Testosterone Deficiency and Supplementation for Women: Matters of Sexuality and Health

by SUSAN RAKO, MD

Each woman has her own individual adjustment to the sexual aspect of life, with her familiar rhythms of sexual feelings, fantasies, dreams, and activities. Life circumstances can certainly disrupt sexual rhythms, but the bottoming out of sexual desire that results from a critical reduction in testosterone is different from the fluctuations experienced with the various ups and downs of life and relationships.1

It has been postulated that, “No matter how hard a woman might try to assemble the building blocks of healthy sexual functioning—the required amounts of other hormones, a loving partner, adequate stimulation, possibly a good sexual fantasy—it cannot work if she does not have the basic foundation of enough testosterone.”2

THE ROLE OF TESTOSTERONE IN FEMALE PHYSIOLOGY

Testosterone, an anabolic steroid and the most potent of the androgens, promotes metabolic efficiency, the physiologic basis for the maintenance of “vital energy.” It has been stated that, “Testosterone and other androgens have some biological activity on virtually every tissue in the body.”3

In girls, as well as boys, it is testosterone that triggers the events of puberty.4 The adolescent girl's growth of pubic and of axillary hair,5 the heightened sexual sensitivity in the nipples and genitals, and the increased susceptibility to psychosexual stimulation (sexual libido) are all generated by a surge of testosterone at adrenarche (the markedly increased production of adrenal cortical androgens that occurs at puberty).

Groundbreaking research published in 1959 made use of clinical observations of women with advanced breast cancer whose ovaries and adrenal glands had been removed in the hope of slowing progression of the disease. This research concluded that androgens, rather than estrogens, are responsible for sexual desire in the human female.6

Two years later, another article emphasized that “androgen is the libido hormone in both men and woman” and that estrogen was “necessary to abolish vaginal dryness and tenderness and so expedite coitus,” but that “androgen was found to increase the sensitivity of the genitals, especially the clitoris, as well as to heighten desire and increase sexual gratification.”7

The symptoms and signs of testosterone deficiency include:1:

2. Decreased sensitivity to sexual stimulation in the nipples and in the clitoris.
3. Decreased arousability and capacity for orgasm.
4. Diminished vital energy and sense of well-being.
5. Loss of muscle tone.
And, in some women:
6. Thinning and loss of pubic hair.

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7. Genital atrophy not responsive to estrogen.
8. Dry and brittle scalp hair; dry skin.

TESTOSTERONE AND BONE DENSITY
Recent research has shown that testosterone contributes substantially to bone density as well as to muscle tone. Testosterone in combination with estrogen supplemental therapy has been shown to produce significant increases in spinal bone mineral density—an effect not produced by estrogens alone.

TESTOSTERONE AND CARDIOVASCULAR RISK
A recent article reviewed the research demonstrating the cardioprotective effects of testosterone. In men, testosterone has been demonstrated to have beneficial fibrinolytic effects and beneficial effects on blood vessel endothelium, on blood sugar and insulin metabolism, and on maintaining coronary artery circulation. Attention is drawn to the need for studies on the potential cardiovascular protective effects of physiologic levels of testosterone in women and in men.

TESTOSTERONE PRODUCTION IN WOMEN
On the average, premenopausal females produce 0.3 mg of testosterone per day. With the establishment of the menstrual cycle, the hormone primarily produced by the ovaries is androstenedione, most of which is then converted to testosterone and subsequently aromatized to estradiol. However, not all of the ovarian testosterone becomes estradiol. Enough testosterone remains unconverted to amount to 25% of a woman’s daily testosterone production, another 25% is produced by the adrenal cortex, and the remaining 50% by peripheral tissues (including the liver, the skin, and the brain) from precursors produced in the ovaries and the adrenals. In other words, the ovaries and the adrenal glands produce all of a woman’s testosterone—directly or indirectly.

TESTOSTERONE IN THE BLOOD
Most of the circulating testosterone (97% to 99%) is carried in the blood bound to sex hormone binding globulin (SHBG). Only unbound or “free” testosterone (1% to 3% of the total) can attach to cellular receptors to produce effects on tissues. If a woman is not using supplementary methyltestosterone, accurate values for both total and free testosterone can be obtained when measuring testosterone blood levels. It is important to know that methyltestosterone, which has the advantage of being optimally absorbed when taken orally, confounds the blood assay for total testosterone.

Sensitivity to testosterone is a variable phenomenon. The adequacy of a particular blood level of testosterone can differ from woman to woman. A woman presenting with the clinical symptoms and signs of testosterone deficiency whose blood levels of total and free testosterone are measured to be in the lower part of the “normal” range may actually be testosterone deficient and will benefit from appropriate physiologic supplementation. In this regard, it is preferable to “treat the patient, and not the numbers.”

MENOPAUSE, ADRENOPAUSE, AND TESTOSTERONE DEFICIENCY
The postmenopausal ovary produces not only markedly lower amounts of estrogens, but also substantially lower amounts of testosterone. Several years before most women reach menopause (by age 40 to 44) adrenal androgen production has already decreased by more than half.

Because the function of the adrenal cortex appears to be linked to the function of the ovary, a woman needs fully functioning ovaries to maintain fully functioning adrenals.

It has long been observed that adrenal cortical hormone production (including testosterone) falls off more quickly in women than in men. This may be due to the fact that, on the average, the testes remain functional for decades longer than the ovaries. The consequence of the connection between ovarian function and adrenal function is that, following menopause, women lose not only a significant portion of their ovarian estrogen and testosterone, but also a significant portion of their adrenal androgens, including testosterone.

In some naturally menopausal women, testosterone production can decrease to the point where it is unmeasurable; signs and symptoms of testosterone deficiency can develop for these women even during their perimenopause. More commonly, testosterone deficiency develops during the several years following natural menopause. Because estrogen has the effect of stimulating the production of SHBG (which will bind up more of whatever available testosterone a woman may be producing), when a woman takes estrogen supplemental therapy, she may be tipped into testosterone deficiency—with loss of libido, energy, and other symptoms.

HYSTERECTOMY AND TESTOSTERONE DEFICIENCY
In 1995, the most recent year for which statistics are available, 583,000 hysterectomies were performed in the United States. Today one-third of American women have had a hysterectomy by age 65—most often before the age of 50.

Although one or both ovaries may be spared at the time of surgery, ovarian failure (postulated to be a consequence of interruption of the blood supply formerly provided by the uterine artery) follows hysterectomy in a significant number of cases.

Within a few days to a few weeks of the surgery, women whose ovaries have been surgically removed or compromised can have dramatic symptoms of both estrogen and testosterone deficiency. Supplementary estrogen, which is often prescribed, cannot help the symptoms of loss of sexual libido and response, lack of gener-
al energy, and diminished sense of well-being that are the consequence of the testosterone deficiency that approximately half of these women develop.\textsuperscript{14}

Studies have demonstrated that women who have undergone surgical menopause and have been treated with both supplemental estrogen and testosterone achieved an optimal balance of sexual energy and well-being as compared with women given either no hormones or estrogen alone.\textsuperscript{15}

At a time when they may be enjoying their sexual and vital energies to the fullest, women who undergo hysterectomy in their 30s and early 40s (and, occasionally, even in their 20s) are particularly unprepared for and aggrieved by these losses. Too often the diagnosis of testosterone deficiency is missed, and many women reporting loss of libido and energy are prescribed antidepressants or referred for counseling; however, what they need is supplementary testosterone.

\textbf{CHEMICAL MENOPAUSE AND TESTOSTERONE DEFICIENCY}

The 1992 publication of “A Neglected Issue: The Sexual Side Effects of Current Treatments for Breast Cancer” addressed the fact that women who have lost ovarian function secondary to chemotherapy for cancer develop testosterone deficiency.\textsuperscript{16} Although they know that definitive research data are not available, chemically menopausal women can be so distressed by their symptoms of testosterone deficiency and compromised quality of life that they choose to take prudently prescribed supplementary testosterone. Of the available forms of supplemental testosterone, methyltestosterone alone does not readily aromatize to estradiol and, therefore, may be the preferred supplement for women for whom it seems prudent to keep estrogen levels as low as possible.

\textbf{TESTOSTERONE SUPPLEMENTATION}

Symptoms of testosterone deficiency are not clinically subtle; however, some women are uncomfortable about initiating discussion about their problems. The most helpful physician is one who inquires about changes in sexual libido, energy, and sense of well-being, and who helps a woman evaluate her particular risk/benefit factors among the options available for treatment.

With the recognition of the cardioprotective, bone-saving, and other benefits of adequate estrogen supplementation, a decision about the risks/benefits of estrogen (with adequate progestin for a woman with an intact uterus) as a foundation for subsequent testosterone supplementation makes good clinical sense. If a woman has already been using estrogen (and, if indicated, adequate progestin), prudent testosterone supplementation, with the goal of keeping blood levels within the physiologic range, can be added to her established hormonal regimen. Clinical experience has shown the effective range of oral dosage to be 0.25 to 0.8 mg of methyltestosterone per day, with most women benefiting from 0.3 to 0.6 mg.\textsuperscript{7} Prescriptions for flexible, low enough dosing of oral methyltestosterone must be compounded to order.

\textbf{AVOIDING VIRILIZING SIDE EFFECTS}

The possibility of undesirable side effects is naturally a major concern of women deciding about supplemental testosterone. Testosterone supplementation within the physiologic range does not produce virilizing side effects.\textsuperscript{17} Only excessive, long-term dosage may result in the development of virilizing side effects—acne, increased downy facial hair, and (in extreme cases) lowered voice.

I have discovered that there is a sensitive “window” of dosage that works best for a particular woman at a particular time. This dose may change—as may the dose of estrogen supplementation she needs—as her ovarian and adrenal functions continue to diminish during the decade following menopause. If a woman takes more testosterone than needed, she will not experience stronger stimulation of libido, but will more likely experience irritability—a signal to reduce the dose.

\textbf{TOPICAL TESTOSTERONE}

Because testosterone deficiency can result in genital atrophy (even for women who have been using supplementary estrogen), women who begin supplementing with oral methyltestosterone may sometimes receive benefits to energy and sense of well-being without significant improvement in genital sensation and libido. I have discovered that testosterone-deficient women sometimes require a once-daily application to the genital mucosa of a small amount of topical testosterone—preparations compounded to order. When the tissue becomes healthy and local testosterone receptors have been well supplied, sensation and libido return.

Topical testosterone is well absorbed by healthy genital tissue and can potentially result in high blood levels—above the physiologic range. Intermittent monitoring of testosterone levels will allow for modification of concentration or dose schedule. Once libido has improved and capacity for genital stimulation has been established, a shift to an oral supplement will usually maintain an adequate effect on the genitals.

Another caution against long-term daily use of topical testosterone on the genital mucosa is the potential for local overstimulation and gradual clitoral enlargement—both reversible on discontinuation of topical testosterone. Should this ensue, a change to physiologic oral dosage is advisable and effective.

\textbf{FOCUS FOR FURTHER RESEARCH}

For more definitive answers on cardiac and cancer risk/benefits, testosterone supplemental therapy must be included in longer-term
research protocols. Shorter-term studies to confirm lowest effective dosage range, comparative effects of routes of delivery, and epidemiologic data are also pressing for attention.

As a recent review of the role of androgens in women’s health concluded: “Future research should be aimed at identifying those women who have not undergone surgical or medical castration but have decreased functional androgenic activity.... Androgen replacement therapy is a neglected area of medical practice and further research is needed to identify all women who will benefit from it.”

REFERENCES