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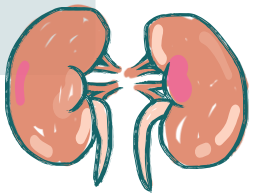
بسم الله الرحمن الرحيم

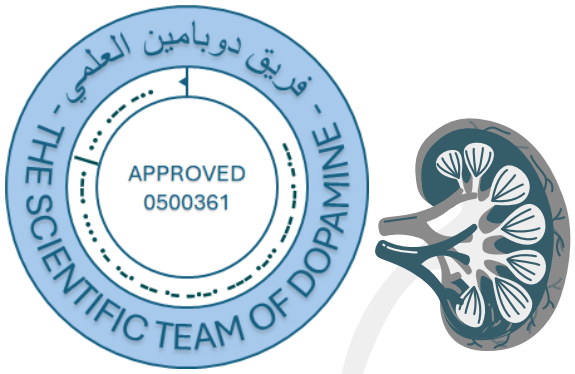
Male Hormones

FINAL | Lecture 11

﴿قُلْ بِفَضْلِ ٱللَّهِ وَبِرَحْمَتِهِۦ فَبِذَٰلِكَ فَلْيَفْرَحُوا۟ هُوَ خَيْرٌ مِّمَّا يَجْمَعُونَ﴾

Written by: Anonymous





"وقيل الحمد لله رب العالمين"...

كتب هذا الموديفايد في اليوم الثامن من شهر ذي الحجة لعام ١٤٤٧ هجرية، وبهذا يكون آخر موديفايد نزولا في مسيرة البيسك...

الحمد لله الذي أتم علينا هذه المرحلة التي مرت كلمح البصر، نسأل الله أن يبارك لنا في ما تعلمناه فيها ويتقبلنا عنده في الصالحين ويبارك لنا في ما بقي...

ملحوظة: إذا بتدرس هذا الموديفايد في يوم عرفة، بنصحك وقف وتكملش، اشتغل بالذكر والدعاء بس للمغرب وأجل الدراسة لبعد المغرب (للعيد) :) وإذا بالعيد، احتسب دراستك لله وأكثر من ذكر الله فأيام العيد أيام ذكر :)

وادعوا لمن كتبه بالفردوس الأعلى والهداية وخيري الدنيا والآخرة...

الله أكبر الله أكبر الله أكبر، لا إله إلا الله...
الله أكبر الله أكبر ولله الحمد...

Male Hormones

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The whole purpose of this lecture, from the physician's perspective, is to understand some of the adverse effects and risks of these steroids in male and female athletes in order to promote awareness.

Male Hormones

Spermatogenesis requires FSH and testosterone.

- **FSH controls gametogenesis, which also requires high local testosterone concentration.**
- **LH stimulates production of testosterone by interstitial or Leydig cells found in the spaces between the seminiferous tubules.**
- **Sertoli cells also secrete inhibin and activin.**
- **Activin stimulates pituitary FSH release,** stimulating spermatogenesis.
- **Inhibin, in conjunction with testosterone and dihydrotestesterone, inhibits FSH secretion,** inhibiting spermatogenesis.

Androgens and Anabolic Steroids

Testosterone and dihydrotestosterone (which is a metabolite of testosterone and more potent):

- **65% of circulating testosterone is bound to SHBG** (Sex hormone-binding globulin), **and most of the rest is bound to albumin** (33%). **(~ 2% free).**
- **SHBG is increased in plasma by estrogen, and thyroid hormone, and in patients with cirrhosis of the liver.**

- **It is decreased by androgen and growth hormone and is lower in obese individuals,** this means that there is a greater free hormone fraction in obese individuals because SHBG levels are decreased.

Androgens and Anabolic Steroids

- **In target tissues, testosterone is converted to dihydrotestosterone (DHT) by 5α-reductase.**
- **Both are responsible for the changes that occur in puberty.**
- **DHT in peripheral tissues is the major active androgen,** not in the testes.
- **Testosterone is metabolized by reduction and the metabolites are excreted in urine as conjugates.**
- Metabolites of male and female sex steroids are excreted in the bile as conjugated compounds.

الله أكبر كبيرا والحمد لله كثيرا
وسبحان الله بكرا وأصيلا...

Androgens and Anabolic Steroids

- **Androstenedione, dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) are also produced in significant amounts in humans largely in the adrenal gland.**
- **They contribute slightly to the normal maturation process.**
- **They improve the sense of well-being and inhibit atherosclerosis** in males.
- In males, low androgen levels accelerate atherosclerosis and osteoporosis.

Androgens and Anabolic Steroids

- **DHEA may be of benefit in patients with SLE. It has an immunomodulatory effect and reduces circulating inflammatory 'drivers' such as interleukin-6 and upregulates interleukin-2**

Physiologic Effects:

- **They are responsible for the secondary sex characteristics and other changes that occur during puberty in males.**

سبحان الله وبحمده سبحان الله العظيم

Androgens and Anabolic Steroids

Metabolic effects:

1. **Reduction of sex hormone-binding proteins,** thus, their free fraction increases.
2. **Increased liver synthesis of clotting factors, triglyceride lipase, α_1-antitrypsin, haptoglobin, and sialic acid,** in cases of androgen excess.
3. **Increased renal erythropoietin secretion.** They can be used in the treatment of aplastic anemia by increasing erythropoietin, which stimulates red blood cell production. However, their efficacy is not absolute, as aplastic anemia is difficult to treat and therapeutic response rates are low.
4. **Reduction of HDL levels,** thus, males are more susceptible to ischemic heart diseases at an earlier age.

Androgens and Anabolic Steroids

- Testosterone has low oral bioavailability (~ 15%) and is administered parenterally.
- Testosterone derivatives alkylated at the 17 position (methyltestosterone and fluoxymesterone) are active after oral administration.

اللهم صل على محمد وعلى آله وصحبه أجمعين

Synthetic Androgenic and Anabolic Steroids

Oxymetholone, oxandrolone, nandrolone decanoate.

TABLE 40–5 **Androgens: Preparations available and relative androgenic:anabolic activity in animals.**

Drug	Androgenic Anabolic Activity
Testosterone	1:1
Testosterone cypionate	1:1
Testosterone enanthate	1:1
Methyltestosterone	1:1
Fluoxymesterone	1:2
Oxymetholone	1:3
Oxandrolone	1:3–1:13
Nandrolone decanoate	1:2.5–1:4

The ratio of androgenic effect to anabolic effect of the compound is important, as some of these steroids are used by athletes to increase muscle mass through their anabolic effects.

Doctor's statement: "It is dangerous; do not use them, as they may cause infertility!!!".

Androgens and Anabolic Steroids

Anabolic steroid and androgen abuse in sports:

- **Usually used at 10-200 times larger than normal production** (Either in quantity or activity; their potency may be 10–200 times greater than that of testosterone. Therefore, physicians advise against their use).
- **The adverse effects of these drugs make their use inadvisable.**

Androgens and Anabolic Steroids

Actions of anabolic steroids:

1. **Increased muscle mass and in strength and increased training intensity** in both sexes.
2. **Growth and mineralization of bone**
3. **Improved competitive performance due to increased strength and aggressiveness. This has been seen only in women.**

Androgens and Anabolic Steroids

Anabolic steroids misuse:

- **Misusers include athletes and body builders.**

Long-term Adverse effects:

1. **Cardiovascular complications**
2. **Liver disease**
3. **Reproductive organs toxicity**
4. **Severe mood swings**
5. **Aggressiveness**

لا إله إلا الله وحده لا شريك له، له الملك
وله الحمد وهو على كل شيء قدير...

Androgens and Anabolic Steroids

Therapeutic Uses:

1. **Androgen replacement therapy in hypogonadal men. Can be used orally, sublingually, IM, TD, and topical gel.**

- **In the presence of pituitary deficiency, androgens are used rather than gonadotropins except when normal spermatogenesis is to be achieved.**

Hypogonadal men who wish to preserve spermatogenesis should be treated with gonadotropins. Therefore, infertility treatment in hypogonadal men involves FSH and LH rather than androgens administration.

Androgens and Anabolic Steroids

2. **In conjunction with dietary measures** (high protein intake and adequate vitamins and minerals) **and exercise to reverse protein loss after trauma, surgery, prolonged immobilization and in patients with debilitating diseases.**
3. **Refractory anemias such as aplastic anemia and others** (Before erythropoietin became available as a pharmaceutical agent). **Recombinant erythropoietin has largely replaced androgens for this purpose.**

This topic is beyond the scope of the lecture; however, it was briefly discussed by the doctor...

- Low muscle mass and assessment of kidney function: a normal plasma creatinine level in debilitated patients with extremely low muscle mass does not necessarily indicate normal renal function, because creatinine production from muscle is reduced. Therefore, assessment of kidney function in such cases requires calculation of creatinine clearance.
- This controversial concept applies to other aspects of medicine. For example, elevated liver enzymes in the blood usually indicate liver injury, but after some time they may normalize or even decrease below normal levels. This may be misinterpreted as recovery and the patient may be discharged, whereas the actual situation may be severe hepatic cell loss leading to death several days later.

Androgens and Anabolic Steroids

أستغفر الله العظيم وأتوب إليه

Adverse effects:

1. **Masculinizing actions in women: hirsutism, acne, amenorrhea, clitoral enlargement and deepening of voice.**
2. **Some exert progestational activity → withdrawal endometrial bleeding.**
3. **They also increase susceptibility to atherosclerosis in women,** especially athletes.
4. **Sodium retention and edema are not common,** however, this can occur because all steroids may produce this adverse effect.

Androgens and Anabolic Steroids

5. Masculinization or undermasculinization of the external genitalia of the female and male fetuses, respectively, if given during pregnancy.
6. Administration of androgens in early life may have profound effects on maturation of central nervous system centers governing sexual development, particularly in the female.

There are animal studies in which pregnant female animals are administered these compounds and maturation of the offspring is observed.

Note: Such studies are unethical and illegal in humans.

Androgens and Anabolic Steroids

7. **Hepatic dysfunction (17-alkyl-substituted steroids): Cholestatic jaundice, and hepatomas and carcinomas.**
8. **Prostatic hyperplasia.**
9. **Increased LDL and lower HDL,** making the lipid profile more atherogenic.

سبحان الله والحمد لله ولا إله إلا الله والله أكبر

Androgens and Anabolic Steroids

10. **Acne, sleep apnea, erythrocytosis, gynecomastia and azoospermia and decrease in testicular size** (We are discussing synthetic androgens rather than testosterone; therefore, they may possess some estrogenic properties). **May take months to recover after cessation of therapy.**
11. **Psychologic dependence** (addiction)**, increased aggressiveness and psychosis.**
12. **Hepatocellular carcinoma.**

سبحان الله وبحمده عدد خلقه ورضا
نفسه وزنة عرشه ومداد كلماته...

Androgens and Anabolic Steroids

Contraindications and Cautions:

1. **Pregnant women.** (Even in female athletes who use these steroids and have a low probability of pregnancy, conception may still occur, and these steroids can produce catastrophic fetal effects).
2. **Male patients with carcinoma of the prostate and breast.**
3. **Infants and young children: special caution is required in giving them to produce a growth spurt** (In short individuals) **(somatotropin is more appropriate).**
4. **Patients with renal or cardiac disease predisposed to edema.**

Antiandrogens

A. 5α-reductase inhibitors:

Since dihydrotestosterone is more potent than testosterone, inhibition of the enzyme responsible for its production (5α-reductase) is beneficial in prostatic hyperplasia.

Finasteride:

- **Is an orally active steroid-like drug.**
- **Decreases dihydrotestosterone levels that begins within 8 hours after administration and lasts for about 24 hours,** thus, a single dose produces suppression for an interval of at least 16 hours.
- **Moderately effective in reducing prostate size in men with benign prostatic hyperplasia**, but Does not apply to prostate cancer.
- **Used for treatment of hirsutism in women and early male pattern baldness in men.**

Further explaination for hirsutism...

- When excessive testosterone is produced by the ovaries in females and converted into dihydrotestosterone, which is more potent, hirsutism may occur. This can be treated with finasteride, which lowers dihydrotestosterone levels, although it may produce significant adverse effects.

يا رب لك الحمد كما ينبغي لجلال وجهك وعظيم سلطانك...

Antiandrogens

Dutasteride:

- **It is a similar orally active steroid derivative with a slow onset of action and a much longer half-life than finasteride.**
- **It is mainly approved for use in for benign prostatic hyperplasia** more than finasteride.

The most important agents in the antiandrogens are the reductase inhibitors, such as finasteride and dutasteride, because they are used in prostatic hyperplasia.

Antiandrogens

Note: These conditions are uncommon or have alternative therapeutic options; therefore, the use of these drugs is limited and their cost is high.

B. Receptor blockers:

1. Cyproterone and cyproterone acetate:

- **Are effective antiandrogens that inhibit the action of androgens at the target organ.**
- **The acetate form** (more effective) **has a marked progestational effect that suppresses the feedback enhancement of LH and FSH, leading to a more effective antiandrogen effect**. (When the receptor is blocked, the body interprets this as testosterone deficiency, resulting in feedback stimulation rather than inhibition).
- **Used to treat hirsutism in women concurrently with an estrogen.** (All drugs used for the treatment of hirsutism in females are administered with estrogen).
- **Used in men to decrease excessive sexual drive.**

Antiandrogens

اللهم اغفر للمؤمنين والمؤمنات والمسلمين
والمسلمات الأحياء منهم والأموات...

2. Flutamide:

- **Nonsteroid antagonist at androgen receptors**
- **Potent antiandrogen.**
- **Used for treatment of prostatic carcinoma.**
- **Causes mild gynecomastia probably by increasing testicular estrogen production.** (The adrenal gland can also produce estrogens and androgens).
- **Occasionally cause mild reversible hepatic toxicity.**
- **Also useful in the management of excess androgen effect in women** such as in hirsutism.

Antiandrogens

3. Bicalutamide, Enzalutamide and Nilutamide:

- **Potent and orally active antiandrogens.**
- **Used in patients with metastatic carcinoma of the prostate.**
- **Bicalutamide is recommended for use in combination with a GnRH analog to reduce tumor flare.**

For these drugs to be effective, cancer cells must be susceptible to the inhibition. However, the effect is limited because cancer cells are not completely responsive to this inhibition; therefore, the therapeutic effect is mainly palliative.

Antiandrogens

اللهم أنت ربي لا إله إلا أنت خلقتني وأنا عبدك وأنا على عهدك ووعدك ما استطعت، أعوذ بك من شر ما صعنت، أبوء لك بنعمتك علي وأبوء بذنبي فاغفر لي فإنه لا يغفر الذنوب إلا أنت...

4. Spironolactone:

- **Aldosterone receptor antagonist.**
- **Also blocks androgen receptors.**
- **Reduces 17α-hydroxylase activity → reduced plasma testosterone and androstenedione levels.**
- **Used in treatment of hirsutism in women.**
- Cause gynecomastia in men.

PHARMACOLOGY QUIZ LECTURE 11

رسالة من الفريق العلمي

"و صادف هذا الدعاء:

1. خشوعًا في القلب،
2. و انكسارًا بين يدي الرَّب،
3. وذُلًّا له،
4. وتضرعًا،
5. و رِقَّةً،
6. و استقبل الداعي القبلة،
7. و كانَ علىٰ طهارة،
8. ورفعَ يديه إلى الله تَعَالىٰ،
9. وبدأ بحمد اللهِ والثناء عليهِ،
10. ثمَّ ثنى بالصَّلاة على مُحمَّد عبده صلى الله عليه وسلم،
11. ثمَّ قدَّم بين يدي حاجته التّوبة والاستغفار،
12. ثمَّ دخلَ على الله،
13. و ألحَّ عليه في المسألة،
14. وتملقَه،
15. ودعاه رغبةً ورهبةً،
16. وتوسل إليه بأسمائه وصفاته وتوحيده،
17. وقدّم بين يدي دعائه صدقةً،

= فإنَّ هذا الدُّعاء لا يكادُ يُرَدُّ أبدًا".

ابن قيّم الجوزية -رحمه الله-.

External Resources

اللهم إن عمر عطية في ذمتك وحبل جوارك، فقِه من فتنة القبر وعذاب النار، أنت أهل الوفاء والحق، فاغفر له وارحمه إنك أنت الغفور الرحيم.

اللهم فرج عن أهلنا المستضعفين في السودان وغزة والإيغور وفي كل مكان وأنزل عليهم شابيب رحمتك وأطعمهم من جوع وآمنهم من خوف، وانتقم اللهم من عدوهم ومن مكن لهم، وارفع عنا إثم الخذلان وأعنا على نصرتهم.

اللهم أهلنا من الأسرى والمعتقلين والمظلومين في كل مكان، كن لهم عونا ونصيرا ومؤيدا وظهيرا، اللهم فرج عنهم وهون عليهم واكفهم شر عدوهم واحرسهم بعينك التي لا تنام، وأعنا اللهم على فكاكهم وأداء حقهم واغفر لنا تقصيرنا معهم.
أخلصوا دراستكم لله لعلها تكون من أقل القليل الذي يقدمه الواحد منا تجاه

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