

# Endocrine Block

"إن الله لا يُعطي  
أصعب المعارك، إلا  
لأقوى جنوده"

■ Text
■ Only in Females' slide
■ Only in Males' slides
■ Important
■ Numbers
■ Doctor notes
■ Extra Notes

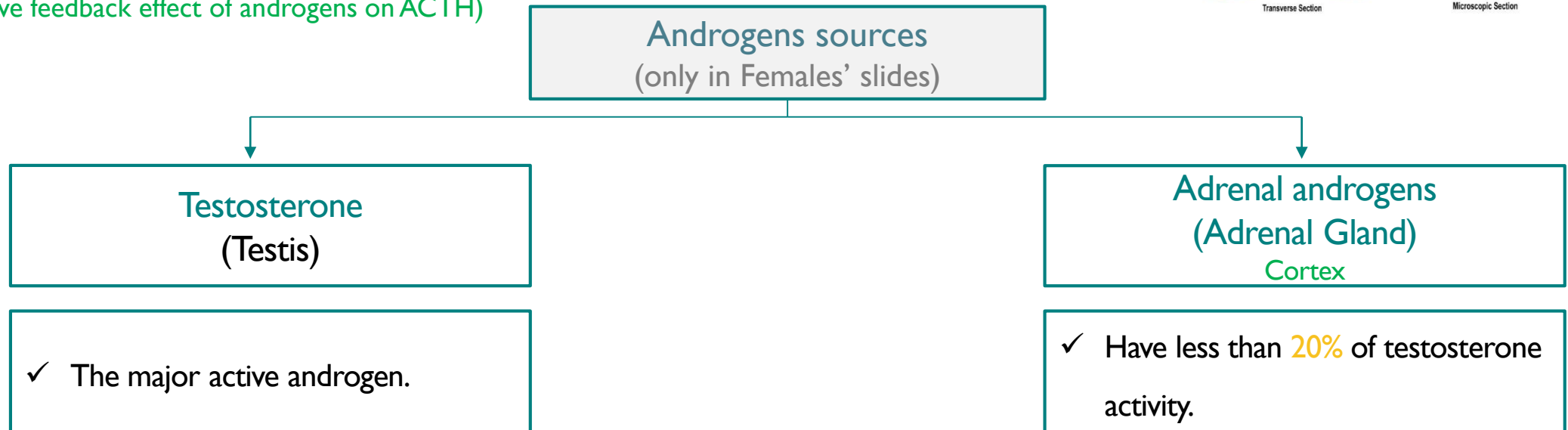
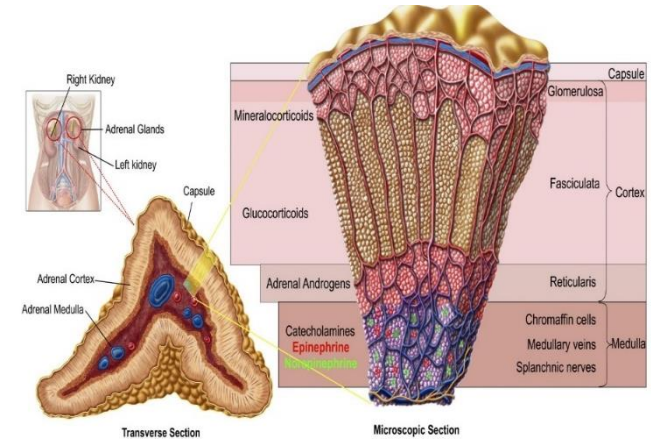
# Adrenal gland hormones (Androgens)

By the end of this lecture, students should be able to describe:

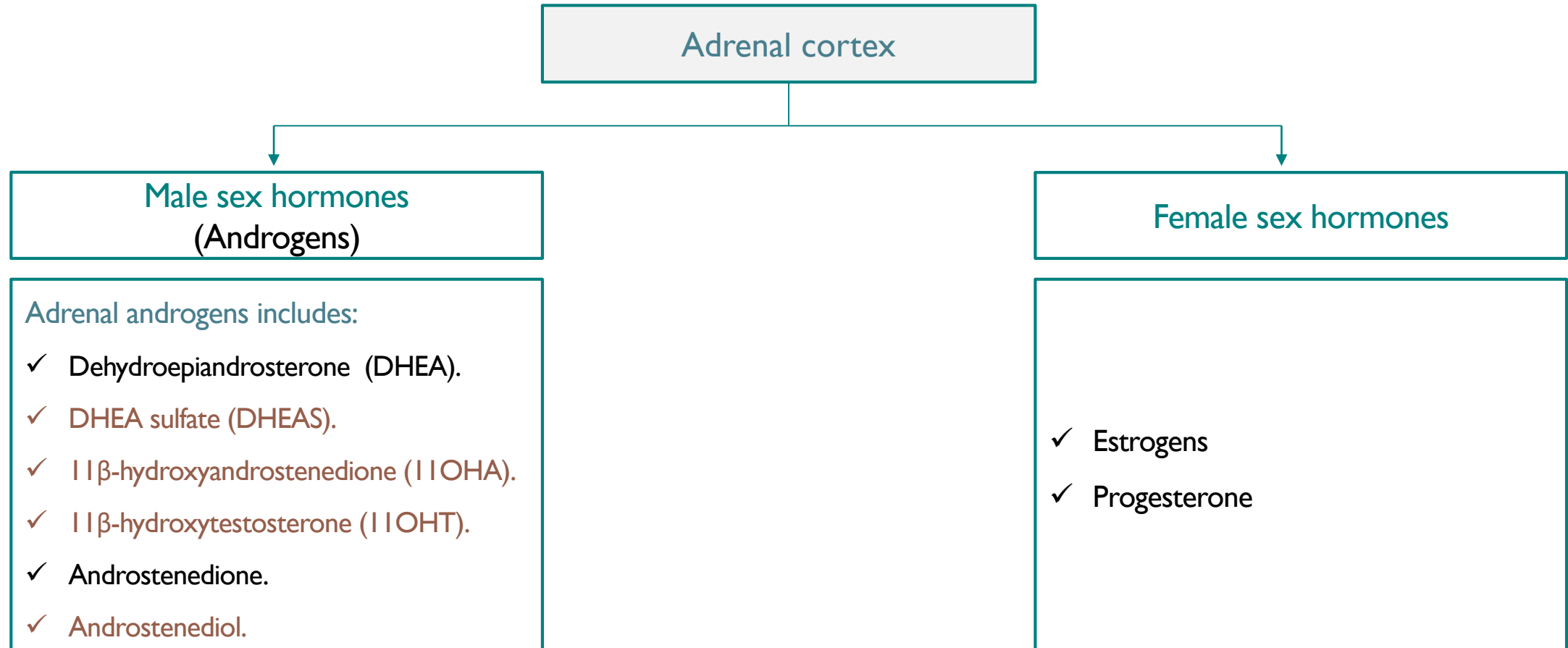
- I. Summarize the actions of adrenal androgens.

# Overview Of Androgens

- ▶ **Definition:** Androgens are the hormones that exert masculinizing ذكورية effects and they promote anabolism and growth.
- ▶ **Synthesis:** The reticularis produces significant amounts of **androgens**, mostly dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS).
- ▶ **Target cells:** General body cells
- ▶ **Hormone control:** Control of secretion of adrenal androgens is by ACTH from the pituitary (There is no negative feedback effect of androgens on ACTH)



# Adrenal Cortex



Estrogen for males is important for Ca homeostasis, deposition of fat and making wise decisions.

# Cont.

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- ▶ The adrenal cortex in both sexes produces small amounts of sex hormone of the opposite sex. **Additional small amounts of sex hormones come from nonadrenal sources.**
- ▶ Some testosterone in males is **converted into estrogen by the enzyme aromatase** found in adipose tissues.
- ▶ In females, ovaries produce androgen as an intermediate step in estrogen production. Little of this androgen is released in the blood instead of being converted into estrogen (**Testosterone in males is linked to aggressive behavior and selfishness**)

# Adrenal Androgens

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- ▶ **Definition:** Adrenal androgens have little androgenic activity, but they provide a pool of circulating precursor for peripheral conversion to more potent androgens (e.g. testosterone) and estrogens (e.g. estradiol).
- ▶ **Synthesis:** Produced from Zona reticularis in small amounts (Adrenal Androgens not androgen) Its secretion is controlled by ACTH.
- ▶ **Adrenarche:** the onset of adrenal androgens in humans is a gradual process that precedes the onset of puberty (6-7 years of age in girls and 7-8 years of age in boys).

Adrenarche: means the 1<sup>st</sup> sign of puberty 1<sup>st</sup> trace of androgens.  
Menarche: means the 1<sup>st</sup> period in females.
- ▶ **Binding:** (only in Males' slides)
- ✓ About 90% of adrenal androgens are bound to albumin, while 3% approximately is bound to sex hormone-binding globulin (SHBG).
- ✓ DHEAS has high affinity to albumin with half-life 7-10 hours, while DHEA has low affinity with half-life 15-30 minutes.
- ✓ DHEA, DHEAS, and Androstenedione are converted to the potent androgens Testosterone and Dihydrotestosterone (DHT) in peripheral tissues (Mostly in adipose tissue, hair follicles and prostate).

# Dehydroepiandrosterone (DHEA) & Androstenedione

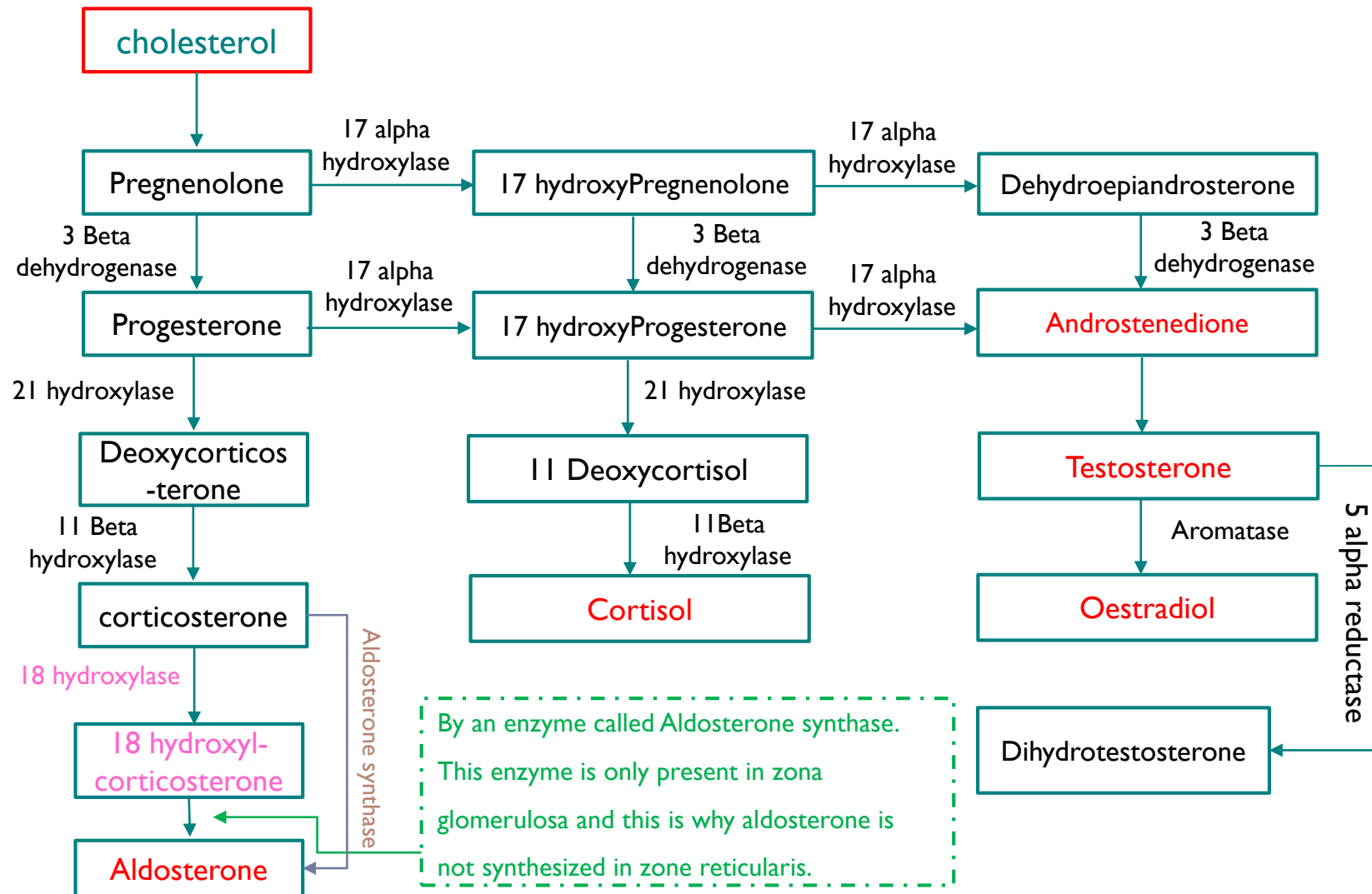
## ▶ Dehydroepiandrosterone (DHEA):

- ✓ It is the most abundant adrenal androgen with DHEAS.
- ✓ **DHEA is the primary precursor of natural estrogens.**
- ✓ Normally they exert very little masculinizing ذكوري effect (weak) when secreted in normal amount (mild effect in female).

## ▶ Androstenedione:

- ✓ An androgenic steroid produced by the testes, adrenal cortex, and ovaries.
- ✓ Androstenediones are converted metabolically to testosterone and to estrogens in the fat and other peripheral tissues. It is an important source of estrogen in men and postmenopausal women.
- ✓ Androstenedione were used as an athletic or body building supplement.

# Steroid synthesis (steroidogenesis)



If there was a deficiency in the enzyme 21-hydroxylase which is responsible for the conversion of progesterone to deoxycorticosterone and 17-hydroxyprogesterone to 11-deoxycortisol there will be a deficiency in aldosterone + cortisol and shift to the pathway for production of androgens (this will lead to excessive amounts of androgens) its usually a congenital defect in the enzyme (Adrenogenital syndrome) and also can be a differential diagnosis for female patients with hirsutism.

Not all androgens will be converted to testosterone. Some of them will be released in the circulation as: Androstenediol & Androstenedion. They are weaker than Testosterone but have androgenic effect.

By an enzyme called Aldosterone synthase. This enzyme is only present in zona glomerulosa and this is why aldosterone is not synthesized in zone reticularis.



# Role Of Androgen (Effects)

The androgens function as paracrine hormones

Only in Females' Slides

## ▶ In males':

1. Spermatogenesis (it acts on Sertoli cells).
2. Inhibition of fat deposition.
3. Muscle mass زيادة بناء العضلات
4. **Brain:** Androgen levels have been implicated in the regulation of human aggression and libido.
5. Masculinization of the developing male fetus (including penis and scrotum formation).

## ▶ In females':

1. **Growth of pubic and axillary hair.**
2. Pubertal growth spurt. يساعد في البلوغ
3. **Androgen have potential roles in relaxation of myometrium** عضلات الرحم **preventing premature uterine contractions in pregnancy.**
4. **Development and maintenance of female sex drive (libido).**

✓ Androgen from the adrenal gland in males is NOT important because it is secreted from testes.

✓ But in females it is important.

# Adrenogenital Syndrome

▶ Definition: Excessive adrenal androgens secretion.

▶ Causes:

1. Adrenocortical tumors.

Adrenocortical tumor secretes excessive quantities of androgens that cause intense masculinizing effects throughout the body.

2. Congenital adrenal hyperplasia.

✓ It is a familial disorder of adrenal steroid biosynthesis, inherited as autosomal recessive diseases.

✓ Affect both boys and girls.

✓ The defect is expressed as adrenal enzyme deficiency.

▶ Most important enzyme deficiencies:

1. 21  $\alpha$ -Hydroxylase (>80% of cases) → enzymes of the cortisol synthesis → Result in deficiency in both Aldosterone and cortisone.

2. 11  $\beta$ -Hydroxylase (5-10% of cases) → There will be deficiency in Cortisone but there will be excessive mineralocorticoid action (signs of Aldosteronemia)

3. 17  $\alpha$ -Hydroxylase.

✓ The enzyme deficiency causes reduction in end-products, accumulation of hormone precursors & increased ACTH production.

▶ The clinical picture reflects the effects of:

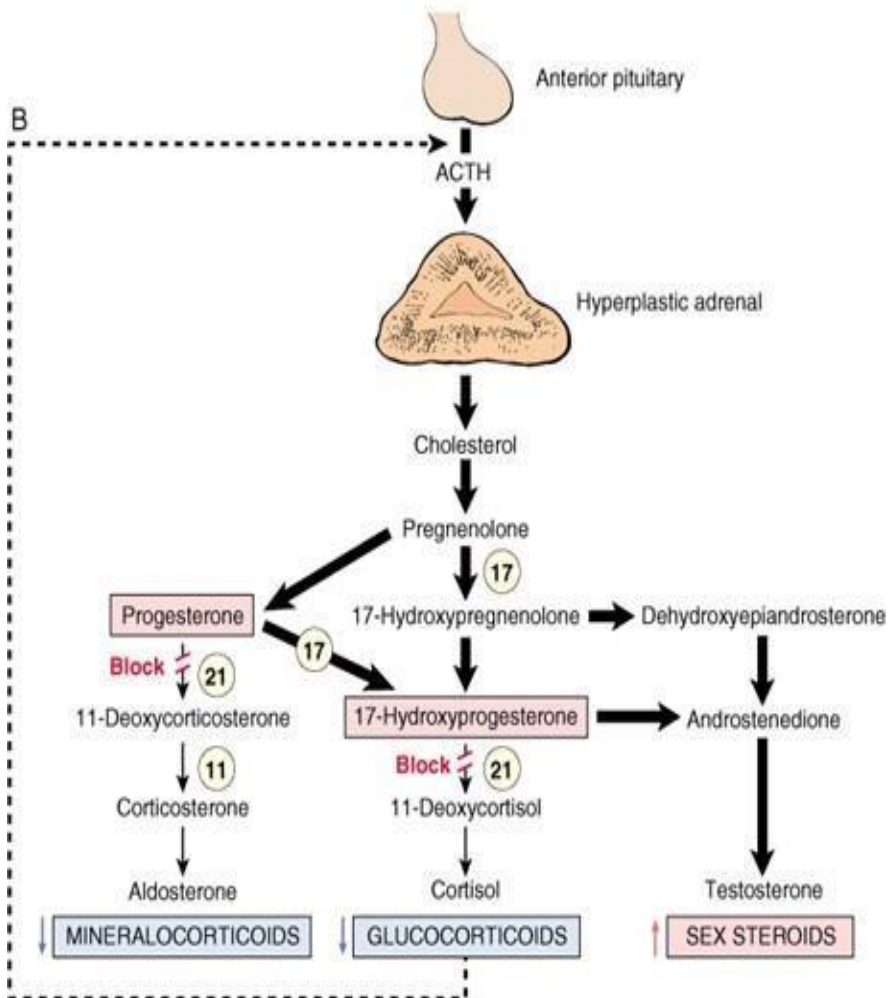
1. Inadequate production of cortisol & aldosterone.

2. The increased production of androgens & steroid metabolites.

▶ Treatment:

Glucocorticoids.

# The 21 $\alpha$ -Hydroxylase Enzyme Pathway



الزبدة:

فيه إنزيم اسمه **21  $\alpha$ -Hydroxylase**

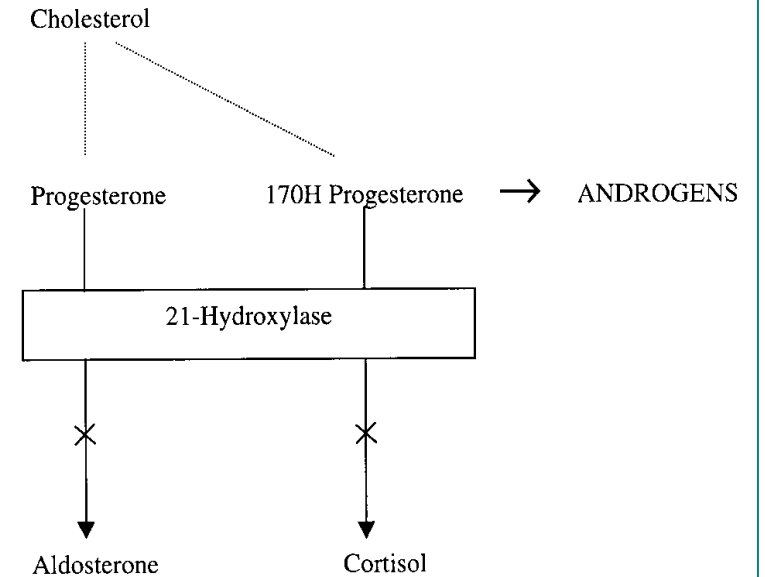
هذا الإنزيم الألدسترون والكورتيزول ما يتصنعون بدونه، بالتالي يتأثرون بأي تغيرات بالإنزيم.

بينما الأندروجين ما يحتاج هذا الإنزيم عشان يتصنع، بالتالي ما يتأثر.

طيب احنا نعرف أن كل هذه الثلاثة هرمونات مصدرها الكوليسترول، فإذا تأثر الإنزيم وما تصنع

عندي الـدسترون وكورتيزول وين راح يروح الكوليسترول؟

كل الكوليسترول راح يتحول إلى اندروجين لأنه الوحيد اللي ما يتأثر بالإنزيم وبالتالي بيصير عندي فائض وزيادة اندروجين.



Patients with of 21-hydroxylase deficiency will have low aldosterone and cortisol and high levels of androgens.

# Sign & symptoms (In Females')

نقصد هنا الأعراض على النساء، مو فقط سلايدات البنات

## Sign & symptoms (In Females')

### Before Birth (only in females' slides)

- ✓ Pseudohermaphroditism خشونة كاذبة
- ✓ XX true female with external male genitalia.
- ✓ Cause: exposure of the mother to excessive androgens, before 12 weeks in female fetus.

### After Birth

- ✓ Virilization الترجل
- ✓ Development of male characters in females.
- ✓ Increase bulk of muscles.
- ✓ Hoarseness بحة الصوت
- ✓ Masculine distribution of body hair & facial hair.
- ✓ Atrophy of the breast.
- ✓ Amenorrhea (is the absence of a menstrual period in a woman of reproductive age).
- ✓ Growth of a beard نمو اللحية
- ✓ A much deeper voice.
- ✓ Occasionally baldness الصلع
- ✓ Growth of the clitoris to resemble a penis.



# Sign & symptoms (In Males')

نقصد هنا الأعراض على الرجال، مو فقط سلايدات الأولاد

## Sign & symptoms (In Males')

### In prepubertal (After birth) male

- ✓ The same characteristics as in the female plus rapid development of the male sexual organ.
- ✓ Precocious puberty بلوغ مبكر
- ✓ Early appearance of male characters.
- ✓ Increase musculature.
- ✓ Development of external genitalia organ to adult size.
- ✓ No spermatogenesis هذي الخاصية اللي تفرق بين هالمرحلة ومرحلة الشباب
- ✓ Increased growth but shorter stature because of early closure of epiphyseal plates.

### In the adult male (only in females' slides)

- ✓ The virilizing characteristics of adrenogenital syndrome are usually obscured by the normal virilizing characteristics of the testosterone secreted by the testes, that's why it is often difficult to make a diagnosis.
- ✓ However, the excretion of 17-ketosteroids (derived from androgens) in urine may be 10 to 15 times more than normal, used in diagnosing the disease.

المقصد من الكلام: صعب نفرق بين الصفات الذكورية الناتجة عن إفراز التيستوستيرون من الخصيتين مثل الرجل الطبيعي وبين الناتجة عن زيادة وفرط إفراز الاندروجين من الادرينال كما في الشخص الغيرطبيعي. فالشيء اللي يساعدنا نفرق ويساعدنا بالتشخيص وجود الـ 17-ketosteroids في Urinell بكمية أكثر من الطبيعي توصل الى 10-15 ضعف الطبيعي!

# Thank you for checking our work!



اعمل لترسم بسمة، اعمل لتمسح دمة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

قادة الفريق:

ليلى مذكور & محمد نصر

خالص الشكر لأعضاء الفريق الكرام:

قيس المهيدب

غادة السكيت

نواف الخضيرى

جومانا القحطاني



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