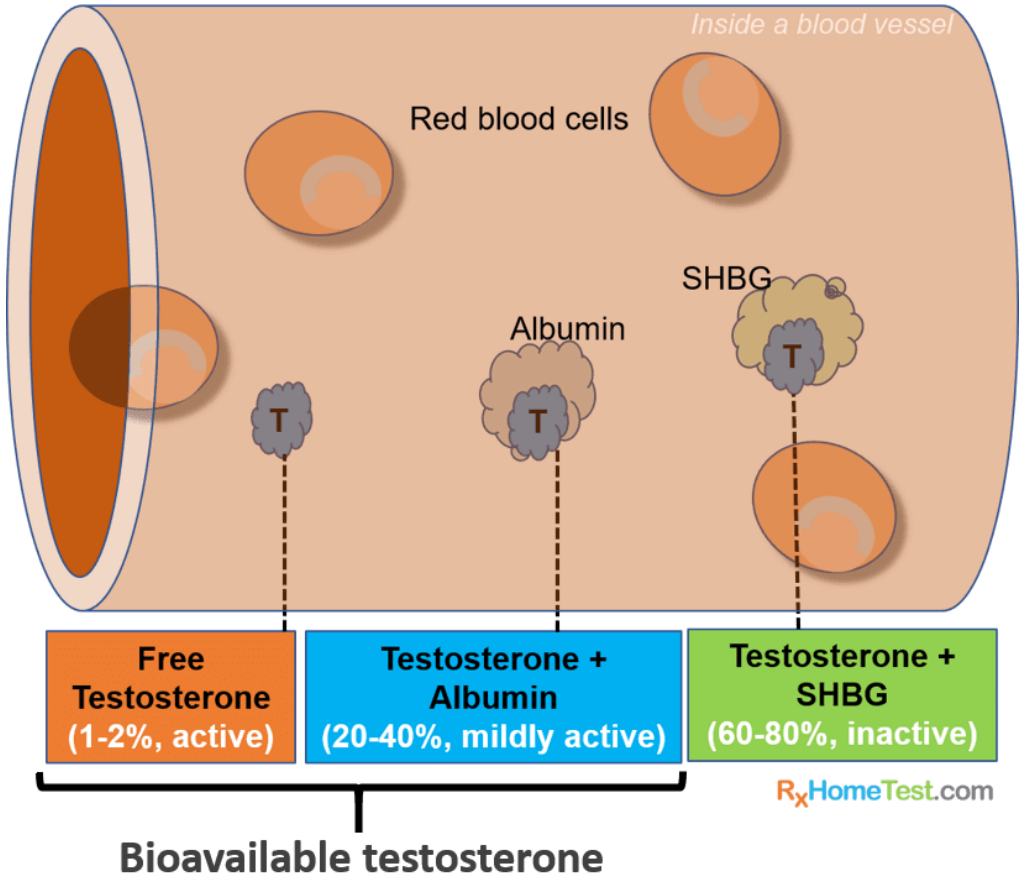
Reproductive Disorders

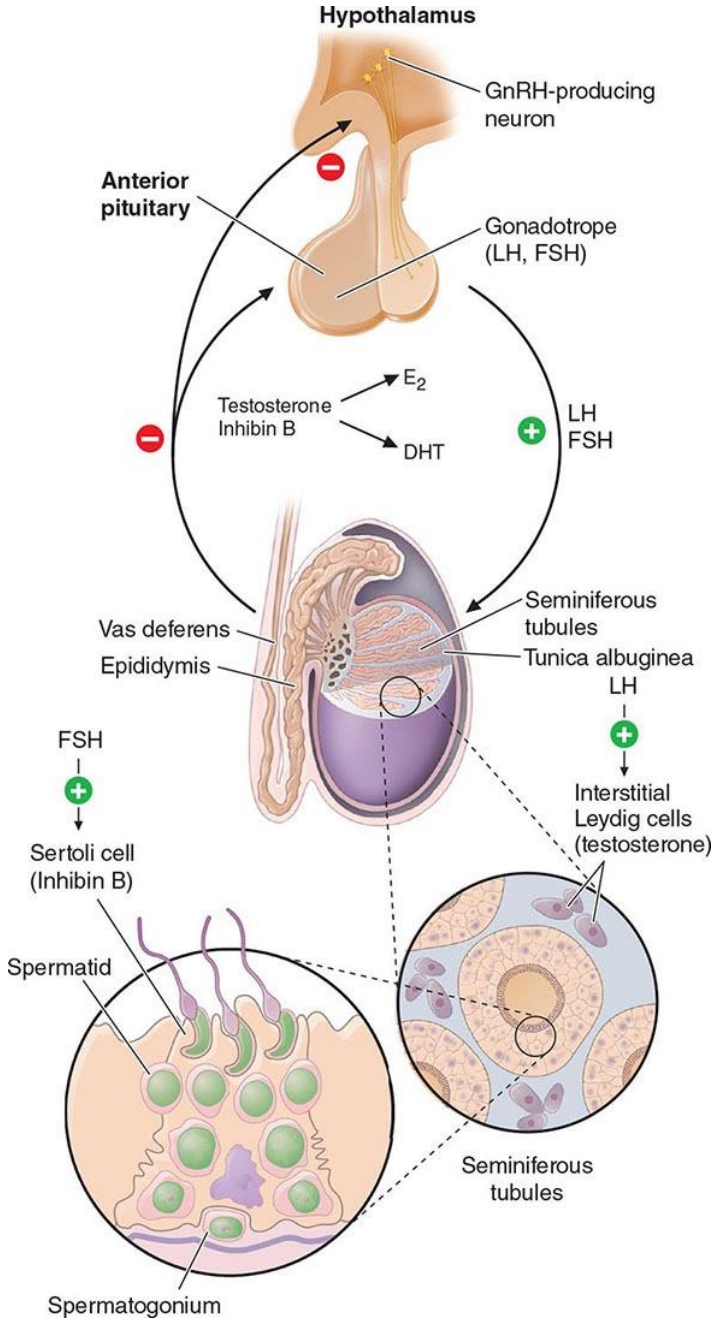
Hypogonadism

- Hypogonadism literally means decrease in function of gonads
- Male hypogonadism means a decrease in the function of the testicle
- Testicles have mainly 2 functions
  - Testosterone production
  - Sperm production

We can say the patient has hypogonadism if there is decreased testosterone production and/or impaired spermatogenesis

Male Physiology





Testosterone

What are the main functions of testosterone?

- Masculinization
- Maintaining bone and muscle mass
- Hair growth
- Influencing libido and mood

What are the symptoms of testosterone deficiency?

- Mild-moderate disease (non-specific): Fatigue, generalized weakness, depression, mood swings, daytime sleepiness, reduced self-confidence and self-esteem, decreased libido, mild erectile dysfunction.
- Advanced disease: Loss of facial hair and muscle mass, gynecomastia.
- Very severe cases: Infertility

Therefore, the physician should have a high index of suspicion for low testosterone

Testosterone Deficiency

- If a patient is suspected to have low testosterone by symptoms and/or is found to have low level of testosterone by blood test the next best step is to perform a proper blood test:
  - Assess for bioavailable testosterone (Not available in Jordan)
  - Free testosterone by equilibrium dialysis (Not available in Jordan)

Alternatively, we measure total testosterone and SHBG and by special calculator we calculate the bioavailable testosterone and the free testosterone

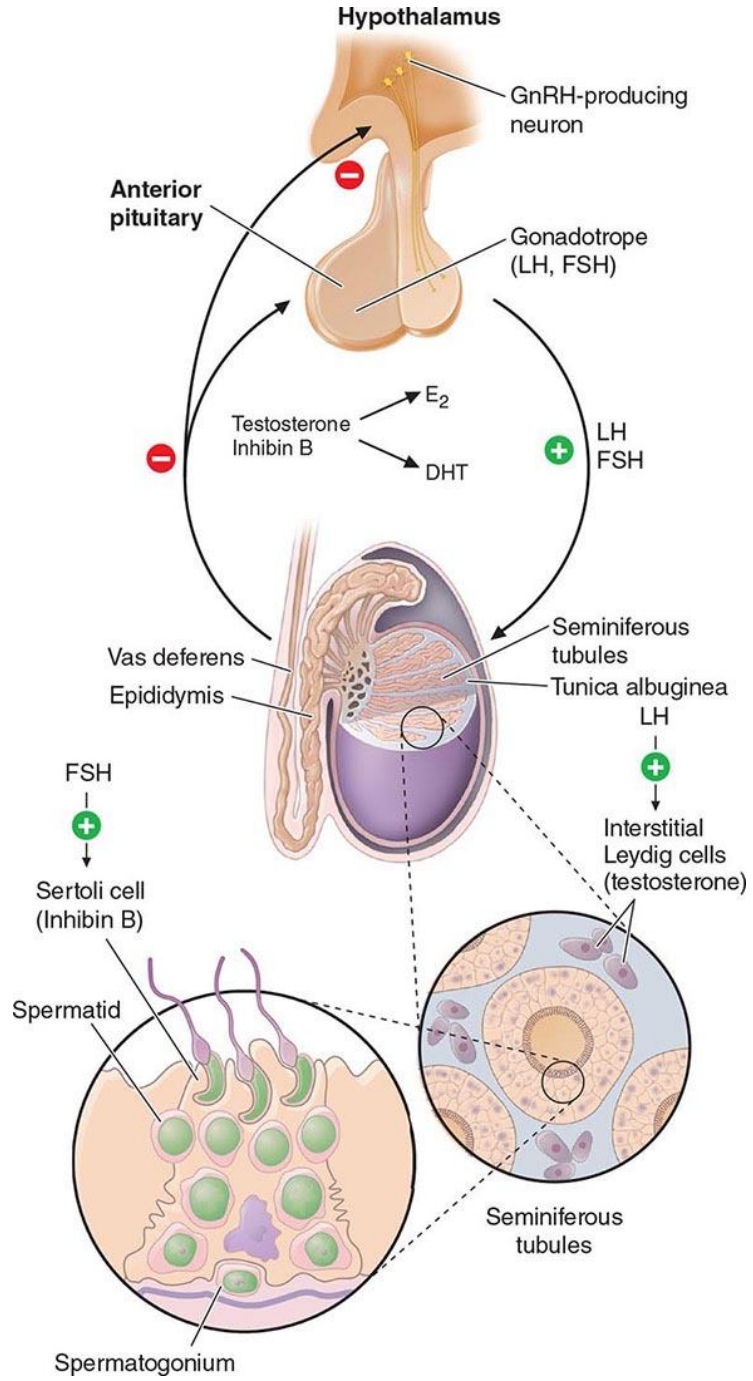
Primary VS. Central

- Primary hypogonadism means the pathology is in the testicles while central hypogonadism means that the pathology is in the pituitary or hypothalamus

- Primary VS. Central: measure LH

Primary Hypogonadism

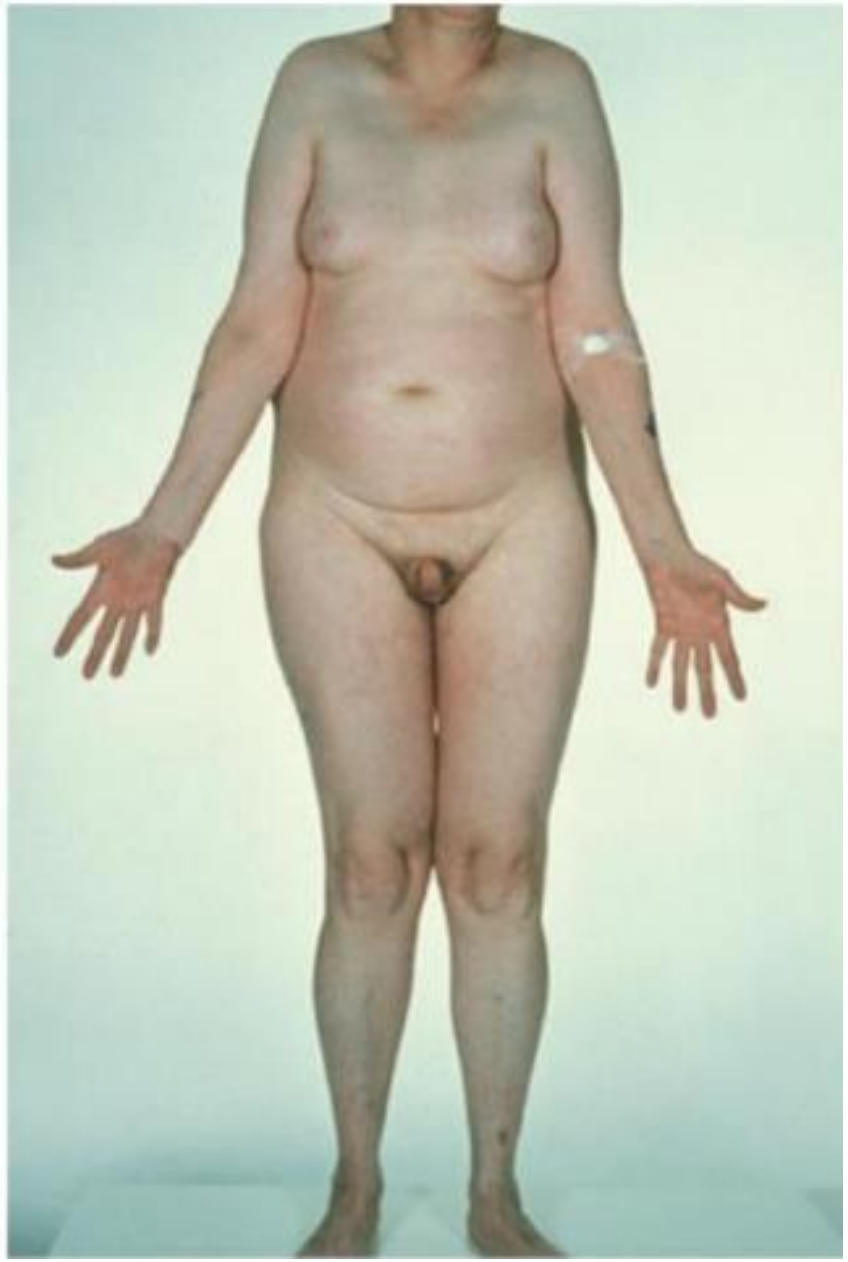
- If the patient has primary hypogonadism; according to negative feedback the LH should be high
- If the LH is not high (low or normal) this means the patient has central hypogonadism
- If the patient has primary hypogonadism, we need to find the specific cause/pathology in the testicles



- What are the possible causes of primary hypogonadism?
  - Klinefelter syndrome
  - Chemotherapy affecting the testicles
  - Testicular removal
  - Radiation
  - Infiltrating diseases (e.g. Hemochromatosis)

Kleinfelter Syndrome

- Chromosomal disorder that occurs in males
- Characterized by the presence of an extra X chromosome, resulting in a karyotype of 47,XXY.
- These patients have certain phenotypic features
- Biochemical features
- Diagnosis



Central Hypogonadism

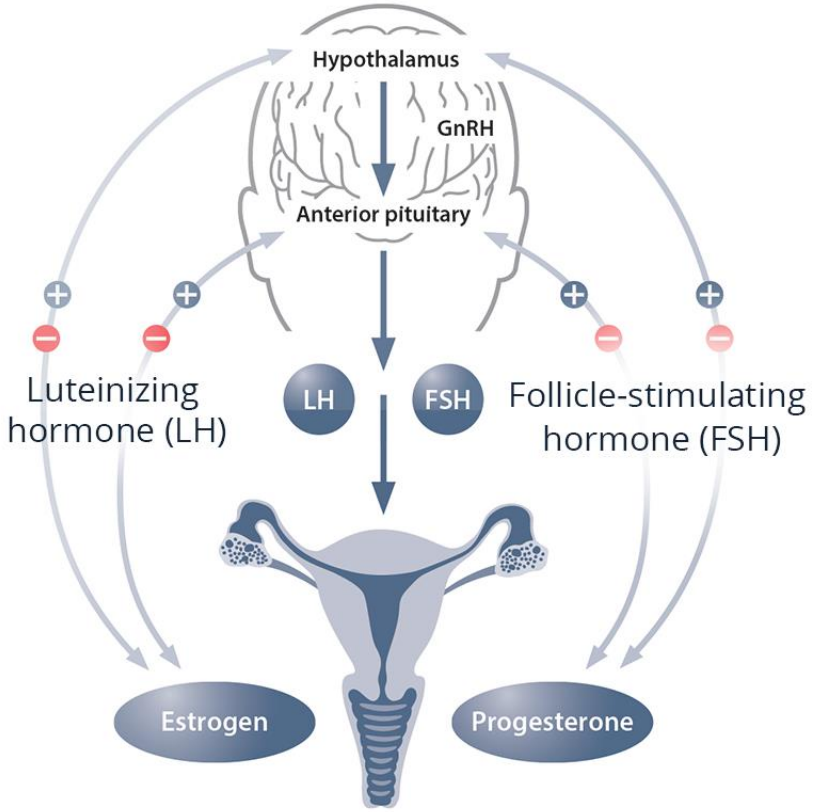
- If the patient has central hypogonadism the next step is to do pituitary MRI to find out the specific pathology in the pituitary or hypothalamus

Kallman Syndrome

- Genetic disorder characterized by failure of episodic GnRH secretion ± anosmia. Results from disordered migration of GnRH-producing neurons into the hypothalamus
- Increased risk of midline defects: cleft lip and palate, Sensorineural deafness, cerebellar ataxia, and renal agenesis
- Low testosterone, LH and FSH levels
- May be inherited as X-linked, AD or AR

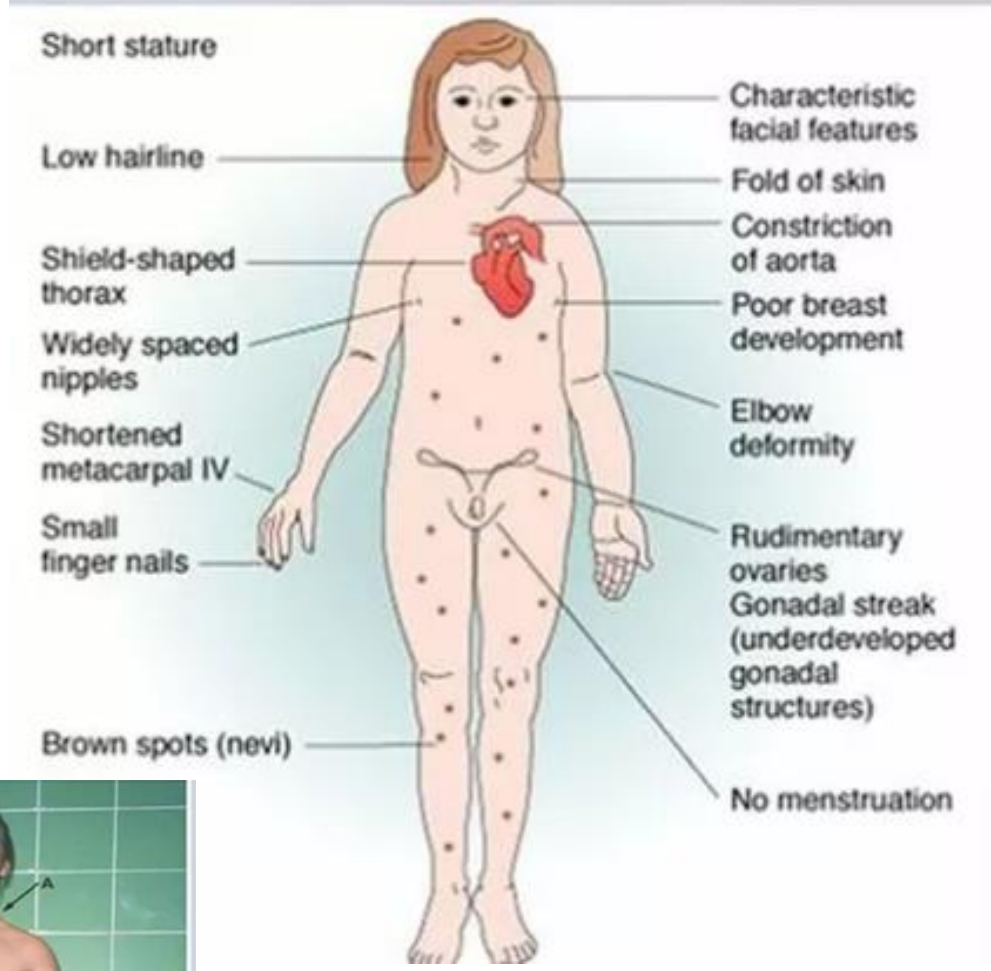
Female Hypogonadism

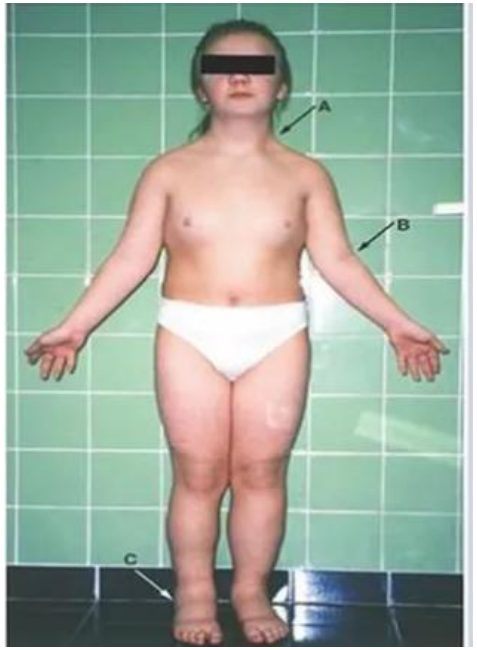
- The principles are similar to male hypogonadism but in females with primary hypogonadism estrogen is low
- The approach to primary and secondary hypogonadism in females is the same as the approach to males.



Turner Syndrome

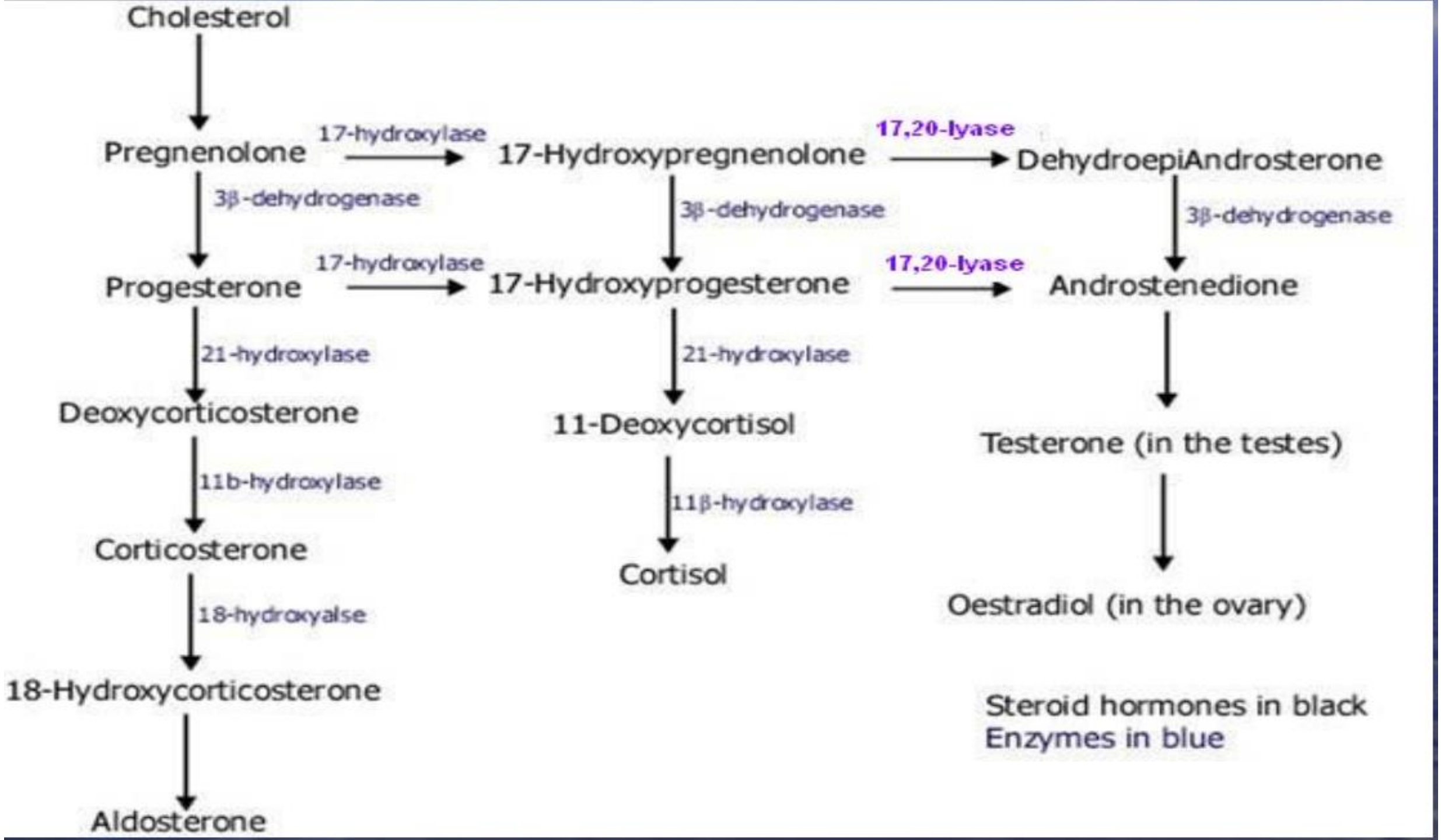
- Genetic disorder that affects females, typically resulting from a complete or partial absence of one of the X chromosomes, thus having a karyotype of 45, XO.
- They have certain phenotypic features

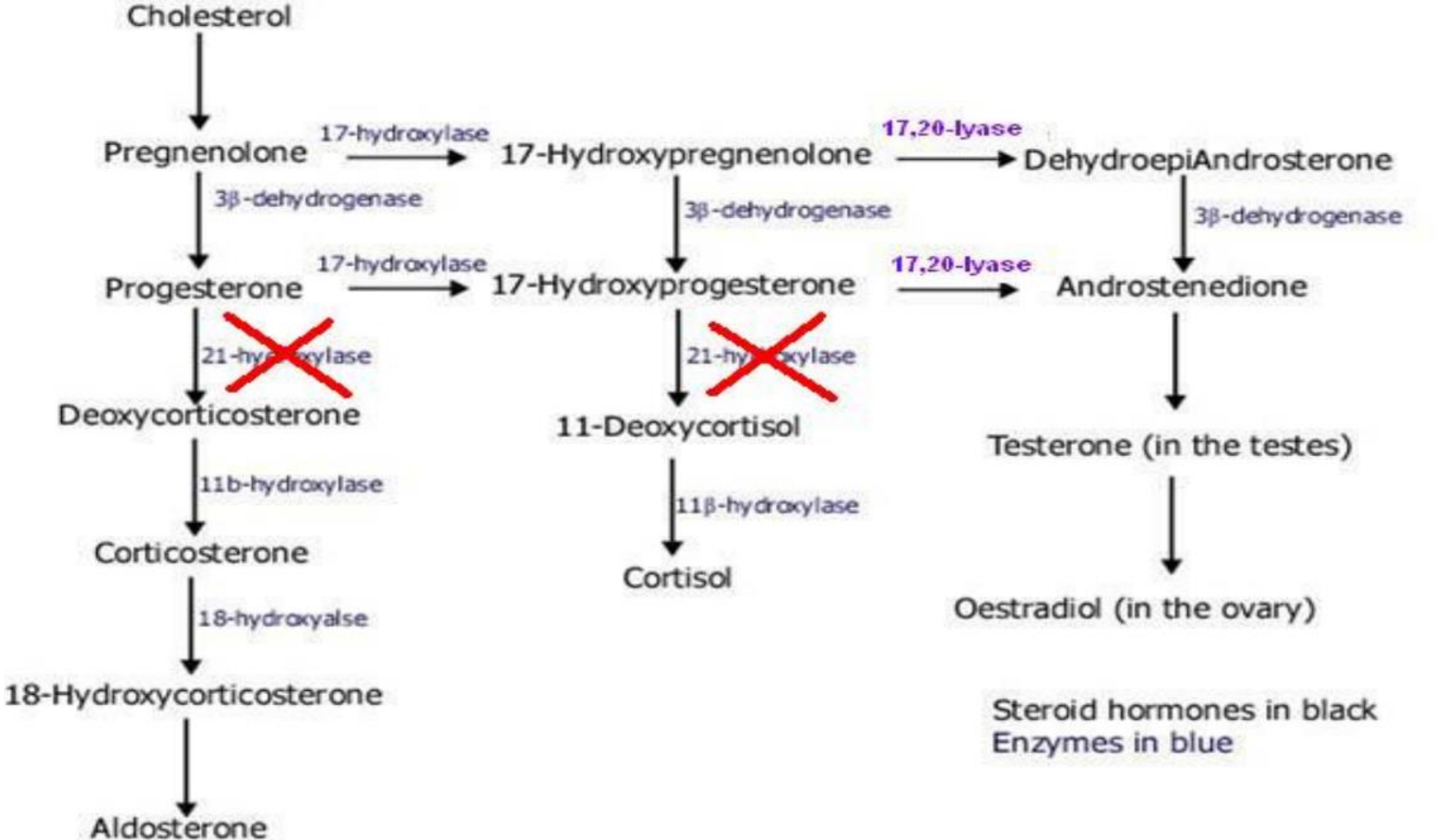




Congenital Adrenal Hyperplasia (CAH)

- It is a disorder which is caused by a defect in one of the enzymes involving the synthesis of adrenal hormones
- The most common enzyme deficiency which causes CAH is 21-hydroxylase deficiency
- Other enzymes include 11beta-hydroxylase deficiency and 17 alpha-hydroxylase deficiency
- There are several types:
  - Classical CAH
    - Salt losing form
    - Non-salt-losing form
  - Non-classical CAH


Cholesterol
Pregnenolone
17-hydroxylase
17-Hydroxypregnenolone
17,20-lyase
DehydroepiAndrosterone
3β-dehydrogenase
3β-dehydrogenase
3β-dehydrogenase
Progesterone
17-hydroxylase
17-Hydroxyprogesterone
17,20-lyase
Androstenedione
21-hydroxylase
21-hydroxylase
Deoxycorticosterone
11-Deoxycortisol
Testerone (in the testes)
11b-hydroxylase
11β-hydroxylase
Corticosterone
Cortisol
18-hydroxyalse
Oestradiol (in the ovary)
18-Hydroxycorticosterone
Steroid hormones in black
Enzymes in blue
Aldosterone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21-hydroxylase
Deoxycorticosterone
11-Deoxycortisol
Testerone (in the testes)
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Cortisol
18-hydroxyalse
Oestradiol (in the ovary)
18-Hydroxycorticosterone
Steroid hormones in black
Enzymes in blue
Aldosterone

- The classical CAH patients usually present at birth with ambiguous genitalia if the newborn is a female
  - In salt-losing form patients also have manifestations of adrenal insufficiency
  - In non-salt-losing form there is ambiguous genitalia without clinical AI

- In non-classical CAH they usually present at puberty or during adolescence; Either with primary amenorrhea or irregular period and hirsutism

- Difference is upon degree of enzyme deficiency
  - Very severe deficiency: salt losing classical CAH
  - Less severe deficiency: non-salt losing classical CAH
  - Mild deficiency: non classic CAH

	Classical type		Non-classical type
Characteristic	Salt-wasting	Non-salt-wasting	
Age at time of diagnosis[1]	Neonatal period	Neonatal period (women) or childhood (men)	From infancy to adulthood
Virilisation/hirsutism	Moderate to pronounced	Moderate to pronounced	None to slight or moderate, may undergo precocious puberty
Percentage enzyme activity	0	1–10 %	30–75 %
Aldosterone	↓↓	↓ Normal	Normal
Cortisol	↓↓	↓	Normal

- To diagnose 21 hydroxylase deficiency, we measure 17 hydroxyprogesterone
- Patient is usually normotensive in contrast to other forms of CAH

Self Reading Topics

- Gynecomastia
- Hirsutism