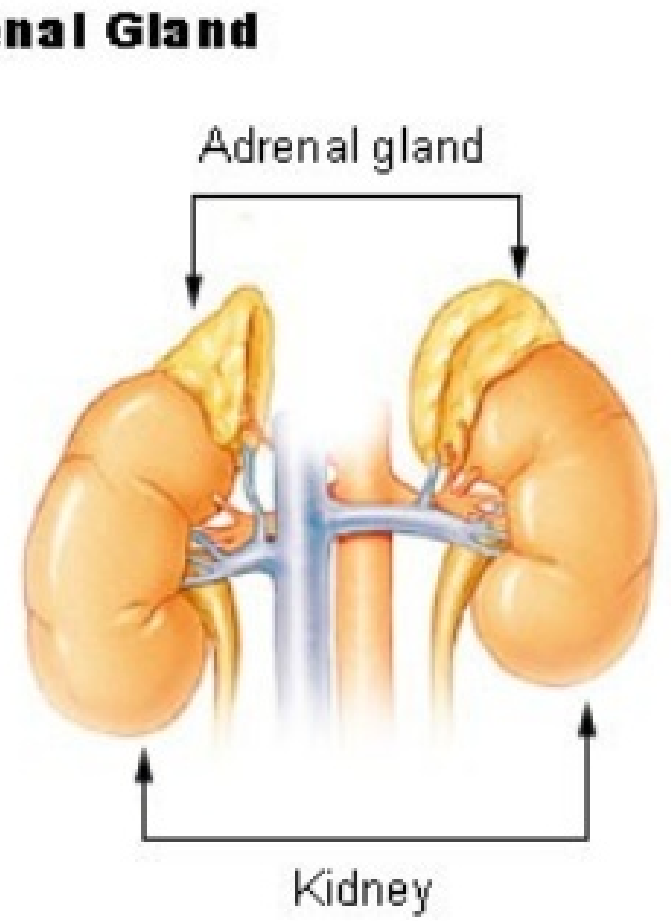
Adrenal Glands

Suprarenal glands

- Paired organ each weight about 4 grams, pyramidal in shape, located on the top of the kidneys, one on each side at the level of the T12

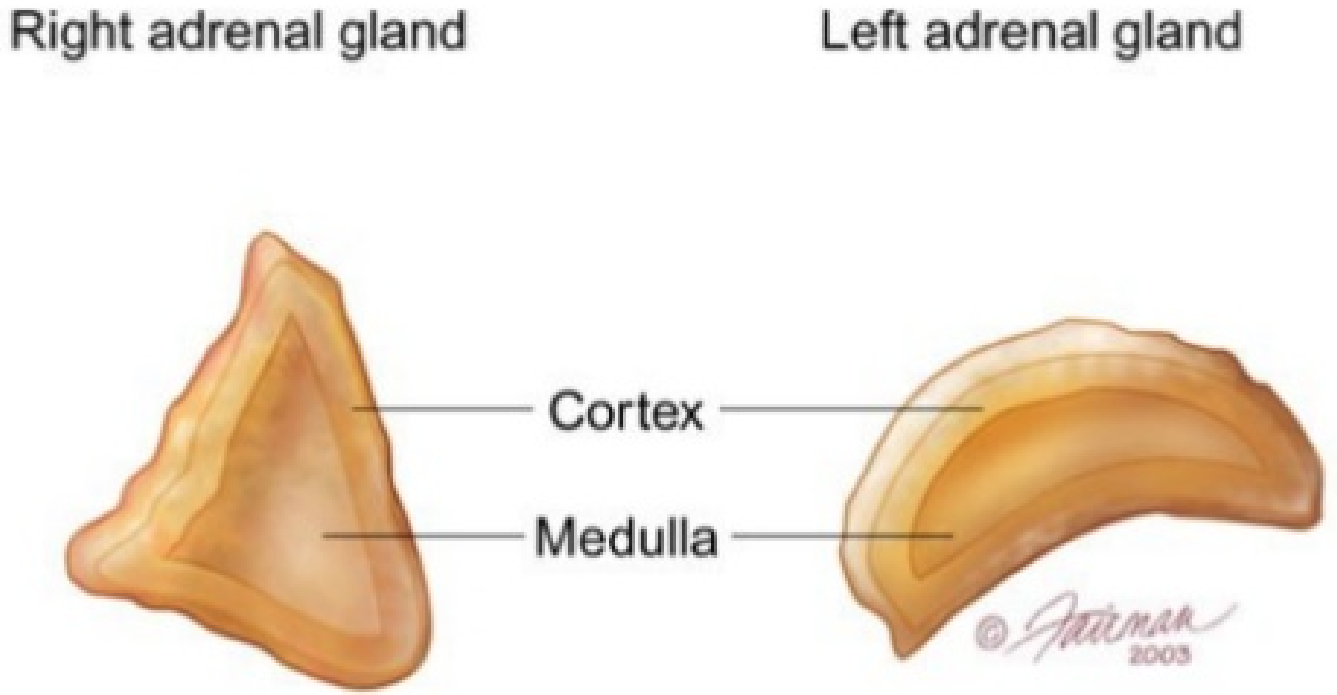
- It enclosed by fibro elastic connective tissue **capsule**.



Adrenal glands

- Each gland is divided into tow parts:
  - **Cortex** – outer part of gland
    - Part of hypothalamus – pituitary – adrenal axis
    - Secrete a variety of steroid hormones
  - **Medulla** – inner part of gland, (20% of gland)
    - Part of sympathetic nervous system
    - Secrete catecholamines
  - Both parts are structurally and functionally different

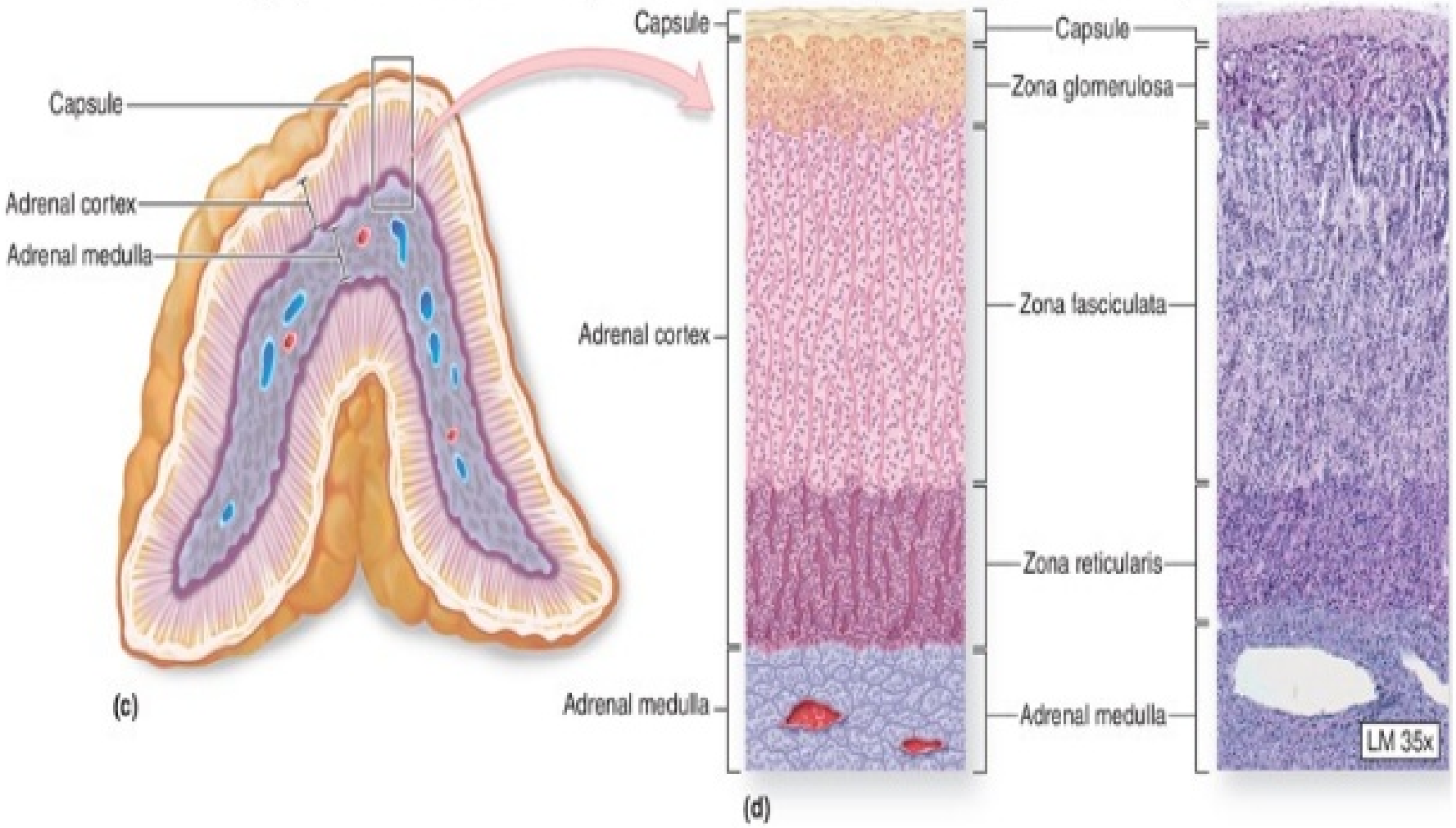
Adrenal glands



Adrenal cortex

- The large cortical cells are arranged into three layers or zones :
  - The **zona glomerulosa**,
    - The thin outermost layer
    - Constitute about 15% of cortex
  - The **zona fasciculata**,
    - The middle and largest portion
    - Constitute about 75% of cortex.
  - The **zona reticularis**,
    - The innermost zone.

Histology of adrenal glands



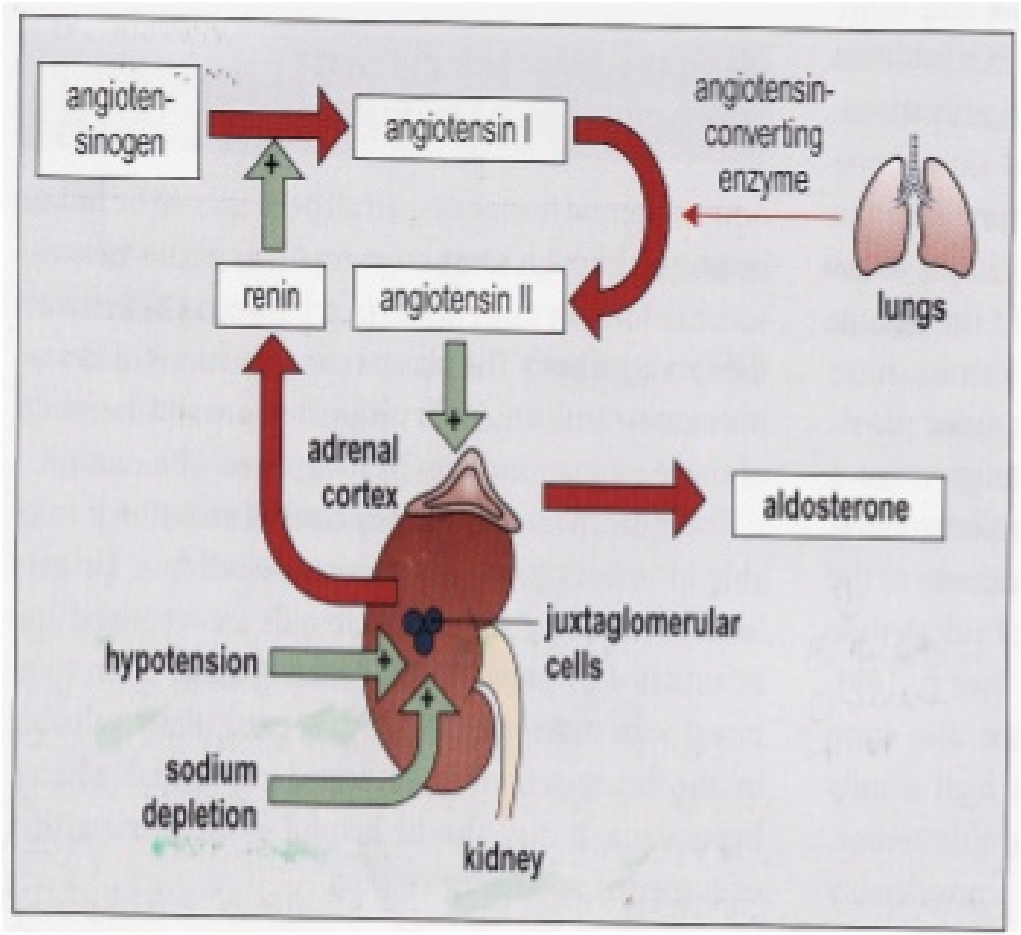
Adrenal cortex

- **Zona glomerulosa:**
  - Produce meniralocorticods
  - Mainly **aldosterone** (because it contain enzyme **aldosterone synthase)**

Hormones that help control the balance of minerals (Na+ and K+) and water in the blood

Adrenal cortex

- **Aldosterone secretion**



Adrenal cortex

- **Zona fasciculata:**
  - Produce glucocorticods
  - Mainly **cortisol and corticosterone**
  - The human adrenal glands produce the equivalent of 35–40 mg of cortisone acetate per day

> Hormone that play a major role in glucose metabolism as well as in protein and lipid metabolism

  - The secretion of these cells is controled by hypothalamic-pituitary axis via ACTH

Adrenal cortex

- **Zona reticularis:**
  - The innermost layer of the adrenal cortex, lying deep to the zona faciculata and superficial to the medulla.
  - These cells produce androgens

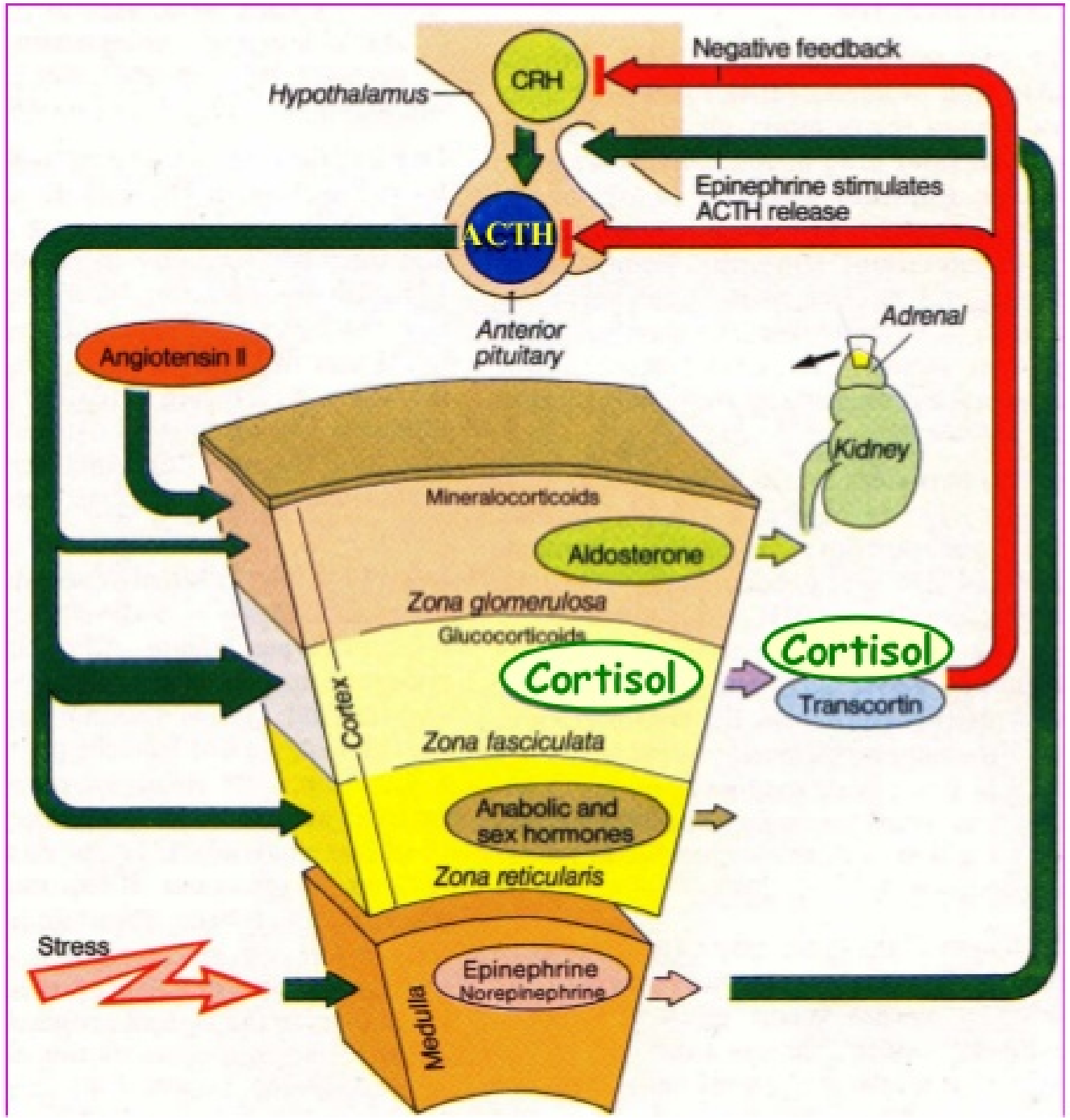
Adrenal cortex

- **Zona reticularis:**
  - The androgens produced includes
    - Dehydroepiandrosterone (DHEA)
    - Androstenedione
      - **Synthesized from cholesterol**
    - DHEA is further converted to DHEA-sulfate via a sulfotransferase

Adrenal cortex

- **Zona reticularis:**
  - The androgens produced are released into the blood stream and taken up in the testis and ovaries to produce *testosterone* and the *estrogens* respectively.

Regulation of adrenal gland secretion



Disorders of adrenal cortex

- Patient with adrenal disorders can present with features related to:
  - **HYPOFUNCTION OF THE GLAND**
  - **HYPERFUNCTION OF THE GLAND**

DISORDERS OF ADRENAL CORTEX

ADRENAL HYPOFUNCTION

Adrenal hypofunction

- Outlines
  - INTRODUCTION
  - AETIOLOGY AND PATHOGENESIS
  - CLINICAL FEATURES
  - INVESTIGATIONS
  - MANAGEMENTS

Adrenal Hypofunction

- Adrenal insufficiency leads to a reduction in the output of adrenal hormones
  - glucocorticoids and/or mineralocorticoids

- Two types of adrenal insufficiency
  - **Primary insufficiency**
    - inability of the adrenal glands to produce enough steroid hormones
  - **Secondary insufficiency**
    - inadequate pituitary or hypothalamic stimulation of the adrenal glands

Adrenal Hypofunction

- **Causes**
  - **Glucocorticoid treatment**
  - **Autoimmune adrenalitis**
  - **Tuberculosis**

  } Common

  - Adrenalectomy
  - Secondary tumor deposits
  - Amyloidosis
  - Haemochromatosis
  - Histoplasmosis, tuberculosis, CMV, AIDS
  - adrenal haemorrhage

Adrenal Hypofunction

- **Causes**
  - Metabolic failure in hormone production
    - Congenital adrenal hyperplasia e.g. 21-hydroxylase deficiency, 3-β-hydroxysteroid dehydrogenase deficiency
    - Enzyme inhibition e.g. ketoconazole
    - Accelerated hepatic metabolism of cortisol e.g. phenytoin, barbiturates, rifampicin

Adrenal Hypofunction

- **Other causes**
  - ACTH blocking antibodies
  - Mutation in ACTH receptor gene
  - Adrenal hypoplasia congenita
  - Familial adrenal insufficiency

Addison disease

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

Adrenal Hypofunction

Addison's disease
Primary hypoaldosteronism

Addison's disease: pathogenesis

- **Progressive destruction of entire adrenal cortex** , This is usually **autoimmune** based.

- Most likely the result of **cytotoxic T lymphocytes**, although 50% of patients have circulating adrenal **antibodies**.

Addison's disease: Clinical features

Common	Less common
Tiredness, generalized weakness, lethargy	Hypoglycemia
Anorexia, nausea, vomiting	Depression
Hyponatremia Hyperkalemia ,Hypercalcemia Convulsions	
Dizziness and postural hypotension	
Pigmentation	
Loss of body hair (woman)	

ADRENAL CRISIS

- **Acute adrenal insufficiency**
- Medical emergency
- Acute in onset; can be fatal if not promptly recognized and treated
- **Clinical features** :
  - Severe hypovolaemia
  - Dehydration
  - Shock
  - Hypoglycaemia
  - possible mental confusion and loss of consciousness

ADRENAL CRISIS

- **Causes :**
  - Precipitated by stress
    - infection, trauma or surgery in patients with incipient adrenal failure/treated with glucocorticoids if dosage is not increase
  - Adrenal haemorrhage
    - due to cx of anticoagulant treatment
  - Meningococcal septicaemia

INVESTIGATIONS (HORMONAL)

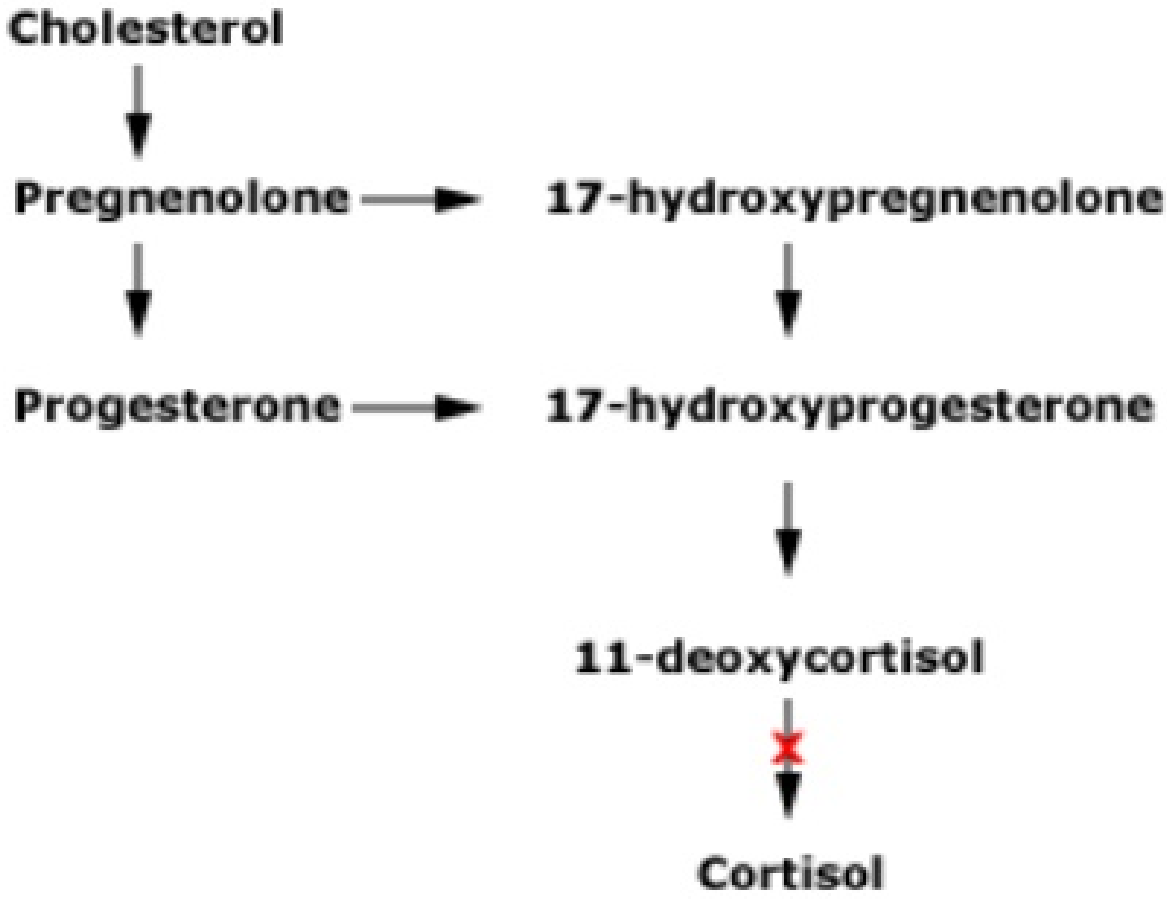
- **Plasma cortisol concentration**
  - <50nmol/L at 0900H → effectively diagnostic
  - >550nmol/L excludes the Dx
- **ACTH stimulation test / Synacthen test**
- Measurement of **plasma ACTH**
- Metyrapone test
- CRH stimulation test
- Plasma **renin** and **aldosterone** levels

PLASMA ACTH MEASUREMENT

- To differentiate between primary and secondary adrenal failure

  - Primary insufficiency - ACTH increased
  - Secondary insufficiency - ACTH decreased

Addison's disease

- 

Disorders of adrenal cortex

ADRENAL HYPERFUNCTION

Adrenal Dysfunction

Increase function

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

Hyperaldosteronism

- A medical condition where too much aldosterone is produced by the adrenal glands, which can lead to sodium retention and potassium loss.

- Types:
  - Primary hyperaldosteronism
  - Secondary hyperaldosteronism

Primary hyperaldosteronism (hyporeninemic hyperaldosteronism)

Conn’s syndrome

Primary aldosteronism

CONN'S SYNDROME

- Characterized by **autonomous** excessive production of **aldosterone** by **adrenal glands**

- Presents with HPT, hypokalaemic alkalosis and renal K+ wasting

Conn's Syndrome

- Causes:
  - Adrenal adenoma
  - Bilateral hypertrophy of zona glomerulosa cells
  - Adrenal carcinoma
    - Rare cause

Secondary aldosteronism

- Is increased adrenal production of aldosterone in response to non-pituitary, extra-adrenal stimuli

- Increase renin secretion
  - (hyperreninemic hyperaldosteronism)
- Commoner than primary aldosteronism

Secondary aldosteronism

- Common
  - CCF
  - Liver cirrhosis with ascites
  - Nephrotic Syndrome
- Less common
  - Renal artery stenosis
  - Sodium – losing nephritis
  - Renin-secreting tumours

Conn's syndrome

- **Clinical features:**
  - Hypertension : *aldosterone induced Na retention with increase in ECF volume*
  - Muscle weakness: *Due to decrease K+*
  - Muscle paralysis: *severe hypokalaemia*
  - Latent tetany and paraesthesiae
  - Polydipsia, polyuria and nocturia: *due to hypokalaemic nephropathy*

INVESTIGATION

- **Electrolyte & blood gasses:**
  - Hypernatraemia
  - Hypokalaemica
  - Alkalosis
  - Urinary potassium loss, *level > 30 mmol daily during hypokalaemia*

INVESTIGATION

- **Plasma aldosterone : renin activity ratio**
  - Sensitive screening test
  - No need to standardize posture

Ratio	Interpretation	Action
<800	Diagnosis excluded	Seek other cause
>1000,<2000	Diagnosis possible	Confirmatory test
>2000	Diagnosis very likely	Establish cause

Treatment

- Tumour
  - Remove surgically

- Bilateral adrenal hyperplasia
  - Spironolactone

Disorders of adrenal cortex

ADRENAL HYPERFUNCTION

CUSHING'S SYNDROME

- Definition
- Clinical features
- Investigations
  - Screening for Cushing's syndrome
  - Elucidation of the cause of Cushing's syndrome

- Management

CUSHING'S SYNDROME

Adrenal cortex hyperfunction

- Any condition resulting from overproduction of **primarily glucocorticoid (cortisol)**

- Mineralocorticoid and androgen may also be excessive

Pseudo-Cushing's syndrome

- Appear cushingoid and have some biochemical abnormalities of true Cushing's disease
- Causes
  - Severe depression
  - Alcoholism
  - Obesity
  - Polycystic ovarian syndrome

Etiology

- **Excessive cortisol (ACTH dependent)~75%**
  - Pituitary disease
    - Adenoma (90%)
    - Hyperplasia (10 %)
  - Ectopic ACTH syndrome
    - Malignancy - (bronchus, thymus, pancreas, ovary)
  - Ectopic CRH syndrome
  - Exogenous ACTH administration

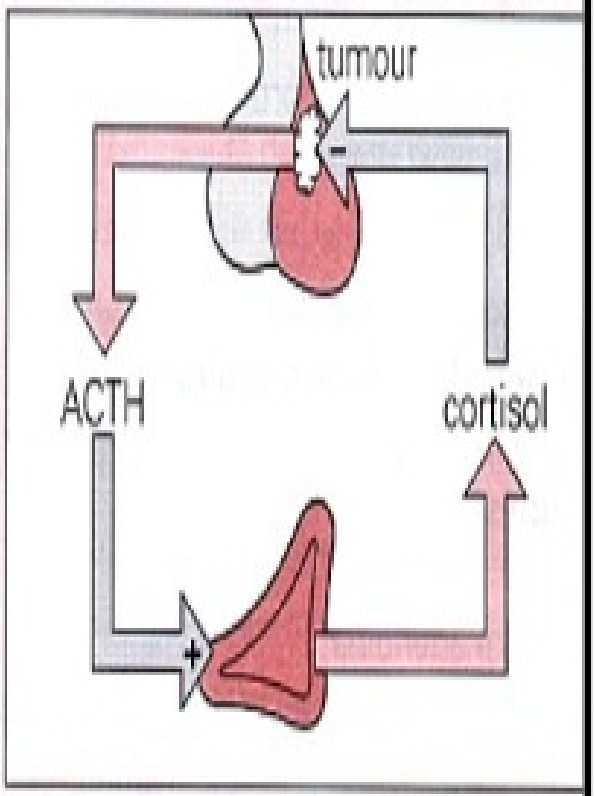
ACTH dependent causes

b. Cushing's disease

ACTH secretion increased

pituitary insensitive to feedback by normal levels of cortisol

higher levels of cortisol required to produce negative feedback effect on ACTH secretion



Laboratory investigations

2. Measuring 24-hour urinary free cortisol

Level (umol/ 24 h)	Interpretation
< 300	Normal
300 - 700	Severe depression Stress
> 700	Diagnostic of Cushing's syndrome

Laboratory investigations

3. Low dose Dexamethasone suppression test :

- 0.5 mg Dexametason (oral) given 6 hourly for 2 days
- blood for plasma cortisol collected 6 hour after last dose
- urine for UFC is collected before & on the 2nd day of Dexa

- Result:
  - UFC suppress by 50% (< 70nmol/24h) normal
  - plasma cortisol suppress < 140 nmol/L pseudo-Cushing
  - no suppression of UFC & Pl. cortisol Cushing's synd

Treatment

- Depend of Cushing's syndrome depends on the etiology:
  - Adrenal adenoma
  - Adrenal Carcinoma – resection
  - Cushing's disease - transphenoidal hyposectomy
  - Drug (block cortisol synthesis) - metyrapone


thankyou