

Androgens

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is a natural or synthetic steroid hormone that regulates the development and maintenance of male characteristics by binding to androgen receptors. Androgens are synthesized in the testes, ovaries, and the adrenal glands.

Although androgens are commonly thought of only as male sex hormones, females also have them, but at lower levels. Also, androgens are the precursors to estrogens in both men and women.

Types of androgens

1-Dehydroepiandrosterone made in the adrenal cortex from cholesterol

2-androstenedione made by the adrenal cortex ,ovaries ,and testes and converted metabolically to testosterone

3-androstenediol main controller of gonadotropin secretion

4-androsterone created when androgens break down and helps to enforce masculinity

5-dihydrotestosterone metabolite of testosterone ,is made in the adrenal cortex

Testosterone

- Bound in plasma albumin & sex hormone binding globulin (SHBG) ,Can be converted to the more potent, dihydrotestosterone (DHT),
- Binds to and activates a single androgen receptor
- Androgen receptors are present in many tissues including reproductive tissue, skeletal muscle, brain, kidney.

Mechanism of action

In the target tissues, androgens enter the cell cytoplasm by simple diffusion across the cell membrane. Once inside the cell, the androgens bind and activate the androgen receptors. The androgen-receptor complex attaches to a specific DNA site and stimulates the production of messenger RNA, which, in turn, stimulates the production of the enzymes and proteins necessary to affect androgen action.

Pharmacokinetics

- Absorption: undergoes high first pass metabolism. Therefore IM injections or synthetic preparations are used
- Transport: highly protein bound 98%, SHBG, albumin.
- Metabolism: by liver enzymes : androsterone & etiocholanolone
- excretion by urine after conjugation

Control of testosterone synthesis

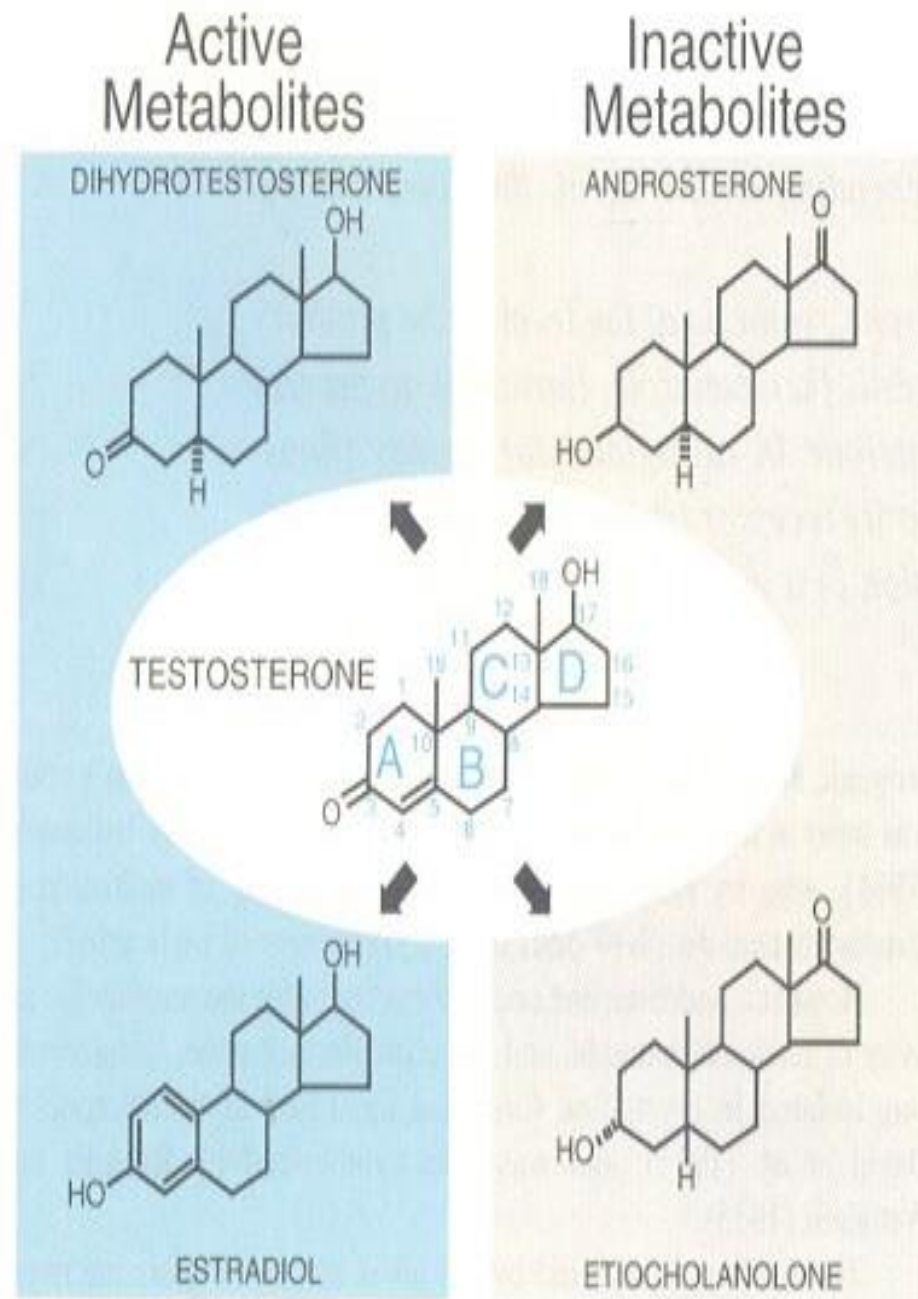
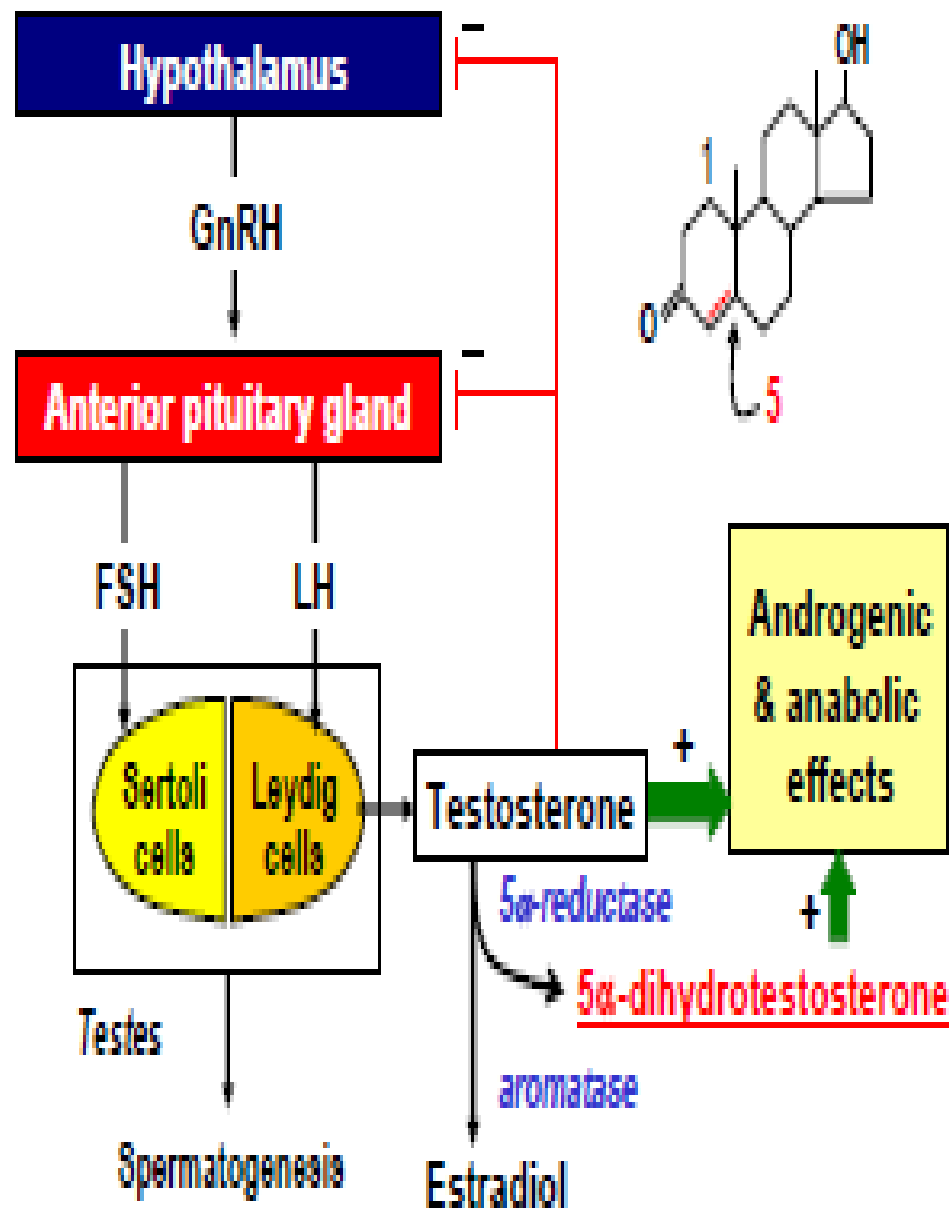


Figure 58-1. Metabolism of androgens.

Therapeutic Androgen Preparations for male patient

1-Testosterone ester is ineffective orally (inactivated by liver), and is usually given as i.m. injections

2-oral androgens

3-transdermal testosterone gel

4- implanted testosterone pellets and patch improve compliance, and symptoms, effects last for months

5- testosterone buccal tablets

Synthetic androgens:

-Methyltestosterone, Fluoxymesterone

-Propionate(25-50 mg), enanthate (100 mg depot preparations) effects last for 2-3 weeks

Testosterone Preparations

Dose

Testosterone aq. suspension

50-100mg / 2 weeks

Testosterone esters:

- Testosterone propionate
- Testosterone phenylpropionate
- Testosterone cypionate
- Testosterone enanthate

25-50 mg / 3 times a week

40-60mg / 1 or 2 week

100 – 200mg / 2 weeks

250 mg / 2 weeks

Orally active preparations:

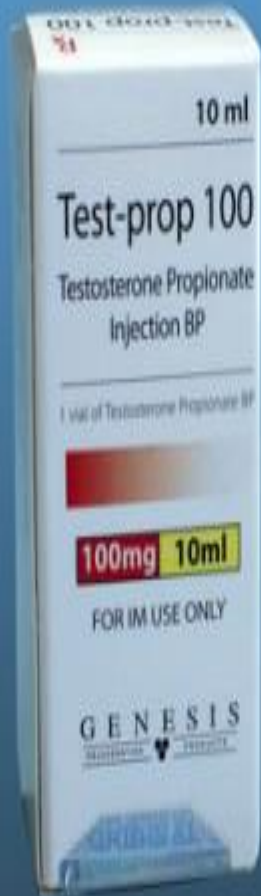
- Methyl testosterone tab.
- Fluoxymesterone
- Mesterolone

Transdermal patches

2 patches /day (back,abdomen,thigh)

Implants

wall of abdomen/thigh



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Androgen replacement therapy (ART)

-ART uses derivatives of testosterone, rather than synthetic Androgens, because they are safe, effective and easy to monitor

1-Hypopituitarism

2-Androgen deficiency (hypogonadism) is usually caused by

-underlying testicular disorders (high LH, but low testosterone levels)

-hypothalamic-pituitary disorders (low LH and low testosterone levels)

Goal: Mimic the normal testosterone concentration as closely as possible (serum concentration monitoring)

If untreated, does not shorten life expectancy, but is associated with significant morbidity (ambiguous genitalia, delayed puberty & infertility).

Treated by androgen replacement therapy (ART), usually for the remainder of life. The aim is to restore tissue androgen exposure by using the natural androgen testosterone

For the treatment of testosterone deficiency in the adult male, one of the two long-acting testosterone esters, testosterone enanthate or testosterone cypionate, should be administered by intramuscular injection, 200 mg every two weeks or 300 mg every three weeks.

-The testosterone derivatives, which can be administered orally, are probably too weak as androgens to be used for the treatment of adult male hypogonadism, but they may have value in situations where full androgenization is not desired, such as adjuvant treatment of breast carcinoma.

3. AIDS related muscle wasting

4. Hereditary angioneurotic edema

5. Ageing

Misuse: involves prescription with no acceptable medical indication, Examples of misuse include:

- male infertility

- male sexual dysfunction or impotence

- “male menopause” (andropause)

- no convincing evidence that androgen therapy is either effective treatment or safe for older men unless there is frank androgen deficiency

Adverse Effects

1-Virilization:

may occur in women receiving relatively high doses for prolonged periods, such as for estrogen dependent mammary carcinoma

2-Cholestatic Jaundice

may be produced by steroids possessing a 17-alpha methyl group-oral Vs parenteral

3-Priapism (sustained erection)

4-Oligospermia

5-Edema-via promotion of salt and water retention.

6-Precocious puberty and short stature

7-Acne

8-Gynecomastia – children and liver disease

contraindications

- Carcinoma of Prostate and male Breast
- Liver and Kidney diseases
- Pregnancy
- CHF, epilepsy and migraine

Thank you