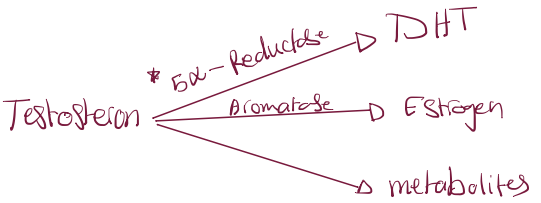
Male hormones

Testosterone
- mainly from testis (Leydig cells)
- small amount from (Adrenal Gland) and (Adipose tissue)



I. Hormonal Regulation of Male Reproductive Function

1. Pituitary Hormones
- FSH (Follicle-Stimulating Hormone):
- Controls gametogenesis (spermatogenesis).
- Requires high local testosterone concentration for full activity.
- LH (Luteinizing Hormone):
- Stimulates Leydig (interstitial) cells to produce testosterone. → mainly!
- Leydig cells are located between the seminiferous tubules.

2. Sertoli Cells
- Secrete inhibin and activin.
- Activin: Stimulates FSH release from the pituitary.
- Inhibin: Inhibits FSH secretion, acting synergistically with testosterone and dihydrotestosterone (DHT).

II. Testosterone and Androgens

1. Circulation and Binding
- 65% of circulating testosterone is bound to SHBG (sex hormone-binding globulin).
- Most of the remainder is bound to albumin.
- Only about 2% is free (biologically active).

Factors Affecting SHBG Levels:

- Increased by:
- Estrogen
- Thyroid hormone
- Liver cirrhosis

- Decreased by:
- Androgens
- Growth hormone
- Obesity

2. Conversion and Activity
- In target tissues, testosterone is converted to DHT via **5α-reductase**.
- Both testosterone and DHT mediate pubertal changes.
- DHT is the **major** active androgen in peripheral tissues.

3. Metabolism and Excretion
- Testosterone is metabolized by reduction.
- Its metabolites are excreted in urine as conjugates.

III. Adrenal Androgens

- Androstenedione, DHEA (dehydroepiandrosterone), and DHEAS (DHEA sulfate):
- Secreted primarily by the adrenal glands.
- Play a minor role in sexual maturation.
- Enhance well-being.
- Inhibit atherosclerosis.

Clinical Relevance of DHEA:

- May benefit patients with systemic lupus erythematosus (SLE):
- Immunomodulatory effects:
- Reduces inflammatory cytokines like IL-6.
- Increases IL-2 production.

IV. Physiological Effects of Androgens

1. Sexual Development

- Responsible for the development of <u>*secondary sexual characteristics*</u> and other pubertal changes in males.

2. Metabolic Effects

1. Decreased SHBG levels.
2. Increased liver synthesis of:
- Clotting factors
- Triglyceride lipase
- α1-antitrypsin
- Haptoglobin
- Sialic acid
3. Increased renal erythropoietin secretion.
4. Reduction in HDL cholesterol levels.

<u>I. Pharmacokinetics of Synthetic Androgens</u>

1. Testosterone (Natural Androgen)

- Has low oral bioavailability (~15%).
- Administered parenterally (injection, transdermal, etc.).

2. Orally Active Testosterone Derivatives

- Alkylation at 17α-position increases oral activity.
- Examples:
- Methyltestosterone
- Fluoxymesterone

Androgenic:Anabolic ratio

- Oxymetholone (~ 1:3)
- Oxandrolone (1:3 to 1:13)
- Nandrolone (1:2.5 to 1:4)

Anabolic ← القدرة البنائية
Androgenic ← القدرة الذكورية
مهم: هاي الهرمونات بستخدموها الرياضيين عشان تعطيهم تأثير بنائي للجسم (بعيداً عن التأثير الذكوري)

<u>II. Actions of Anabolic-Androgenic Steroids (AAS)</u>

1. Anabolic Effects

- Increased muscle mass and strength.
- Enhanced training intensity.
- Promotion of bone growth and mineralization.
- Improved performance (strength & aggression) — especially noted in females.

III. Anabolic Steroid Abuse in Sports

1. Usage Patterns
   - Athletes and bodybuilders may use doses 10–200× higher than physiological levels.

2. Common Misusers
   - Athletes
   - Bodybuilders

3. Adverse Effects of Abuse
   - Cardiovascular complications
   - Liver disease
   - Reproductive organ toxicity
   - Severe mood swings
   - Increased aggressiveness

⚠️ These adverse effects outweigh potential benefits, making non-medical use inadvisable.

IV. Therapeutic Uses of Androgens and Anabolic Steroids

1. Androgen Replacement Therapy
   - For hypogonadal men.
   - Routes of administration:
   - Oral
   - Sublingual
   - Intramuscular (IM)
   - Transdermal (TD)
   - Topical gel
   - In pituitary deficiency, androgens are used (instead of gonadotropins), unless fertility/spermatogenesis is the goal.

2. Treatment of Protein Loss
   - Used in combination with diet and exercise to reverse catabolism in:
   - Trauma
   - Surgery
   - Prolonged immobilization
   - Debilitating diseases

3. Treatment of Refractory Anemias ⟶ انيميا لاتستجيب للعلاجات العاديه
   - Examples:
   - Aplastic anemia
   - Note: Recombinant erythropoietin has now largely replaced androgens for this indication.

🚨❌❗ Contraindications and Cautions:

Absolute Contraindications
1. Pregnancy
2. Men with prostate or breast cancer

Caution Required In:
3. Infants and children
   - Risk of premature epiphyseal closure
   - Somatotropin (GH) is preferred for growth stimulation.
4. Patients with renal or cardiac disease
   - Due to potential for fluid retention and hypertension.

🚨Adverse Effects of Androgenic and Anabolic Steroids:

1. Masculinizing Effects in Women → بنت دكاية
   •Hirsutism (excess hair growth) •Ace •Amenorrhea •Clitoral enlargement •Deepening of voice

2. Progestational Activity
   - Some steroids exert progestin-like effects,
     leading to withdrawal endometrial bleeding upon discontinuation.

3. Increased Atherosclerosis Risk in Women

4. Fluid and Electrolyte Effects > Sodium retention and edema are rare but possible.

5. Teratogenicity
   - If administered during pregnancy:
   - May cause masculinization of female fetus.
   - May cause undermasculinization of male fetus.

6. Neurologic Effects
   - Early administration may alter CNS sexual development, especially in females

7. Hepatic Dysfunction
   - Especially with 17-alkylated steroids:
   - Cholestatic jaundice • Hepatomas •Hepatocellular carcinoma *with long-term use.*

8. Prostatic Effects
   - Benign prostatic hyperplasia (BPH) or stimulation of latent prostate cancer.

9. Lipid Profile Alteration
   - Increased LDL. • Decreased HDL

10. Other Physical Effects
   - Acne. •Obstructive sleep apnea. •Erythrocytosis. •Gynecomastia •Azoospermia
   - Testicular atrophy •*Recovery may take months after stopping treatment.*

11. Psychological Effects
   - Psychological dependence •Increased aggression •Psychosis

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🫀***Antiandrogens:***

Antiandrogens function by either inhibiting the production of androgens (like DHT)
or blocking androgen receptors at target tissues. They are used in both male and female patients depending on the condition.

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كتكوت ، هانت ضايل
اخر صفحة 🥳

Remember: testosterone —5α Reductase→ DHT

A. 5α-Reductase Inhibitors

(Inhibit conversion of testosterone → dihydrotestosterone [DHT])

1. Finasteride
   - Orally active steroid-like drug.
   - Reduces DHT levels within 8 hours of administration; effect lasts ~24 hours.
   - Moderately effective in reducing prostate size in benign prostatic hyperplasia (BPH).
   - Also used for:
   - Early male-pattern baldness (androgenic alopecia)
   - Hirsutism in women

2. Dutasteride
   - Similar to finasteride; orally active steroid derivative.
   - Slower onset but much longer half-life than finasteride.
   - Mainly approved for benign prostatic hyperplasia (BPH).

B. Androgen Receptor Blockers

1. Cyproterone and Cyproterone Acetate
   - Steroidal antiandrogens that block androgen action at target tissues.
   - Cyproterone acetate has progestational activity:
   - Suppresses LH and FSH via negative feedback.
   - Enhances antiandrogenic effect.
   - Clinical uses:
   - Hirsutism in women (given with an estrogen).
   - Decreased libido and sexual drive in men.

2. Flutamide
   - Nonsteroidal androgen receptor antagonist.
   - Potent antiandrogen.
   - Uses:
   - Treatment of **prostatic carcinoma.**⭐
   - Management of androgen excess in women (e.g., hirsutism).
   - Adverse effects:
   - Mild gynecomastia (likely due to increased testicular estrogen production).
   - Occasional mild, reversible hepatic toxicity.

3. Bicalutamide, Enzalutamide, and Nilutamide
   - All are potent, orally active antiandrogens.
   - Used in metastatic prostate cancer.
   - Bicalutamide is often combined with GnRH analogs to reduce tumor flare from initial LH/FSH surge.

4. Spironolactone
   - Primarily an aldosterone receptor antagonist (diuretic).
   - Also:
   - Blocks androgen receptors
   - Inhibits 17α-hydroxylase → lowers testosterone and androstenedione levels.
   - Clinical use:
   - Hirsutism in women

Done by
Shahed jumah