TESTOSTERONE

Steroid hormone produced primarily in the testes of the male; responsible for the development of secondary sex characteristics in the male.

About Testosterone

Function

Testosterone (Pic.1) is a steroid hormone from the androgen group. Androgen is any natural or synthetic compound, usually a steroid hormone, that stimulates or controls the development and maintenance of male characteristics in humans by binding to androgen receptors. This includes the activity of the primary male sex organs and development of male secondary sex characteristics. Androgens are also the original anabolic steroids and the precursor of all estrogens. In general, androgens promote protein synthesis and growth of those tissues with androgen receptors.

Testosterone is produced primarily by the testes in men, although it also can be produced by the adrenal glands and other sites including adipose tissue and bone. It is responsible for testes descent and reproductive tract development in the fetus, development of male secondary sex characteristics in puberty, and the production of sperm. Testosterone production in men begins in utero, rises sharply in puberty, and then declines with age (Pic. 2). Indeed, the Massachusetts Male Aging Study showed that total serum testosterone levels decline by 1.6% per year starting at age 40. Testosterone is also produced by the ovaries, the adrenal glands, and tissues such as adipose tissue and skin in women, although serum concentrations are almost 20-fold lower in pre-menopausal women compared to age-matched men. Interestingly, testosterone levels also decline with age in women. This age-dependent reduction in testosterone is not restricted to humans, as it is also seen in older male rats and mice (>20 months of age) in conjunction with a decline in fertility, although whether levels decline in aged female animals has not been investigated.

Hormonal regulation

In males, testosterone is synthesized primarily in Leydig cells. The number of Leydig cells in turn is regulated by luteinizing hormone (LH) and follicle-stimulating hormone (FSH). In addition, the amount of testosterone produced by existing Leydig cells is under the control of LH.

The amount of testosterone synthesized is regulated by the hypothalamic-pituitary-testicular axis (Pic. 3). When testosterone levels are low, gonadotropin-releasing hormone (GnRH) is released by the hypothalamus, which in turn stimulates the pituitary gland to release FSH and LH. These latter two hormones stimulate the testis to synthesize testosterone. Finally, increasing levels of testosterone through a negative feedback loop act on the hypothalamus and pituitary to inhibit the release of GnRH and FSH/LH, respectively.

Before birth

The prenatal androgen effects occur during two different stages. Between 4 and 6 weeks of the gestation.

- Genital virilization (midline fusion, phallic urethra, scrotal thinning and rugation, phallic enlargement); although the role of testosterone is far smaller than that of dihydrotestosterone.
- Development of prostate and seminal vesicles.
- During the second trimester, androgen level is associated with gender formation. This period affects the feminization or masculinization of the fetus and can be a better predictor of feminine or masculine behaviours such as sex typed behaviour than an adult’s own levels. A mother’s testosterone level during pregnancy is correlated with her daughter’s sex-typical behavior as an adult, and the correlation is even
stronger than with the daughter's own adult testosterone level.

**Early infancy**

In the first weeks of life for male infants, testosterone levels rise. The levels remain in a pubertal range for a few months, but usually reach the barely detectable levels of childhood by 4–6 months of age. The function of this rise in humans is unknown. It has been speculated that “brain masculinization” is occurring since no significant changes have been identified in other parts of the body. The male brain is masculinized by the aromatization of testosterone into estrogen, which crosses the blood–brain barrier and enters the male brain, whereas female fetuses have alpha-fetoprotein, which binds the estrogen so that female brains are not affected.

Testosterone effects can be classified as virilizing and anabolic, though the distinction is somewhat artificial, as many of the effects can be considered both.

**Pre-pubertal effects**

The first observable effects of rising androgen levels at the end of childhood, occurring in both boys and girls:

- adult-type body odor
- pubarche (appearance of pubic hair)
- axillary hair
- growth spurt, accelerated bone maturation
- hair on upper lip, on chin, and growth of sideburns

**Pubertal effects**

Begin to occur when androgen has been higher than normal adult female levels for months or years. In males, these are usual late pubertal effects, and occur in women after prolonged periods of heightened levels of free testosterone in the blood.

- enlargement of sebaceous glands
- penis or clitoris enlargement
- increased libido and frequency of erection or clitoral engorgement
- pubic hair extends to thighs and up toward umbilicus
- facial hair (sideburns, beard, moustache)
- foss of scalp hair (androgenetic alopecia)
- chest hair, periareolar hair, perianal hair
- leg hair, armpit hair
- subcutaneous fat in face decreases
- increased muscle strength and mass
- deepening of voice
- growth of the Adam’s apple
- growth of spermatic tissue in testicles, male fertility
- shoulders become broader and rib cage expands
- completion of bone maturation and termination of growth. This occurs indirectly via estradiol metabolites and hence more gradually in men than women
- more aggressive, active attitude - interest in sex develops

**Androgenic effects**

- maturation of the sex organs, particularly the penis
- formation of the scrotum in the fetus
- deepening of the voice
- growth of the beard and axillary hair

**Anabolic effects**

- growth of muscle mass and strength
- increased bone density and strength
- stimulation of linear growth and bone maturation

**Romantic relationships**

Falling in love decreases men’s testosterone levels while increasing women’s testosterone levels. There has been speculation that these changes in testosterone result in the temporary reduction of differences in behavior between the sexes. However, it is suggested that after the “honeymoon phase” ends—about one to three years into a relationship—this change in testosterone levels is no longer apparent. Men who produce less testosterone are more likely to be in a relationship and/or married, and men who produce more testosterone are more likely to divorce; however, causality cannot be determined in this correlation. Marriage or commitment could cause a
Female sexual arousal

Androgens may modulate the physiology of vaginal tissue and contribute to female genital sexual arousal. Women’s level of testosterone is higher when measured pre-intercourse vs pre-cuddling, as well as post-intercourse vs post-cuddling. There is a time lag effect when testosterone is administered, on genital arousal in women. In addition, a continuous increase in vaginal sexual arousal may result in higher genital sensations and sexual appetitive behaviors.

Insufficiency

Testosterone insufficiency (also termed hypotestosteronism or hypotestosteronemia) is an abnormally low testosterone production. It may occur because of testicular dysfunction (primary hypogonadism) or hypothalamic-pituitary dysfunction (secondary hypogonadism) and may be congenital or acquired. An acquired form of hypotestosteronism is the decline in testosterone levels that occurs by aging, sometimes called andropause in men, as a comparison to the decline in estrogen that comes with menopause in women.

Regulator of cognitive and physical energy

Testosterone regulates the population of thromboxane A2 receptors on megakaryocytes and platelets and hence platelet aggregation in humans. High androgen levels are associated with menstrual cycle irregularities in both clinical populations and healthy women.

Cancer prevention and health risks

As testosterone affects the entire body (often by enlarging; males have bigger hearts, lungs, liver, etc.), the brain is also affected by this sexual differentiation. The literature suggests that attention, memory, and spatial ability are key cognitive functions affected by testosterone in humans. Preliminary evidence suggests that low testosterone levels may be a risk factor for cognitive decline and possibly for dementia of the Alzheimer's type. Testosterone does not cause deleterious effects in prostate cancer. In people who have undergone testosterone deprivation therapy, testosterone increases beyond the castrate level have been shown to increase the rate of spread of an existing prostate cancer.
Androgen replacement therapy (ART), often referred to as testosterone replacement therapy (TRT), is a class of hormone replacement therapy in which androgens, often testosterone, are replaced. ART is often prescribed to counter the effects of male hypogonadism. It typically involves the administration of testosterone, either by injection or by use of testosterone skin creams or gels. ART may also be prescribed to lessen the effects or delay the onset of normal male aging.

However, this is controversial and is the subject of ongoing clinical trials, assessing the benefits and harms of its use in otherwise healthy older men. As men enter middle age they may notice changes caused by a relative decline in testosterone: fewer erections, fatigue, thinning skin, declining muscle mass and strength, more body fat. This dissatisfaction with the changes of aging has led to the development of the idea of androgen replacement therapy. Androgen replacement therapy is also used for men who have lost testicular function to disease, cancer, or other causes. For men who have had prostate cancer or at elevated risk, androgen replacement therapy remains controversial because some studies have shown that it increases the risk for prostate cancer; others refute that risk.

**Non-medical use**

Testosterone can be used by an athlete in order to improve performance, but it is considered to be a form of doping in most sports. There are several application methods for testosterone, including intramuscular injections, transdermal gels and patches, and implantable pellets. Hormone supplements cause the endocrine system to adjust its production and lower the natural production of the hormone, so when supplements are discontinued, natural hormone production is lower than it was originally. Anabolic steroids (including testosterone) have also been taken to enhance muscle development, strength, or endurance. They do so directly by increasing the muscles' protein synthesis. As a result, muscle fibers become larger and repair faster than the average person’s.

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**Find more about related issues**

**Diagnoses**

**Amenorrhoea**
The absence of a menstrual period in women of reproductive age.
Learn more at: [www.fertilitypedia.org/therapy/diag/amenorrhoea](http://www.fertilitypedia.org/therapy/diag/amenorrhoea)

**Cryptozoospermia**
Male infertility diagnosis characterized by extremely low concentration of sperm in semen.
Learn more at: [www.fertilitypedia.org/therapy/diag/cryptozoospermia](http://www.fertilitypedia.org/therapy/diag/cryptozoospermia)

**Ejaculatory disorders**
A class of sexual disorders defined as the subjective lack of normal ejaculation.
Learn more at: [www.fertilitypedia.org/therapy/diag/ejaculatory-disorders](http://www.fertilitypedia.org/therapy/diag/ejaculatory-disorders)

**Erectile dysfunction**
The inability (that lasts more than 6 months) to develop or maintain an erection of the penis during sexual activity.
Learn more at: [www.fertilitypedia.org/therapy/diag/erectile-dysfunction](http://www.fertilitypedia.org/therapy/diag/erectile-dysfunction)

**Hypogonadism**
A medical term which describes a diminished functional activity of the gonads – the testes and ovaries.
Learn more at: [www.fertilitypedia.org/therapy/diag/hypogonadism](http://www.fertilitypedia.org/therapy/diag/hypogonadism)

**Hypospermia**
A condition in which a man has an unusually low ejaculate (or semen) volume.
Learn more at: [www.fertilitypedia.org/therapy/diag/hypospermia](http://www.fertilitypedia.org/therapy/diag/hypospermia)

**Idiopathic male infertility**
A condition in which fertility impairment occurs spontaneously or due to an unknown cause.
Learn more at: [www.fertilitypedia.org/therapy/diag/idiopathic-male-infertility](http://www.fertilitypedia.org/therapy/diag/idiopathic-male-infertility)
Obesity
A disease of excess body fat that can have a negative effect on health, leading to reduced life expectancy and other health problems.
Learn more at: www.fertilitypedia.org/therapy/diag/obesity

Oligozoospermia
Semen with a low concentration of sperm and is a common finding in male infertility.
Learn more at: www.fertilitypedia.org/therapy/diag/oligozoospermia

Orchitis
An inflammation of the testes, involving swelling and heavy pains.
Learn more at: www.fertilitypedia.org/therapy/diag/orchitis

Ovariectomy
Surgical removal of one or both ovaries.
Learn more at: www.fertilitypedia.org/therapy/diag/ovariectomy

Polycystic ovary syndrome
A condition in which a woman has an imbalance of female sex hormones. This may lead to changes in the menstrual cycle, cysts in the ovaries, trouble g
Learn more at: www.fertilitypedia.org/therapy/diag/polycystic-ovary-syndrome

Prostatitis
An inflammation of the prostate gland.
Learn more at: www.fertilitypedia.org/therapy/diag/prostatitis

Retrograde ejaculation
The semen, which would normally be ejaculated via the urethra, is redirected to the urinary bladder.
Learn more at: www.fertilitypedia.org/therapy/diag/retrograde-ejaculation

Sperm autoantibodies
Antibodies that bind to sperm, inhibiting their movement, stopping recognition and entry into the egg.
Learn more at: www.fertilitypedia.org/therapy/diag/sperm-autoantibodies

Teratospermia
Teratospermia is a condition characterized by the presence of sperm with abnormal morphology that affects fertility in males.
Learn more at: www.fertilitypedia.org/therapy/diag/teratospermia

Testicular failure
The inability of the testicles to produce sperm or testosterone.
Learn more at: www.fertilitypedia.org/therapy/diag/testicular-failure

Testicular torsion
Emergency medical condition occurring when the spermatic cord twists and cuts off the testicle’s blood supply.
Learn more at: www.fertilitypedia.org/therapy/diag/testicular-torsion

Thyroid disorders
A medical condition impairing the function of the thyroid.
Learn more at: www.fertilitypedia.org/therapy/diag/thyroid-disorders

Undescended testes
In the case of cryptorchidism one or both testes are absent from the scrotum. It is is the most common etiologic factor of azoospermy in the adult.
Learn more at: www.fertilitypedia.org/therapy/diag/undescended-testes
Varicocele
An abnormal enlargement of the pampiniform venous plexus in the scrotum.
Learn more at: www.fertilitypedia.org/therapy/diag/varicocele

Y-chromosome deletions
A family of genetic disorders caused by missing gene(s) in the Y chromosome.
Learn more at: www.fertilitypedia.org/therapy/diag/y-chromosome-deletions

HDR Reproductive functions

Spermatogenesis
Process in which spermatozoa are produced from male primordial germ cells in testicles by way of mitosis and meiosis.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/spermatogenesis

HDR Gallery

**Pic**
Molecular structure of testosterone

**Pic**
Regulation of testosterone production

<table>
<thead>
<tr>
<th>Testosterone</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, overall</td>
<td>8,10 230,300</td>
<td>27,35 780-1000</td>
<td>nmol/L ng/dL</td>
</tr>
<tr>
<td>Male &lt; 50 years</td>
<td>10</td>
<td>45</td>
<td>nmol/L</td>
</tr>
<tr>
<td>Male &gt; 50 years</td>
<td>290</td>
<td>1300</td>
<td>ng/dL</td>
</tr>
<tr>
<td>Female</td>
<td>6.2</td>
<td>26</td>
<td>nmol/L</td>
</tr>
<tr>
<td></td>
<td>180</td>
<td>740</td>
<td>ng/dL</td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>2.8-3.0</td>
<td>nmol/L</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>80-85</td>
<td>ng/dL</td>
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Sources

"Androgen replacement therapy" [https://en.wikipedia.org/wiki/Androgen_replacement_therapy] —sourced from Wikipedia licensed under CC BY-SA 3.0

"Anatomy and Physiology of the Female Reproductive System" [http://cnx.org/contents/FPtK1zmh@8.1:nMy6WSQ@5/Anatomy-and-Physiology-of-the-] —sourced from OpenStax College licensed under CC BY 4.0 Download for free at http://cnx.org/content/col11496/latest/

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