with androgen therapy must be determined, but once these have been identified, and researchers have defined normal testosterone ranges for women and the proper treatment of a woman with androgen deficiency, Onel said, the potential of the research is "phenomenal." □

Addiction Medicine Specialists Add a New Therapeutic Approach

Stephen Lurie, MD, PhD

CHICAGO—The last 10 years have witnessed the growth of drug courts in the United States. Instead of being sentenced through the criminal justice system, people who have been convicted of nonviolent drug-related crimes are being given the option of participating in rigorous, court-supervised rehabilitation. This approach relies on the concept of therapeutic jurisprudence, which has been defined as the use of social science to study the extent to which legal processes promote the psychological and physical well-being of the people they affect. These issues received renewed attention at a meeting here last month of the American Society of Addiction Medicine.

At a session entitled "Addiction Medicine in the Courtroom," Sidney H. Schnoll, MD, PhD, professor of internal medicine and psychiatry at the Medical College of Virginia, said that the criminal justice system can play a vital and therapeutic role in the treatment of chronic substance abuse. Schnoll admitted that most participants in the session would find it difficult to imagine judges and attorneys functioning in a healing capacity, a role that the courts have historically turned over to therapists and social workers.

However, he said, it is time to get past the traditional argument about whether criminal behavior arising from drug addiction should be treated as a medical or a criminal problem. Schnoll said that instead of dwelling on these theoretical distinctions, drug courts focus on the specific reasons that people commit drug-related crimes, and develop practical and individualized approaches to changing these behaviors.

SHUT THE REVOLVING DOOR

William G. Schma, a judge in the ninth judicial circuit court in Kalamazoo, Mich, said that after several years as a judge in a traditional courtroom, he began to notice that the same defendants would appear before him repeatedly on charges of having committed nonviolent offenses to support their drug habits. He found that repeatedly sentencing these individuals usually did not deter them from further criminal behavior.

However, he said, most attorneys and judges usually are unconcerned about such poor outcomes of the criminal justice system, because they are trained to believe that the court's mission is to administer a blind and impersonal legal process and not necessarily to produce humane outcomes.

In contrast, Schma said that the operation of drug courts is based on the premise that "the pathology of crime brings with it a person with predicaments." These may include a lack of inner emotional and mental resources and unmet external problems, such as poor housing, unemployment, or lack of child care and transportation. Thus, a drug court functions as an "interdisciplinary problem-solving community institution" that coordinates the input of police and probation officers, social workers, drug counselors, physicians, and family members. Schma presented data showing that the long-term costs of this approach are considerably less than those of the traditional criminal justice system. For instance, when compared with 2 years of imprisonment, 1 year of court-supervised drug rehabilitation followed by a year of employment may produce a direct savings of more than $60 000. The results would be even more impressive if the other social costs of nonviolent crime were taken into account. The success of this approach, Schma said, is based on a "recognition of the therapeutic potential of the court's coercive power. We must move from a focus on retribution to a focus on healing."

Peggy Fulton Hora, a Superior Court judge in Hayward, Calif, emphasized that the advent of drug courts is "revolutionary and transforming." Hora said that drug-court judges typically mandate that participants (who are deliberately not called "defendants" to avoid implications of guilt or innocence) develop their own treatment plan in conjunction with legal and medical authorities. Participants must then appear regularly in court to report on their progress. Hora said that drug court judges enforce adherence to the plan, using rewards for good behavior as well as imposing sentencing and imprisonment for failure to comply.

For example, Hora said she may reduce participants' court costs if they perform supervised volunteer work or complete a job-training program. On the other hand, she may order participants to spend a weekend in jail for missing a treatment session or to spend even more time there if they are found