Androgens and antiandrogens (Pharmacology)

Male sex hormones

Androgens are male sex hormones. They are responsible for the **development of the male** type of **genitalia** during prenatal development as well as for the **growth of the genitals** and **the development of secondary sex characteristics** during puberty.

Testosterone

Testosterone is the basic male sex hormone. It is responsible for most of the physiological effects of androgens. In addition to the development and growth of male genitals, it has a significant **effect on the skin** , an **anabolic effect** , increases the **density of bone tissue** and supports **erythropoiesis** .

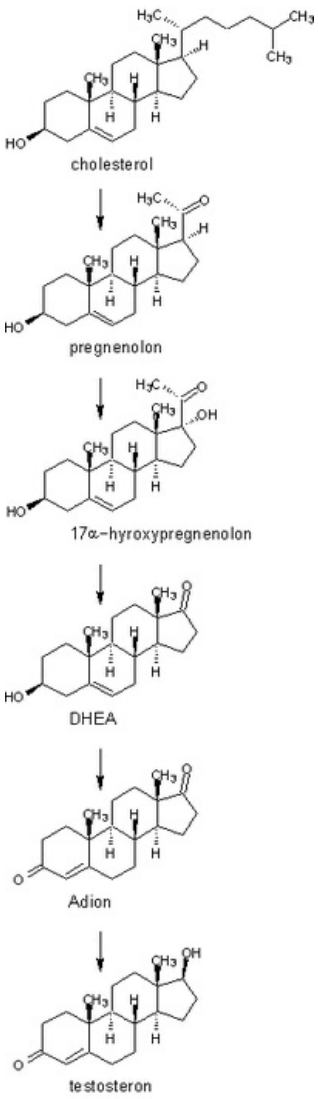
🔎 *For more information see Testosterone.*

Dihydrotestosterone

Dihydrotestosterone (DHT) is formed from testosterone in some target tissues (prostate, scrotum, penis, bones). It has **higher androgenic effects** than testosterone, thereby amplifying the signal.

Dihydroepiandrosterone

Dihydroepiandrosterone (DHEA) is unable to activate the androgen receptor and therefore **lacks androgenic effects**. However, it is an important **substrate for the production of testosterone** .



Scheme of testosterone synthesis from cholesterol.

Androgen secretion and its regulation

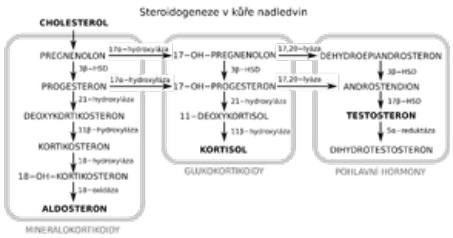
Most of the testosterone secreted into the blood comes from the **Leydig cells** in the testicles (60–95 % depending on the state of the organism and the literature used), the rest is secreted by the **adrenal cortex**. Secretion from both glands is controlled by the hypothalamo-pituitary system, however, individual glands respond to different hormones.

- Leydig cell secretion is **controlled by pituitary luteinizing hormone**. The hypothalamus produces **gonadoliberin**, which stimulates the pituitary gland to produce *luteinizing hormone* and *follicle-stimulating hormone*. Luteinizing hormone subsequently stimulates the Leydig cells to secrete testosterone. The production of gonadoliberin from the hypothalamus and luteinizing hormone from the pituitary gland is feedback inhibited by testosterone, but also by *estrogens*.
- The secretion of the adrenall cortex is under the control of another pituitary hormone - **adrenocorticotropin** (ACTH). The hypothalamus secretes **corticoliberin**, which stimulates the pituitary gland to secrete ACTH, and which stimulates the adrenal cortex to secrete *androgens* and *glucocorticoids*. Feedback is also different in this case. The secretion of corticoliberin and ACTH is inhibited by the presence of glucocorticoids in the blood, not androgens as is the case with secretion by Leydig cells.

Androgen synthesis

Testosterone synthesis takes place mainly in the Leydig cells of the testicles and adrenal cortex. The starting substance for synthesis is **cholesterol** (the synthetic pathway from cholesterol to testosterone is shown in the figure).

🔎 *For more information see Steroid Hormone Synthesis.*



Scheme of steroidogenesis.

The first three reactions can only take place in glands with internal secretion, i.e. testicles and adrenal glands, other tissues lack the appropriate enzymatic equipment. However, many target tissues can synthesize androgens from DHEA circulating in the blood.

> The adrenal cortex not only secretes testosterone from androgens, but also DHEA - mainly int its sulfated form and androstenedione, i.e. the last two products of testosterone biosynthesis. These then serve as substrates for the synthesis of testosterone directly in target tissues, such as the prostate or sex organs. This biosynthesis directly in the target tissue plays an important role in the humoral control of organs whose proper function is dependent on the supply of androgens. These processes are controlled by the expression of enzymes catalyzing these reactions, such a control method is called intracrine modulation.

Primarily in the prostate, testes, penis and bone tissue, testosterone is reduced to DHT, its product with a much higher affinity for receptors and therefore with a much higher effect.

Androgens used in therapy

Androgens used in therapy are substances that have effects similar to physiologically produced hormones.

Indications

- **Hypogonadism**;
- Improving the condition of the organism (it is possible to indicate them to patients in whom it is necessary to support anabolic pathways - patients with AIDS, osteoporosis, previously also with anemias);
- Breast cancer (in post-menopausal women);
- Misuse as anabolics in athletes.

Medicaments and methods of administration

Testosterone
: The basic remedy is testosterone. When administered orally (p.o.), it has a **high first pass effect**, thus it must be administered by other ways. It is applied **transdermally** in the form of **gels'** or **patches'** - these are able to maintain testosterone levels for up to a week.

Testosterone esters
: Testosterone can also be administered in the form of esters. These **can also be administered p.o.** as due to their high lipophilicity they travel with other lipids through the lymph after absorption and bypass the high first pass effect of the liver. Another option is intramuscular (i.m.) administration. The registered representative is ***testosterone undecanoate*** (for p.o. and i.m. administration).

Anabolic steroids
: Anabolic steroids have enhanced anabolic effects and suppressed androgenic effects. The representatives are ***mesterolone*** (for p.o. administration) and ***nandrolone*** (with injectable administration).

Side effects

Side effects are based on the physiological effects of androgens. They mainly include:

- Puberty-like symptoms - administration before puberty stops growth;
- Gynecomastia;
- Increased sodium and water retention;
- Reduced physiological testicular function resulting in decreased spermatogenesis, which can lead to infertility - the condition is reversible;
- Virilisation in women.

Some side effects are exacerbated with anabolic steroids, most notably hepatotoxicity, testicular atrophy, personality disorders associated with an increase in aggression, and the risk of increased IHD and sudden cardiac death.

Antiandrogens

Antiandrogens are pharmaceuticals that reduce the effect of androgens. This group includes androgen receptor antagonists and 5α-reductase blockers.

Androgen receptor antagonists

Drugs from this group are used **in the therapy of prostate cancer** in combination with gonadoliberin analogues.

Side effects are considerable and include, in particular:

- Hot flashes, gynecomastia, mastodynia;
- Diarrhea, nausea, vomiting;
- Impotence;
- Depression, fatigue, malaise;
- Hepatotoxicity.

Representatives of androgen receptor antagonists

- **Cyproterone** - a steroidal partial androgen receptor agonist and progestin.
- **Flutamide** and **Bicalutamide** - non-steroidal antagonists.

5α-reductase inhibitors

5α-reductase inhibitors inhibit the metabolism of testosterone to dihydrotestosterone. Representatives are **dutasteride** and **finasteride**. They are used to treat benign prostatic hyperplasia or, for example, androgenetic alopecia (finasteride).

Links

Related articles

- Testosterone
- Steroid hormones synthesis

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