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

Cholesterol → Pregnenolone → Progesterone

Testosterone ← Androstenedione ← Hydroxyprog.

5α-reductase

5α-dihydrotosterone
GnRH → LH; FSH → Testosterone; spermatogenesis
Transport & MOA of androgens:

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

5α-reductase

Testosterone \[\rightarrow\] 5α-dihydrotestosterone (sex organs)
(skeletal muscles)

\[\rightarrow\] cytosolic; nuclear receptors \[\rightarrow\] increase
transcription of a specific protein \[\rightarrow\] androgen effects

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

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Pharmacological effects

- **Virilizing=musculinizing effect**
  - $1^\circ$ & $2^\circ$ 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 (masculinization)
  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:** Diethylstilbesterol; mestranol...

- **Progestins:** Cyproterone acetate

- **GnRH superagonists (Leuprolide acetate); GnRH antagonists (Ganirelix)**

- **Flutamide; Bicalutamide and Nilutamide**

- **5α- reductase inhibitors:** Finasteride

- **Ketoconazole**

- **Spironolactone**

- **Gossypol**
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 (Cyoctol = topical antiandrogen; Finasteride)
Side Effects of Antiandrogens

↓ Libido
Impotence
↓ Spermatogenesis
↓ Ejaculate