Bio 1

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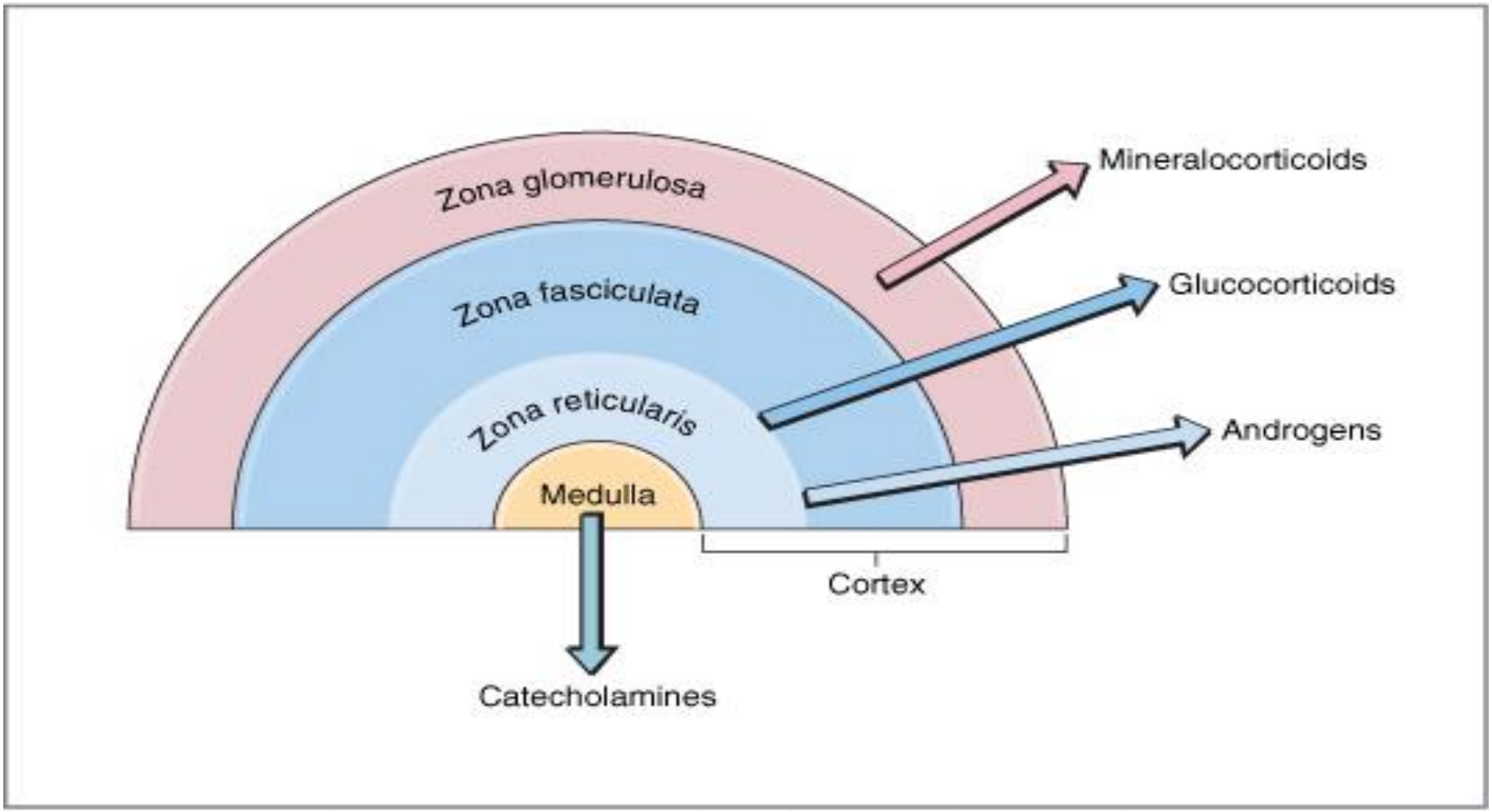
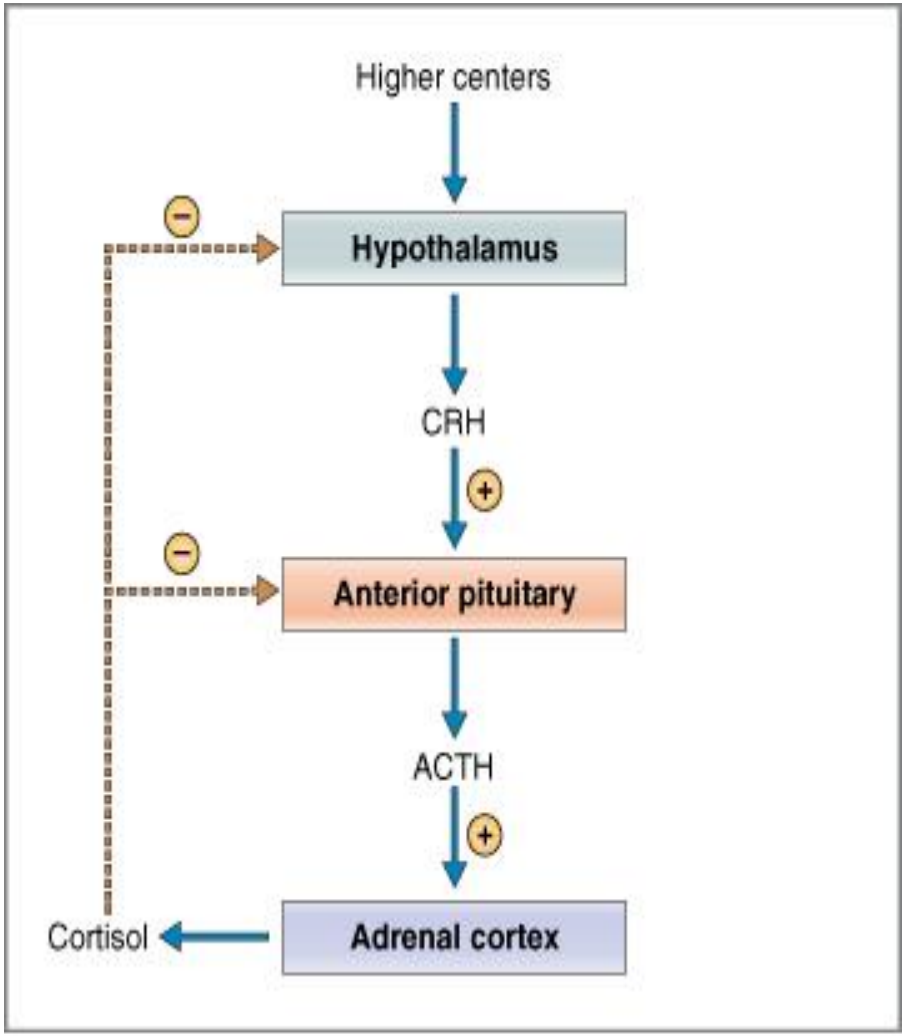


- Androgens
- Chatecholamines
- Glucocorticoids:
  - cortisol-like activity
  - Potent metabolic regulators & immunosuppressants
- Mineralocorticoids:
  - aldosterone-like activity
  - Promote renal sodium retention

- Intersex: A person has neither standard male or standard female anatomy
- True hermaphrodite :
  - Ovaries and testis
- Female pseudohermaphrodite is :
  - A person with XX chromosomes (female)
  - MALE external genitals
  - Person has ovaries
- Male pseudohermaphrodite
  - A person with XY chromosome (male)
  - FEMALE external genitals
  - Person has testis

- CRH causes the pituitary to release ACTH
- ACTH works on the adrenal gland to release hormones
- Cortisol negatively inhibits ACTH release

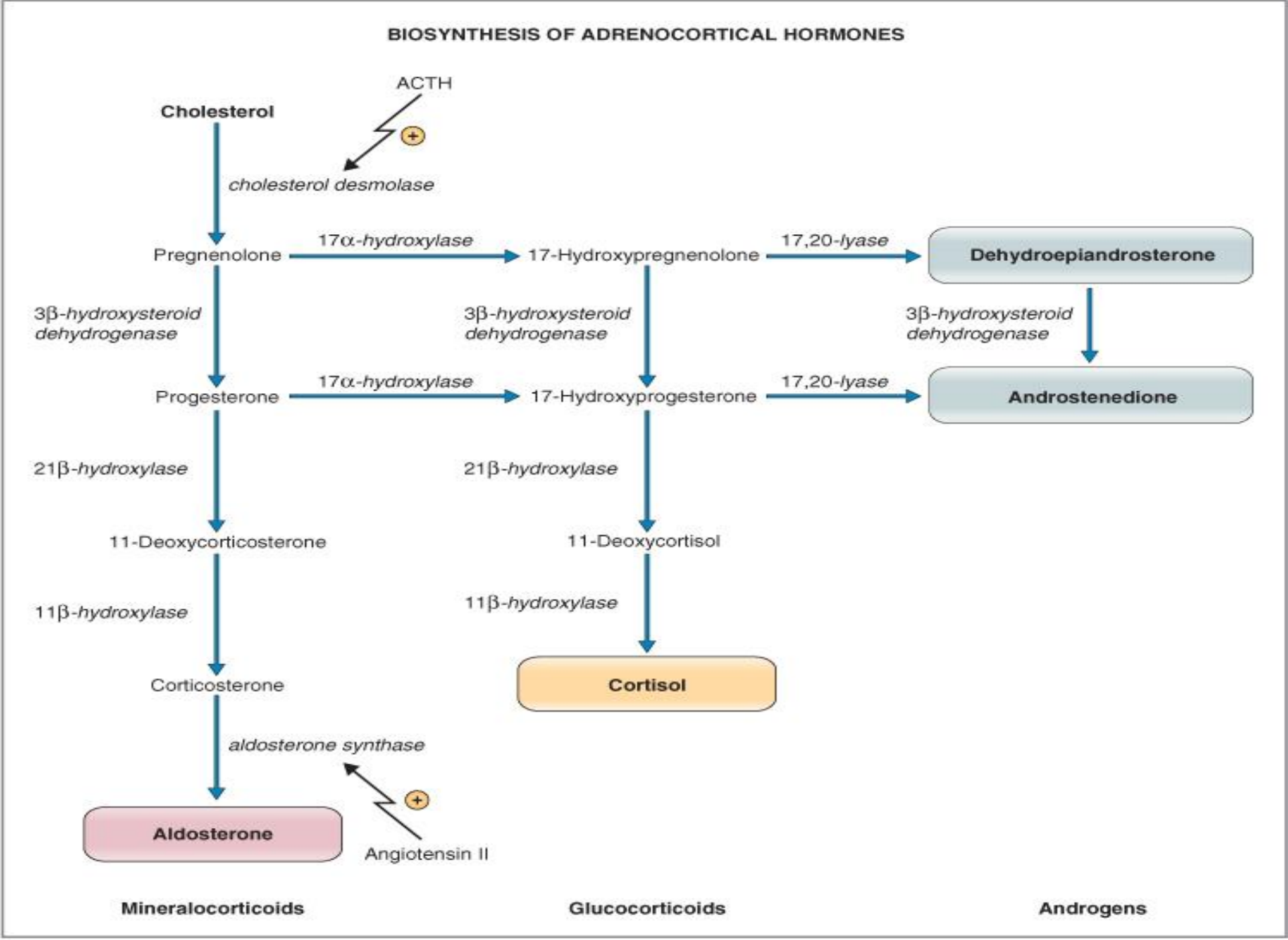


Congenital adrenal hyperplasia

- result of an inherited enzyme defect in steroid biosynthesis
- If there are no enzymes then >> no cortisol(cortisol cannot be synthesized) >> if there is no cortisol there will be no negative feedback on ACTH secretion >> ACTH levels will continue to go up
- If there is no cortisol to give negative feedback then? ACTH will drive the adrenal gland to undergo HYPERPLASIA (compensation)

- No cotrisol
  - adrenal hyperplasia
  - accumulation of cortisol precursors
- No aldesterone
  - Hyponatremia (because aldesterone causes sodium water retention)
  - Hypokalemia (because aldersterone causes K+ secretion)

- Diagnosis of the most common type (21-hydroxylase deficiency) is be finding ↑ plasma [17-hydroxyprogesterone] as early as 4 days after birth
- ↑ stimulation of adrenal androgen production
  - virilization in baby girls
  - precocious puberty in boys.
- Partial enzyme defect → late onset form → menstrual irregularity & hirsutism in young females



21 α-Hydroxylase diff

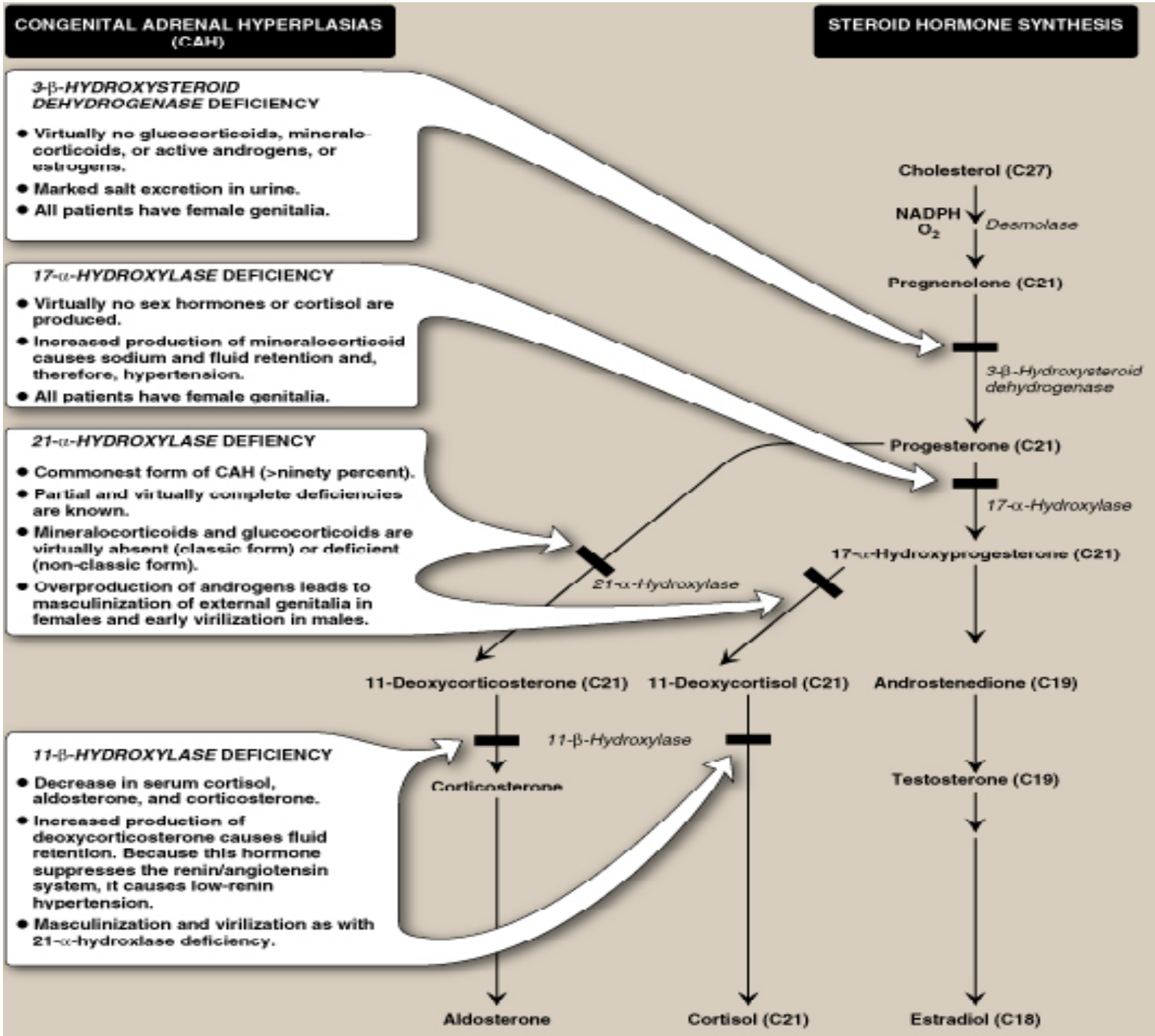
- cause progesterone to take another pathway causing increased levels of androgens
- 95% of all cases of CAH
- Autosomal recessive
- None or few mineralocorticoid synthesis
- signs of androgen excess:
  - ambiguous genitalia in newborn girls (FPH)
  - rapid postnatal growth in both sexes

- Genetics : in the CYP21 gene
  - Miss sense
  - Deletetion
  - Nonsense
- Enzyme mutation is not severe
  - Late presentation
- Enzyme mutation is severe
  - salt & H_2O loss → hypovolaemia & shock → neonatal adrenal crisis
  - Due to lack of mineralocorticoid that cause retention of NA and H2O

- Diagnosis of the most common type (21-hydroxylase deficiency) is be finding ↑ plasma [17-hydroxyprogesterone] as early as 4 days after birth
  - Why 4 days ? because in the first 2 days the maternal levels of [17-hydroxyprogesterone] are high
- What if the levels are normal but the clinical presentation suggest (21-hydroxylase deficiency) ?
  - We do provoking test which is injecting bolus of corticotrophin and we take measurements before and after the injection – base line and stimulated levels – if it is high then it is diagnostic

11 β -Hydroxylase Deficiency

- leads to >>> high levels of 11-deoxy-corticosterone
- 11-deoxy-corticosterone has a mineralocorticoid action so it will cause sodium and water retention
- That leads to suppression of renin/angiotensin >>>>> LOW RENIN HYPERTENSION
- If in the question he presents with hypertension then think of 11 β -Hydroxylase Deficiency

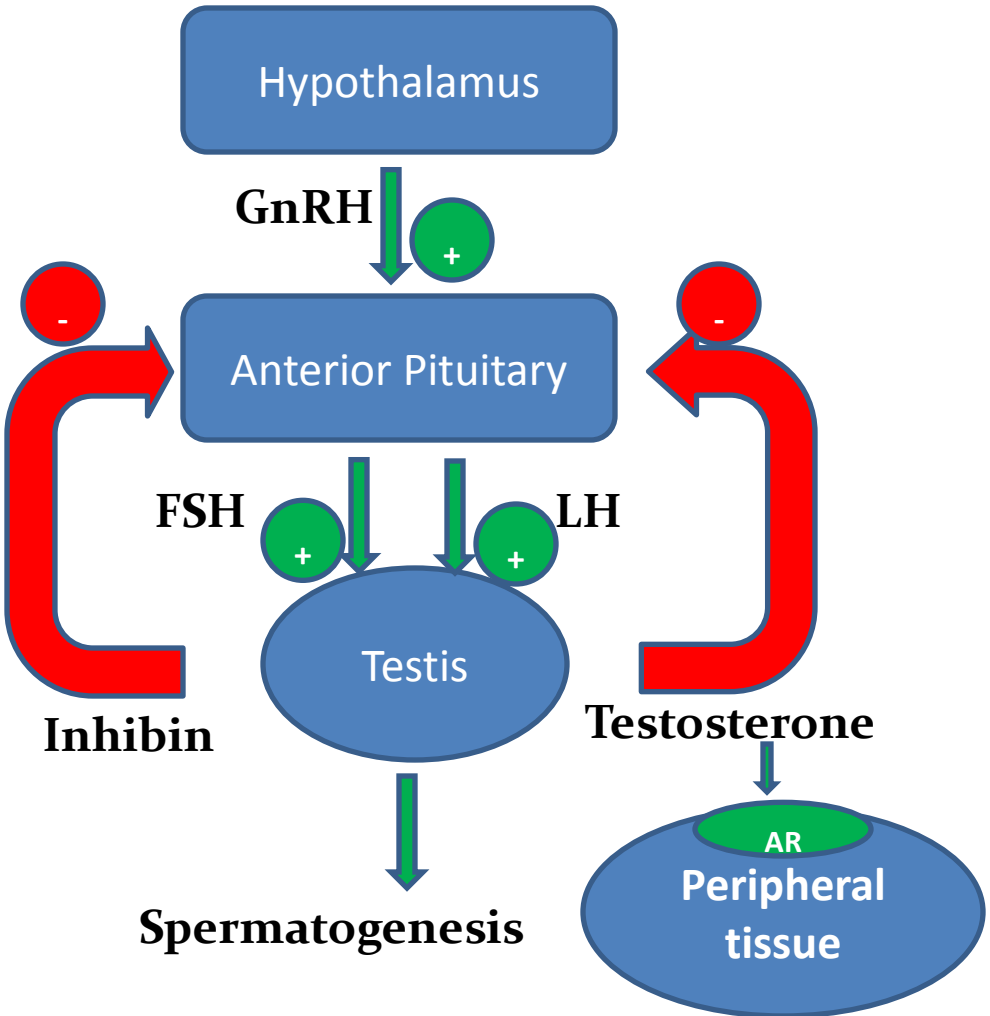

CONGENITAL ADRENAL HYPERPLASIAS (CAH)
STEROID HORMONE SYNTHESIS
3-β-HYDROXYSTEROID DEHYDROGENASE DEFICIENCY
Virtually no glucocorticoids, mineralocorticoids, or active androgens, or estrogens.
Marked salt excretion in urine.
All patients have female genitalia.
17-α-HYDROXYLASE DEFICIENCY
Virtually no sex hormones or cortisol are produced.
Increased production of mineralocorticoid causes sodium and fluid retention and, therefore, hypertension.
All patients have female genitalia.
21-α-HYDROXYLASE DEFIENCY
Commonest form of CAH (>ninety percent).
Partial and virtually complete deficiencies are known.
Mineralocorticoids and glucocorticoids are virtually absent (classic form) or deficient (non-classic form).
Overproduction of androgens leads to masculinization of external genitalia in females and early virilization in males.
11-β-HYDROXYLASE DEFICIENCY
Decrease in serum cortisol, aldosterone, and corticosterone.
Increased production of deoxycorticosterone causes fluid retention. Because this hormone suppresses the renin/angiotensin system, it causes low-renin hypertension.
Masculinization and virilization as with 21-α-hydroxlase deficiency.
Cholesterol (C27)
NADPH
O2
Desmolase
Pregnenolone (C21)
3-β-Hydroxysteroid dehydrogenase
Progesterone (C21)
17-α-Hydroxylase
17-α-Hydroxyprogesterone (C21)
21-α-Hydroxylase
11-Deoxycorticosterone (C21)
11-Deoxycortisol (C21)
Androstenedione (C19)
11-β-Hydroxylase
Corticosterone
Testosterone (C19)
Aldosterone
Cortisol (C21)
Estradiol (C18)

Disorders of Male Sexual Differentiation

- They are **rare** group of disorders
- The defect may be in:
  - **Testosterone** production (impaired testosterone production)
  - Androgen **receptors** (inactive androgen receptors → target tissues cannot respond to stimulation by circulating testosterone; e.g., **Testicular feminization syndrome**)

- Androgen Insensitivity Syndrome is a disease of receptor resistance
  - like diabetes mellitus when insulin cannot bind to the receptors
  - like diabetes insipidus when ADH cannot bind to receptors

Control of testicular function by the gonadotrophins



Diagnosis

- **Clinical Diagnosis:**
  - Three phenotypes:
    - Complete androgen insensitivity syndrome (**CAIS**) Female ("testicular feminization“, MPH)
    - Partial androgen insensitivity syndrome (**PAIS**)
    - Mild androgen insensitivity syndrome (**MAIS**) Male ("undervirilized male syndrome")

Testicular Feminization Syndrome

- 46,XY karyotype
- X-linked recessive disorder
- Androgen receptor resistance ⟶ high testosterone blood level
- In peripheral tissue, testosterone will be converted by aromatase into estradiol ⟶ feminization

- **Laboratory Diagnosis:**
  - Increased (or normal) testosterone blood level
  - Increased luteinizing hormone (LH) production by the pituitary gland

- usually if there is high levels of testosterone that will block LH secretion but in this disease we find high LH levels in the blood also (something strange)
- excess testosterone. in the peripheral tissue will be converted into estradiaol
  - why is there excess ? because it cant bind to the receptor