PALS – Peer Assisted Learning Scheme

Tim Buckeridge

Cushing's Syndrome and Addison's Disease

Aim

- To develop an understanding of the presentation, diagnosis and management of Cushing's Syndrome and Addison's Disease

Objectives

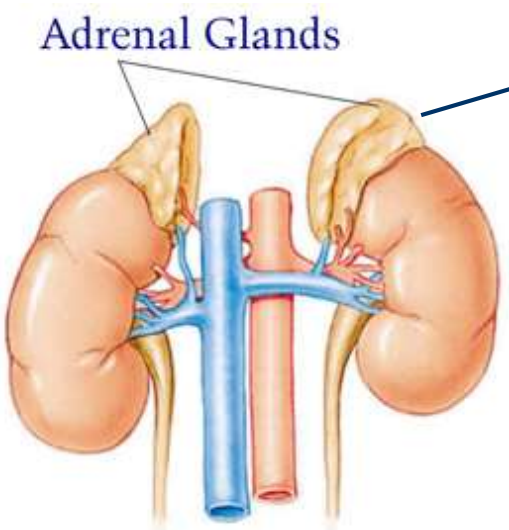
- By the end of the session you should be able to:
  - Describe the pituitary-adrenal axis.
  - Explain the actions of cortisol and aldosterone.
  - Name the signs and symptoms associated with Cushing's and Addison's.
  - Explain the basic investigations and treatment for these conditions.

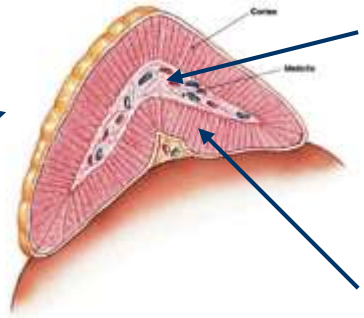
Plan

- Pituitary-adrenal axis
- Actions of cortisol, aldosterone and androgens
- Terms and definitions
- Symptoms and signs (Quiz!)
- Investigations
- Treatment
- Case studies and picture quiz (!)
- Summary
- Feedback

Brainstorm!

Pituitary-adrenal axis





Medulla – catecholamines
e.g. adrenaline

Cortex

Glucocorticoids
e.g. cortisol

Gonadocorticoids
e.g. androgens

Mineralocorticoids
e.g. aldosterone

Cortisol

-ve

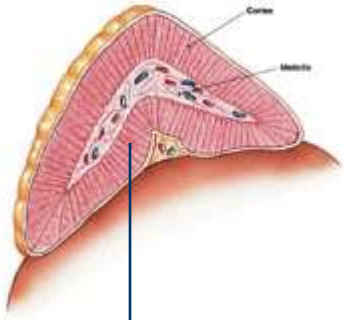
Hypothalamus

CRH

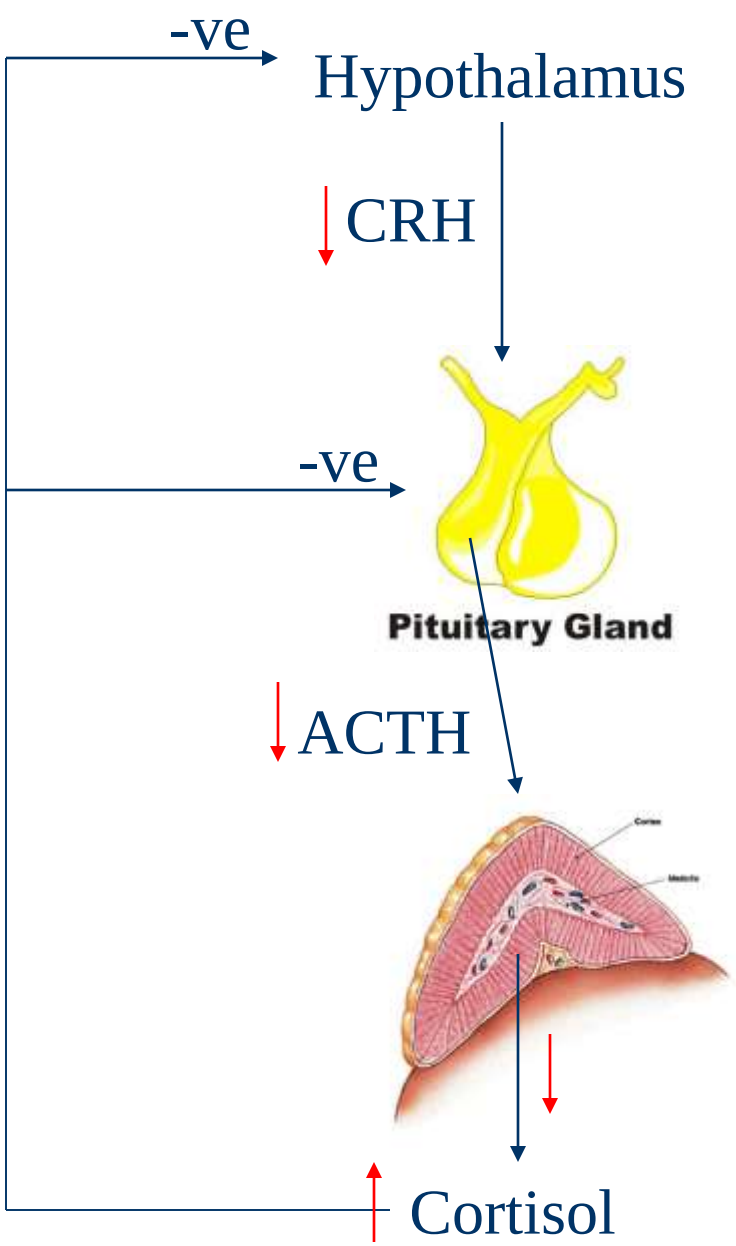
-ve

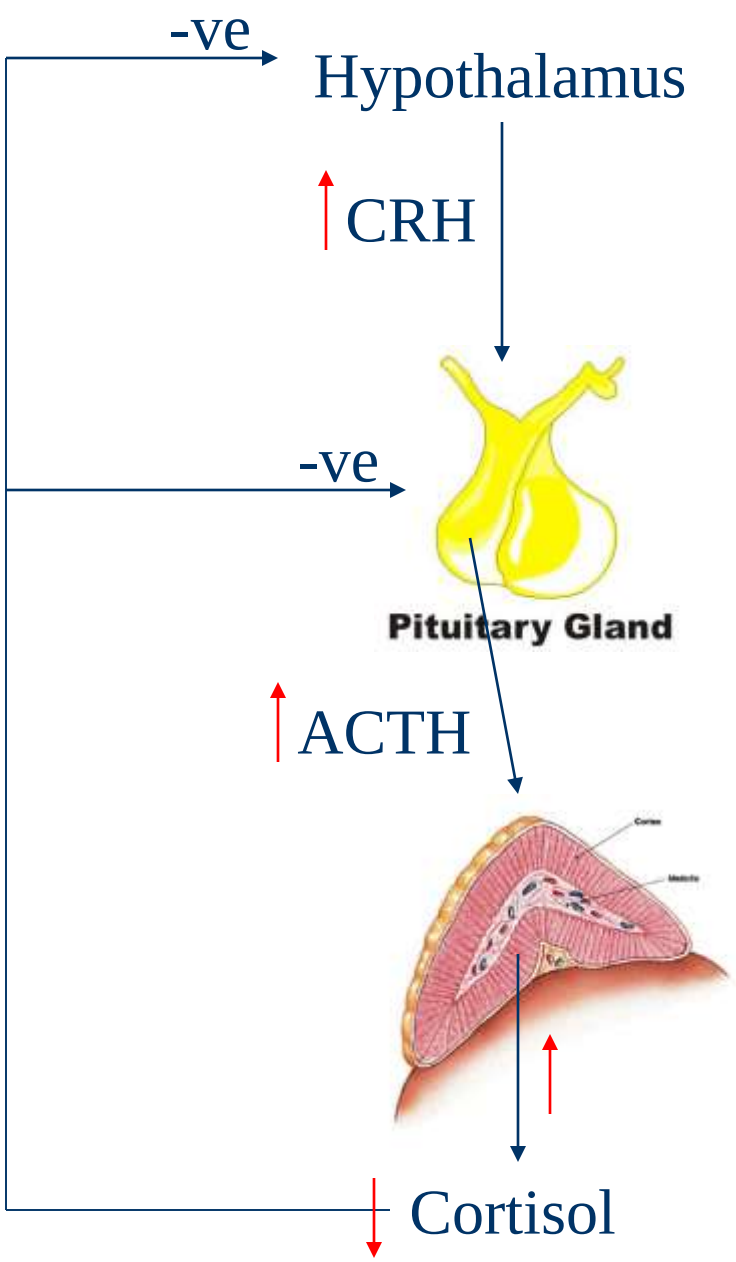
Pituitary Gland

ACTH



Cortisol


-ve
Hypothalamus
CRH
-ve
Pituitary Gland
ACTH
Cortisol

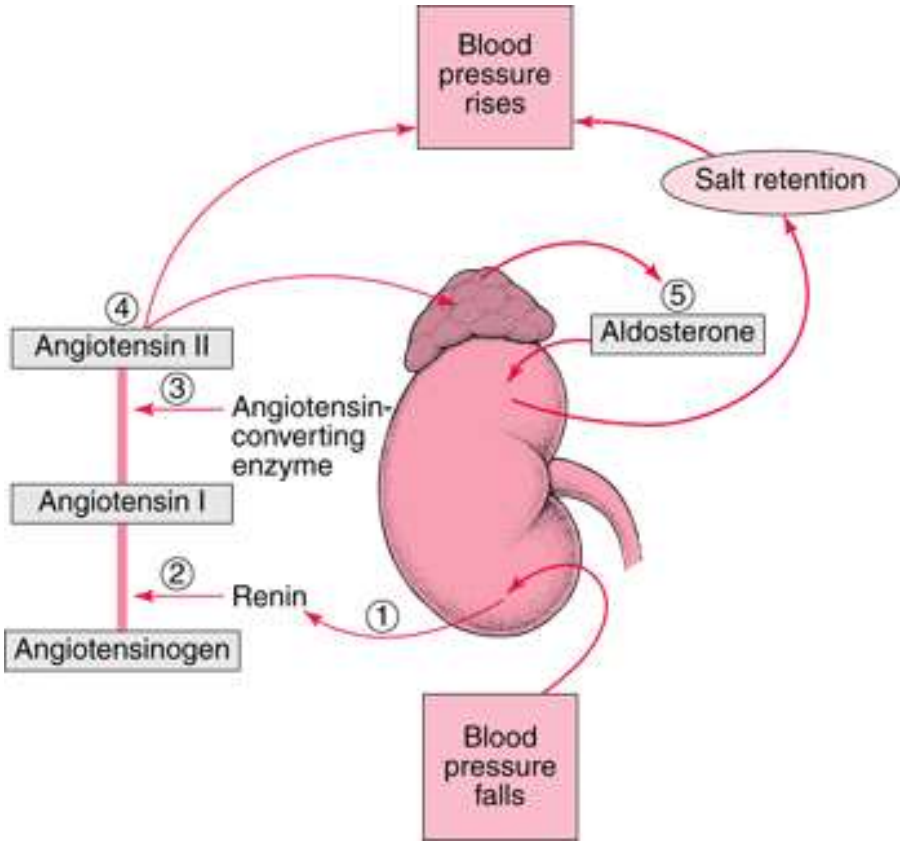

-ve
Hypothalamus
CRH
-ve
Pituitary Gland
ACTH
Cortisol

Cortisol

- Stress hormone
- Released in times of stress to restore homeostasis.
- Glycogenolysis ↑
- Gluconeogenesis ↑
- Lipolysis ↑
- Protein breakdown ↑
- + other actions

Aldosterone

Renin-angiotensin system



Aldosterone increases blood pressure

(ACE-inhibitors inhibit the system)

Androgens

- Male sex hormones
- Act on androgen receptors to produce male sexual characteristics
- E.g. testosterone
- Can act in both males and females

Cushing's Syndrome and Addison's Disease – Terms and definitions

Cushing's Syndrome – any condition where there is chronic glucocorticoid excess i.e. increased cortisol

ACTH-dependent causes

ACTH-independent causes

Cortisol

-ve

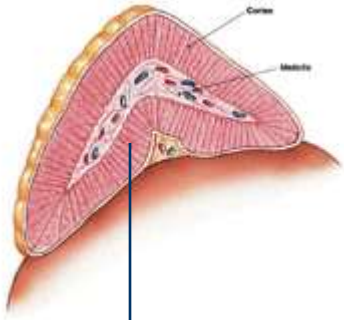
Hypothalamus

CRH

-ve

Pituitary Gland

ACTH



Cortisol

Cushing's Syndrome – any condition where there is chronic glucocorticoid excess i.e. increased cortisol

ACTH-dependent causes

1) **Cushing's Disease** – bilateral adrenal hyperplasia due to ACTH secreting pituitary adenoma

2) Ectopic ACTH production e.g. small cell lung cancers

ACTH-independent causes

1) Iatrogenic – steroids – **commonest cause**

2) Adrenal adenoma or carcinoma

3) Adrenal nodular hyperplasia

Adrenal insufficiency/hypoadrenalism – underactive adrenal glands – cortisol, aldosterone and androgens

Primary – **Addison's Disease** – originating from adrenal cortex

1) Autoimmune (80%)
2) Tuberculosis
3) Adrenal metastases

Secondary – originating from elsewhere

Iatrogenic – withdrawal of long term steroid therapy that had led to suppression of pituitary-adrenal axis

Pituitary problems.

Cortisol

-ve

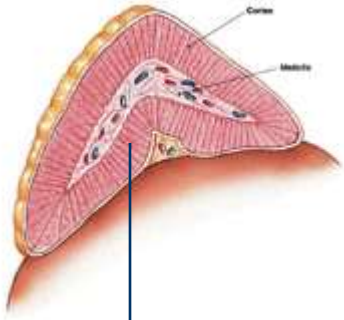
Hypothalamus

CRH

-ve

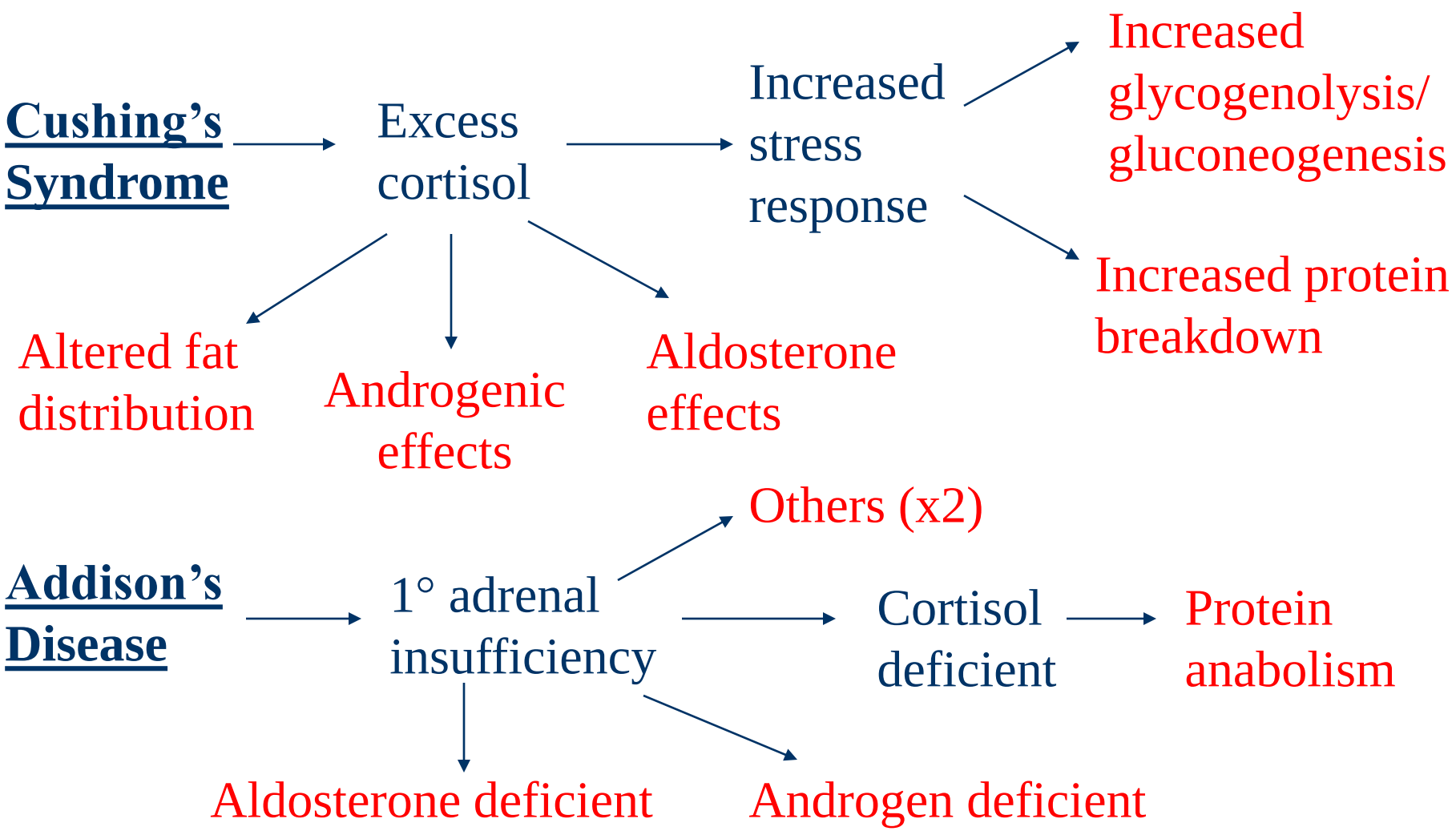
Pituitary Gland

ACTH



Cortisol

Cushing's Syndrome and Addison's Disease – Presentation



N.B. Pigmentation is due to increased ACTH.

Addison's is commonly an autoimmune condition.

Cushing's Syndrome

- Increased glycogenolysis/gluconeogenesis:
  - Diabetes (20%), impaired glucose tolerance (50%)
- Increased protein breakdown:
  - Thinned hair, thin skin, poor wound healing, purple abdo striae, infections, muscle wasting, osteoporosis, peptic ulcer, proximal myopathy.
- Altered fat distribution:
  - Moon face, buffalo hump, supraclavicular fat pad
- Androgenic effects:
  - Dysmenorrhoea, acne, hirsuitism, impotence (?)

Cushing's Syndrome

- Aldosterone effects:
  - Hypertension, premature IHD.
- Others:
  - Pigmentation (ACTH-dependent types), psychosis, depression.

Addison's Disease

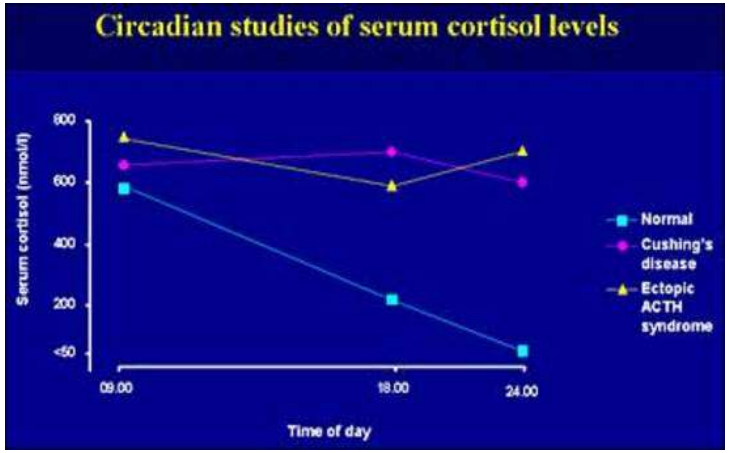
- Protein anabolism
  - lethargy
- Aldosterone deficient
  - Postural hypotension, fainting, dizziness
- Androgen deficient
  - Impotence
- Others
  - Hyperpigmentation – palmar creases, buccal mucosa, scars (increased ACTH), vitiligo (autoimmune), Abdo (diarrhoea, constipation, vomiting), depression, anorexia, weight loss, myalgia, arthralgia, hair loss

Onset of symptoms is gradual
- Diagnosis is often made late

Cushing's Syndrome and Addison's Disease – Investigations

Cushing's Syndrome

- Random cortisol levels are of no value – affected by diurnal variation, stress, illness – may do as initial test.
- 1st line diagnostic tests:



- Overnight dexamethasone suppression test (low dose). 1mg PO at night. Cortisol levels checked before and at 8am. Normal = suppressed. Cushing's = not suppressed.

- 24h urinary free cortisol – measure amount in urine/24h – normal is <280nmol/24h.

Cushing's Syndrome

- Other possible diagnostic tests - 48h dexamethasone suppression test, and midnight cortisol.
- Localising tests:
  - **Plasma ACTH** – differentiates ACTH-dependent/ independent causes. Low in ACTH-independent.
  - **High-dose dexamethasone test** (2mg/6h PO for 2 days) – differentiates ACTH-dependent causes (pituitary or ectopic source). No suppression of cortisol with an ectopic source.

Cortisol

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Hypothalamus

CRH

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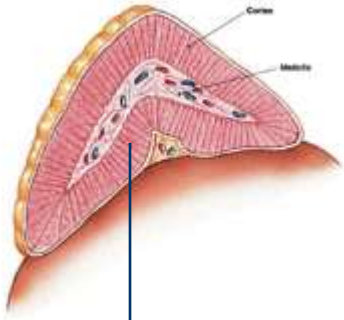
Pituitary Gland

ACTH



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Cushing's Syndrome

- Other investigations
  - U and Es
  - Glucose
  - Adrenal CT
  - CXR, bronchoscopy, CT chest – ectopic ACTH.

Adrenal insufficiency

- **Short synacthen test** – 1st line screening test. Plasma cortisol measured before and 30 mins after tetracosactide 250ug IM (synthetic ACTH). Addison's excluded if 2nd cortisol >550nmol/L.

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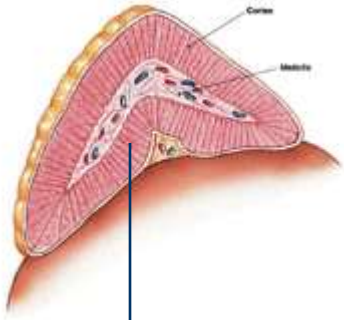

Cortisol

Adrenal insufficiency

- Localising tests:
  - **Plasma ACTH levels** – inappropriately high in primary causes, low in secondary causes.
  - **Long Synacthen test -** higher dose of synacthen and cortisol levels measured at 30min, 60min, 5hr and 24hr. With secondary causes, get cortisol response after 24 hrs – adrenal cortex wakes up.

Adrenal insufficiency/hypoadrenalism – underactive adrenal glands – cortisol, aldosterone and androgens

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Pituitary problems.

Adrenal insuffiency

- Other investigations:
  - U and Es – low Na/high K, uraemia
  - Glucose – low
  - Calcium – high
  - FBC – anaemia, eosinophilia
  - Adrenal autoantibodies
  - AXR/CXR – signs of past TB e.g. upper zone fibrosis or calcification of adrenals.

Cushing's Syndrome and Addison's Disease – Treatment

Cushing's Syndrome

- Depends on the cause…
- Iatrogenic – stop steroids if possible.
- Cushing's Disease - selective removal of pituitary adenoma. Bilateral adrenalectomy if source cannot be located, or recurrence post surgery. Pituitary radiotherapy in children.
- Ectopic ACTH – surgery if possible/appropriate
- Medical treatment – metyrapone, ketoconazole (both block cortisol synthesis) - To reduce cortisol secretion pre-surgery or while waiting for radiation to become effective.

Adrenal insufficiency

- Replace the steroids.
- Glucocorticoid replacement – **hydrocortisone**. Avoid giving late in the day because it can cause insomnia.
- Mineralocorticoid replacement may be needed e.g. if postural hypotension or abnormal U + Es – **fludrocortisone**.

Any Questions?

Case studies

Cushing's Syndrome

- Increased glycogenolysis/gluconeogenesis:
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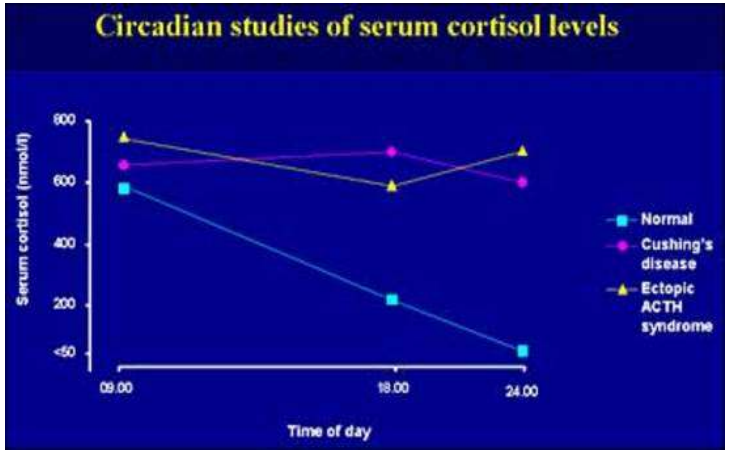

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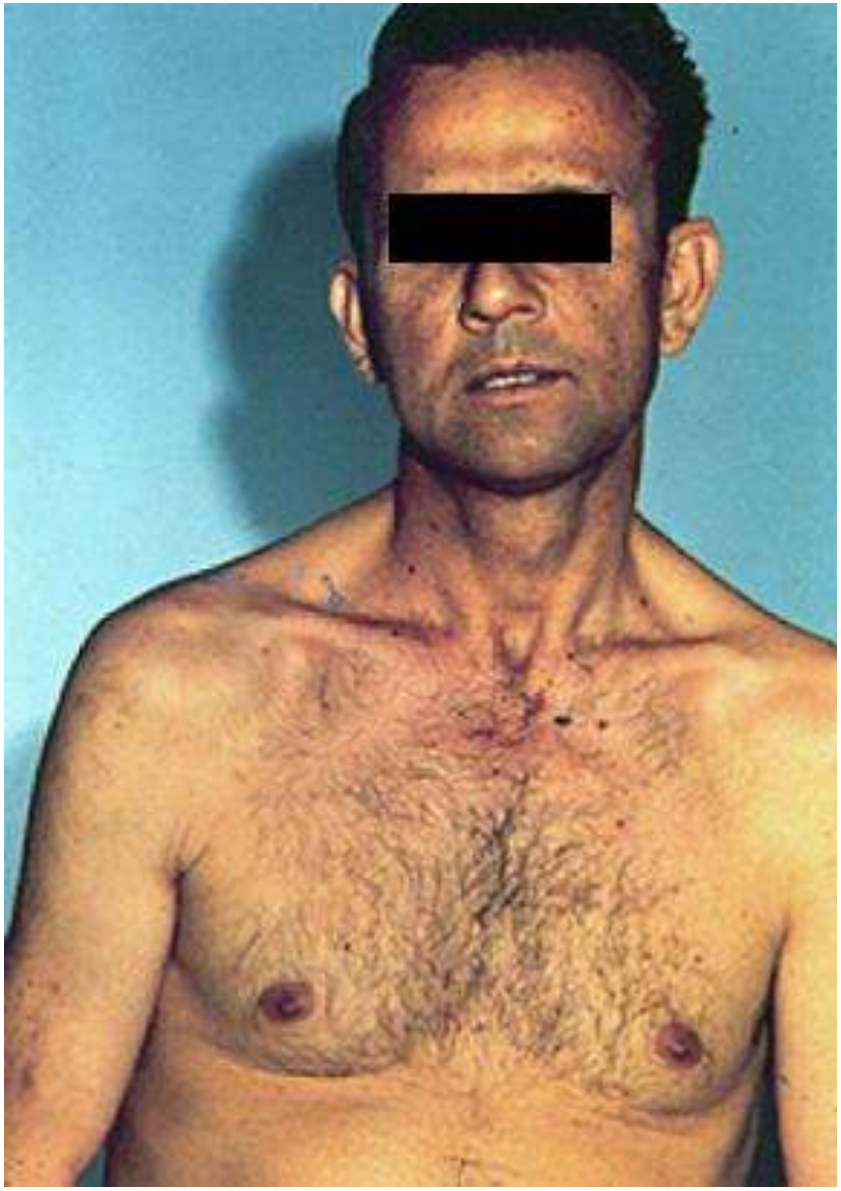
Summary

- Cushing's Syndrome is any condition where there is an excess of cortisol.
- Addison's Disease is primary adrenal insufficiency.
- The presentation of these conditions can be predicted from the actions of the effected hormones.
- Diagnostic investigations require an assessment of hormone levels.
- The treatment of Cushing's Syndrome depends on the cause.
- Addison's Disease is treated with steroid replacement.
- Addisonian crisis is a medical emergency.

Feedback, MCQs and next week's tutorial

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