

Androgens & Antiandrogens

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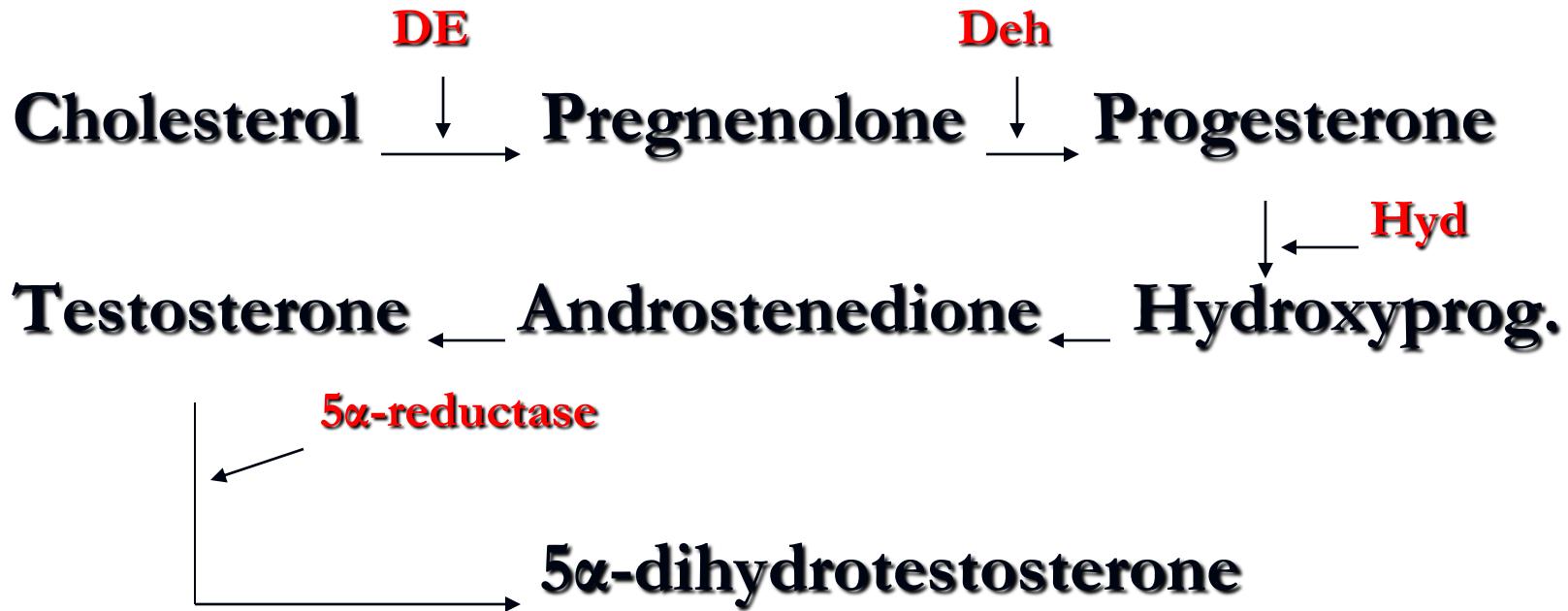
Androgens

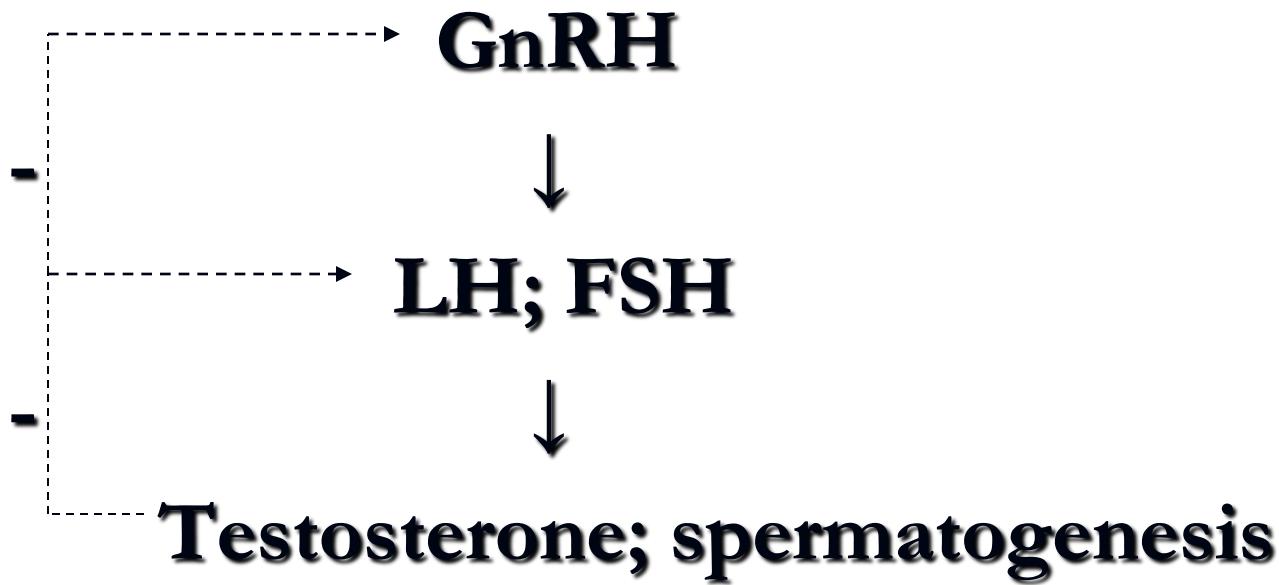
- The testes have two major functions:
 1. Spermatogenesis occurring within the seminiferous tubules
 2. Production of androgenic hormones

Androgens

- Naturally occurring androgenic hormones are:
 1. Testosterone, the principal androgenic hormone, is mainly produced by the Leydig cells of testes .
 2. Dehydroepiandrosterone (DHEA) is produced by adrenal cortex.
 3. Androstenedione
- The testes also produce other hormones:
 - Estradiol
 - Inhibin(feedback inhibits FSH)
 - Activin

Testosterone synthesis



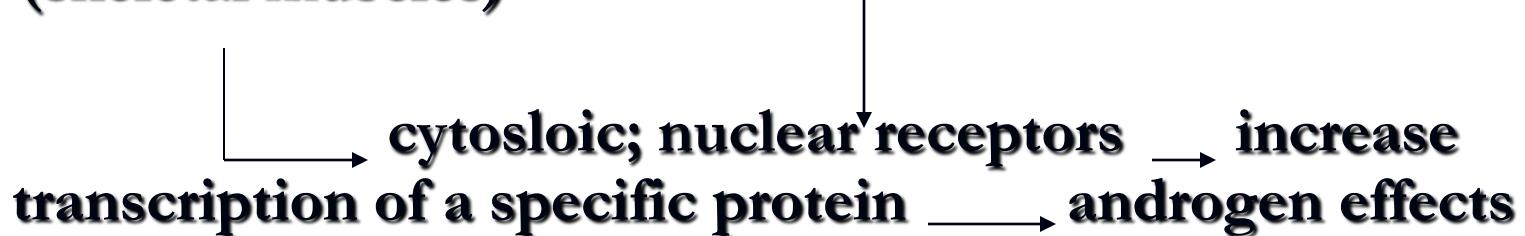


Transport & MOA of androgens:

- 65% is bound to SHBG, 2% is free, rest bound to albumin.

5 α -reductase

Testosterone $\xrightarrow{\quad}$ 5 α -dihydrotestosterone (sex organs)
(skeletal muscles)



DHT is 10 times more potent than testosterone and mediates the effects of testosterone on skin and sexual apparatus (prostate; seminal vesicle, epididymis...)

Pharmacological effects

- **Virilizing=musculinizing effect
1° & 2° sexual characteristics**
- **Spermatogenesis**
- **Erythropoiesis**
- **Anabolic or growth promoting effect (bone;
skeletal muscles)**

Clinical Uses

- **Testosterone deficiency**
Hypogonadism; impotence; ↓ libido; aging; infertility.
- **Anemia; leukemia; lymphoma**
- **Endometriosis (Danazol is particularly used)**

Clinical Uses

- **Antiestrogenic effect:**

Breast cancer.

- **Anabolic effect.**

Osteoporosis

Abused by athletes.

Testosterone preparations

For androgen replacement:

- **Testosterone I.M; S.C**
- **Testosterone propionate I.M, S.L**
- **Testosterone cypionate I.M; depo I.M**
- **Methyltestosterone O; S.L**
- **Fluoxymestrone O**

For breast cancer:

Testolactone (progesterone derivative and aromatase inhibitor) O

Testosterone preparations

For anabolism (osteoporosis):

Androgen:anabolic ratio=1:2 or 1:3 (promote +ve anabolism and muscular growth but little effect on sex)

- Ethylestrenol O
- Stanozolol O
- Oxandrolone O
- Nandrolone decanoate I.M
- Methandienone O

Side Effects of Testosterone

- **Virilization (musculinization)**
Hirsutism; acne; menstrual disorders in ♀'s
- **Precocious puberty & hirsutism in children**
- **Salt & water retention**
- **Jaundice; gall bladder stones (methyltestosterone)**
- **Enlargement of prostate**
- **? Liver cancer**

Antiandrogens

- **Estrogens:** **Diethylstilbestrol;**
mestranol...
- **Progestins:** **Cyproterone acetate**
- **GnRH superagonists (Leuprolide acetate); GnRH antagonists (Ganirelix)**
Flutamide; Bicalutamide and
Nilutamide
- **5 α - reductase inhibitors:** **Finasteride**
- **Ketoconazole**
- **Spirostanolactone**

Gossypol

- Cottonseed derivative, China.
- Destroys elements of the seminifrous epithelium, but does not affect the endocrine function of the testes.
- Irreversible if continued more than 2 years.
- Can cause hypokalemia and paralysis.
- Not used in western medicine.

Clinical Uses of Antiandrogens

- **Ca prostate**
- **Benign hyperplasia of the prostate
(Finasteride)**
- **Severe acne and hirsutism in ♀'s
(Spironolactone; Cyproterone acetate)**
- **Precocious puberty**
- **♂ antifertility agents (♂ contraceptive)
(Gossypol)**
- **♂ baldness (Cytoctol=topical antiandrogen;
Finasteride)**

Side Effects of Antiandrogens

↓ Libido

Impotence

↓ Spermatogenesis

↓ Ejaculate