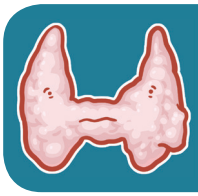

NOTES
ADRENAL HYPERPLASIA

CONGENITAL ADRENAL HYPERPLASIA

osms.it/congenital-adrenal-hyperplasia

PATHOLOGY & CAUSES

- Congenital adrenal hyperplasia (CAH) is a group of autosomal-recessive metabolic disorders characterized by defects in certain genes resulting in a partial/total lack of an enzyme involved in steroidogenesis within the adrenal cortex
  - ↓ steroid hormone production → compensatory ↑ ACTH → adrenal hyperplasia
  - ↓ cortisol → cortisol precursor accumulation → steroid precursors shunted to overproduction of other ACTH-dependent adrenal steroids

TYPES

21-hydroxylase deficiency
- *Defective gene:* *CYP21A2*
- Most common type of CAH
  - *Classic:* neonatal/early infancy genital ambiguity in females, adrenal insufficiency; classic non-salt-losing (simple virilizing): female fetus virilization; classic salt-losing
  - *Non-classic (late onset):* presents later in life (child-adult) with androgen excess signs; non-salt-losing

17-alpha hydroxylase deficiency
- *Defective gene:* *CYP17A1*
- Rare
- Steroid precursors for testosterone, cortisol synthesis shunted to aldosterone

11-beta-hydroxylase deficiency
- *Defective gene:* *CYP11B1*
- 7% of CAH cases
- Lack of enzyme prevents conversion of 11-deoxycortisol to cortisol
- 11-deoxycortisol (aldosterone precursor) has mild mineralocorticoid effect → biphasic effect on mineralocorticoid balance

SIGNS & SYMPTOMS

21-hydroxylase deficiency
- Varies by subtype

17-alpha hydroxylase deficiency
- ↓ cortisol → corticosterone presence prevents adrenal crisis
- Mineralocorticoid excess → secondary hypertension; hypokalemic alkalosis
- Gonadocorticoid deficiency (males: mildly underdeveloped genitalia, hypergonadotropic hypogonadism; females: abnormal pubertal sexual development, infertility)

11-beta-hydroxylase deficiency
- Androgen excess → external genitalia virilization, sexual ambiguity (females)
- Biphasic mineralocorticoid balance → possible salt-wasting crisis in early infancy; secondary hypertension and hypokalemia in childhood and adult life

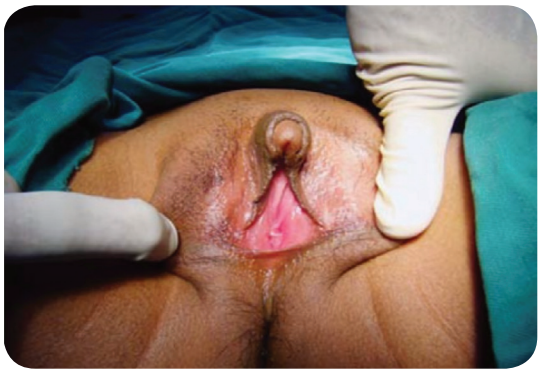

Figure 12.1 Clitoromegaly with normal labia and introitus in a biologically female individual with 21-hydroxylase deficiency.

DIAGNOSIS

- Clinical presentation
  - Steroid imbalance evidence
- Most cases identified via newborn screening

LAB RESULTS

Serum hormone levels

- 21-hydroxylase deficiency
  - ↓ sodium (salt-losing type), ↑ potassium (salt-losing type)
  - *Serum markers:* ↑↑ serum 17-hydroxyprogesterone, ↑ 21-deoxycortisol)
- 17-alpha hydroxylase deficiency
  - ↑ sodium, ↓ potassium
  - *Serum markers:* ↑ pregnenolone, ↑ progesterone, ↑ 11-deoxycorticosterone, ↑ 11-deoxycortisol
- 11-beta-hydroxylase deficiency
  - ↑ sodium, ↓ potassium
  - *Serum markers:* ↑ 11-deoxycorticosterone, ↑ 11-deoxycortisol)

Genetic testing

Prenatal diagnosis

- By chorionic villus sampling at 10–12 weeks

TREATMENT

MEDICATIONS

- 21-hydroxylase deficiency
  - Exogenous glucocorticoid (hydrocortisone), mineralocorticoid (fludrocortisone)
- 11-beta-hydroxylase deficiency
  - Exogenous glucocorticoid (hydrocortisone), antihypertensives
- 17-alpha hydroxylase deficiency
  - Exogenous glucocorticoid (hydrocortisone), sex steroid replacement beginning at puberty, antihypertensives
- If CAH diagnosed prenatally
  - Dexamethasone

SURGERY

- Potential atypical genitalia correction

OTHER INTERVENTIONS

- Address complications (e.g., fluid, electrolyte imbalance)
- Monitor
  - Serum 17-hydroxyprogesterone, renin, electrolytes
  - Blood pressure
  - Bone age and density
  - Tanner staging
  - Weight
  - Growth velocity

21-HYDROXYLASE DEFICIENCY OVERVIEW

	CLASSIC SALT-LOSING	CLASSIC SIMPLE VIRILIZING	CLASSIC
AGE AT PRESENTATION	- Early neonatal period	- Neonatal - 4 years	- Adult-child (late onset)
EFFECTS ON GENITALIA	- Females: ambiguous - Males: normal; may have scrotal hyperpigmentation; enlarged phallus	- Females: ambiguous - Males: normal; early virilization (pubic hair, growth spurt, adult body odor) at 2-4 years of age; testicular adrenal rest tumors may develop between 10-20 years of age	- Females: virulized - Males: normal
HORMONE PRODUCTION	- ↓ cortisol - ↓ aldosterone - ↑ androgens	- ↓ cortisol - Normal aldosterone - ↑ androgens	- Normal cortisol, aldosterone - ↑ androgens
OTHER EFFECTS	- First 2 weeks of life: may present with hypotension and salt-wasting crisis (poor feeding, vomiting, failure to thrive, lethargy), hypoglycemia, hypotension	- Males: premature pubarche (pubic hair, growth spurt, adult body odor) at 2-4 years of age; testicular adrenal rest tumors may develop between 10-20 years of age - Premature epiphyseal closure → adult height diminished	- Males/females: premature pubarche -Females: hirsutism, menstrual irregularity -↑ risk of stress-induced adrenal insufficiency