# Testosterone

Testosterone, the most important representative of androgens, is a steroid hormone produced in men primarily by Leydig cells. One third of its production is provided by *zona reticularis* of adrenal gland (not testosterone but another androgen with a similar function is produced here – *dehydroepiandrosterone*, shortly *DHEA*). Testosterone is derived from progesteron, which is created by gradual modifications of the carbon skeleton of cholesterol (dehydrogenation, isomerization,...).

endocrine

determines the development of the male phenotype, sexual organs, occurrence of secondary sexual characteristics, stimulates spermatogenesis (in men)

613498 (https://omim.org/entry/613498)

## Morphology

### Brief anatomy of testes

Testicles are an ellipsoid-shaped paired organ measuring between 3.6-5.5 cm in length and 2.1-3.2 cm in width. Their volume is around 18.6 ml.
They are stored in a scrotum, which on the one hand has the function of a protective cover and at the same time plays an important role in regulating the temperature, which should be 3–4   ° C lower than the abdominal temperature. **Testicle cover** consists of 3 layers of membranes: *tunica vaginalis*, *tunica albuginea* and *tunica vasculosa*. The testes themselves are functionally and morphologically divided into two sections: **intersticium** and **seed-forming canals**. These individually provide two main functions: spermatogenesis and steroidogenesis.

### Leydig cells

The endocrine elements of the testes, Leydig cells, are found in the interstitium, which occupies approximately 10-15% of the testes and fills the area between the seminiferous tubules. The cells themselves are represented by 20% in number (about 350 million). Along with Leydig cells, it contains the interstitium and cells of the immune system (macrophages and lymphocytes), which by their production of cytokines affect the proliferation, differentiation and endocrine function of steroidogenic cells. Leydig cells are of mesenchymal origin and originated from the differentiation of fibroblast-like interstitial cells due to luteinizing hormone. These cells are rich in endoplasmic reticulum and mitochondria and at the same time we can find abundant lipid droplets and lipofuscin residues in them. Their main function is **testosterone secretion**.

## Production and transport

The androgen production of men is from 2/3 testes and from 1/3 adrenal glands. Women, on the other hand, have the adrenal glands as the main source of male hormones, but testosterone is also produced in ovarium. Androgens are excreted directly into the blood, where they are transported tied to globulin, specifically *SHBG* . Furthermore, the newly formed testosterone diffuses into Sertoli cells, where it binds to the nuclear receptor and to ABP (which provides transport to the lumen) or converts to estradiol, which diffuses back into Leydig cells. Androgens are metabolized mainly in liver and their metabolites are excreted by urine.

## Secretion regulation

The main regulatory mechanisms of androgenic hormone production are **hypothalamic-pituitary system** and then **local** autocrine and paracrine signaling. These take place along the way:

### LH a hCG

Specific, high-affinity, and low-capacity luteinizing hormone receptors are abundant (up to 15,000 per cell) on the outer membrane of Leydig cells.

In laboratory experiments, testosterone levels in the interstitium and seminiferous tubules were found to be directly proportional to the time elapsed since LH antiserum administration, and a significant increase in the number of locally produced interstitial hormones stimulated basally was observed. with hCG-stimulated testosterone production in isolated purified Leydig cells. [1]

The maximum answer occurs when 1% of them is occupied, on the contrary, when they are oversaturated, their number is suddenly reduced. At the same time, a large part of the binding abilities is lost, for example, during fetal testicular irradiation, testicular fixation in the abdomen or after vas deferens ligation. LH is the only hormone capable of activating steroidogenesis on its own even in *in vitro* conditions. While at low doses the effect of *in vivo* is maximal, at high doses cells can be desensitized to both hCG and exogenous cAMP.

Upon binding of LH to the receptor, adenylate cyclase is stimulated, which induces increased cAMP production in the cell. Thus, protein kinase is activated, which ensures the biosynthesis of specific protein. Other messengers are also involved in protein kinase activation: cGMP and $Ca^{2+}$. At the same time, the activity of enzyme, which is involved in the cleavage of the cholesterol side chain and its release from the ester bond, is stimulated. The Leydig cell population is heterogeneous and therefore does not respond to uniform stimulation. In the event of high levels

of hCG, the cleavage of the cholesterol side chain is blocked, while long-term mild stimulation has a positive effect - it causes the proliferation of Leydig cell organelles (mainly smooth endoplasmic reticulum, mitochondria and Golgi complex).

### Estradiol

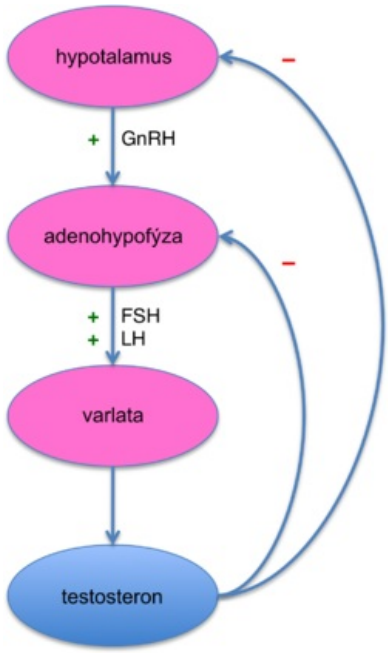
Locally produced estradiol can be a mediator of desensitization processes and its level is sensitive to hCG stimulation (after two hours its level is maximal). Estrogens also inhibit the production of progesterone.

### Adenohypophyseal hormones

Unlike Sertoli cells, cells do not have Leydig receptors for FSH, but they do carry receptors for **prolactin**. However, it can only act synergistically in the current presence of LH. Prolactin probably **increases the affinity of LH for the receptor** and at the same time affects lipid metabolism by mobilizing cholesterol esters and stimulating some steroidogenesis enzymes. However, too high levels have an inhibitory effect on testosterone synthesis.

### Substances produced directly by the testicles

This group includes, for example, LH receptor binding inhibitor, gonadokinin, inhibin... These substances largely have effects that slow down to stop estrogen production.



Axis hypothalamus → pituitary → testes

### Other substances and influences

Steroidogenesis is inhibited by ACTH, glucocorticoids and stress, and the effect of serotonin and its metabolites on testicular endocrine function is also known.

## Mechanism of action

Androgenic hormones, like other tissue agents of steroid origin, accumulate only minimally at the site of origin, most products steroidogenesis are excreted in the blood immediately after formation. Testosterone (or DHEA) passively diffuses into the cells of the target tissue, where it binds to the androgen receptor and then forms a hormone-receptor complex that enters the nucleus, inducing the formation of new mRNA and thus the formation of a specific protein.

## Biological effects of testosterone

1. Testosterone has an indispensable function in the embryonic period, when it determines the development of the male phenotype (and in the last two months of the embryonic period, it initiates the descent of the testes into the scrotum).
2. It is necessary for the growth of the genitals and the occurrence of secondary sexual characteristics (hair, mutations), which are most pronounced during puberty, when its level gradually increases.
3. In men, it stimulates spermatogenesis.

This fact was experimentally verified in 1968, when the presence of androgens (testosterone and DHEA) in the rabbit epididymis was first demonstrated. In the same year, these steroids were also detected in excrement from the *caput epididymis* of the ram. In 1969, the synthesis of testosterone *in vitro* from radioactive precursors from the rat epididymis was successfully described. (The study of A. I. Frankel and K. B. Eik from 1970 deals with the different concentrations of these hormones in individual sections of the epididymis!). [2]

In addition, it influences male sexual behavior and, through its anabolic effects, promotes proteosynthesis. At the same time, it enhances the formation of bone (increases bone mass and storage calcium) and stimulates muscle growth. Its increased level has a negative effect on the quality of skin (the formation of acne). It also increases erythropoiesis through increased erythropoietin secretion.

## Developmental and functional disorders associated with abnormalities in testosterone production

1. **Pseudopubertas** is a false form of premature puberty beginning in boys before 9 years of age and in girls before 8 years of age. One of the reasons for its formation may be autonomous overproduction of sex hormones in the gonads or adrenal glands. The main goal of treatment is to prevent premature growth termination.
2. We call **late puberty** the absence of signs of puberty in boys over 14 years of age, and in girls from 13 years of age. On the contrary, it is caused by a reduced level of sex hormones and we treat it by substituting them.
3. We talk about **anorchia** in the absence of one or both testicles. In bilateral anorchy, the testicles do not disappear until after the 16th gestational week. Although the victim has a masculine external genitalia, he is sterile and is characterized by a eunuchoid habit due to low androgen production. Testosterone must be substituted for life.
4. **Cryptorchidism**, occurring in 5% of boys born, persists after 1 year of age in almost 1/5 of them. The

testicles are often dystopian or ectopic in terms of the usual descent path. Testosterone production is maintained, but there is a risk of gradual deterioration of spermiogenesis. At the same time, it increases the risk of malignancy reversal by up to thirty times.
5. **Klinefelter's syndrome** arises from the nondisjunction of XY in meiosis. Classically, it is a XXY gonadotype, but there are also cases of multiple X or Y chromosomes. The frequency is 1: 500 live births. Small (often azoospermic) testes, eunuchoid growth due to low testosterone production, and gynecomastia due to increased estradiol production are typical. Hair and beard are thinner.
6. **"Male menopause" syndrome (PADAM)** is natural from a certain age (see Image 5) decrease in endocrine activity of testes responsible for decreased libido, decreased erectility, loss of muscle mass and development osteoporosis.
7. **Androgen insensitivity syndrome** is due to partial or complete depletion of the androgen receptor. It is genetically located at the Xp11-12 locus. In the XY genotype, we speak of the so-called Moris syndrome, in which the phenotype and psyche of a woman develop, but with a blindly ending vagina (testicular feminization syndrome). The prevalence of the disorder is 5 / 100,000 women and its treatment consists in the replacement of female hormones and the removal of retained testes.

# Links

## Related article

- Renin-angiotensin-aldosterone system
- Synthesis of steroid hormones

## External links

- Testosteron (Czech wikipedia)
- Testosterone (English wikipedia)

## Source

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## References


1. SHARPE, R. M – BARTLETT, J. M. S. Intratesticular distribution of testosterone in rats and the relationship to the concentrations of a peptide that stimulates testosterone secretion. *Journal of Reproduction and Fertility.* 1985, y. 25, no. 74, p. 223, ISSN 1741-7899.
2. FRANKEL, A.I – EIK-NES, K. B. Testosterone and dehydroepiandrosterone in the epididymis of the rabbit. *Journal of Reproduction and Fertility.* 1970, y. 10, no. 23, p. 441, ISSN 1741-7899.


## Bibliography


- STANISLAV, Trojan, et al. *Lékařská fyziologie.* 4. edition. Praha : Grada, 2003. ISBN 80-247-0512-5.
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