



# **Low Testosterone**

## Consultation Information



**UrologyAustin**

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# Andropause or Male Menopause

This syndrome has been nicknamed ADAM, which stands for *androgen deficiency of the aging male*. It differs most markedly from female menopause in the speed with which the symptoms occur. In women, the menopause (which means the ceasing of menses or periods) is a universal and comparatively sudden change. In men, the change is much more gradual and difficult to pinpoint. This difference suggests that referring to the syndrome in men as "*male menopause*" is not accurate and we prefer the term *Andropause*.

## Testosterone and Age

Aging in men is associated with a one percent decline in total testosterone level each year starting at around age forty. About twenty percent of men in their sixties and fifty percent of men in their eighties have a testosterone level significantly below normal. Men who develop a serious illness, take certain kinds of medications, or who don't eat a healthy variety of foods are even more likely to have low testosterone levels. Furthermore, about one in three men with symptoms of Andropause turn out to have a testosterone level lower than normal. Andropause is defined in terms that relate to *low testosterone levels* in men regardless of age. One doctor in a recent journal article defined it as "a decline in serum (blood) testosterone in older men to levels below the normal range for young men, with associated clinical manifestations consistent with androgen deficiency." Many of these men will simply feel better when their testosterone level is raised through hormone replacement therapy.

## Testosterone Production in the Body

Testosterone, a steroid hormone is produced in the testes by the Leydig cells. In women testosterone is produced in the ovaries. However, small amounts are made in the outer layer of the adrenal glands in both sexes.

The process that carefully regulates the amount and timing of testosterone production is complex and begins in the brain which sends a signal to another part of the brain called the hypothalamus. The hypothalamus is an area at the base of the brain that regulates much of the body's hormonal activity. It does this by sending chemical signals to the pituitary gland, a cherry-sized organ that produces a wide variety of hormones involved in the regulation of growth, thyroid function, blood pressure, pregnancy, birth and other critical body functions.

To stimulate testosterone production, the hypothalamus releases a substance to the pituitary gland called gonadotropin-releasing hormone (GnRH). GnRH then travels a short distance to the pituitary gland, and stimulates the pituitary to release FSH (follicle stimulating hormone) and LH (luteinizing hormone).

The majority of testosterone circulates in the blood bound to a carrier protein (many hormones that are produced in one area and affect another area have a carrier protein that helps their travel through the bloodstream). In this case the carrier protein is called "sex hormone binding globulin," or SHBG. When testosterone is being carried by SHBG, it is considered "bound". Bound testosterone does not play an active role in the body; only the unbound or "free" testosterone is able to enter the different cells of the body and exert its androgenic and anabolic effects. Thus, anything that affects the function or the amount of SHBG can also affect the total circulating amount of active testosterone.

These hormones travel through the bloodstream to activate the sex organs in both men and women. Subsequently, these hormones have a role in regulating testosterone levels in the bloodstream.

# What are the causes of low testosterone?

The human body functions within a relatively narrow range of normal. When chemicals such as hormones fall outside those normal levels, there can be consequences that affect the body at a cellular, organ, or systemic (body-wide) level. With advancing age, in both men and women, the amount of testosterone the body produces gradually falls. After the age of thirty, a man may lose up to two percent of testicular function each year. We know that twenty to fifty percent of healthy men between the ages of 50 and 70 have lower than normal levels of testosterone. This statistic indicates that up to five percent of all men are at risk for low testosterone states, a staggering number if you think about it.

When the problem is in the organs that produce testosterone (the ovaries or testes, for the most part), it is called a "**primary problem**". In medical terminology, the decrease in normal testosterone production is called "**hypogonadism**." Some common causes of **primary hypogonadism** or failure of the gonads (the medical term for the sex organs, or testes and ovaries) may include the following:

- **Undescended testicles:** If the testes fail to migrate from inside the abdomen into the scrotum during fetal development or in the first year or two of life, the testes may become damaged and unable to produce adequate amounts of testosterone.
- **Injury to the scrotum:** If the testes are injured, they may not be able to produce adequate testosterone. Damage to one testicle does not often lead to low levels if the other testis remains normal.
- **Cancer therapy:** Chemotherapy and radiation therapy can damage the interstitial cells in the testes responsible for testosterone production. This decrease in testosterone production may be temporary as the cells recover, or it may be permanent.
- **Aging:** Testosterone levels decrease with aging. Usually, enough testosterone is manufactured to allow for adequate bodily functions.
- **Mumps orchitis:** The mumps virus can cause inflammation of the testes in males, and if the illness occurs in puberty or adulthood, the damage to the testes may lead to low testosterone production. Immunization against the mumps has significantly decreased the incidence of this illness.
- **Chromosomal abnormalities:** A normal male has one X and one Y chromosome (a normal female has two X chromosomes). In Klinefelter's syndrome, in males, an extra X chromosome is present and among other anatomic issues, there is abnormal development of the testes and decreased ability to manufacture testosterone.
- **Ovary conditions in women:** Premature ovarian failure and surgical removal of both ovaries (bilateral oophorectomy) are conditions associated with lower circulating testosterone levels.

When the problem is related to the pituitary and its ability to regulate testosterone, it is called "**secondary hypogonadism**". If the problem is thought to be at the level of the hypothalamus, it is called "**tertiary hypogonadism**." **Secondary and tertiary hypogonadism** may be due to damage of the hypothalamus or pituitary and/or the failure of the production of hormones (GRH, FSH and/or LH) to stimulate the gonads.

Causes of secondary and tertiary hypogonadism include:

- Damage to the pituitary gland may occur because of tumors of the gland itself or because of damage caused by the side effects of treatment of nearby brain tumors.
- Hypothalamus malformations can prevent normal function. Kallman's syndrome is one example.
- Compromised blood flow to these glands from other conditions such as excessive systemic blood loss.
- Inflammation caused by tuberculosis and sarcoidosis may affect the pituitary gland.
- HIV and AIDS may also cause inflammation of both the hypothalamus and pituitary.
- Illegal use of anabolic steroids, for example in body building, can cause hypogonadism and low testosterone levels.
- Chronic narcotic pain medicine use.
- Obstructive Sleep Apnea (OSA) or snoring.

# Physical Symptoms of Low Testosterone

Each individual may experience a different number and type of symptoms.

**Genital development:** If there is inadequate testosterone in the fetus, genital development may be affected. There may be poor development of the penis and scrotum, with an appearance of female genitalia or ambiguous genitalia that are neither male nor female.

**Sexual Maturation:** If low testosterone occurs before or during puberty, there may be a lack of sexual maturation. Signs may include failure to develop muscle mass, failure of the voice to deepen, poor growth of body hair, enlarged breasts (gynecomastia), and failure of the penis and testes to enlarge.

**Sexual Symptoms:** Sometime during a **man's** fourth or fifth decade of life, and sometimes as early as his thirties, his body's production of *testosterone* may begin to slow. The gradual decline, most often fully realized between the ages of 50 and 55, can produce a variety of changes and effects on the male body: The symptoms of decreased testosterone depend upon when the low levels occur. Low testosterone may lead to decreased sexual function and desire, infertility, and erectile dysfunction.

**Others:** Decreased muscle mass, and osteoporosis or decreased bone density may occur.

**Women:** While low testosterone is usually thought of as a male disease, **low levels may occur in women and cause significant issues.** Symptoms may include hot flashes, irritability, loss of sexual desire (decreased libido), and sleep disturbances. Loss of muscle mass, decreased bone density (osteoporosis), and loss of body hair may also be seen.

## Mood/Intellect Effects of Low Testosterone

Studies in humans and other animals have clearly demonstrated that testosterone has receptors in the brain and that it affects how we think and act. Low testosterone also affects men's psychosocial functioning, leading to depression, anxiety, irritability, reduced cognitive ability, and a loss of a sense of wellbeing.

In studies, researchers find that, after adjusting for age, higher levels of testosterone are associated with better self-rated health. Men with lower serum (blood) testosterone concentrations, in contrast, were more likely to experience symptoms of depression. In fact, men who have the lowest levels of testosterone have a much higher prevalence of depression, even when researchers account for other co-existing conditions, such as obesity, which is also tied to depression. Depression is more common in women than men until age 65. At that point, the incidence is comparable between the genders. Physicians suspect the decline in male hormones is behind the increased prevalence of male depression.

## Steps for Diagnosing Low Testosterone

The number of symptoms and signs of low testosterone may not be obvious to a man. As added source of confusion is that many of the symptoms overlap with symptoms of depression or with what we consider normal ageing. In spite of amazing medical advances, one of the most important diagnostic tools is the information a patient provides a doctor in the form of a medical history. Your participation in providing as complete information as you can will be important in this diagnosis. At the first visit, a doctor will ask many questions about general health as well as specific questions about sexual interest and activity that relate to low testosterone. Some of the specific topics asked about may include:

## ***Diagnosing Low Testosterone continued***

### **History**

#### ***Personal History:***

- Date of birth
- Allergies
- All prescription and non-prescription drugs currently being taken
- Previous and existing conditions and major illnesses
- Names of current and previous doctors
- Dates/reasons for previous medical visits
- Dates and kinds of surgeries
- Copies of past test results
- Lifestyle habits – smoking, alcohol consumption, drug use
- Family and relationship problems, including any sexual ones
- Major life events or changes that have occurred

#### ***Family History:***

- Alcoholism
- Blood diseases (hemophilia or sickle cell)
- Cancer (all types)
- Diabetes
- Heart disease, hypertension or stroke
- Kidney disease
- Mental illness
- Other illnesses and disorders

Your doctor will also ask you questions about your sexual history and development. These may include:

- Any genital abnormalities present from birth
- When and how quickly puberty took place
- Current status of sexual function
- Status of secondary sexual characteristics such as beard growth, muscular strength and energy level
- Rate of nocturnal emissions
- Degree of penile rigidity during erections
- Frequency of sexual thoughts, desires and fantasies
- Frequency of masturbation or sexual intercourse

Once the doctor has a general idea about your past and current situation, he or she will conduct a thorough physical examination. In addition to a typical exam that includes blood pressure, heart rate and other basic measures, the doctor will look at the amount and distribution of body hair, presence and degree of breast enlargement, size and consistency of the testes, abnormalities in the scrotum, and the size of the penis. These tests should be repeated at 6 weeks, 6 months and annually thereafter. Monitoring your health while on treatment is very important.

# Blood Tests

**Total Testosterone:** The most obvious test required is a measurement of testosterone level in your blood. The test for total testosterone has been widely available for many years but in many cases it is misleading. In the United States at present, it also remains the standard for indicating a need for replacement therapy.

**SHBG:** Another test available is for SHBG. By running a test for total testosterone and another for SHBG, your doctor can use these values to calculate the amount of free testosterone in the blood. This is done by dividing the total testosterone value by the value of the SHBG and multiplying by 100 to arrive at a percentage value called the free androgen index. In normal men, this value should stay between 70 to 100 percent, but in Andropause men, it may fall to below 50 percent

**Free Testosterone:** There is general agreement among experts (at least in theory) that free testosterone is the best indicator of a man's testosterone status. Free testosterone levels can be measured and normal levels depend upon an individual's age. However, this depends to some extent on the individual laboratory being used, and the range can vary as a result. A number of test have been used to measure free testosterone, but there has been so much controversy over the quality and interpretation of these various tests that many community physicians have given up on the free testosterone and depend primarily on the total testosterone.

**LH:** LH levels will show whether your pituitary gland is working properly to regulate and stimulate testosterone production. Low levels raise the possibility of a problem with the pituitary gland or hypothalamus. High levels mean that the problem has arisen because the testicles are unable to produce testosterone adequately despite a strong stimulus to do so.

**Prolactin:** Very high levels of prolactin may reveal the presence of a tumor of the pituitary gland which in turn can cause low testosterone.

**HCT or HGB:** The hematocrit and hemoglobin tests indicate whether there are normal numbers of red blood cells in the bloodstream. A side effect of testosterone replacement is a rise in red blood cells, thus blood donation may be suggested.

**PSA:** A PSA should be obtained to have a baseline value prior to beginning testosterone treatment and to make sure it is within normal limits.

**Women:** In women, there is debate about the accuracy of testosterone measurements, because the circulating values are so much lower than in males and are harder to accurately measure. Interestingly, menopause itself does not seem to play a role in a reduction of testosterone levels in women beyond that of advancing age.

**Misc:** When to take the blood sample for these tests is important because the level of testosterone normally varies from a high point in the morning to lower points throughout the day – most significantly in men 45 and younger. The blood sample should be drawn between 8:00 and 9:00 AM to be sure it will provide the highest level of testosterone during the cycle. The normal range for total testosterone is 300 - 1000 ng/dl. The average concentration of total testosterone in men over forty years old is approximately 450/ng/dl.

Other tests may be indicated by the medical history or physical exam. For example, a doctor may order bone density testing if bone loss is suspected, or genetic testing may be useful to confirm an inherited condition. If tests indicate that there might be a problem with the pituitary gland, the doctor may want to examine the gland itself through a computed tomography (CT) scan or magnetic resonance imaging (MRI.)

In any case, these tests are chosen to augment an Andropause diagnosis

## Which Treatment is Best for Me?

### Treatment of low testosterone in men

When testosterone therapy was first developed more than 60 years ago, the only form of treatment was a daily injection. Fortunately, we now have a much wider and more convenient set of treatments modalities, including patches, gels and even pellets. The variety of treatment options leads to the question “Which treatment is best for me?”

**Injections:** The first form of T-Therapy was an intramuscular injection. Usual dosage is 50-400 mg of testosterone cypionate or testosterone enanthate every 2-4 weeks. Some clinicians recommend testosterone cypionate or testosterone enanthate dosage of 50-100 every 7-10 days or 100-150 mg every 2 weeks. While dosage of 300 mg every 3 weeks also may be considered for convenience, such dosing is associated with wider testosterone fluctuation and generally is inadequate to ensure a consistent clinical response. Serum total testosterone concentration generally should exceed 250-300 ng/dl just before the next dose.

Adult males with prepubertal onset of hypogonadism who are going through puberty for the first time with testosterone replacement: initially, 50 mg every 3-4 weeks: increase dosage gradually in subsequent months as tolerated up to full replacement within 1 year.

**Patches:** The first real advance over injections was the patch which offered more uniform testosterone concentration eliminating the roller coaster effect that frequently occurs with injections. One major problem with patches is that testosterone levels only tend to reach the lower range of normal and in some men the absorption may be too poor to achieve beneficial response at all. Some men feel the visible patch itself if awkward especially with sexual partners. A major limitation is that patches cause skin irritation or fall off of many men.

**Topical (Gel:)** Before the introduction of pellets, gels were the fastest growing form of treatment in the US. Once a day, the men applies the prescribed amount of gel to his skin and rub it in. Skin irritation is rare. The advantages of the gel are that it is not visible and there are no red blotches, no injections. Their absorption rate is faster than patches, however there is great variability in absorption from one individual to another and early blood test are necessary to evaluate and adjust dosage to achieve a good testosterone concentration. The gel should be applied daily. The average cost is high (cash pay).

## ***Low testosterone treatment in men continued***

**Pellets:** The most appealing treatment choice is the use of extended-release pellets that are inserted under the skin, usually in the buttocks. The advantages of these pellets is that they maintain good levels of testosterone for three to six months, so patients don't need to apply gel every day or receive injections every couple of weeks. These pellets are each about the size of a grain of rice and six to eight of them usually are inserted at a time. Insertion is painlessly performed in the office with local anesthesia and requires only a few minutes. The average cost, by comparison, is low.

**HCG (Human Chorionic Gonadotropin) or Clomid:** Can be used to stimulate the patients own testosterone production as well as preserving normal sperm production.

## **Treatment of low testosterone in women**

In women, in the United States there are currently no preparations that are FDA approved for testosterone replacement. Esterified estrogens and methyltestosterone (Estratest), manufactured by Solvay Pharmaceuticals, a combination of estrogen and methyltestosterone that was formerly available, was discontinued by the manufacturer in the spring of 2009.

Some doctors will advise women to cut the patches for men into smaller sizes, or to use the gel in smaller doses; however, the accuracy of these methods is questionable, as is the safety.

## **What is the outlook (prognosis) for a patient with low testosterone?**

The ability to treat the condition depends upon recognizing symptoms and seeking medical care. Once the cause for the low testosterone levels is diagnosed, testosterone replacement therapy may be helpful in reversing the symptoms related to those low levels. Maintaining adequate testosterone levels within the body may minimize future risk of muscle and bone loss.