Diseases of hypophysis and adrenal gland

Diseases of hypophysis

Hypophysis

In sella turcica

0,4 - 0,9 g

Together with hypothalamus is the main controling and regulating endocrine system

= **hypothalamo-hypophyseal axis**

- Anterior lobe
- Posterior lobe
- Stalk

Hypophysis

Neurohypophysis

= posterior lobe

- from extension of hypothalamus

- axons of neurons from hypothalamus (paraventricular and supraoptic nucleus) with Herring bodies
- pituicytes
  = modified glial cells
- blood vessels

Hypophysis

Neurohypophysis

- Oxytocin
- Antidiuretic hormone (ADH)

Hypophysis

Adenohypophysis

= anterior lobe

- from Rathke's pouch

- Eosinophilic cells
- Basophilic cells
- Chromophobic cells

Hypophysis

Adenohypophysis

- Growth hormone (GH) 50%
  = somatotropin (STH)
- Adrenocorticotropic hormone (ACTH) 15%
- Thyroid-stimulating hormone (TSH) 5%
- Gonadotropic hormones 10%
  - Luteinizing hormone (LH)
  - Follicle-stimulating hormone (FSH)
- Prolactin (PRL) 20%
- Melanocyte-stimulating hormone (MSH)

Developmental disorders

- **Ectopia**
  - adenohypophyseal cells in the nasopharynx
  - residual squamous epithelium between neuro- and adenohypophysis

- **Hypoplasia / Aplasia**
  - rare

Hypopituitarism

= disorder caused by destruction of at least 80% of adenohypophysis

- Causes:
  - Sheehan syndrome
    (hypoperfusion caused by massive bleeding during labor)
  - Trauma
  - Tumours of sella turcica
  - Inflammatory disorders (autoimmune diseases, TBC, sarcoidosis...)
  - Radiotherapy
  - ...

Hypopituitarism

Signs and symptoms

- ↓ GH ⇢ proportional nanism (only in children)
- ↓ prolactin ⇢ no lactation after labor
- ↓ ACTH ⇢ secondary adrenal insufficiency (=“white Addison”)
- ↓ TSH ⇢ central hypothyreosis
- ↓ LH and FSH ⇢ amenorrhea, atrophy of gonads, decrease of libido, loss of secondary sex characteristics, osteoporosis...
- ↓ ADH ⇢ central type of diabetes insipidus

Hyperplasia of hypophysis

= diffuse of nodular enlargement of hypophysis

- **Physiological**:
  - During pregnancy
- **Pathological**:
  - Peripheral hypothyrerosis
  - Peripheral hypogonadism (castration)
  - Paraneoplastic
    (tumours producing hormones similar to hypothalamic “releasing” hormones)

Pituitary adenomas

= benign tumours of adenohypophysis

- The most common cause of **hyperpituitarism**
  (oversecretion of 1/more pituary hormones)
  ! but most are **non-secretory** !

- <u>Gross</u>:
  - Capsulated soft tumour
  - Size differs from mm to cm

Pituitary adenomas

Signs and symptoms - based on size

- **Microadenomas** (< 10 mm)
  - ussually asymptomatic
- **Macroadenomas** (> 10 mm)
  - hypopituitarism
- **Giant adenomas** (> 40 mm)
  - hypopituitarism, **bitemporal hemianopsia** and intracranial hypertension
    +/- slighly ↑ PRL

Pituitary adenomas

Signs and symptoms - based on producing hormone

- PRL
- GH
- ACTH
- TSH
- FSH / LH

- Plurihormonal adenomas

Pituitary adenomas

Signs and symptoms - based on producing hormone

- **PRL (prolactinomas)** = most common (30 %)

  ♀ amenorhea, galactorhea

  ♂ gynecomastia, decreased libido, galactorhea

Pituitary adenomas

Signs and symptoms - based on producing hormone

- **GH**
  - **Gigantism** (children)
    - proportianal
    - organomegaly
  - Acromegaly (adults)

Pituitary adenomas

Signs and symptoms - based on producing hormone

- **GH**
  - Gigantism (children)
  - **Acromegaly** (adults)
    - prominent acral parts of body
    - organomegaly
    - osteoporosis, hypertension, DM...

Pituitary adenomas

Signs and symptoms - based on producing hormone

- **ACTH**
  - Cushing disease
- **TSH**
  - Hyperthyreosis
- **FSH / LH**
  - Asymptomatic

Pituitary adenomas

Familiar syndromes

- **Multiple endocrine neoplasia 1** (MEN 1)
  - mutation of gene *MEN1* (encodes protein *Menin*); AD
  - manifestation in middle age
  - **hyperplasia** / **adenoma of parathyroid gland**
    + **pituitary adenomas** (prolactinoma with/without production of GH)
    + **tumours of endocrine pancreas** (insulinoma / gastrinoma / ...)
    +/- adrenal cortical adenomas
    +/- bening mesenchymal tumours of skin (lipoma / angiofibroma / ...)
- Other genes associated with familiar pituary adenomas: *CDKN1B*, *PRKAR1A* and *AIP*

Other tumours of hypophysis

- **Pituitary carcinoma**
  - extremely rare, most of them secretory
  - defined by presence of **distant metastasis**
    - subarachnoideal
    - hematogenic - liver, lung, bones...
- **Craniopharyngeoma**
  - probably arises from remnants of Rathke's pouch
  - bening
  - manifestation depends on size
- Gliomas, germ cell tumours, chordoma, metastases...

Diseases of adrenal glands

Adrenal gland

Pair organ

8-10 g

- Adrenal cortex
- Adrenal medulla

Adrenal gland

Medulla

- from neural crest

- chromaffin cells
- sustentacular cells
- ganglion cells
- blood vessels

- catecholamins
  (norepinephrin and epinephrin)

Adrenal gland

Cortex

- from mesoderm

- Zona glomerulosa
- Zona fasciculata
- Zona reticularis

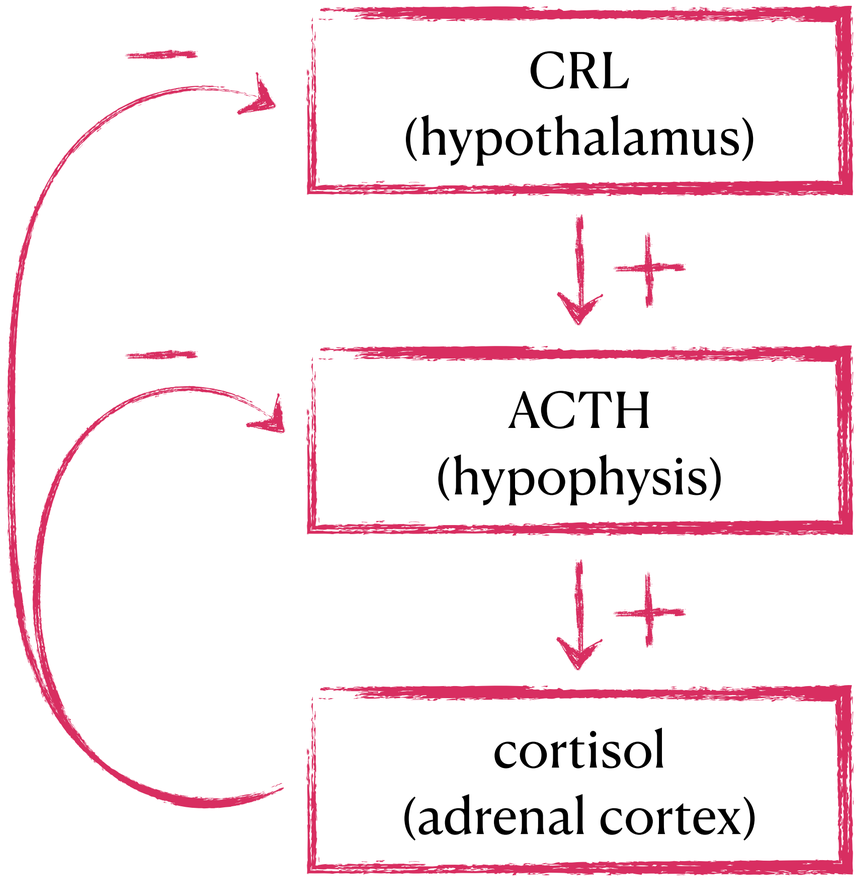
Adrenal gland

Cortex

- from mesoderm

- **Zona glomerulosa**
  - mineralocorticoids (aldosteron)
  - regulation mainly through renin-angiotensin-aldosteron system (RAA)
- Zona fasciculata
- Zona reticularis

Adrenal gland



Cortex

- from mesoderm

- Zona glomerulosa
- **Zona fasciculata and reticularis**
  - glucocorticoids (cortisol)
  - androgens
  - regulation through hypothalamo-hypophyseal axis (ACTH)

Primary adrenal insufficiency

= disorder caused by destruction of at least 80% of adrenal cortex

- ussually insufficiency of all 3 types of hormones
- Causes:
  - inflammatory disorders (autoimmune epinephritis, TBC...)
  - haemorrhage (Waterhause-Friedrichsen syndrom...)
  - adrenal tumours (primary / metastasis)
- Laboratory markers:
  - ↓ cortisol and ↑ ACTH
    (vs. secondary adrenal insufficiency - ↓ cortisol and ↓ ACTH)

Primary adrenal insufficiency

Chronic adrenal insufficiency (Addison disease)

- mostly caused by **autoimune epinephritis**
  - associated with **autoimune polyendocrine syndrom** (mutation of gene *AIRE*)
- Signs and symptoms:
  - fatigue, weekness, depression, weight loss, loss of body hair...
  - abdominal pain, diarrhoea/constipation...
  - hypotension, hypoglycaemia, ↓Na+, ↑K+
  - hyperpigmentation - skin creases (palms), nipple, buccal mucosa... +/- vitiligo

Primary adrenal insufficiency

Acute adrenal insufficiency (Addisonian crisis)

- endocrinologic emergency with high mortality rate
- Causes:
  - **acute stress event in patients with chronic adrenal insufficiency**
  - massive haemorrhage (Waterhause-Friedrichsen syndrome...), iatrogenic...
- Signs and symptoms:
  - extreme fatigue and weekness, vomiting, diarrhoea, abdominal pain
  - hypotension, hypoglycaemia, fainting
  - arrhythmia, mineral disbalance

Hypercortisolism

= overproduction of cortisol

- **Primary hypercortisolism** = **Cushing syndrome**
  - tumours of adrenal cortex (adenoma / carcinoma)
  - iatrogenic (exogenic intake)
  - ↑ cortisol, ↓ ACTH
- **Secondary hypercortisolism** = **Cushing disease**
  - hyperplasia / tumours of pituitary gland
  - *paraneoplastic (ectopic production of ACTH in tumours - SCLC...)*
  - ↑ cortisol, ↑ ACTH

Hypercortisolism

Signs and symptoms

- disproportional (centrally dominant) obesity
- muscle atrophy
- “moon face” with facial flush, buffalo hump
- skin atrophy, red striae, hematomas
- poor wound healing
- hypertension, steroid diabetes
- osteoporosis (risk of pathological fractures)
- ↑ risk of infectious diseases

Hyperaldosteronism

= overproduction of aldosteron

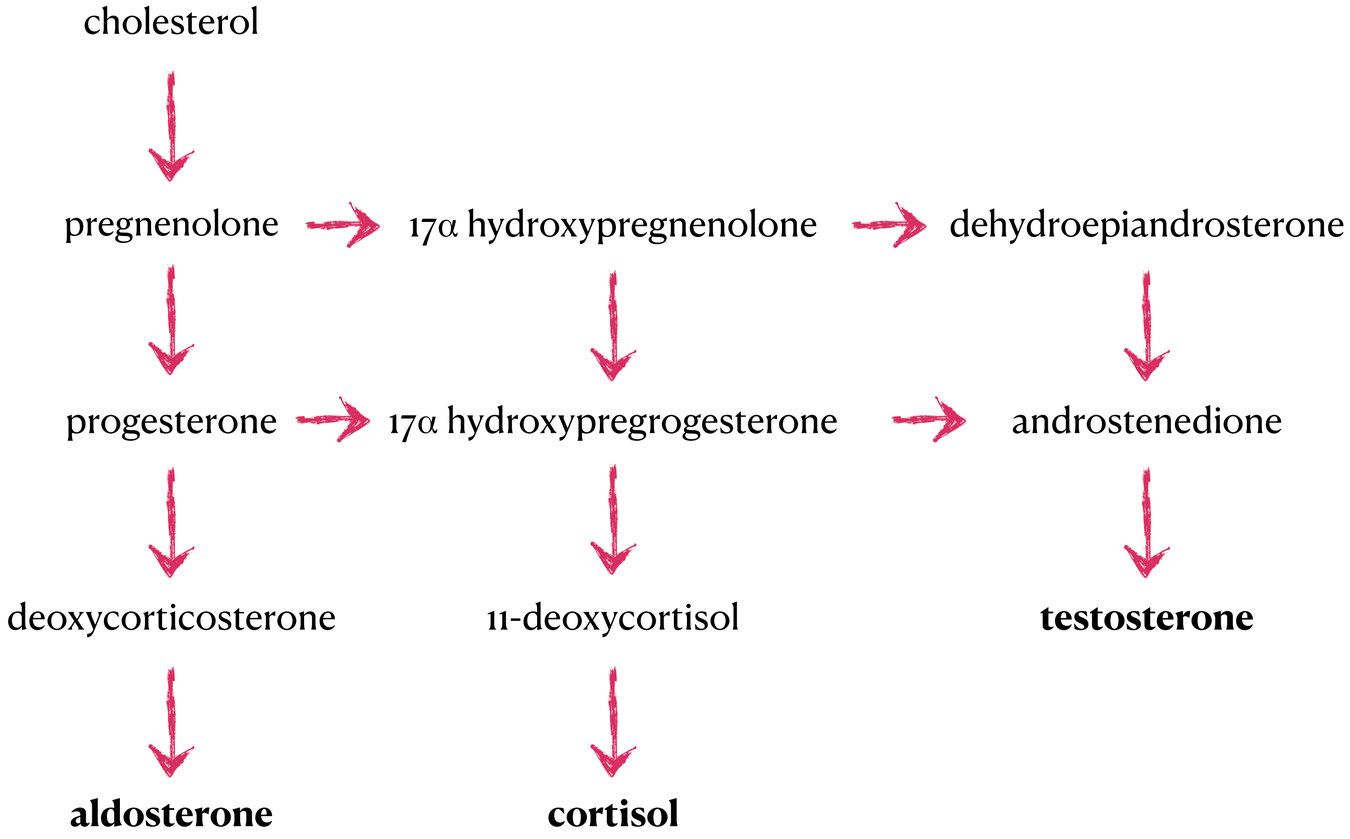
- **Primary hyperaldosteronism**
  - adrenal cortical **adenoma** (= Conn's syndrome) / hyperplasia of adrenal cortex
- **Secondary hyperaldosteronism**
  - activation of RAA system in ↓ renal perfusion

- <u>Signs and symptoms</u>:
  - ↑ Na+ ⇢ systemic hypertension, oedema...
  - ↓ K+ ⇢ fatigue, obstipation, arrhythmia...

Adrenogenital syndrome

= overproduction of androgens

- **Aquired**
  - adrenal cortical adenoma
  - adrenal cortical carcinoma
- **Congenital**
  = congenital adrenal hyperplasia
  - enzyme deficiencies
  - most common
    = deficiency of 21-hydroxylase



Adrenogenital syndrome

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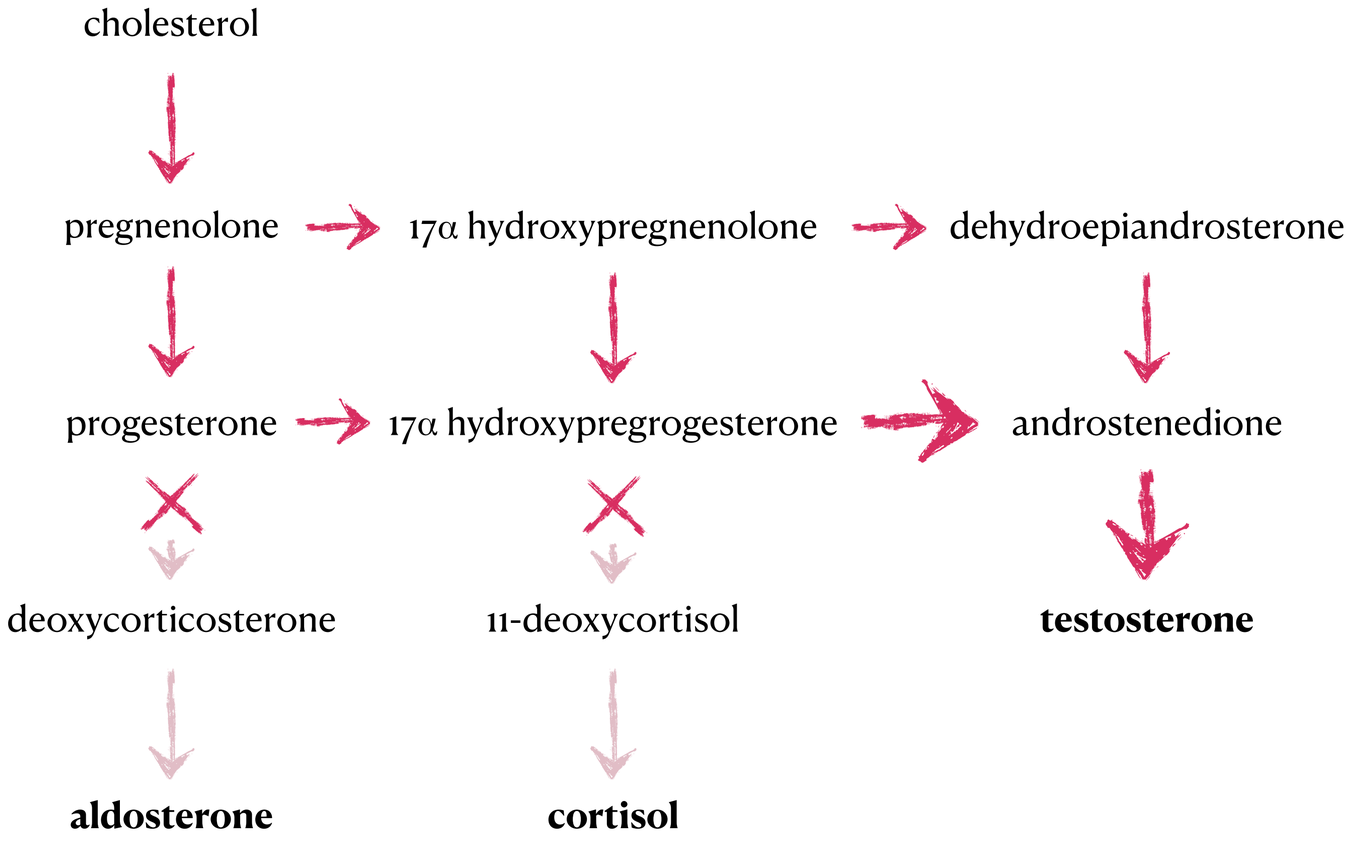

Adrenogenital syndrome

Symptoms and signs

- **Childhood**

  ♀ virilisation of external genitals
  / pseudopubertas heterosexualis praecox

  ♂ pseudopubertas isosexualis praecox

  +/- hypotension, ↓ Na+, ↑ K+

- **Adulthood**

  ♀ virilisation (acne, hirsutism, frontal hair thining,
  deepening of voice, anovulation...)

  ♂ asymptomatic

  +/- hypotension, ↓ Na+, ↑ K+

Tumours of adrenal cortex

Adrenal cortical adenoma

Adrenal cortical carcinoma

Myelolipoma

Tumours of adrenal cortex

Adrenal cortical adenoma

- often accidental finding of CT / MRI
- ussually in adults (5th - 7th decade), ♀ > ♂
- most are non-secretory
- if secretory than ussually production of cortisol / aldosteron
- Gross:
  - encapsulated ovoid mass
- Histopathology:
  - resembling normal adrenal cortex
- Genetic syndromes: von Hippel-Lindau syndrome

Tumours of adrenal cortex

Adrenal cortical carcinoma

- less common
- any age, ♀ > ♂
- approximately 50% are non-secretory
- Gross:
  - invasive, hemorrhage, necrosis...
- Histopathology:
  - atypia, mitosis...
- Genetic syndromes:
  - Li-Fraumeni syndrome...

Tumours of adrenal cortex

Myelolipoma

- bening mesenchymal tumour
- adults (5th - 7th decade), ♀ = ♂
- ussually asymptomatic
- Gross:
  - encapsulated yellow to red mass
- Histopathology:
  - mature adipocytes
  - trilineage hematopoesis
    (with full maturation)

Tumours of adrenal medulla

Pheochromocytoma

Neuroblastoma

Tumours of adrenal medulla

Pheochromocytoma

= intra-adrenal sympatic paraganglioma

- “rule of 10%”
  - 10% familial
  - 10% bilateral
  - 10% extrarenal (= paraganglioma)
  - 10% malignant

→ neuroendocrine tumour with production of catecholamins (norepinephrine)
⇢ hypertension typically paroxysmal with headache

- Genetic syndromes: von Hippel-Lindau, MEN 2, neurofibromatosis type 1

Tumours of adrenal medulla

Pheochromocytoma

- neuroendocrine tumour with production of catecholamins (norepinephrine)
  ⇢ hypertension typically paroxysmal
  + headache
- Gross:
  - pink-gray soft mass +/- hemorrhage
- Histopathology:
  - solid alveolar architecture
  - polygonal tumour cells
  - sustentacular cells

Tumours of adrenal medulla

Neuroblastoma

- neuroectodermal tumour
- in little children (first years of life)
- mostly in adrenal medulla, but also extraadrenal
- Gross:
  - white to soft greys mass
    +/- hemorrhage, calcificaions, necrosis...
- Histopathology:
  - neuroblasts forming Homer-Wright rosettes
  - sustentacular cells