









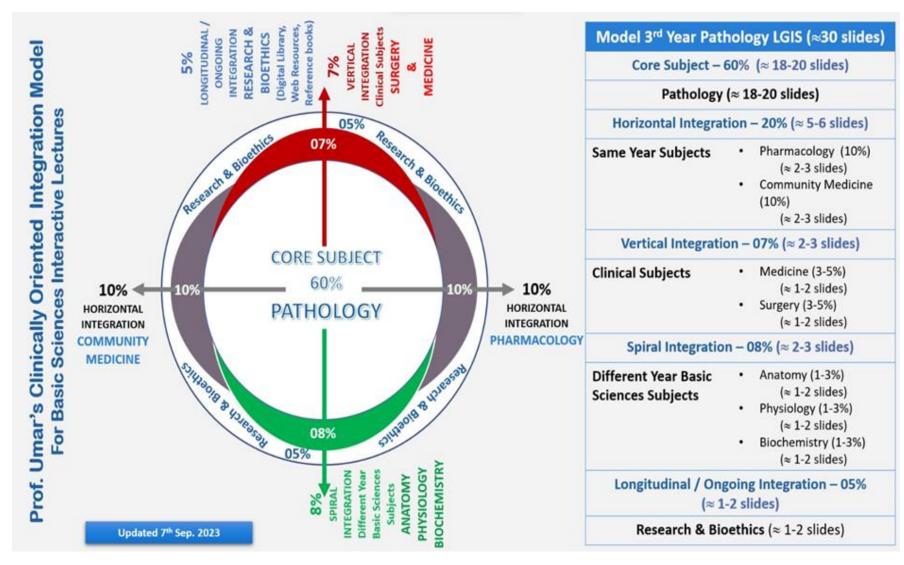
To impart evidence based research oriented medical education

To provide best possible patient care

To inculcate the values of mutual respect and ethical practice of medicine













Androgens & Anabolic Steroids (LGIS)

Reproduction Module 4th YEAR MBBS 2024

Sources:

BERTRAM G. KATZUNG BASIC & CLINICAL PHARMACOLOGY 15TH EDITION

DR.MUHAMMAD ZAHEER SHEIKH





LEARNING OBJECTIVES

At the end of the lecture, students should know:

- Enumerate Androgenic prepration
- Describe uses and adverse effects of androgenic preprations.
- Discuss Pharmacokinetics and Pharmacodynamics of Anti-Androgens

















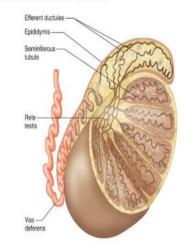


ANDROGENS & ANABOLIC STEROIDS

Two major functions of testis:

- Spermatogenesis
- Production of androgenic hormones
 - ✓ Testosterone
 - **✓** Dihydrotestosterone

Testis & seminiferous tubules



✓ Androstenedione & Dehydroepiandrosterone

Spiral Integration



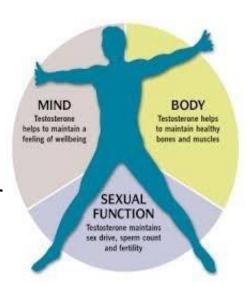
TESTOSTERONE – PYSIOLOGICAL EFFECTS



ANABOLIC EFFECTS

- Pubertal spurt of growth at puberty both boy & girl
- Rapid bone growth, both in thickness & length.
- Skeletal growth stimulated & epiphysial closure accelerated
- Decreased bone resorption
- Positive nitrogen balance, increase protein synthesis or decrease.protein breakdown
- Increase in appetite

Other effects: HDL, erythropoiesis by stimulating renal erythropoietin secretion & by direct action on haeme synthesis



Spiral Integration





Classification of androgens

NATURAL

- Testosterone
- Dihydrotestosterone
- Androstenidone
- Dehydroepiandrosterone (DHEA)
- Dehydraepiandosterone sulfate (DHEAS)





SYNTHETIC ANDROGENS

- Testosterone
- Testosterone cypionate
- Testosterone enanthate
- Testosterone propionate
- Fluoxymesterone
- Methyltestosterone
- Dromostanolone propionate





Mechanism of action of testosterone

Intracellular receptor transduction mechanism





Anabolic steroids

- Synthetic androgens with higher anabolic and lower androgenic activity
- Drugs include
 - nandrolone
 - oxymetholone
 - stanozolol
 - mathandienone
 - oxandrolone
 - oxymesterone
 - norethandrolone



Pharmacologic actions of anabolic steroids



- Anabolic effects are similar to testosterone
- Therapeutic doses, anabolic action more prominent
- Higher doses and prolonged treatment, androgenic effect become more and more prominent





Effects of anabolic steroids

- Anabolic effect
- Progestational effect (norethandrolone)
- Androgenic effect
- Increase well being & appetite





Uses of anabolic steroids

- Osteoporosis
- Catabolic states
- Suboptimal children growth
- Hypoplastic , hemolytic and malignancy associated anemias
- Renal failure
- CA breast
- To enhance physical activity in athletes



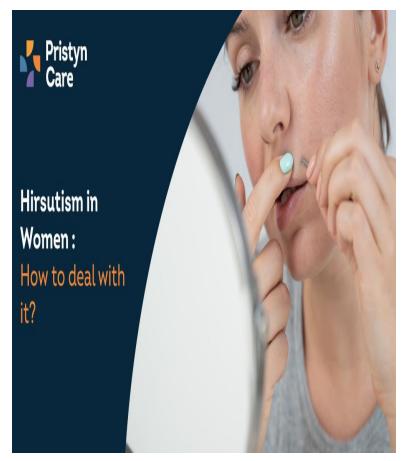


Adverse effects of anabolic steroids

- Testicular atrophy , impotence , sterility , gynecomastia
- Inhibition of ovulation, hirsutism, voice deepening, alopecia, acne
- Short stature
- Increased aggressiveness
- Use in pregnancy virilization
- Increased risk of coronary heart disease in athletes









Vertical Integration

Contraindications anabolic steroids

- Prostate and breast CA
- Cardiac, renal, hepatic disease
- Pregnancy

- Drug interactions:
 - Anabolic sterodis and glucocorticoids (potentiated effects)



Anti-androgens Classification



GnRH antagonists

- Ganerelix
- Cetrorelix
- Adarelix
- Degarelix

GnRH agonists (continuous administration)

- Leuprolide
- Goserelin
- Naferelin
- Buserelin

Testosterone and its metabolites synthesis inhibitors

- Ketoconazole
- Spironolactone
- Abiraterone





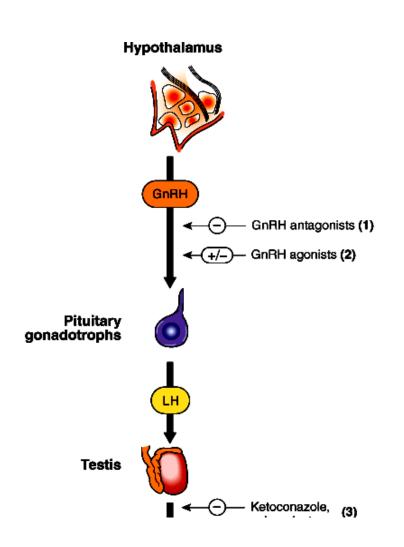
- Decreased conversion of testosterone into dihydrotestosterone (5 alpha reductase inhibitors)
 - Finasteride
 - Dutasteride

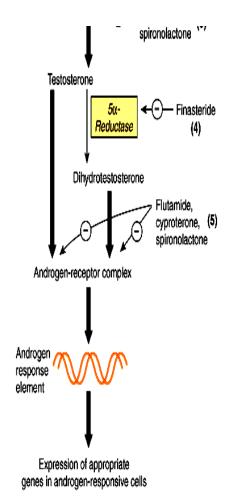
Androgen receptor blockers

- Cyproterone acetate
- Flutamide
- Spironolactone
- Bicalutamide
- Nilutamide









Spiral Integration





GnRH antagonists:

- Gonadotropin releasing hormone is inhibited by the GnRH antagonists, resulting in diminished release of gonadotropins (LH, FSH)
- Ultimately synthesis of testosterone and its active metabolites are inhibited

– Use:

- CA prostate (adarelix, degarelix)
- Controlled ovarian stimulation (ganerelix, cetrorelix)

Adverse effects:

- Gyneacomastia
- Nausea , headache , drowsiness
- Less hematocrit
- Weakness
- depression





GnRH agonists

– Uses:

- Prostatic cancer
 - Initial flare up can be treated with a combination of GnRH agonists and flutamide or bicalutamide

– Adverse effect:

 Hot flushes , sweats , edema , guneacomastia , decreased libido , decreased hematocrit , muscle weakness





Testosterone synthesis inhibitors

KETOCONAZOLE:

- Mechanism of action:
 - displace testosterone from protein sites
 - Inhibits 450 c 17, 17-20 lyasedecreased dehydotestosterone, androstenedione
- Uses:
 - CA prostate
- Adverse effects:
 - Gyneacomastia, loss of hair and libido, oligozoospermia





Abiraterone:

- It inhibits 17 hydroxylase enzyme and thus inhibits the conversion of progesterone and pregnenolone into dehydroepiandrosterone and androstenedione
- With resultant testosterone synthesis inhibition
- Use:
 - CA postate



<u>Decreased conversion of testosterone to</u> <u>dihydrotestosterone</u>



FINASTERIDE:

- Mechanism of action
 - Competitive inhibitor of 5 alpha reductase
 - It is the enzyme that converts testosterone into dihydrotestoterone (active metabolite) in skin, hair, prostate, seminal vesicles, epididymis

Uses

- BPH (reduce size of prostate)
- CA prostate
- Hirsutism
- Male pattern baldness

Adverse effects

Decreased libido , impotence , skin rashes





Androgen receptors blockers

FLUTAMIDE:

Competitive inhibitor of androgen receptors

– Uses:

- CA prostate
- Hirsutism

– Adverse effects:

Gyneacomastia , breast tenderness , liver damage , GIT disturbance





CYPOTERONE AND CYPOTERONE ACETATE

Mechanism of action

- Compete with dihydrotestosterone for receptor binding
- Acetate has progestational activity, it suppresses the feedback enhancement of LH & FSH more anti-androgenic activity

Uses

- Female hirsutism
- Masculinization in women
- Precocious puberty in boys
- Male pattern baldnesss
- acne





SPIRONOLACTONE:

- Competitive inhibitor of aldosterone and androgen receptors
- Also lowers 17 alpha hydroxylase thus reduced conversion of dehydrotestosterone and androstenedione into testosterone
- Spironolactone used for treatment of hirsutism

– Adverse effects:

 Gyneacomastia , hyperkalemia , hyponatremia , hypotension in large doses





 Bicalutamide and nilutamide are oral antiandrogens with similar anti-androgenic effects as previous drugs but less hepatotoxic





BIOMEDICAL ETHICS

Medical ethics is involved because of the crucial role of physicians in anti-doping policies and practices as well as developing and administering ergogenic substances or methods for athletes. This raises ethical questions regarding physician-patient relationship, principle of non-male faience, privacy and confidentiality of patient, and fairness and justice in the macro allocation of resources. The aim of this paper is to discuss anti-doping practices and policies in the context of medical ethics. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5 215887

Vertical Integration





RESEARCH ARTICLES

- Treatment of Anabolic-Androgenic Steroid
 Dependence: Emerging Evidence and Its Implications
 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC287

 5348/
- Diagnosis and Management of Anabolic Androgenic Steroid Use

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC651 7163/





How To Access Digital Library

- 1) Go to the website of HEC National Digital Library.
- 2) On Home Page, click on the INSTITUTES.
- 3) A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.
- 4) Select your desired Institute.
- 5) 5. A page will appear showing the resources of the institution

Further Reading





