Common Adrenal Disorders in Children

Dr Sarar Mohamed

FRCPCH (UK), MRCP (UK), CCST (Ire), CPT (Ire), DCH (Ire), MD

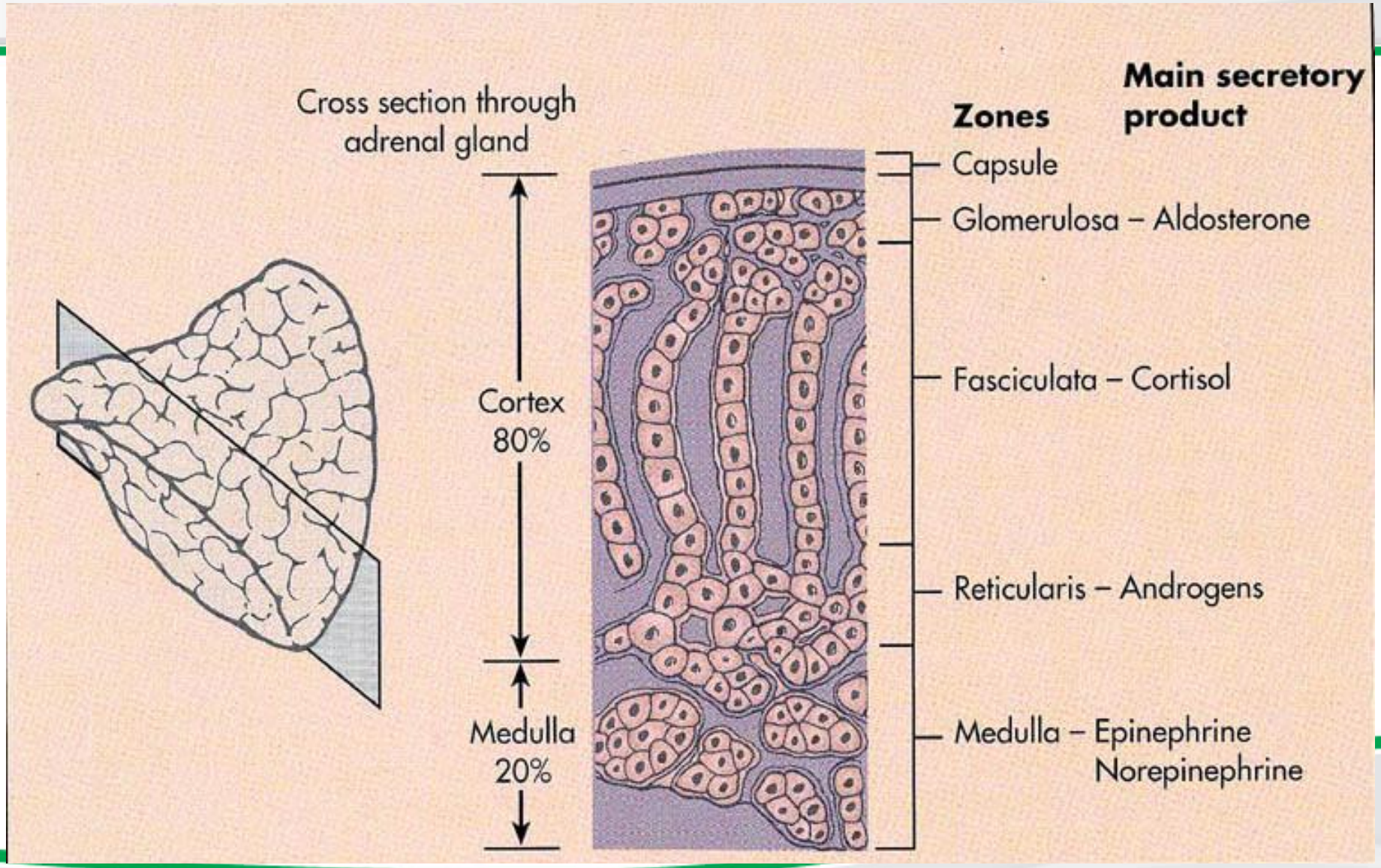
Consultant Paediatric Endocrinologist & Metabolist

Assistant Professor of Pediatrics

King Saud University

Agenda

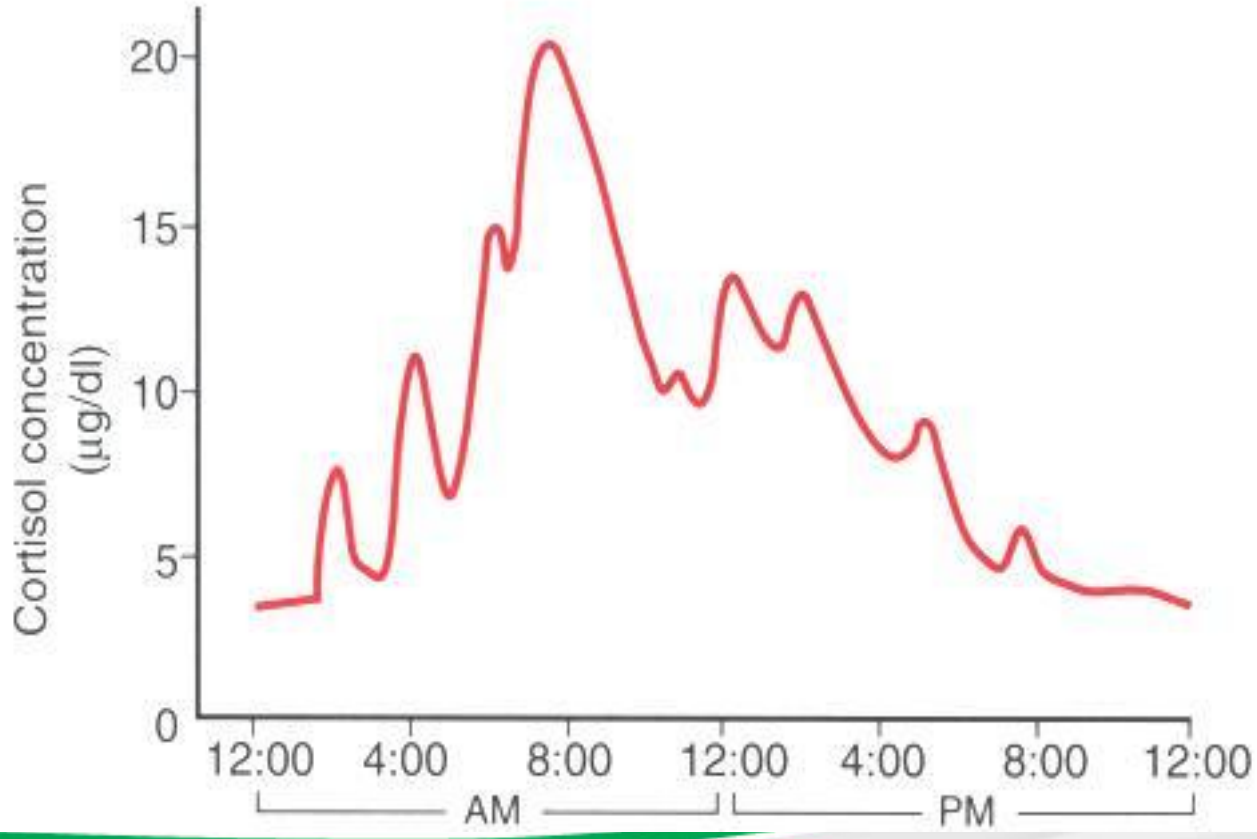
- Physiology of adrenal
- Causes of adrenal insufficiency
- Addison Disease
- Adrenal crisis
- Congenital adrenal hyperplasia
- Cushing Syndrome


Cross section through adrenal gland
Cortex 80%
Medulla 20%
Zones
Main secretory product
Capsule
Glomerulosa – Aldosterone
Fasciculata – Cortisol
Reticularis – Androgens
Medulla – Epinephrine
Norepinephrine

Aldosterone

- Mineralocorticoid
- Regulates concentration of Na+ and K+.
  - Kidney conserves Na+.
  - Kidney excretes K+.
- Responds to changes in composition of plasma.
- Regulated by renin-angiotensin system of kidney

Pattern of cortisole level during the day



Adrenal Dysfunction

Decrease function

- Adrenal insufficiency
- Low cortisol, aldestrone
- Eg Addison disease

Increase function

- Cushing syndrome
  High Cortisol
- Hyperaldosteronism
  High aldestrone
- Pheochromocytoma
  High catecholamine

Causes of Adrenal insufficiency

- Congenital adrenal hyperplasia
- Addison disease
- Infection (TB, sepsis)
- Adrenoleukodystrophy

Addison disease

- Autoimmune
- Isolated or associated with other autoimmune disease
- Presents with tiredness, weight loss, skin pigmentation
- Hypotension, hyponatremia, hyperkalemia
- Aldestrone & cortisol low, high ACTH, high renin
- Low sodium , high potasium
- ACTH stimulation test
- Adrenal antibodies
- Treatment : cortisol + aldestrone

Addisonian crisis

- Life threatening complication
- Severe vomiting and diarrhoea followed by dehydration
- Low blood pressure and shock
- Hypoglycemia
- Loss of consciousness
- Treatment: IV fliuds+IV hydrocortisone

Congenital Adrenal Hyperplasia

- Family of inherited disorders of adrenal synthesis
- Autosomal Recessive (M=F)
- Each disorder results from a deficiency of one five enzymes necessary for steroid synthesis
- 21-hydroxylase ↓ is the commonest form

(90–95% of CAH cases)

Steroid biosynthetic enzymes

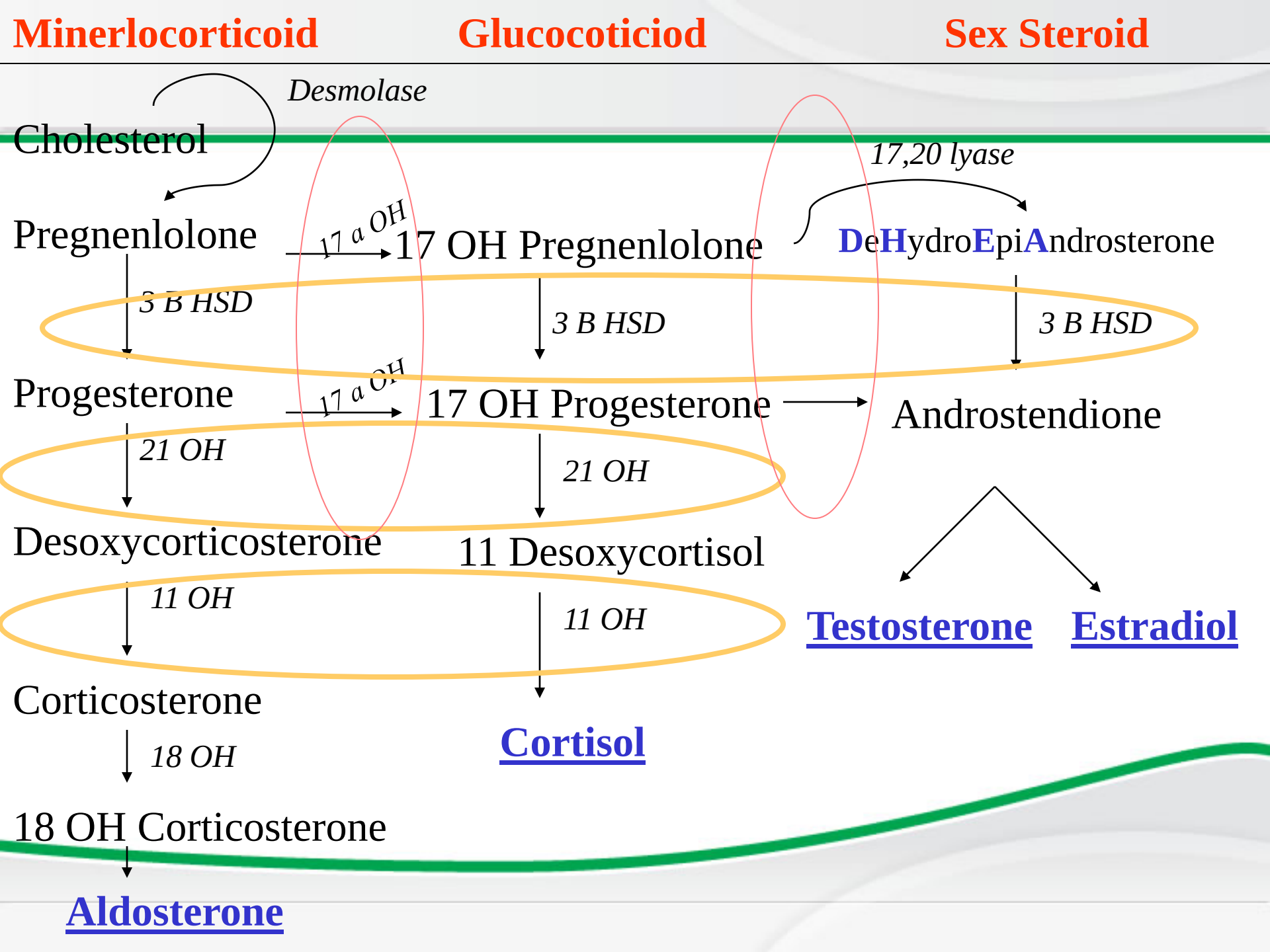
1) Cholesterol side chain cleavage= desmolase)

2) 3β-Hydoxysteroid dehydrogenase

3) 17 α hydroxylase

4) **21β-Hydroxylase**

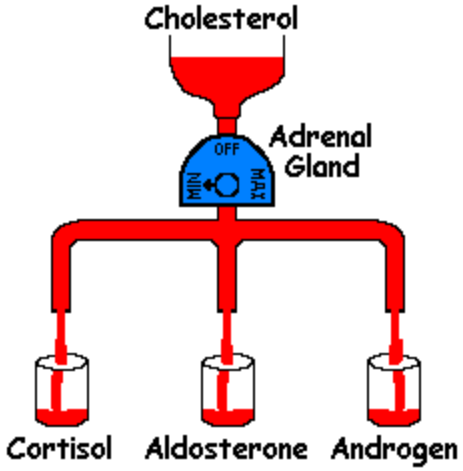
5) 11β-Hydroxylase


Minerlocorticoid
Glucocoticiod
Sex Steroid
Desmolase
Cholesterol
Pregnenlolone
17 a OH
17 OH Pregnenlolone
17,20 lyase
DeHydroEpiAndrosterone
3 B HSD
3 B HSD
3 B HSD
Progesterone
17 a OH
17 OH Progesterone
Androstendione
21 OH
21 OH
Desoxycorticosterone
11 Desoxycortisol
11 OH
11 OH
Testosterone
Estradiol
Corticosterone
18 OH
Cortisol
18 OH Corticosterone
Aldosterone

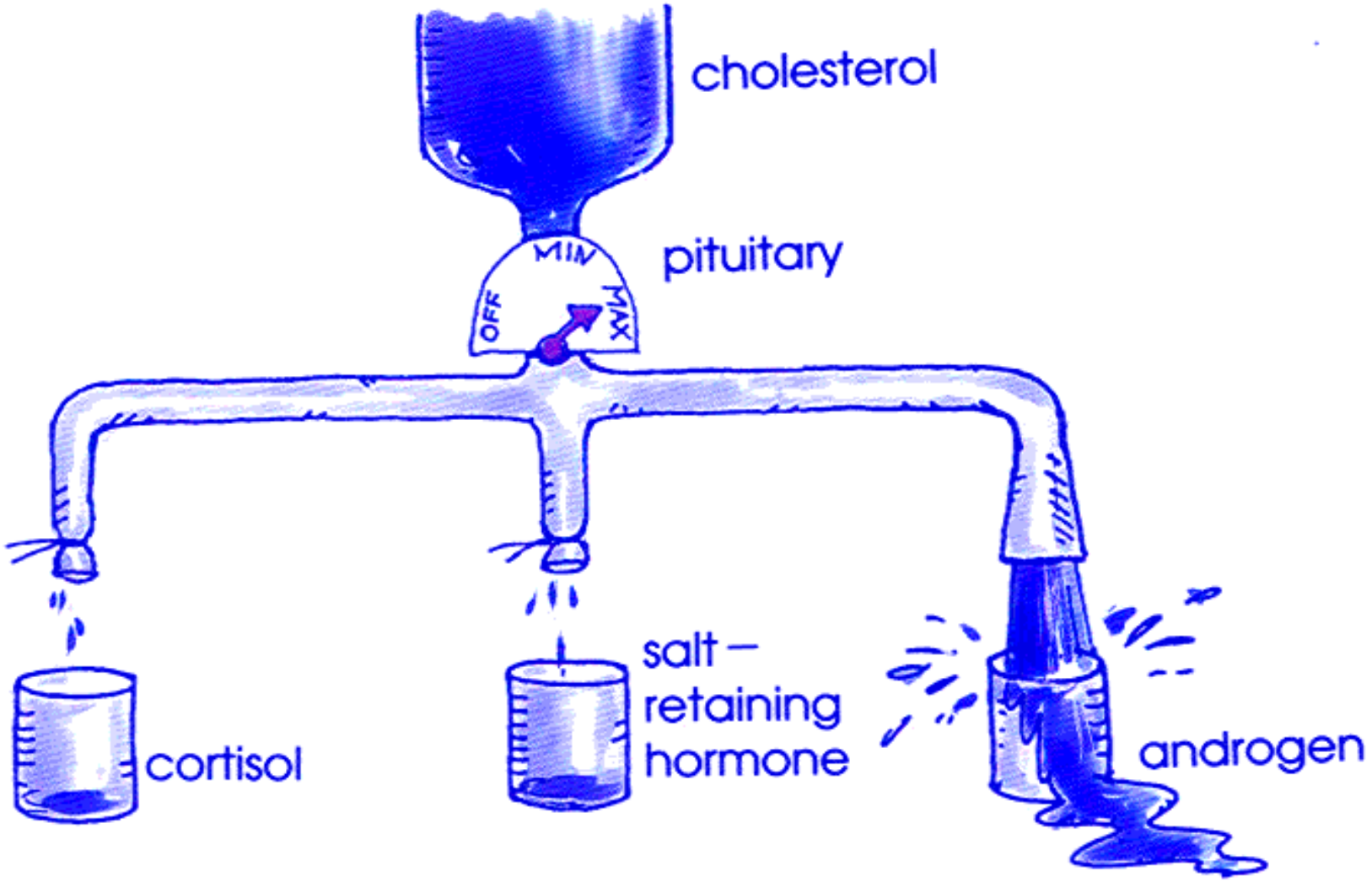
21-OH CAH: Pathophysiology

- 21-OH deficiency → cortisol deficiency ± aldosterone deficiency
- Cortisol deficiency → increased ACTH secretion → excess secretion of the precursor steroids 17-OHP → hyperplastic changes of the adrenal cortex
- The increased circulating 17-OHP: diagnostic for 21-OH deficiency
- The precursor steroids metabolized by the androgen biosynthetic pathway→ excess androgen production → virilizes the genitalia
- Females affected with severe, classic 21- OHD are exposed to excess androgens prenatally and are born with virilized external genitalia
- Aldosterone deficiency → SW

Congenital Adrenal Hyperplasia



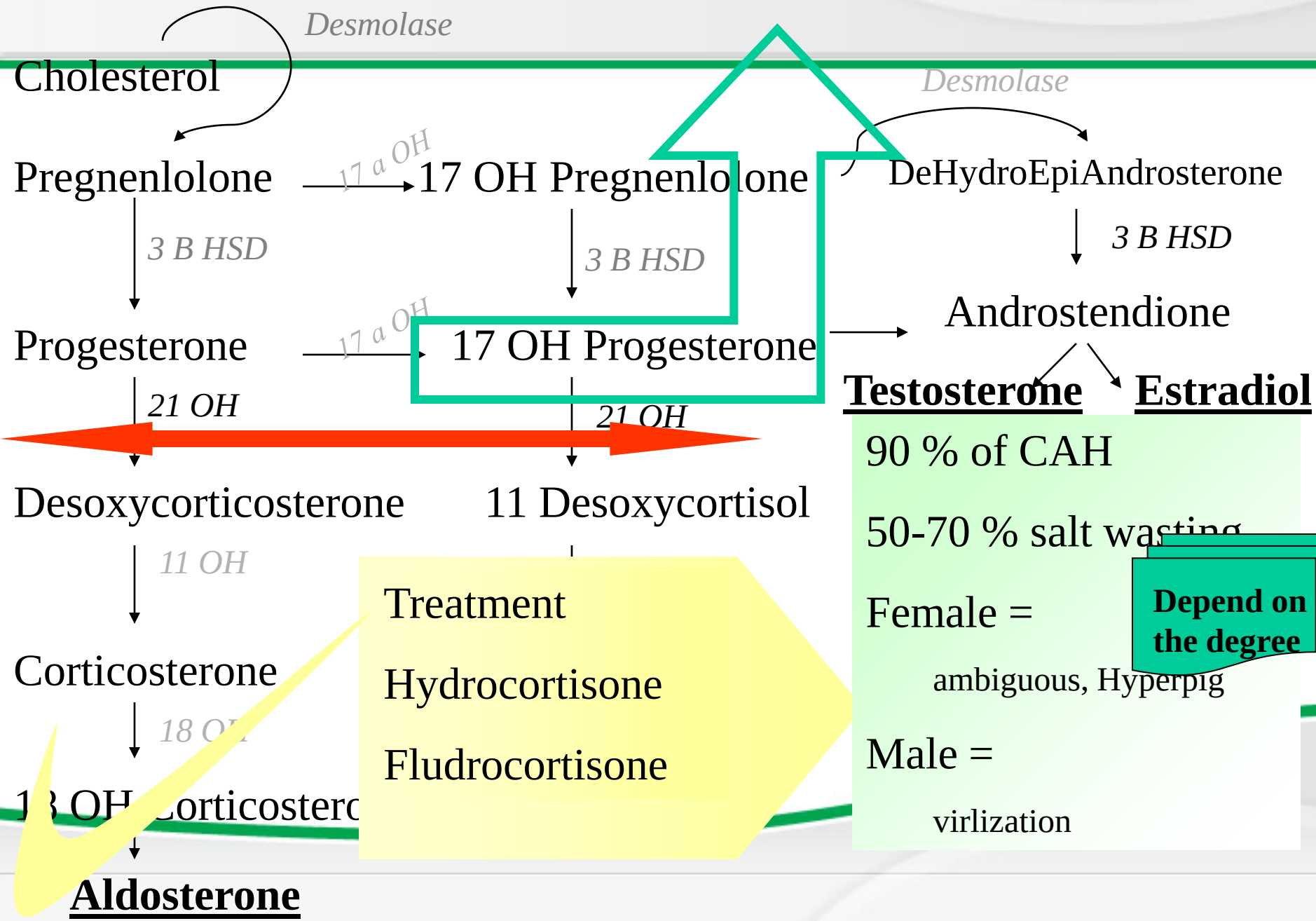
Congenital Adrenal Hyperplasia



21-OH CAH: Clinical phenotypes

1. “Classic, severe” salt-wasting (SW) form
2. “Classic, less severe” simple-virilizing (SV)
3. “Mild, non-classic” forms

21-OH CAH:


Desmolase
Cholesterol
Pregnenlolone
17 a OH
17 OH Pregnenlolone
Desmolase
DeHydroEpiAndrosterone
3 B HSD
3 B HSD
3 B HSD
Androstendione
Progesterone
17 a OH
17 OH Progesterone
Testosterone
Estradiol
21 OH
21 OH
Desoxycorticosterone
11 Desoxycortisol
11 OH
Corticosterone
18 OH
Aldosterone
Treatment
Hydrocortisone
Fludrocortisone
90 % of CAH
50-70 % salt wasting
Female =
ambiguous, Hyperpig
Male =
virlization
Depend on the degree

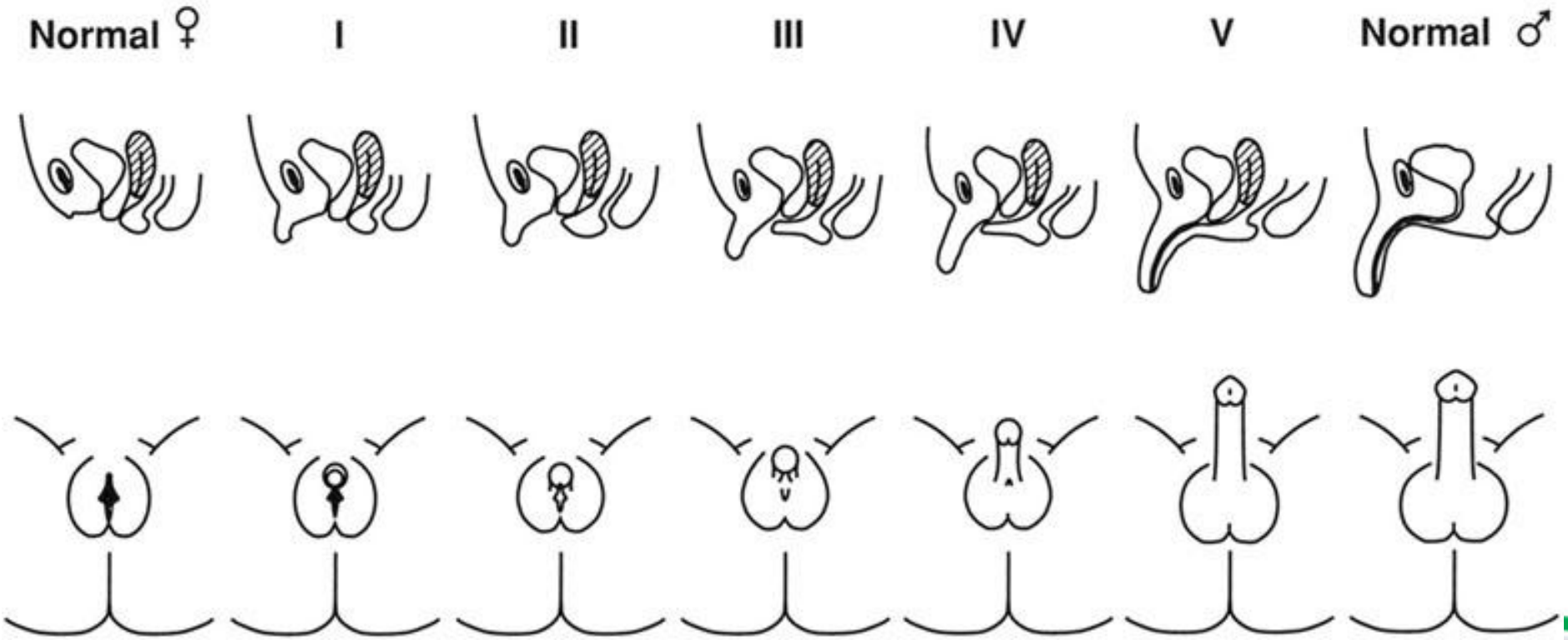
Salt wasting form

- Salt wasting form
  - Adrenal crisis in the 1st-4th weeks of life, peaking at 3rd
  - Poor feeding, vomiting, diarrhea, FTT
- Dehydration
- Shock
- Electrolytes imbalance
  - Hyponatremia
  - Hyperkalaemia
- Hypoglycemia
- Hyperpigementations
  - If untreated → circulatory collapse → shock → death
  - Perminant brain injury due to shock and hypoglycemia → lower IQ

Simple virilizing form 21-OH CAH

- Simple virilizing form
  - No adrenal-insufficiency symptoms unless subjected to severe stress but exhibit virilization
  - Girls present with ambiguous genetalia at birth
  - Males usually not diagnosed until later (virilization, precocious, growth acceleration)
  - Advanced skeletal age diagnosed late → short adult stature

Prader Classification of Virilization



Nonclassical CAH

- Residual enzyme activity.
- Non salt losing CAH
- present late in childhood with precocious pubic hair and/or clitoromegaly and accelerated growth.
- Present in adolescence or adulthood with varying virilizing symptoms ranging from oligomenorrhea to hirsutism and infertility.

Diagnosis

- Serum electrolytes & glucose
  - Low Na & high K
  - Fasting hypoglycemia
  - Elevated serum urea due to associated dehydration
- Elevated plasma Renin & ACTH levels
- Low Cortisol
- High 17 – OHP
- High androgens especially testosterone level
- Low Aldosterone
- Urinary steroid profile
- Chromosomes
- Pelvic US

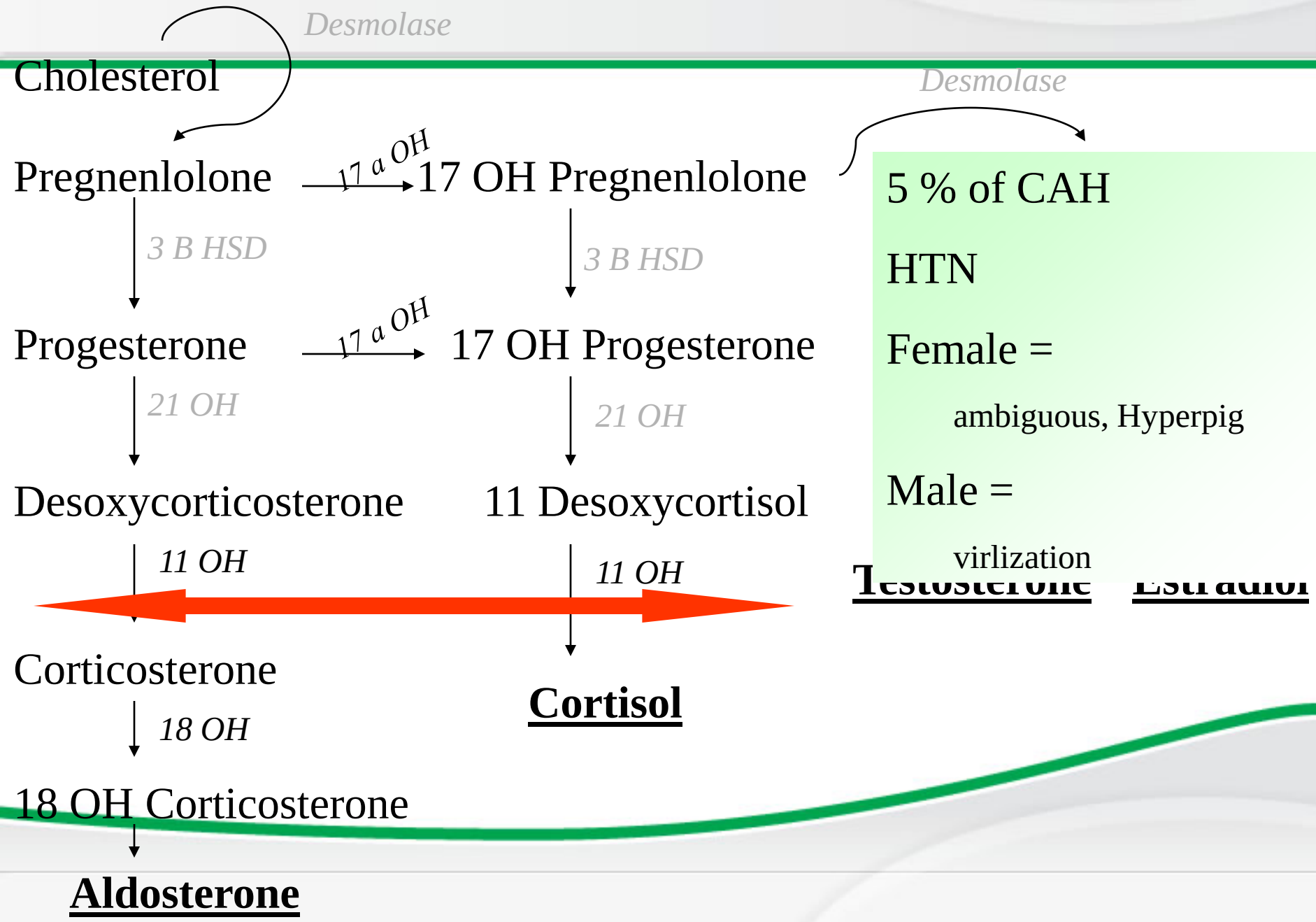
Management

- Hydrocortisone
- Fludrocortisone 0.05 - 0.2 mg/day
- Triple hydrocortisone duiring stress.
- During adrenal crisis intravenous hydrocortisone and IV fliud
- Surgery for female external genetalia
- Antenatal diagnosis and treatment

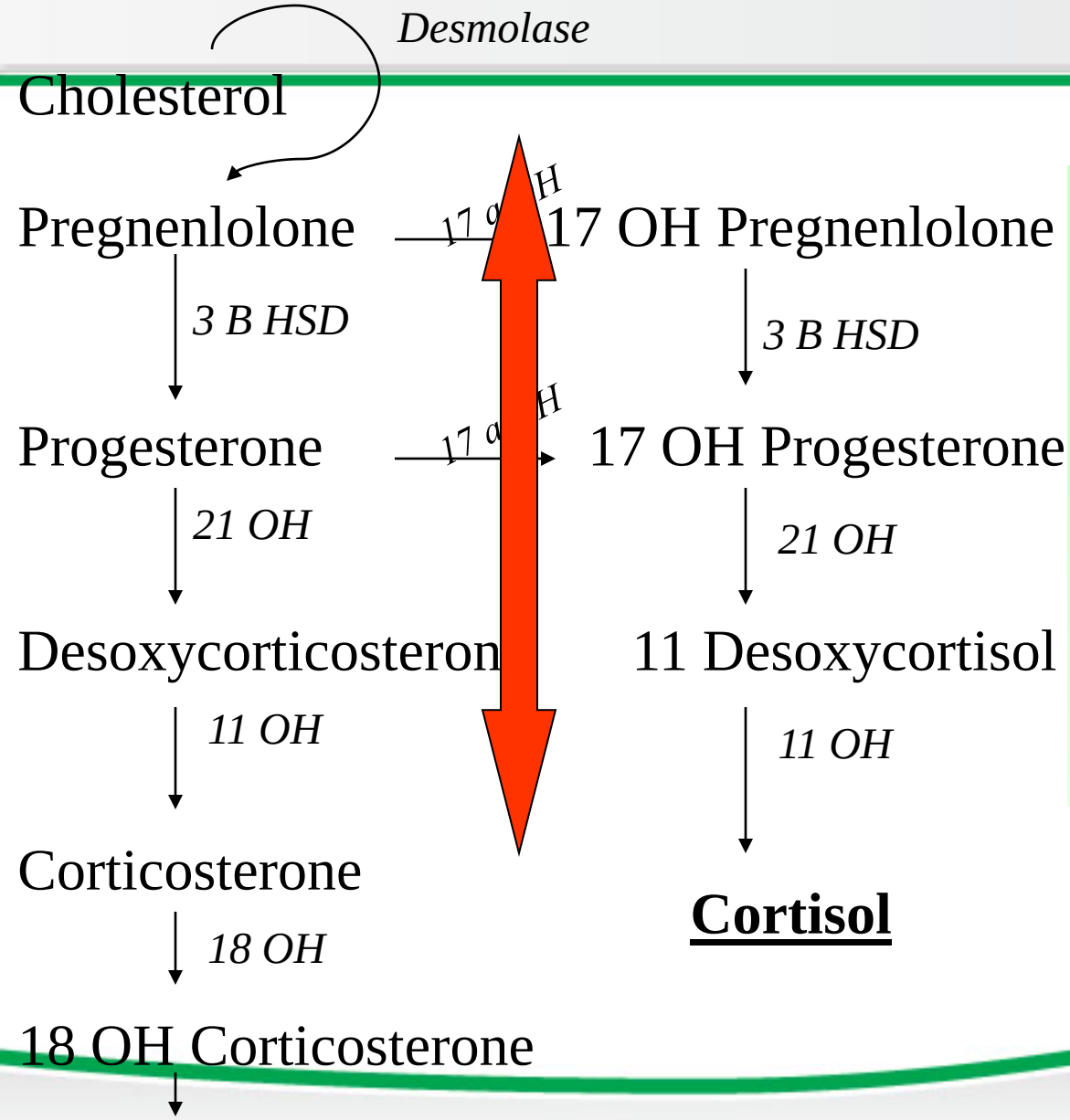
Newborn screening for CAH

- Neonatal screening by filter paper on 3rd day of life
- 17 Hydroxyprogestrone blood level (17 OHP)

11 Hydroxylase Deficiency:



17 Hydroxylase Deficiency:



Desmolase

HTN

Hypokalemic alkalosis

Female =

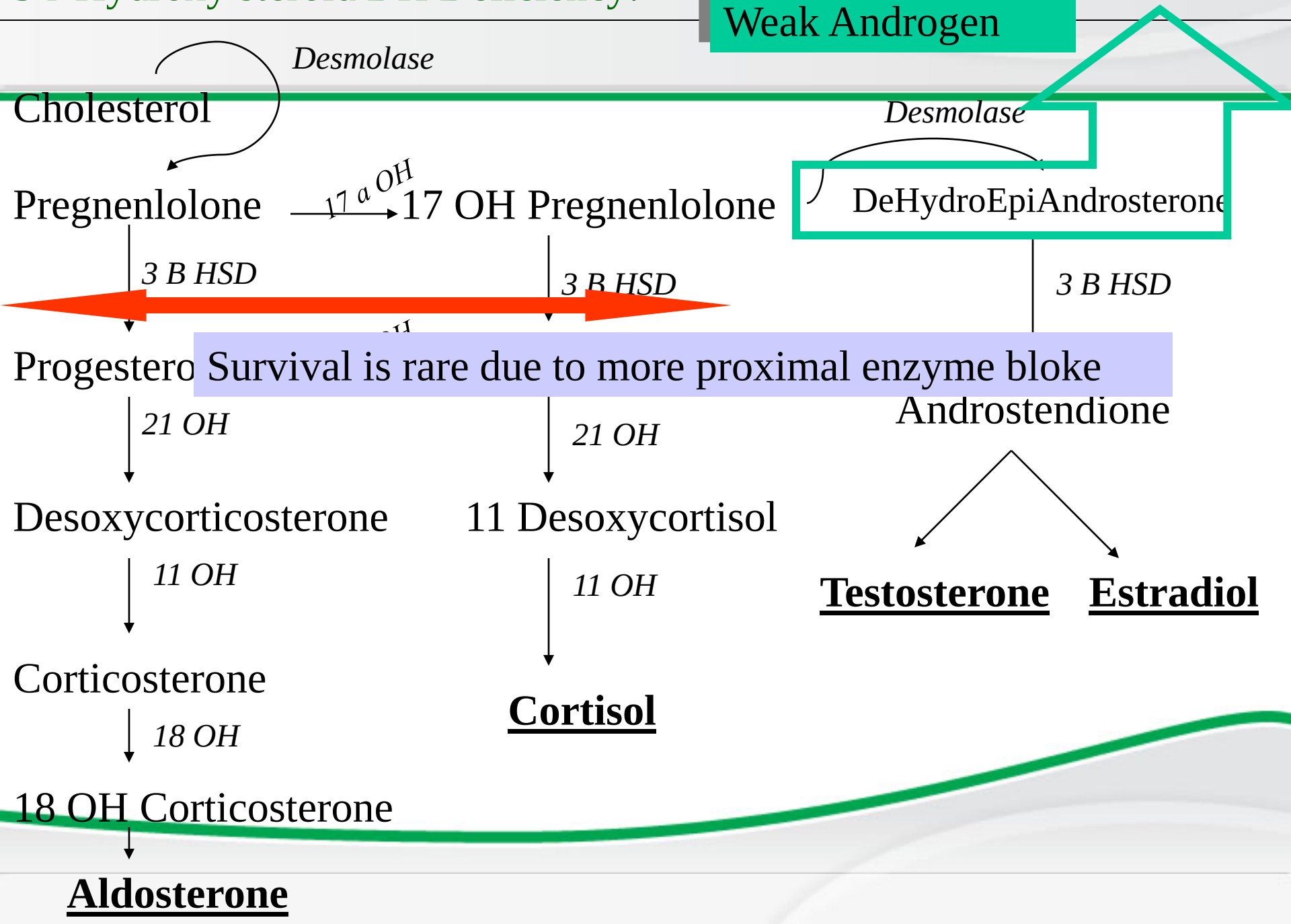
Normal

Male =

Ambiguous

3 β Hydroxy steroid DH Deficiency:

Weak Androgen

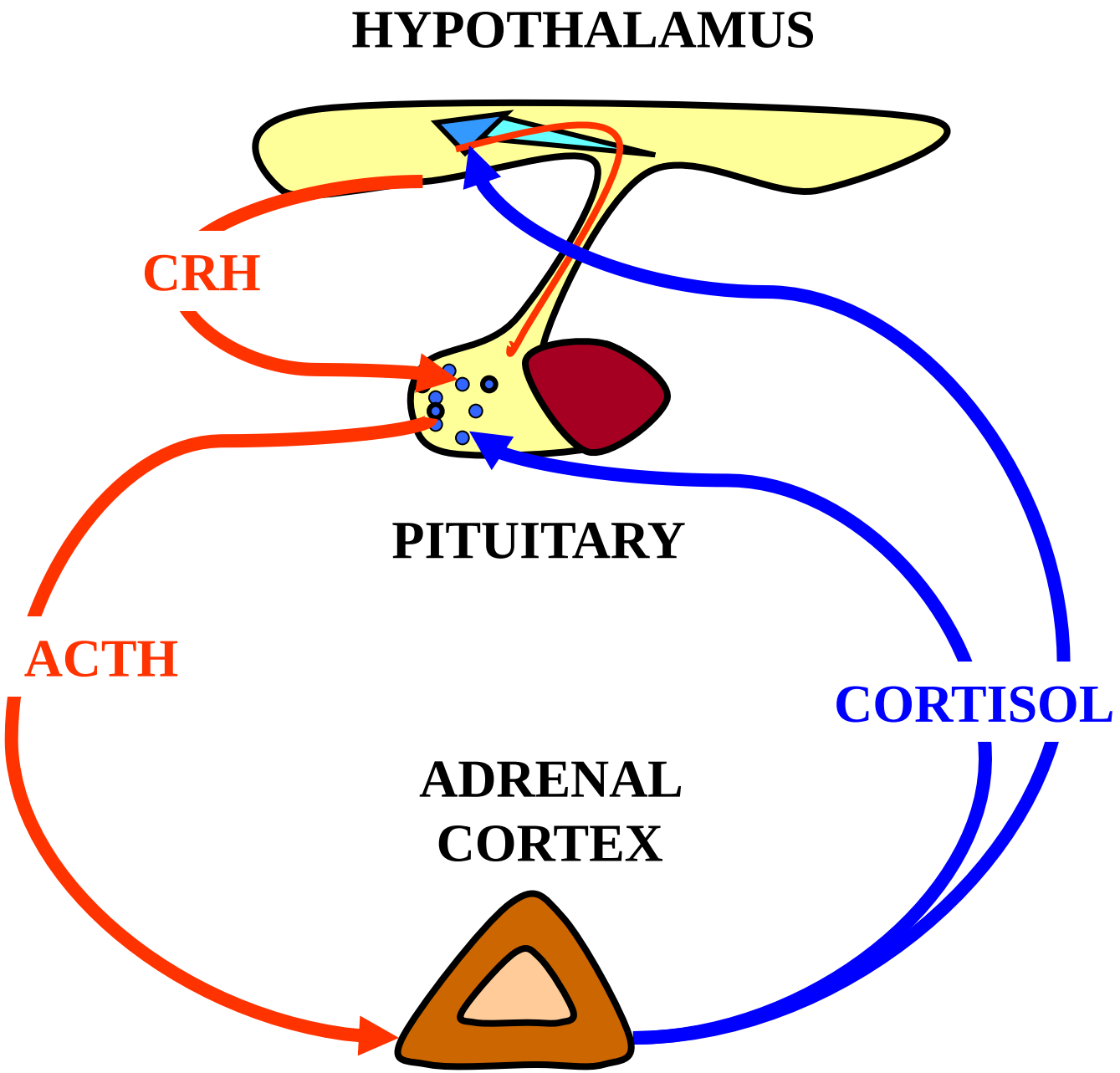


Congenital Lipoid Adrenal Hyperplasia

- **Inability to convert cholesterol to pregnenolone thus all 3 classes of steroids are absent**
- **Clinical Manifestations:**
  - Salt-losing crisis
  - XX and XY have female genitalia
  - Massive cholesterol accumulation in adrenal cortex
  - Absent puberty in males
  - Females may have puberty

Definitions

- Cushing's Syndrome
  - Excess cortisol in the blood
- Cushing's Disease
  - Excess cortisol in the blood due to an ACTH secreting pituitary tumour


HYPOTHALAMUS
CRH
PITUITARY
ACTH
CORTISOL
ADRENAL
CORTEX

Cushing's syndrome

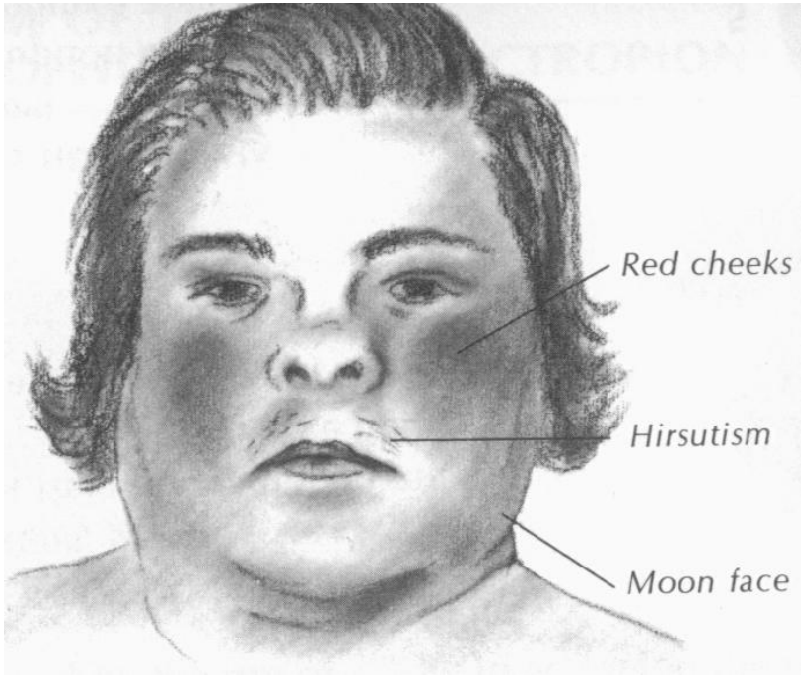
- Cushing's Syndrome
  - Results from increased adrenocortical secretion of cortisol
  - Causes include:
    - ACTH-secreting tumor of the pituitary (Cushing's disease)
    - excess secretion of cortisol by a neoplasm within the adrenal cortex
    - ectopic secretion of ACTH by a malignant growth outside the adrenal gland
    - excessive or prolonged administration of steroids

Differential Diagnosis of Cushing's Syndrome

Diagnosis	ACTH	Cortisol
Pituitary tumor	High	High
Ectopic ACTH	High	High
Adrenal tumor	Low	High
Exogenous cortisol	Low	High
Exogenous prednisone or dexamethasone	Low	Low

Cushing's syndrome

- Cushing's Syndrome
  - Characterized by:
    - truncal obesity
    - moon face
    - buffalo hump
    - acne, hirsutism
    - abdominal striae
    - hypertension
    - psychiatric disturbances
    - osteoporosis
    - Amenorrhea
    - Diabetes



Establishing the Cause

- Serum ACTH, cortisol and urine free cortisol
- CRH stimulation test
- Dexamethasone Suppression testing
- Localisation of the ACTH source
  - Imaging (MRI)

Treatment of Cushing's syndrome

- Treatment of underline cause
- Surgery for neoplasia