

Testosterone notes from IFM

The market for testosterone replacement treatments has grown in recent years and remains strong. A 2017 *JAMA* study documented a huge increase in direct-to-consumer advertising for testosterone supplementation, which has also been associated with increased prescribing trends.¹ In 2013, testosterone supplementation brought in \$2 billion in sales for pharmaceutical companies.² Although trends suggest that that rapid growth in prescriptions has slowed,³ many men visit the doctor specifically seeking a testosterone prescription. Yet 80-85% of men supplementing testosterone discontinue treatment after a year.⁴ In healthy men under 50 years of age, serum testosterone ranges from 300-1,000 ng/dl, and levels start to drop after the age of 50.⁵ The American Urological Association (AUA) guidelines state that testosterone therapy can be considered if serum levels of testosterone are under 300 ng/dl *and* clinical symptoms are present.⁶

*Despite this, up to 25% of men receiving testosterone therapy did not have their levels tested prior to the prescription.*⁶

Lifestyle Interventions

Suboptimal testosterone levels are often amenable to lifestyle interventions. For instance, high-intensity interval training increases free testosterone in older, sedentary men,⁷ as well as masters athletes.⁸ Reducing alcohol intake also increases free testosterone.⁹

One intervention to consider prior to exogenous testosterone is nutritional: natural aromatase inhibitors. A range of foods and vitamins naturally inhibit aromatase, which decreases the conversion of testosterone into estradiol, resulting in increased testosterone levels. A 2021 systematic review found that two herbal extracts, fenugreek seed extracts and ashwagandha root and root/leaf extracts, may have positive effects on testosterone concentrations in men.¹⁰

In one large trial, aromatase inhibitors and testosterone supplementation resulted in similar outcomes to placebo for many cardiovascular measures, but aromatase inhibitors significantly reduced abdominal fat, an effect not seen in the testosterone group.¹¹ In both the exogenous testosterone and aromatase inhibitor groups, testosterone levels were significantly increased.¹² Other studies support the finding of increased testosterone in men with aromatase inhibition.¹³ However, in this study at least, estradiol increased in the testosterone group and decreased in the aromatase inhibitor group.¹² This may be of particular interest because the role of estradiol as a male hormone has been drawing increasing interest.¹³ For men with suboptimal testosterone, addressing lifestyle considerations and nutritional interventions first is not only safe but may lead to the desired results.

There are several foods, herbs, and supplements that can be used to inhibit or slow aromatase activity. For men who have suboptimal testosterone, lowering aromatase activity may help support and optimize healthy testosterone levels. IFM has created a handout called "Aromatase Inhibitors" for clinician and patient use in the IFM Toolkit, which includes a list of foods, herbs, and nutrients that inhibit aromatase. To access this educational resource, log in to the IFM website and select "My Toolkit," then search for "Aromatase Inhibitors."

Dosing and Optimum Levels

If supplementation is required, the dose of testosterone needed to create specific effects in the body varies widely.¹⁴ Ongoing monitoring is needed to ensure supplementation is reaching the desired range of free testosterone,⁶ yet reporting suggests that nearly half of patients' blood levels are not monitored after testosterone therapy.⁶

Optimal ranges for testosterone levels have not been well established.⁶ A study published in July 2019 suggested optimal circulating testosterone target levels for healthy aging men through the analysis of survey data and previously measured serum total testosterone concentrations.¹⁵ Data was collected from men who participated in the National Health and Nutrition Examination Surveys (NHANES).¹⁵

Comparison data between a healthier target population of never-smoking, lean men of 20 years of age or more without specific comorbidities and a general population of all men who took the surveys showed the following:

NHANES III – phase I (1988-1991) data:¹⁵

- Median testosterone level was 4-9% higher in the target population than all men.
- Median total testosterone by age in years (20 to 39; 40 to 59; 60 or more):
 - Target population: 624 ng/dl; 537 ng/dl; 461 ng/dl
 - All men: 599 ng/dl; 486 ng/dl; 435 ng/dl

Continuous NHANES (1999-2004) data:¹⁵

- Median testosterone level was 13-24% higher in the target population than all men.
- Median total testosterone by age in years (20 to 39; 40 to 59; 60 or more):
 - Target population: 626 ng/dl; 586 ng/dl; 422 ng/dl
 - All men: 542 ng/dl; 445 ng/dl; 392 ng/dl

The study aimed to use its findings to both better inform clinical guidelines used to address testosterone deficiency and to help establish target total serum testosterone levels for men in nondrug intervention trials.¹⁵

Therapy Risks & Side Effects

Testosterone therapy can cause a range of side effects,^{6,16} such as:

- Reduced fertility
- Fluid retention
- Obstructive sleep apnea

There may be other risks, including cardiovascular and respiratory risks,¹⁷ although data is not yet conclusive,¹⁸ and those risks may be due to flaws in study design.¹⁸ At least one study suggests testosterone may be cardioprotective.²⁰ In addition, the as-yet-inconclusive role of testosterone in prostate cancer continues to garner controversy and attention.^{21,22}

A 2020 review conducted for the American College of Physicians reported on the analysis of 38 randomized controlled trials, finding that:²³

- Testosterone therapy improved sexual function and quality of life for older men who had low testosterone levels and who did not have a medical condition known to cause hypogonadism; however, the improvements were small, with low to moderate-sized effects reported.
- Testosterone therapy had little to no effect on other symptoms such as physical functioning, depressive symptoms, energy and vitality, and cognition.
- The trials often excluded men who were at high risk of cardiovascular events or prostate cancer; therefore, no relationship could be established between those conditions and testosterone therapy.
- According to the review, "Harms evidence reported in trials was judged to be insufficient, or of low certainty for most harm outcomes."
- The long-term efficacy and safety of testosterone therapy is unknown among the noted population.

As with other hormonal imbalances, low testosterone may indicate a change in a patient's overall physiology. From a functional medicine perspective, low testosterone levels may be a marker for the presence of an underlying physiological imbalance, and low levels have been associated with comorbidities such as hypertension and type 2 diabetes.²⁴ The functional medicine model assesses an individual patient's genetic, biochemical, and lifestyle factors to help create a personalized treatment plan for their testosterone deficiency diagnosis. To learn more about optimizing testosterone function, consider attending IFM's Hormone Advanced Practice Module (APM):



Functional Nutrition Fundamentals

Maintaining Healthy Testosterone Levels: 5- α Reductase Inhibitors

5- α reductase is a key enzyme in the body which regulates the conversion of testosterone to a hormone called dihydrotestosterone (DHT). When testosterone is converted to DHT, testosterone is lowered and can no longer work effectively. This can result in conditions such as enlargement of the prostate in men, hair loss in both men and women, and extra facial hair and acne in women. There are several foods, herbs, and supplements that can be used to inhibit or slow 5- α reductase activity and thus decrease or prevent these symptoms.

Foods that Inhibit 5- α Reductase

- Green Tea
- Flax seed (lignans)
- Soy Isoflavones
- Fatty fish (Omega-3 fats)

Herbs that Inhibit 5- α Reductase

- Saw Palmetto (*Serenoa repens*)
- Stinging Nettle Root (*Urtica dioica*)
- Chaste Tree Berry (*Vitex agnus-castus*)
- Black Cohosh (*Actaea racemosa*)
- Pygeum (*Pygeum africanum*)

Nutrients/Phytonutrients that Inhibit 5- α Reductase

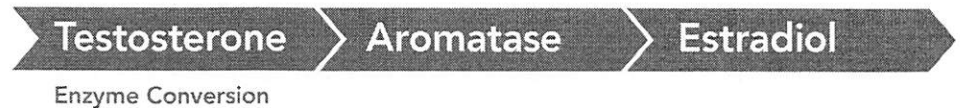
- Quercetin
- Omega-3 fish oils
- Krill (astaxanthin)
- Beta-sitosterols
- L-lysine
- Rice bran

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Aromatase Inhibitors

Aromatase is a key enzyme in the body which regulates the conversion of testosterone to estradiol. It is important to consider strategies to lower or inhibit that conversion when men have lower than optimal levels of testosterone. There are several foods, herbs and supplements that can be used inhibit or slow aromatase activity. Therefore, for men who have suboptimal testosterone, lowering aromatase activity can help support and optimize healthy testosterone levels.



Use the following foods and supplement support as instructed by your clinician:

Foods that Inhibit Aromatase

- Dietary fiber
- Flax seeds (lignans)
- Soy (isoflavones)
- Grape seed extract
- White button mushrooms
- Green tea

Herbs that Inhibit Aromatase

- Stinging nettle root (*Urtica dioica*)

Nutrients and Phytonutrients that Inhibit Aromatase

- Quercetin
- Vitamin C
- Chrysin
- Zinc

These recommendations should be followed under the supervision and guidance of a qualified healthcare professional.

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Sex Hormone Binding Globulin (SHBG)

Sex hormone binding globulin (SHBG) is a protein that binds to sex hormones (i.e., testosterone and estrogen) in the blood and helps transport the hormones into tissues to do their job. In this way, SHBG plays an important balancing role for sex hormones in the body.

When hormones bind to SHBG, they are essentially inactivated. High concentrations of SHBG in the body can lead to increased bound testosterone, as SHBG more easily binds to testosterone than to estrogen. This can cause symptoms associated with testosterone deficiency, including fatigue, decreased libido, weight gain, mood changes, decreased muscle mass, and decreased bone mineral density, to name a few.

On the other hand, when SHBG levels in the body are low, there is not enough binding power to keep sex hormones within the optimal range. This can lead to increased free testosterone and estrogen in the body, which can lead to symptoms like hair loss, acne, and excess fluid retention.

Some health conditions can affect the level of SHBG in the body. In order to help normalize SHBG levels in the body, your practitioner may have specific recommendations. The table below lists some common health conditions associated with increased or decreased SHBG, and recommendations for addressing both. Talk to your functional medicine practitioner before beginning any interventions.

Increases SHBG

Health Conditions:

- Aging
- Cirrhosis
- Hepatitis
- Hyperthyroidism
- HIV
- Pregnancy

Medications and Supplements:

- Anticonvulsants
- Exogenous estrogens
- Vitamin D

Diet and Nutrition:

- Low-fat diet
- Low-protein (vegetarian) diet

Decreases SHBG

Health Conditions:

- Diabetes mellitus (Type 2)
- Hypothyroidism
- Metabolic syndrome
- Nephrotic syndrome
- Obesity

Hormones:

- Androgens
- IGF-1 and growth hormone
- Insulin
- Progesterone
- Prolactin

Medications and Supplements:

- EPA/DHA
- Glucocorticoids
- Stinging nettle (Urtica dioica)
- Whey protein

Adrenal Exhaustion

Your adrenal glands sit on top of the kidneys and secrete important hormones: cortisol, adrenaline, and dehydroepiandrosterone (DHEA). These hormones help you to buffer stress and adapt to everyday life demands by determining the stress response.

Under stress, healthy adrenals increase their output of cortisol and DHEA to enable you to preserve health. They also secrete adrenaline, giving you a boost of energy when needed. If this becomes chronic, the adrenals can no longer keep up with the demand, and DHEA levels begin to fall, signifying adrenal exhaustion. In addition, the oversecretion of adrenaline can cause you to feel anxious and nervous. Complaints of insomnia, fatigue, depression, irritability, and digestive difficulties are also common. As adrenaline surges during stress, digestive enzymes are simultaneously lowered, and blood sugar levels initially rise. As this becomes a more chronic occurrence, the results of high cortisol and adrenaline levels from prolonged stress include:

- Diminished immune function
- Depletion of cortisol, resulting in low blood sugar
- Less restful sleep
- Increased lipid levels of blood fats
- Water retention
- Loss of cellular potassium, a very important mineral
- Lowered insulin sensitivity, with a higher susceptibility to diabetes
- Loss of the capacity to produce sufficient DHEA

Functions of cortisol

- Converts proteins into energy by increasing amino acids in the bloodstream
- Stimulates the liver to convert amino acids to glucose as needed for energy
- Counters inflammation and allergies
- Helps maintain blood pressure
- Aids in stress reactions

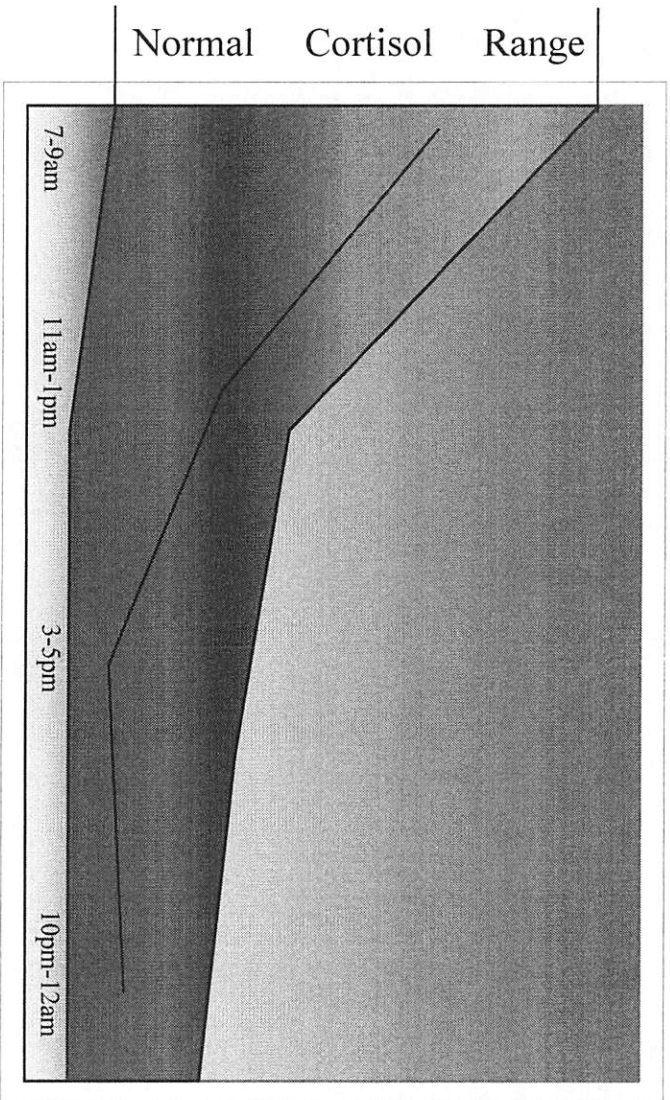
Functions of DHEA

- Precursor to testosterone and estrogen
- Improves resistance to viruses, bacteria, parasites, allergies, and cancer
- Prevents osteoporosis
- Lowers total and LDL cholesterol
- Increases muscle mass and decreases body fat

Restoration

- Diet should avoid refined sugars, caffeine, and alcohol and should include several small meals containing protein.
- Determine allergic foods and avoid them.
- Ginseng and/or licorice tea can be supportive.
- Adequate vitamin C is important.
- Get adequate sleep and go to bed by 10pm
- Use stress-management techniques.
- Deal with emotions as needed with laughter, breathing, and/or professional help.
- Engage in light exercise.
- Get daily outdoor light.

The following is an example of a typical cortisol curve throughout the day.



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Functions of DHEA

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- Increases muscle mass and decreases body fat

Restoration

- Determine trigger foods and avoid them.
- Avoid refined sugars, caffeine, and alcohol in the diet.
- Eat several small meals containing protein each day.
- Consume ginseng and/or licorice tea for support.
- Get adequate vitamin C.
- Get adequate sleep and go to bed by 10:00 pm.
- Use stress management techniques.
- Deal with emotions as needed with laughter, breathing, and/or professional help.
- Engage in light exercise.
- Get daily exposure to outdoor light.

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