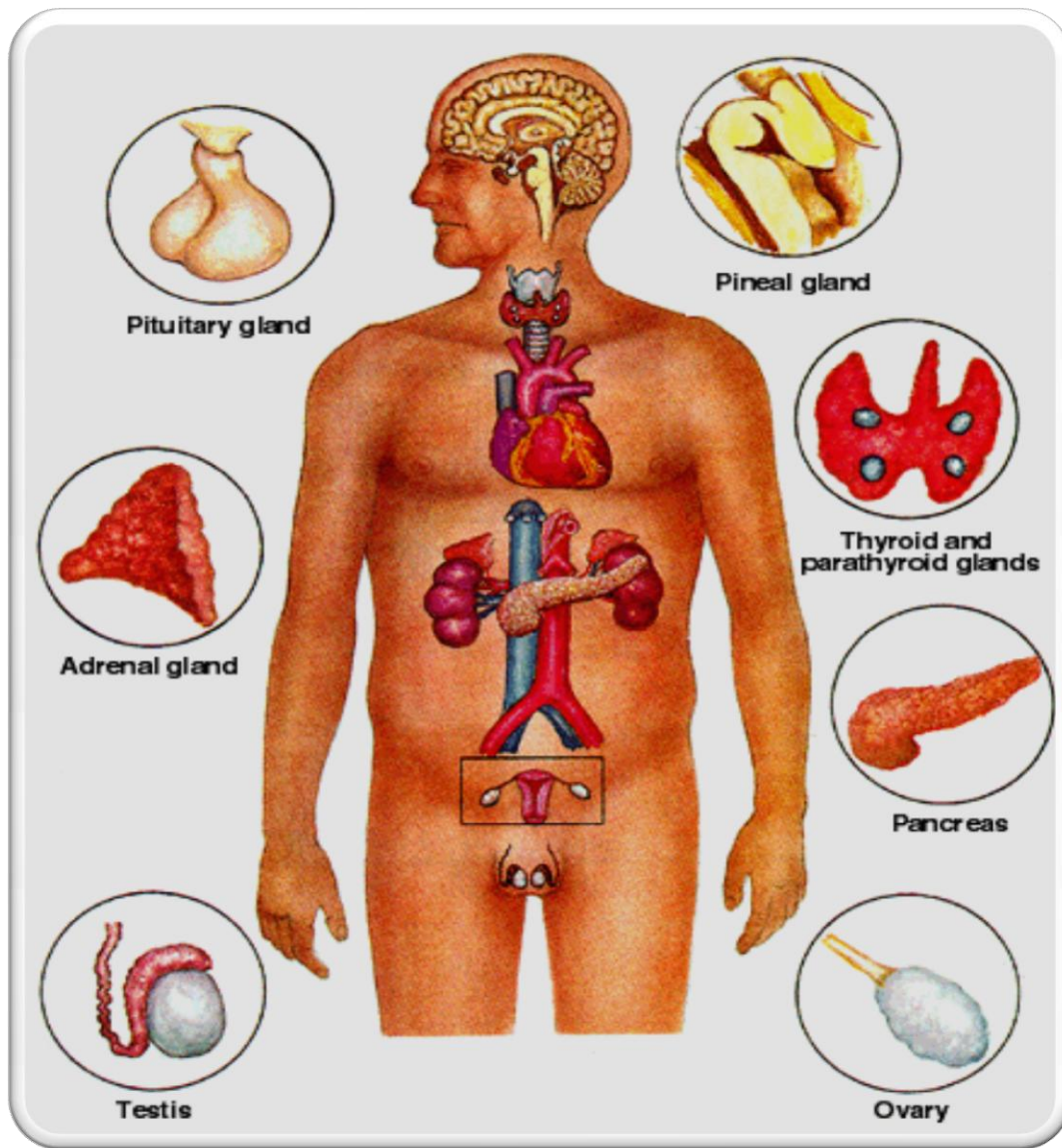


ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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Before going to this let's have a quick revision,

Each adrenal is composed of two endocrine organs, one surrounding the other. The outer layers composing the **adrenal cortex** secrete a variety of **steroids** hormones; the inner portion the **adrenal medulla**, secrete **catecholamines**.

Now let's focus on the cortex,

The adrenal cortex produces a number of different **adrenocortical hormones**, all of which are **steroids derived from the common precursor molecule, cholesterol**.

On the basis of their primary actions, the **adrenal steroids can be divided into three categories**:

1. **Mineralocorticoids**, mainly **aldosterone**, influence mineral (electrolyte) balance, specifically Na^+ and K^+ balance.
2. **Glucocorticoids**, primarily **cortisol**, play a major role in glucose metabolism as well as in protein and lipid metabolism and in adaptation to stress.
3. **Sex hormones** are identical or similar to those produced by gonads (testes in males, ovaries in females). **The most abundant and physiologically important of the adrenocortical sex hormone is dehydroepiandrosterone (DHEA)**, an androgen, or "male" sex hormone.

And that leads us to the topic of our lecture, Adrenal androgens

INFO WAS OBTAINED FROM SHERWOOD'S HUMAN PHYSIOLOGY "FROM CELL TO SYSTEMS", 7E

First, what are androgens?

Androgens are the hormones that exert masculinizing effects (to produce masculine qualities in the sexually maturing male or in the female). They promote anabolism and growth (increase growth reaction specifically for the muscle and bones). **Testosterone from the testis is the major active, androgen. The adrenal androgens have less than 20% of its (testosterone) activity.**

So androgen (male sex hormone) has to 2 sources, Nonadrenal (Testosterone from the testes) and Adrenal (dehydroepiandrosterone and androstenedione), and if we compare their activity (ex.in masculinizing effects) we will find that testosterone exerts about 100 times greater "androgenicity" than DHEA.

What is the site of adrenal androgens production?

Zonal Reticularis (inner most layer of the adrenal cortex): Produces small amounts of androgens, **mostly dehydroepiandrosterone (DHEA)**, DHEA may be converted into estrogens (we will discuss this in the next point) **Hormone Control:** Believed to be **ACTH**. **Target tissue:** General body cells.

What are the 2 component of Adrenal androgens?

A subset of androgens, adrenal androgens, includes:

1. Dehydroepiandrosterone (DHEA),

It is the most abundant adrenal androgen, a steroid hormone produced in the adrenal cortex from cholesterol. It is the primary precursor of natural estrogens.

2. Androstenedione,

An androgenic steroid produced by the testes, ovaries, and adrenal cortex.

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.

You can read the details of this at the end

★ The adrenal cortex in both sexes produces small amounts of sex hormone of the opposite sex. (Meaning in both sexes,) the adrenal cortex produces both androgens i.e. “Male sex hormones” and estrogens or “Female sex hormones”. (How is that possible? Remember when it said “DHEA may be converted into estrogens” that exactly what happens!).

★ Additional small amounts of sex hormones (of the opposite sex) come from Nonadrenal sources. How?

(In males): Some testosterone (from the testes) 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.

(It's correct that Nonadrenal sources (gonads) produce sex hormone of the opposite sex, however that is in small amounts in comparison to the adrenal cortex, especially for menopausal women when their ovaries in the first place have little androgens to produce estrogen, so they rely on the androgens coming from their cortex to make that estrogen).

What are the actions of adrenal androgens?

Effects of adrenal androgens (Normally):

Control androgen-dependent processes in the female as:

- 1- Growth of pubic and axillary hair
- 2- Pubertal growth spurt (During puberty, the rate of growth speeds up. Girls and boys may go through a growth spurt, which lasts about two years. During this time, girls generally grow from 2.5 to 4.5 inches per year, while boys grow 3 to 5 inches a year. The pubertal growth spurt accounts for about 17% of adult male height and 12% of adult female height—and leads to much of the difference in height between adult men and women).
- 3- Development and maintenance of female sex drive

(Why are we focusing on females? cause in males, adrenal androgens play only a minor role because de nova synthesis of testosterone from cholesterol in the testes is much greater than testosterone synthesis from adrenal androgenic precursors. In females, however, adrenal androgens are the major androgens, and they are responsible for the development of pubic and axillary hair and for libido).

Disorders of androgens secretion

- Congenital adrenal hyperplasia (adrenogenital syndrome)

Causes:

The different types of adrenogenital syndrome are inherited as autosomal recessive diseases and can affect both boys and girls. The defect is lack of an enzyme (21-hydroxylase) (genetically induced enzyme deficiency) needed by the adrenal gland to make the major steroid hormones of the adrenal cortex: cortisol and aldosterone (the adrenal cortex doesn't synthesize glucocorticoids and mineralocorticoids). Due to the block in synthesis of these hormones, there is abnormal 'feedback' and steroids are 'diverted' to becoming androgens, a form of male sex hormones. (ACTH levels will be high because of negative feedback on the anterior pituitary by the low cortisol levels, and these high ACTH levels will have a trophic effect on the adrenal cortex and cause adrenocortical hyperplasia).

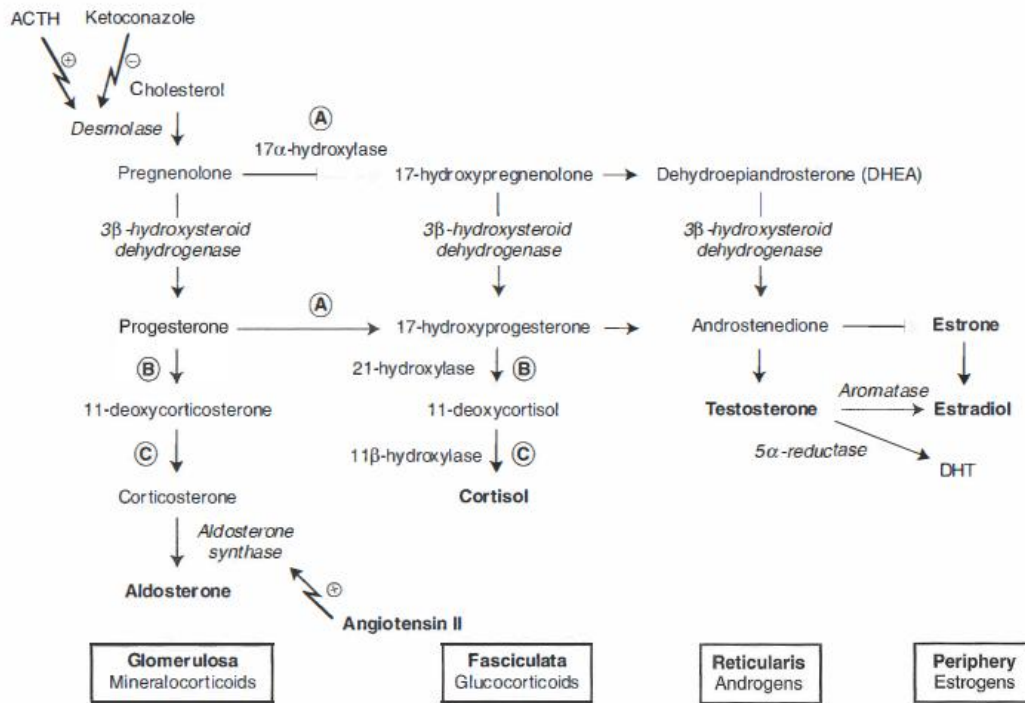
Hyper-secretion: Adrenogenital Syndrome

- 1- In pre-pubertal males, it causes the rapid development of secondary sexual characters.
- 2- In females, causes beard growth, deeper voice, masculine distribution of body hair, and growth of the clitoris to resemble a penis.

Virilizing adrenal hyperplasia in a newborn female baby, DHEA was converted to testosterone. (Virilization means that the clitoris of girls is enlarged, and may resemble the male penis to the point that the sex of the child is questioned or mistaken).



Adrenal steroids

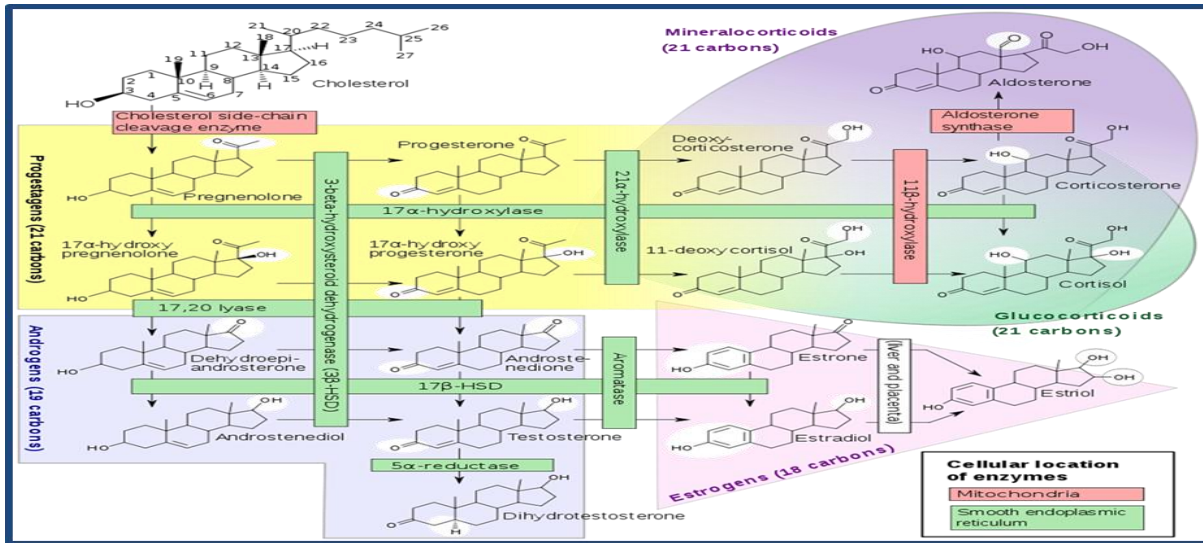


Congenital bilateral adrenal hyperplasias*

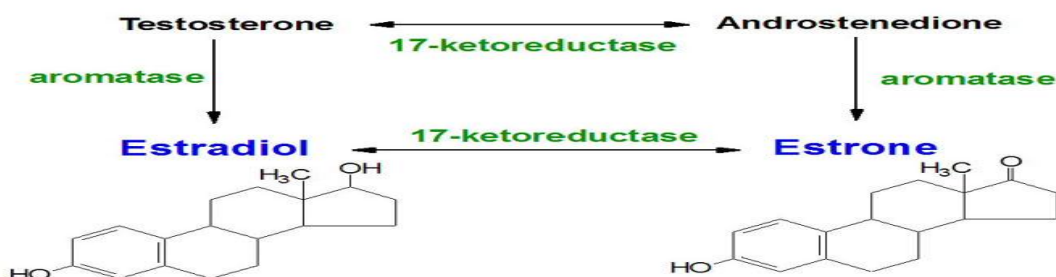
Deficiency	Mineralocorticoids	Cortisol	Sex hormones	Notes
Ⓐ = 17α-hydroxylase deficiency	↑	↓	↓	HYPER tension, hypokalemia. XY: ↓ DHT → pseudohermaphroditism (phenotypic female, no internal reproductive structures due to MIF). XX: externally phenotypic female with normal internal sex organs, lacks 2° sex characteristics.
Ⓑ = 21-hydroxylase deficiency	↓	↓	↑	Most common form. HYPOT ension, hyperkalemia, ↑ renin activity, volume depletion. Masculinization, female pseudohermaphroditism.
Ⓒ = 11β-hydroxylase deficiency	↓ aldosterone ↑ 11-deoxycorticosterone	↓	↑	HYPER tension (11-deoxycorticosterone is a mineralocorticoid and secreted in excess). Masculinization.

*All congenital adrenal enzyme deficiencies are characterized by an enlargement of adrenal glands due to ↑ ACTH stimulation because of ↓ cortisol.

most common







Ok, first of all you have to remember that using cholesterol to produce sex hormones is not only confined to the adrenal cortex, but the gonads use a similar pathway to do so. These organs have a common step which is the conversion of DHEA to Androstenedione; the difference comes in what they do to Androstenedione. The adrenal gland secretes Androstenedione into the circulation then peripheral tissues (as the adipose tissue and even the gonads) convert it to either testosterone or estrogen. Conversion of androstenedione to testosterone requires the enzyme 17β -hydroxysteroid dehydrogenase, whereas conversion of androstenedione to estrogen (estrone) requires the enzyme aromatase. Remember that these 2 enzymes are not found in the adrenal cortex. **So now we have understood how the adrenal cortex in both sexes produces small amounts of sex hormone of the opposite sex. Now what about the statement that additional small amounts of sex hormones of the opposite sex come from Nonadrenal sources?!** That's easy, in males the main sex hormone is testosterone that dominantly comes from the testes, and some of that testosterone can also be converted to estrogen (Estradiol) in adipose tissue by the enzyme aromatase. Ok what about females? As we said that Androstenedione is also produced by the ovaries; the common step. Some of that Androstenedione is released in the blood and instead of being converted into estrogen; it gets converted to testosterone (mainly in premenopausal women)



Note that: 17β -Hydroxysteroid dehydrogenase (17β -HSD), also known as 17-ketosteroid reductase (17-KSR)

summery

- Adrenal androgen as a steroid hormone with a Keaton group attached to C-17 (testosterone has a hydroxyl group attached to the same carbon) , secreted mainly from zona retuclaris in the adrenal cortex .
- subsets of adrenal androgen include **DHEA** (most abundant) and **Androstenedione** .
- Adrenal androgen plays a **minor role** in males (because de novo synthesis of testosterone is much greater than its synthesis from androgens precursors) . **however** in females it's very important for pubic development , axillary hair and for libido in famales .
- commonly the defect in congenital adrenal hyperplasia is in **21-hydroxylase** (which is essential for gluco and mineralocorticoids synthesis  loss of -ve feedback  more ACTH  high level of androgen  rapid development of 2ndry sexual characters in **males** and beard growth , deeper voice, masculine distribution of body hair and growth of the clitoris to resemble a penis in **famales** .

Questions

1- adrenal androgen is stimulated by :

- A. CRH
- B. ACTH
- C. Renin-Angiotensin system
- D. Neural stimulus

2- The greatest androgen secretory activity occurs at :

- A. Evening
- B. Early morning
- C. After noon
- D. Midnight

3- which enzyme is commonly defected in congenital adrenal hyperplasia :

- A. 11-hydroxylase
- B. 17-hydroxylase
- C. 21-hydroxylase
- D. 27-hydroxylase

4- which of the following is the most abundant adrenal androgen :

- A. DHEA .
- B. Testosterone .
- C. Androstenedione .
- D. Androstenediole

answers : 1-B . 2-B . 3-C . 4-A