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Testosterone and Libido

Introduction:
There is much written in the lay literature about the benefits of testosterone for enhancing libido. There is some truth and a lot of exaggeration. In the Gyn community, I think the manufacturer of Estratest spreads some of the misinformation. Estratest (see my comments below) is the only commercial product containing "testosterone" that is FDA approved for use in menopause. I will share my experience.

Normal Testosterone levels:
Most labs give a normal serum Testosterone range of 30-75 ng/dl. That is nanograms/deciliter. In a healthy young woman, the Ovary makes about half of the Testosterone and half comes from the Adrenal. The commercial laboratory "normal" range is two standard deviations on each side of the mean. That is 90% of the population. Only the 5% above 75 and the 5% below 30 are considered abnormal. I have asked the PhDs that run Quest if they have the actual curve of distribution, but they say they do not, that their figures don't work that way. It is not an even distribution, I suspect. PCOS is a fairly common disorder; more than 5% of the population. That means that PCOS women pull up the top of the normal range with Testosterone levels between 60 and 90.

Libido within the normal range: I see many young women with various menstrual and hormonal disorders. It is extremely rare for a patient in her teens or twenties to list low libido amongst her complaints. In addition, young women don't complain of excess libido. The young women with PCOS complain, as expected, of acne, abnormal hair growth and irregular periods. **They are not noted for excessive sexual behavior**. Most commonly, I see serum Testosterone in PCOS between 60 and 90. The levels of DHEA-S and Androstenedione are also elevated. They are virtually entirely of adrenal origin. On the low end, it is not unusual for me to see Testosterone below 30 in young, sexually active women, with no apparent sexual problems. Placing a woman on oral contraception, suppresses ovarian Testosterone production and the levels fall. Although some individuals have reported reduction of libido on oral contraception, it is not universally or even frequently a problem. In short, in **young patients** in their teens and twenties, **I see little relationship between testosterone and libido for values within, or even near, the normal range.**

Sexual response to Testosterone therapy: Occasionally I see women who have been treated by other physicians for low libido complaints. One popular therapy is injections with testosterone in oil. These injections are usually given on a monthly basis. It is not unusual for me to find levels of 250-500 ng/dl in these women. These levels are many multiples of the levels of any woman I have ever tested with naturally occurring Testosterone elevation. Some of these women do report a significant increase in libido. **I do not feel that it is ever appropriate to send a patient into extremes of super-physiologic levels of any of the hormones.** In the long run, this will probably cause hirsutism, a deepened voice and male pattern baldness. Even if no immediate problems are seen, my goal is to normalize conditions, not to make a normal situation into an abnormal one.

What determines libido? A woman's sex drive at any point in time is multifactorial. Her general health is of great importance. Is she getting adequate exercise and rest? How does she feel about her current sexual relationship? Does she have the time and motivation to devote to her sexuality? Although libido can be

improved by using extreme levels of Testosterone supplementation, I have not found that raising a woman from the low end of the range into the middle or high end of the normal range has much of an effect on libido.

Do I use supplemental Testosterone? Yes. Testosterone has a small effect on mood. It also improves decision-making. As I have pointed out to patients, men tend to make decisions more rapidly and with more certainty than women. They may be wrong, but they are less frequently in doubt. In addition, Testosterone stimulates osteoblasts to repair and build bone, thus protecting against osteoporosis.

What is in Estratest? Estratest and Estratest HS is a brand name of two synthetic hormone sets in a single tablet. The estrogen part is esterified estrogens. These are various estrogens with added molecules to increase water solubility and power. The testosterone is actually methyltestosterone. This is also a synthetic molecule that stays in the body for prolonged periods because it is difficult to metabolize and excrete. Neither of these medications show up on hormone blood work. It is difficult to compare either of these medications to natural hormones because they cannot be easily measured and their exact actions are unknown. In addition, the ratio of estrogen to androgen is fixed. They cannot be custom mixed for the individual patient's needs.

Some observations about Testosterone lab work: In the medical literature it is frequently reported that Total Testosterone levels are not reliable, that they vary randomly. I don't believe this. Laboratory testing is very precise now; it is automated and consistent. If nothing has changed for an individual patient, the values are fairly consistent and repeatable. It is common in science and in medicine that data that is not understood is considered to be in error. Anything that affects either ovarian or adrenal output will affect testosterone levels.

1. **Oral contraception** or any similar method including OrthoEvra patches or Nuva ring will lower Testosterone output.
2. **Any cortisone therapy** including nasal sprays and inhalers lower ACTH and shut down adrenal output. I have seen many menopausal women's Testosterone and DHEA-S virtually disappear after only a few days on a cortisone inhaler or nasal spray for asthma or sinus problems. The prior levels return when the adrenal suppression is stopped. This is despite the fact that these medications are marketed with the supposed advantage of minimal systemic effects.
3. **Adrenal exhaustion** is fairly common. These women have reduction of DHEA-S in addition to Testosterone. They tend to have generalized fatigue. Low libido is one part of the syndrome.
4. Many menopausal women, even women after removal of the ovaries, maintain normal Testosterone levels on adrenal output alone. I have one patient who is eighty years old with Testosterone of 45 ng/dl on no supplemental therapy. She looks terrific.
5. **Total v Free Testosterone:** There is much discussion in the literature of measurement and importance of total Testosterone versus the free component. This involves levels of Sex Hormone Binding Globulin (SHBG). At one time I was measuring all these levels. **I generally found that total and free Testosterone rise or fall together**. Much of the Testosterone in the blood is also loosely bound to albumin. Since there is much more albumin than SHBG in the blood, this amounts to a significant portion of the total Testosterone. Many things, including Estrogen, Thyroxin, Testosterone, BMI, insulin and insulin resistance affect **SHBG** levels. Free Testosterone is not directly measured, but is actually mathematically calculated using SHBG levels. I am not sure that the numbers the labs report for Free Testosterone precisely reflect Testosterone activity within a specific individual. In addition, for most target tissues, Testosterone must be converted to **dihydrotestosterone** to be active. The individual's level of **5-alpha reductase** activity governs testosterone activity at most target tissues. I have found it easier and less expensive to just measure total Testosterone. All the hormones affect the activity of each other. There is little to be gained by getting too hung up on any one blood level. My goal is to holistically balance the patient's health and life style as well as individual hormone levels.

Testosterone supplementation: Bioidentical testosterone can be given orally in a capsule, in a sublingual troche, as a topical cream, vaginal cream or topical gel. My experience is that many women have little or no

rise in Testosterone when it is given in an oral capsule. The **topical gel** can be very effective. I start with a concentration of **one-half mg/ml gel having the patient use one ml/day**. Since topical Testosterone can induce hair growth if put on the same piece of skin every day, I tell patients to move the site around. They have two upper arms, two lower arms, thighs front and back, a rear end and belly. There are lots of places. Most of the hormone is actually absorbed through the palm of the hand, so the site rubbed on doesn't matter much. The alcohol-based gels are fairly rapidly absorbed and are not very messy. Some physicians have suggested putting a little **Testosterone directly on the clitoris**. If this is done, the compounding pharmacist must be instructed to make a **vaginal cream**. The alcohol based gel will burn if placed anywhere on the vulva. After six weeks, serum Testosterone can be tested again to check the levels. If insufficient levels have been achieved, either the concentration or quantity of hormone can be increased. **There is a great deal of individual variation!** Some women will have a big rise in levels with the starter concentration of ½ mg/ml. Other patients can use up to 2-3mg/ml concentrations without getting too high a level. **My goal is to return Testosterone, and all hormone levels, only to normal levels, as tolerated. <u>I am never comfortable putting a patient into a super-physiologic state</u>.** If Testosterone is over 80mg/dl you are using too much; either, reduce the concentration or the quantity used, or both.

<u>Conclusion:</u> Testosterone is a normal component of a woman's hormonal milieu. It is important for mood, muscle development, bone health and brain function. Supplementation can be used to bring low levels into the normal range. When supplementing Testosterone, follow up blood levels are important to insure sufficient but not excessive serum levels. A woman's libido is affected by many factors in her health and life. Testosterone is only one of those factors. **Raising Testosterone levels from below normal into the normal range, or even to the top of the normal range, has only a small effect on libido**. I do not feel it is appropriate, safe, or good medical care, to raise any hormone to super-physiologic levels.

<u>Of note:</u> A study was recently reported in the NAMS *First to Know* series. A pharmaceutical company desired to market a testosterone patch for female use. There were three groups of women, each group given a different dose level of patch. Before treatment, each woman wrote a survey of libido and sexual frequency and activity. Repeat surveys were filled out during and after treatment. There was no statistically significant change in libido between the various levels of testosterone supplementation. **No serum testosterone levels were obtained on any of the women, either before or during the trial.** There seems to me to be very little reason to expect improvement in libido if a woman already has normal testosterone and you raise her levels a little more. The pharmaceutical company wants to treat everyone, regardless of hormonal need. **We need to change this approach! Hormone balance should be the goal, not blind treatment of symptoms regardless of the cause.** The FDA did not approve the patches. Patches might be a very effective way to enhance Testosterone levels. It is possible that a new approach, with a goal of restoring normal levels, would meet FDA approval.