Congenital Adrenal Hyperplasia

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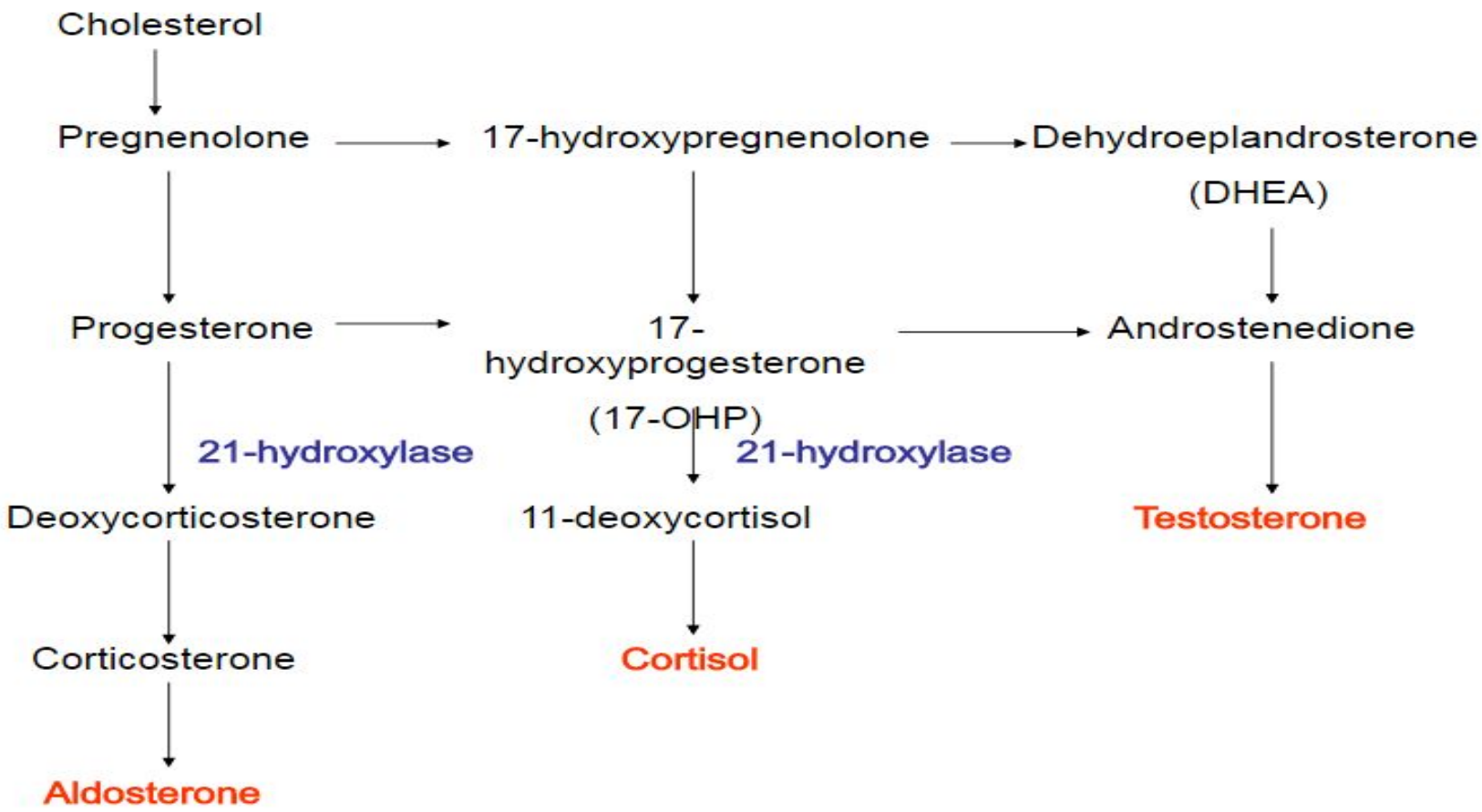
?What is CAH

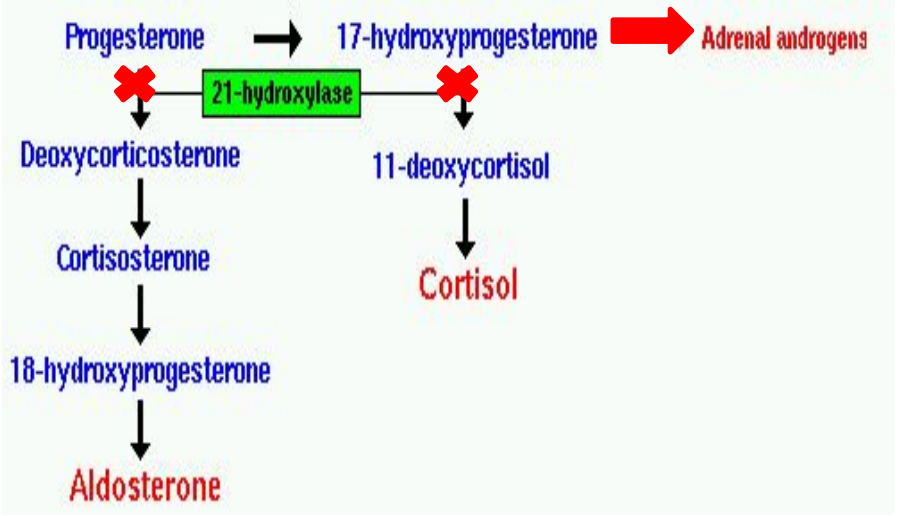
- It is a familial disorder of adrenal steroid biosynthesis due to adrenal enzyme deficiency with autosomal recessive mode of inheritance.
- Classical CAH is a sever homozygotic disorder with an incidence of 1 : 7,000-15,000
- Non-classical CAH is less sever heterozygotic disorder with an incidence of 1 : 500-1,000
- 3 major enzymes deficiency are clinically important
    - 21-Hydroxylase deficiency (90%-95%)
    - 11-b-Hydroxylase deficiency
    - 17-a-Hydroxylase deficiency

Adrenal steroids biosynthesis



Hydroxylase deficiency-21

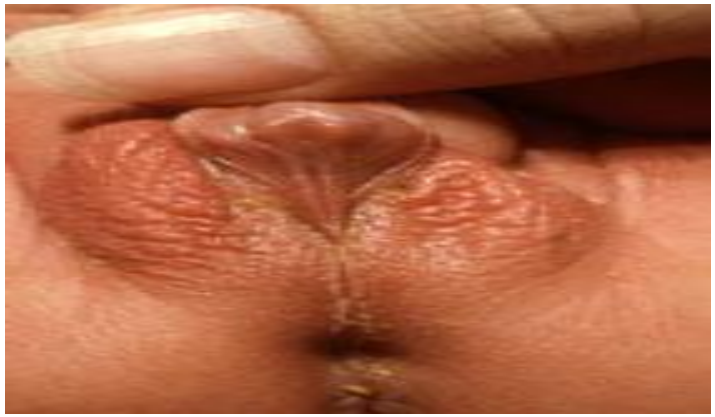
- The most common CAH type
- reduced production of cortisol and aldosterone and increased production of progesterone; 17-OHP, and sex steroids.
- Heterozygous carriers can be detected by ACTH stimulation test.

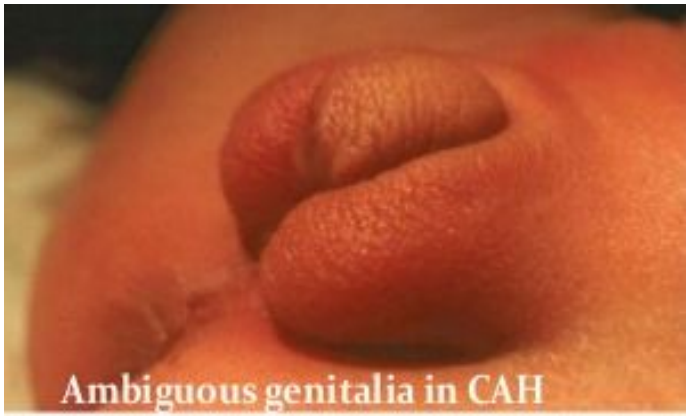


Classical 21-hydroxylase deficiency

- *Salt-wasting form (75%)*: unable to synthesize adequate amounts of cortisol and aldosterone, lose large amounts of sodium in urine, which can lead to fatal electrolyte and water imbalance. Babies usually present with "adrenal crisis" on week 1-4 (poor appetite, vomiting and failure to grow).

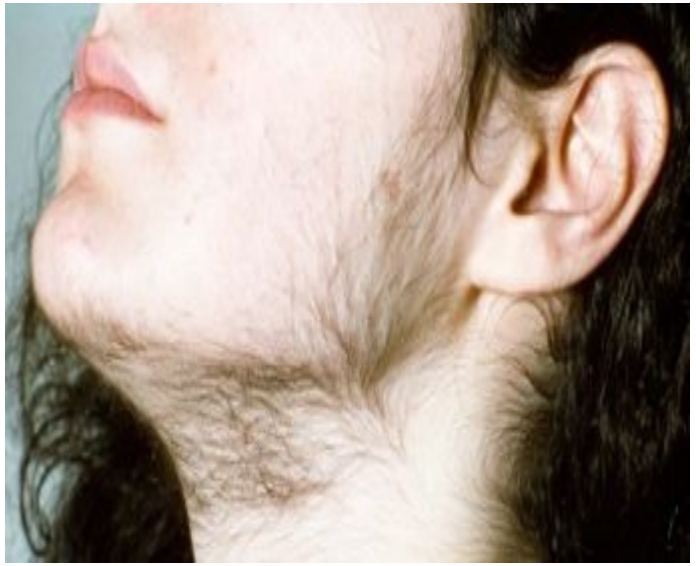
- *Simple virilizing form (*25%): Excessive prenatal production of androgens in females results in ambiguous genitalia. Males are usually normal at birth with precocitous puberty. In both sexes, linear growth is accelerated, but the epiphyses fuse early, leading to short stature with a well-developed trunk.





Non-classical 21-hydroxylase deficiency

- Usually is mild and manifest as an androgen excess later in life. Aldosterone and cortisol deficiency isn't usually observed.
- Female manifestations: hirsutism, acne, male-pattern balding, oligomenorrhea, infertility.
- Male manifestations: general asymptomatic, short stature, sometimes oligospermia.



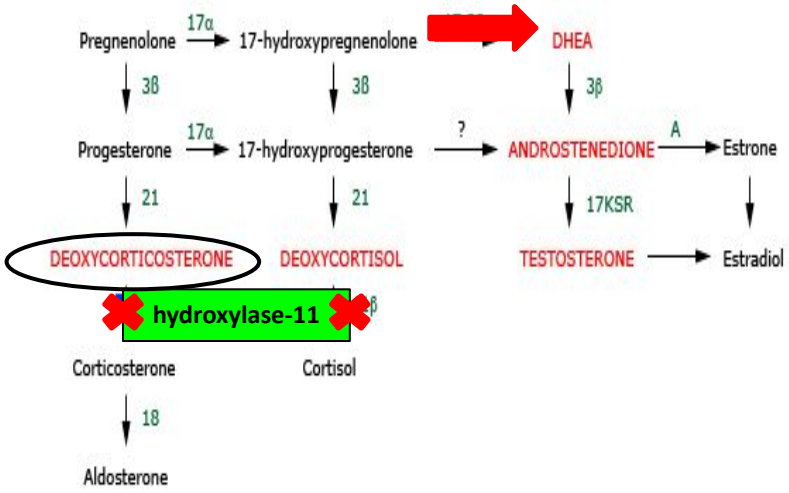
Diagnosis of 21-hydroxylase deficiency

- Screening: high blood level of 17-OH Progesterone

- 250 MKG SYNACTHEN TEST:
  high level of 17-OHP
  low/normal cortisol and aldosterone

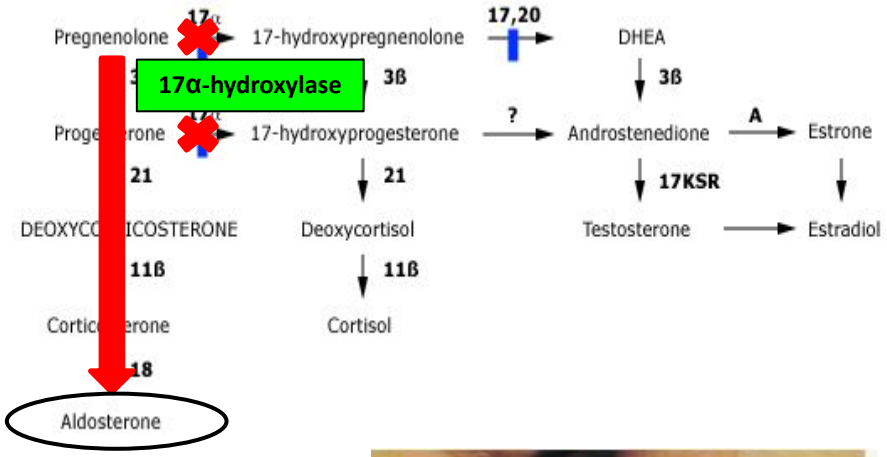
hydroxylase (CYP11B1) deficiency-11

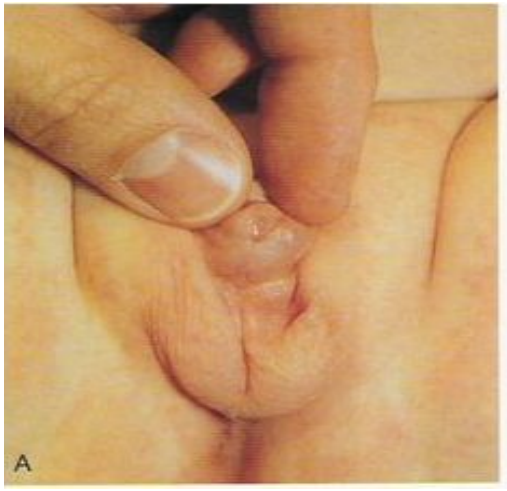
- Hypertension and hypokalemia occur because of accumulation of 11-deoxycorticosterone, a potent mineralocorticoid, which causes the excessive salt retention.
- Girls with ambiguous genitalia
- Girls and boys with precocious puberty



hydroxylase (CYP11B1) deficiency-17

- Hypertension and hypokalemia occur due to accumulation of aldosterone
- No female virilizaton
- Male ambiguous genitalia or female phenothype





Diagnosis

11-hydroxylase deficiency

- 250 MKG SYNACTHEN TEST: high serum level of 11-deoxycorticosterone and 11-deoxycortisol
- elevated 24-hour urinary 17-ketosteroids

17-hydroxylase deficiency

- low K, high Aldosterone, suppressed Renin
- Low 17-OHP, androgens

TREATMENT PRINCIPLES

- In classical CAH treatment is life-long
- Treatment goals are:
  - to maintain growth velocity & skeletal maturation.
  - to normalize electrolytes & hormone levels using the smallest dose of glucocorticoids.
  - mineralocorticoid replacement may be needed to sustain normal electrolyte homeostasis.
- Plastic surgery for ambiguous genitalia at early age
- Genetic counseling
- Psychological support

Prenatal diagnosis and treatment

- Done by chorionic villus sampling at 8-12 wk & amniocentesis at 18-20 wk.
- Prenatal treatment of 21-hydroxylase deficiency prevents intrauterine virilization of female fetuses.
- The mother with nonclassical CAH is treated with dexamethasone as soon as the pregnancy is recognized until fetus sex determination.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