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Testosterone Therapy in Women – July 2025

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Disclosures

- **Scientific Advisory Boards**
  - Integrative Therapeutics
  - Symphony Natural Health
  - Nutritional Fundamentals for Health

- **Director of Education and Research; co-owner**
  - Vitanica

- **Speaker's Bureaus**
  - Natural Factors
  - Doctor's Data
  - Enzyme Science
  - Precision Analytical

Testosterone in Menopausal Women - Overview

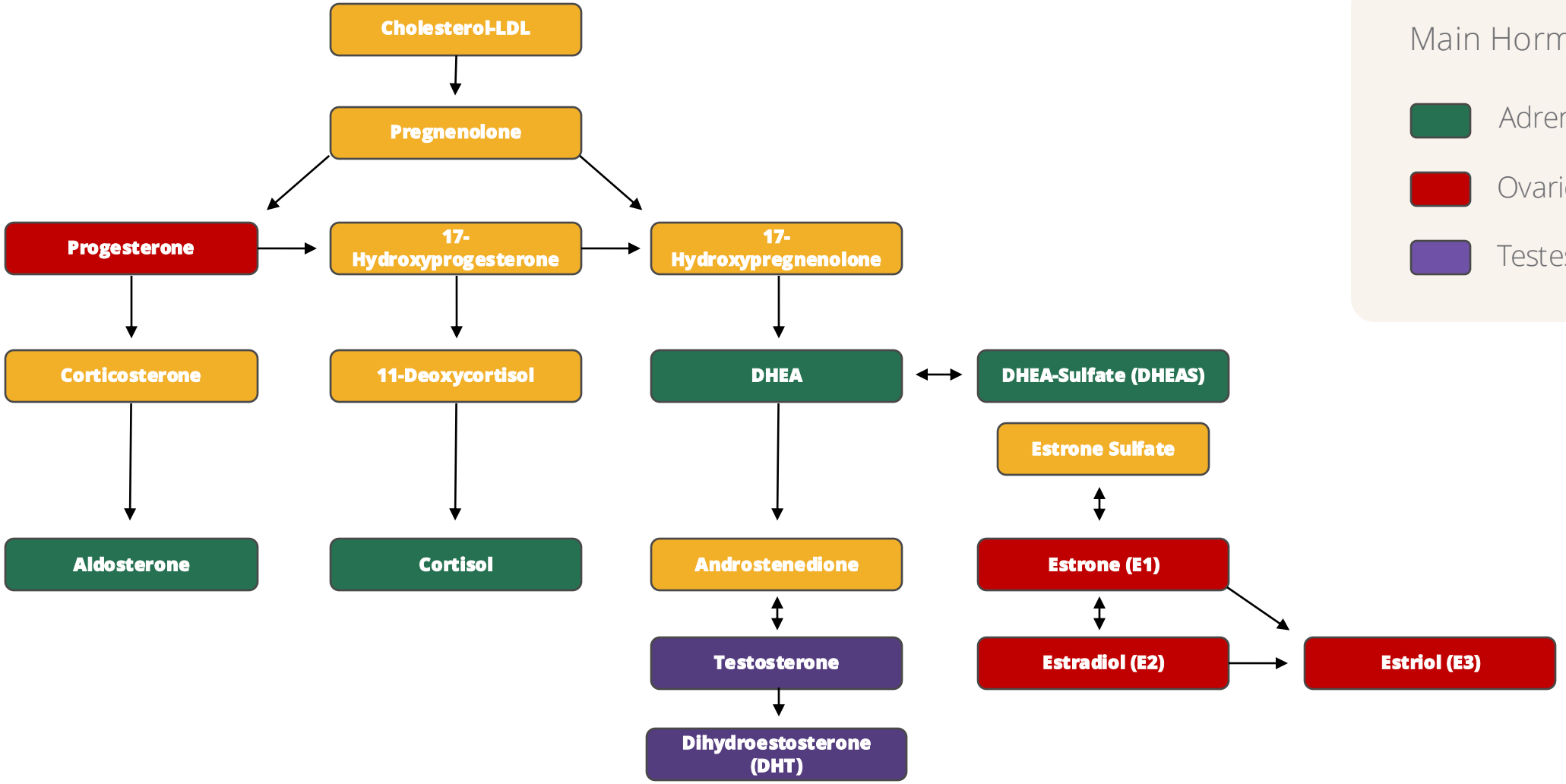
- Acts directly as an androgen in addition to being an obligatory precursor for biosynthesis of estradiol.
- Control of testosterone production in women is not well understood; no feedback loop governing its production has been described.
- Exerts physiological effects in reproductive and non-reproductive tissues in women.
- Concentrations of testosterone are positively associated with sexual function in women
- Postmenopausal ovary= androgen-secreting organ; levels of testosterone are not directly influenced by the menopausal transition or the occurrence of menopause.

Davis SR, Wahlin-Jacobsen S. Testosterone in women--the clinical significance. Lancet Diabetes Endocrinol. 2015 Dec;3(12):980-92.

Testosterone in Menopausal Women - Overview

- Serum testosterone levels in women: approximately 1/10th those in men; increase 20–30% at midcycle due to higher ovarian production
- Oophorectomy in younger, premenopausal women = even greater reduction in testosterone levels than in postmenopausal women
- Approximately 66% of testosterone in women is bound to SHBG, a significantly larger proportion than in men
- Increases in serum estrogen and thyroid hormone levels result in increased SHBG levels

Testosterone in Menopausal Women - Overview



Testosterone - Production

Ovaries

The ovaries, specifically the theca cells, produce a portion of circulating testosterone.

Adrenal Glands

The adrenal glands, located on top of the kidneys, also produce testosterone and its precursors like DHEA.

Peripheral Tissues

Other tissues, like skin and muscle, convert androstenedione (another androgen) into testosterone.

Estrogen can be converted to testosterone in adipose tissue in women.

Testosterone - Production

- Quantitatively, women secrete greater amounts of androgen than of estrogen
- The major circulating steroids -classified as androgens include
  - Pre-androgens: dehydroepiandrosterone sulphate (DHEAS), dehydroepiandrosterone (DHEA), androstenedione (A)
  - Androgens: testosterone (T), and dihydrotestosterone (DHT)
  - (in descending order of serum concentration)
  - (only the latter two bind the androgen receptor)
- Pre-androgens:
  - DHEA= primarily an adrenal product; regulated by adrenocorticotropic hormone (ACTH) ; acts as a precursor for the peripheral synthesis of more potent androgens. DHEA- produced by both the ovary and adrenal; also derived from circulating DHEAS.
  - Androstenedione and testosterone; products of the ovary and the adrenal
  - Dihydrotestosterone (DHT) is primarily a peripheral product of testosterone metabolism.

Testosterone – Transport in Women

- In women, testosterone= primarily transported in the bloodstream bound to proteins, with the majority being bound to sex hormone-binding globulin (SHBG) and albumin.
- A small fraction exists as "free" testosterone, which is the biologically active form. Free testosterone, along with testosterone bound to albumin (bioavailable testosterone), is available for use by the body's tissues.

Testosterone – Transportation Continued

Binding Proteins

Testosterone's transport in the blood is largely mediated by proteins= SHBG and albumin are the main proteins involved.

SHBG

SHBG binds testosterone with high affinity. In women, a significant portion of testosterone is bound to SHBG.

Albumin

Albumin binds testosterone with lower affinity but has a faster dissociation rate

Free Testosterone

Only a small percentage of testosterone is unbound and free in the bloodstream. This free testosterone is considered the biologically active form

Bioavailable Testosterone

The combination of free testosterone and albumin-bound testosterone is referred to as bioavailable testosterone. This fraction is readily available for tissues to utilize.

Conversion to Estradiol

In women, testosterone can be converted into estradiol, by aromatase.

Dynamic Regulation

Testosterone levels in women are lower than in men, but does have some fluctuation. For instance, testosterone levels can increase slightly during the ovulatory surge.

Menopause

Testosterone production declines with age, particularly after menopause, due to decreased ovarian and adrenal function. Surgical menopause = more significant and permanent drop in testosterone levels.

Testosterone – Metabolism

- Dihydrotestosterone (DHT) is primarily a peripheral product of testosterone metabolism.
- Testosterone is converted to DHT by the enzyme 5-alpha reductase in target tissues like the skin
- DHT is a more potent androgen than testosterone (~4x more potent)
- Testosterone can be converted to estradiol by the enzyme aromatase, also in target tissues.

Testosterone – Excretion

- In women, testosterone is primarily excreted through urine, both as conjugated and unconjugated (free) forms.
- A small portion of unchanged testosterone is also excreted in the urine, along with metabolites formed through hydroxylation and oxidation in the liver.
- DUTCH Urine measurements: T-glucuronide and T-sulfate

Menopause Steroid Hormone Levels

- Marked changes in ovarian and pituitary hormone secretion
- Few changes in hormone metabolism
- Metabolic clearance of E and T do not change with menopause
- Shift in 1 pathway; aromatization of androstenedione and testosterone to estrogen in peripheral tissues

Androgen Production in the Female

Tissues	Adrenals	Ovaries	Peripheral
Testosterone	X	X	X
Androstenedione	X	X	
DHEA	X	X	
DHEAS	X		

Daily Ovarian Secretion of Androgens

Androgen	Premenopausal	Postmenopausal
Androstenedione	1.5 mg/d	0.3 mg/d
Dehydroepiandrosterone (DHEA)	1-2 mg/d	0 - 0.1 mg/d
Testosterone	60 mg/d	60 mg/d

Adashi, 1994

Serum Hormone Levels

	Premenopausal	Postmenopausal
Estrogens, pg/mL *	Estrone 40-170 *** Estradiol 29-318 ***	Estrone 53-71 Estradiol 13-16
Progesterone, ng/mL **	0.47	0.17
Adrogens, ng/mL **	Androstenedione 1.9 DHEA 4.2-8.3 DHEA Sulfate 1600 Testosterone 0.32	Androstenedione 0.5-0.6 DHEA 1.8-2.3 DHEA Sulfate 300 Testosterone 0.25

*pg/mL = 10.0E-10 mg/mL (or 1.0E-9)
**ng/mL = 10.0E-7 mg/mL (or 1.0E-7)
*** The amounts vary depending on the phase of the menstrual cycle.

Ref-Abraham and Maroulls, 1975; Baird and Guevara, 1969; Judd, et al, 1982; Buster, et al 1992.

Blood Production Rates (daily) OF Androgens in Women

According to Reproductive Status

Androgen	Premenopausal	Postmenopausal	Oophorectomized
Androstenedione, mg/d	2-3	0.5 - 1.5	0.4 - 1.2
DHEAS, mg/d	6-8	1.5 - 4.0	1.5 - 4.0
DHEA, mg/d	8 - 16	4 - 9	4 - 9
Testosterone, pg/d	200 - 250	50 - 100*	20 - 70

*Age Dependent

Adashi, 1994, Longcope, 1988

Testosterone Therapy for Women

- "Global Consensus Position Statement on the Use of Testosterone Therapy for Women (1-13 points)"

- Endorsements:
  - International Menopause Society
  - Endocrine Society
  - European Menopause and Andropause Society
  - International Society for Sexual Medicine
  - International Society for the Study of Women's Sexual Health
  - NAMS
  - Royal College of Ob/Gyns
  - International Society of Endocrinology
  - Endocrine Society of Australia
  - Royal Australian and NZ College of Ob/Gyns

Davis SR, et al. Climacteric. 2019 Oct;22(5):429-434.

Measurement of FSD and Endogenous Androgen Levels (postmenopausal women)

1. Measurement of circulating testosterone
   - Testosterone concentrations decline during reproductive years but are maintained during menopause
   - Direct assays - highly unreliable for diagnosis within the normal female range of values but useful to exclude high baseline concentrations in the setting of suspected pathology or to rule/out supra-physiologic doses during treatment
   - Use high accuracy liquid/gas chromatography and tandem mass spectrometry assays for total testosterone

     "(LC/GC-MS/MS)"
   - Total testosterone is the main biomarker rather than free testosterone

Measurement of FSD and Endogenous Androgen Levels (postmenopausal women)

2. Terminology for female sexual dysfunction (FSD)

Distinct Conditions and categorized separately:

- HSDD: hypoactive sexual desire disorder
- FSAD: Female sexual arousal disorder
- Different etiologies, risk factors, clinical features and responses to psychological and biological interventions, including androgen therapy
- Diagnose through a thorough clinical assessment and diagnostic criteria- ISSWSH

Measurement of FSD and Endogenous Androgen Levels (postmenopausal women)

3. Associations between endogenous androgen concentrations and FSD

- Using androgen concentrations as a diagnostic test for sexual function categorized as “insufficient”
- There is no cut-off blood level for any measured circulating androgen to differentiate women with and without sexual dysfunction

Systemic Testosterone Therapy for Postmenopausal Women

4. Testosterone Treatment of naturally or surgically postmenopausal women with HSDD, with or w/o concurrent estrogen therapy

- Testosterone replacement can have beneficial effects on sexual function at physiologic levels in naturally or surgically postmenopausal women with HSDD
- Benefit over placebo= average of one satisfying sexual event per month and increases in desire, arousal, orgasmic function, pleasure and sexual responsiveness; reduction in sexual distress

Systemic Testosterone Therapy for Postmenopausal Women

5. Effects of Testosterone therapy on wellbeing, mood and cognition in postmenopausal women

- Insufficient evidence: cognitive performance or delay in cognitive decline, well being, mood

6. Musculoskeletal Effects of Testosterone Therapy

- High quality evidence that testosterone does not improve bone density or increase lean body mass or total body fat or improve muscle strength

Systemic Testosterone Therapy for Postmenopausal Women

7. Possible Androgenic side–effects of testosterone therapy

- At physiologic doses: systemic testosterone therapy in postmenopausal women is associated with mild side effects in some women:
  - (acne, increased body/facial hair)
  - but not alopecia, clitoromegaly or voice changes

Systemic Testosterone Therapy for Postmenopausal Women

8. Cardiovascular Health and Testosterone Therapy

- Oral testosterone therapy is associated with adverse lipid profiles with negative effects on HDL cholesterol and LDL cholesterol levels AND IS NOT RECOMMENDED
- Percutaneous and injectable testosterone therapy in doses that approximate physiological testosterone concentrations for premenopausal women, have shown NO significant adverse effects on lipid profiles over the short term
- Testosterone therapy-no association with increases in BP, glucose or A1c levels
- Non-significant trend for an increased risk of DVT has been seen in testosterone therapy; but it was used with concurrent estrogen therapy
- No good data on effects of testosterone therapy and myocardial infarction or death
- Recommendations regarding the effect of physiologic doses of testosterone in postmenopausal women on cardiovascular health are not generalizable to a more at risk population or to long term therapy

Systemic Testosterone Therapy for Postmenopausal Women

9. Breast health and testosterone therapy

- Short-term TD testosterone therapy does not increase mammographic breast density or affect breast cancer risk;
- Insufficient data exist to assess long-term breast cancer risk or to support safety in women with hormone sensitive breast cancer

Systemic Testosterone Therapy for Postmenopausal Women

10. Testosterone therapy and serious adverse events

- Testosterone therapy for postmenopausal women, in doses that approximate physiological testosterone concentrations for premenopausal women, is not associated with serious adverse events
- RCTs of testosterone therapy have excluded women at high cardiometabolic disease risk; most have included women taking concurrent estrogen therapy, therefore, the recommendation above is not generalizable to a more at risk population
- Safety data for testosterone in physiologic doses are not available beyond 24 months of treatment

11. Full Assessment of FSD before Rx Testosterone

- Multiple etiologies including biopsychosocial factors: neuroendocrine imbalance, physical ill health or disease, interpersonal difficulties, psychological distress and sexually repressive cultural or religious values
- Treatments should follow the biopsychosocial model and include pharmacologic options (hormone therapies and other agents), psychotherapy or multimodal treatments that combine both

12. Testosterone therapy in postmenopausal women

- The only evidence based female indication for the use of testosterone is HSDD in postmenopausal women
- Supraphysiologic doses are not recommended
- Measure SHBG: if above normal range; less likely to benefit
- Measure baseline total testosterone prior to treatment and repeat 3-6 weeks later
- Total testosterone after treatment should not exceed 27-38.6 ng/dL (lab differences)
- Monitor for signs of androgen excess
- Monitor total testosterone levels every 4-6 months
- Typical response time: 6-8 weeks; as early as 4; maximum effects at 12 weeks
- Discontinue treatment at 6 months if no sexual function benefits

13. Other Androgenic Preparations

- DHEA is not recommended for HSDD

Testosterone for Perimenopause/Menopause Women – Cochrane Review

Cochrane Review for postmenopause and libido, 2005

> "There is good evidence that adding testosterone to hormone therapy (HT) has a beneficial effect on sexual function in postmenopausal women. However, the combined therapy is associated with a higher incidence of hair growth and acne and a reduction in high-density lipoprotein (HDL) cholesterol. These adverse events may vary with different doses and routes of administration of testosterone. Adding testosterone to HT did not increase the number of women who stopped HT therapy."

Conclusion: Testosterone with standard MHT Tx= improved sexual function

Somboonporn W, Bell RJ, Davis SR. Testosterone for peri and postmenopausal women. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD004509.

Testosterone – Surgical Menopause Women

- **Design:** RDB parallel group, P controlled CT; 24 weeks
- **Patients:** women, aged 26-70 yr, with HSDD after bilateral salpingo-oophorectomy who were receiving concomitant estrogen therapy. Placebo (n = 279) or testosterone 300 microg/d (n = 283) was administered. 19 patients withdrew due to adverse events in the placebo group and 24 in the 300 mug/d testosterone group.
- **Intervention:** Testosterone (300 microg/d) or placebo patches were applied twice weekly.
- **Main outcome measure(s):** The primary end point was the change in the frequency of total satisfying sexual activity at 24 wk. Secondary end points included other sexual functioning end points and safety assessments.
- **Results:** At 24 wk= increase from baseline in the frequency of total satisfying sexual activity of 2.10 episodes/4 wk in the testosterone group, which was significantly greater than the change of 0.98 episodes/4 wk in the placebo group (P = 0.0003). The testosterone group also experienced statistically significant improvements in sexual desire and a decrease in distress. The overall safety profile was similar in both treatment groups.
- **Conclusion:** In the Intimate SM 1 study, the testosterone patch improved sexual function and decreased distress in surgically menopausal women with HSDD and was well tolerated in this trial.

Simon J, et al. J Clinical Endocrinol Metab. 2005 Sep;90(9):5226-33.

Testosterone – Surgical Menopause Women

Objective:

- Assess the efficacy and safety of a 300 µg/d testosterone patch for HSDD in surgical menopause women also using ET.

Methods:

- 535 women with HSDD; Hysterectomy/BSO; 24 weeks, DBPCT. Tx: P or the testosterone patch twice weekly.
- The primary efficacy endpoint: change from baseline at week 24 in the frequency of total satisfying sexual activity, measured by the Sexual Activity Log. Secondary measures =sexual desire using the Profile of Female Sexual Function and personal distress as measured by the Personal Distress Scale. Hormone levels, adverse events, and clinical laboratory measures were reviewed.

Results:

- Total satisfying sexual activity significantly improved in the testosterone patch group vs placebo after 24 weeks (mean change from baseline, 1.56 compared with 0.73 episodes per 4 weeks. Treatment with the testosterone patch also significantly improved sexual desire (mean change, 10.57 compared with 4.29) and decreased personal distress.
- Serum free, total, and bioavailable testosterone concentrations increased from baseline. Overall, adverse events were similar in both groups ($P > .05$). The incidence of androgenic adverse events was higher in the testosterone group; most androgenic adverse events were mild.

Conclusion:

- In surgically menopausal women with hypoactive sexual desire disorder, using ET and a 300 µg/d testosterone patch significantly increased satisfying sexual activity and sexual desire, while decreasing personal distress, and was well tolerated through up to 24 weeks of use.

Buster, J, et al. ***Obstetrics & Gynecology*** 105(5 Part 1):p 944-952, May 2005.

Testosterone - HSDD

- HSDD; 814 women over 52 weeks; received trandermal patch of either 150 mcg /day or 300 mcg/day testosterone or placebo patch. None were taking estrogen. Testosterone at both doses increased desire and decreased distress; the number of satisfying sexual episodes was greatest in those who received 300 mcg/day patch
- Also significant improvements in desire, arousal, responsiveness, orgasm, pleasure, satisfaction

Davis S, NEJM 2008;359(19):2005-2017

Testosterone Cream – HSDD Hysterectomized Women

- DBRPCT of 36 menopausal women; hysterectomy;HSDD.
- Tx: all women received Estradiol gel 1 mg/day (if she had been stable on an estradiol patch); + 1% testosterone cream (10 mg/gm) or placebo cream for 12 weeks. And then crossed over.
- Results:
  - Active treatment group had increased testosterone by an average of 1.8 nmol/l.
  - No increase in the placebo group.
  - Testosterone cream significantly improved sexual desire, frequency of sex, receptivity
  - Testosterone cream did not change mood, energy, lipids, blood pressure or weight over the study period....
  - No side effects of the 3 month of active treatment.

El-Hage G, et al. Climacteric. 2007 Aug;10(4):335-43.

Vulvo-Vaginal Testosterone

- FAD/FOD: testosterone 1-10 mg/gm; apply ½ gm-1 gm before sex to clitoris up to biw
- Trial of 80 healthy postmenopausal women for 12 weeks with compounded vaginal cream containing 300 mcg of testosterone propionate improved vaginal signs and symptoms.

Menopause 2016;23:792

Testosterone – Adverse Effects

Can happen even with physiological doses:

- Acne
- Hair thinning
- Increased body hair
- Anger/irritability

Likely only to happen with supraphysiological doses:

- Polycythemia, clitoromegaly, voice changes

IF ADVERSE EVENTS ARE OBSERVED, REDUCE DOSE

IF ADVERSE EVENTS DO NOT DIMINISH WITH LOWER DOSES, DISCONTINUE THERAPY

Testosterone Contraindications

Similar to those associated with estrogen therapy

Do not initiate testosterone therapy in postmenopausal women with:

- Breast or Uterine Cancer
- Cardiovascular Disease
- Liver Disease

Compounded Testosterone Formulations for Women

Creams

- Systemic: compounded 2.5-10 mg/Gm; Maximum = 10 mg/gm=1 gm/day to skin

  Sample conomical Rx: 20 mg/gm- apply ¼ gram per day= 5mg; (or apply ½ gm/day = 10 mg)

- Vulvar: 1-10 mg/gm; apply 1/4-1/2 gm to clitoris before sex, up to twice per week

  these doses will not induce clitoromegaly

Gels

- Systemic: compounded= same as cream

Or…1/10 of men's doses:

- One-tenth of a 1% testosterone tube or packet approved for men = ex/3 tubes or packets per month
- Apply to the back of calf, upper outer thigh or buttock

Less Effective:

Oral Micronized USP testosterone

- low dose = 1-3 mg/day
- common dose= 4-6 mg/day

Troche

- low dose = 1-3 mg/day
- common dose = 4-6 mg/day

Supraphysiologic and not recommended:

- Pellets, Injectables

Testosterone Products For Men

Androgel

1%= 10mg/Gm; starting dose 5 gm once daily; other doses= 7.5 gm and 10 gm/day

Testim

1% gel; 5 gm delivers 50 mg or 10 gm/day delivers 100 mg

Striant

One buccal system (30 mg) to the gum region twice daily; morning and evening (about 12 hours apart).

Testoderm; Testoderm TTS

4 mg over 24 hours or 6 mg patch

Two versions of Testoderm patches. One that is made for scrotal application Testoderm TTS) and another that is made for application on other areas of the body.

Testosterone injections

Brand Names: *Andro LA 200, Delatestryl, Depandro 100, Depo-Testosterone, Testosterone Cypionate, Testosterone Enanthate*

Testosterone Enanthate is usually injected every 7 to 21 days. Some of the others are injected every 7-30 days

Resources

- Buster, J, et al. Obstetrics & Gynecology https://journals.lww.com/greenjournal/toc/2005/05000
- Davis SR, et al. Testosterone for low libido in postmenopausal women not taking estrogen. N Engl J Med. 2008 Nov 6;359(19):2005-17.
- Davis SR, et al. Global Consensus Position Statement on the Use of Testosterone Therapy for Women. Climacteric. 2019 Oct;22(5):429-434.
- El-Hage G, et al. A double-blind, randomized, placebo-controlled trial of the effect of testosterone cream on the sexual motivation of menopausal hysterectomized women with hypoactive sexual desire disorder. Climacteric. 2007 Aug;10(4):335-43.
- Fernandes T, et al. Efficacy of vaginally applied estrogen, testosterone, or polyacrylic acid on vaginal atrophy: a randomized controlled trial. Menopause. 2016 Jul;23(7):792-8
- Simon J, et al. Testosterone patch increases sexual activity and desire in surgically menopausal women with hypoactive sexual desire disorder. J Clin Endocrinol Metab. 2005 Sep;90(9):5226-33.
- Somboonporn W, Bell RJ, Davis SR. Testosterone for peri and postmenopausal women. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD004509.

Dr. Tori Hudson Resources

- Women's Encyclopedia of Natural Medicine, 2008, second edition
- Menopause Companion; 2023
- www.drtorihudson.com
- Ndresidency.org
- www.Vitanicapro.com
- www.awomanstime.com
- www.instituteofwomenshealth.com
- www.naturopathicresidency.org
- www.womenshealthmentorship.com

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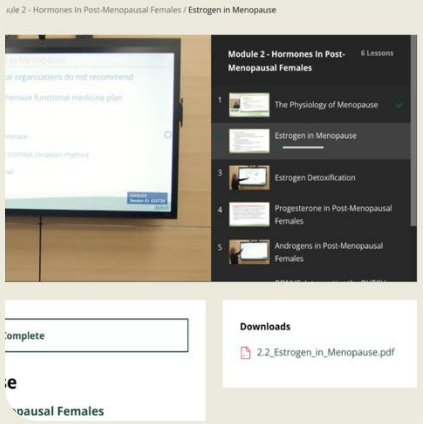

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Dr. Tori Hudson, N.D.

July, 2025

Testosterone Therapy in Women

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