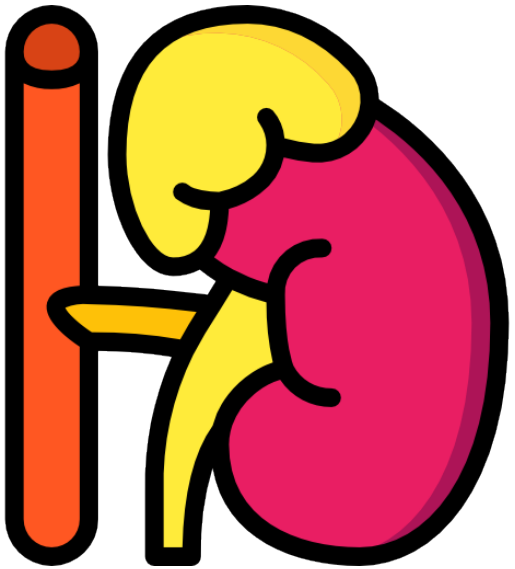
Phaeochromocytoma and Cushing's disease

Pathophysiology, differentials, investigations and management.

Cases Quiz



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BITE Medicine
Endocrinology series

Case 1

History
A 28-year-old female presents to the GP complaining of recurrent headaches and is aware of a fluttering in her chest from time to time. The patient takes the progesterone-only pill but no other medication.

There is strong family history of cancer, as her mother and grandmother both have had thyroid cancer.

Observations
HR 94, BP 176/104 mmHg, RR 14, SpO2 97%, Temp 36.8

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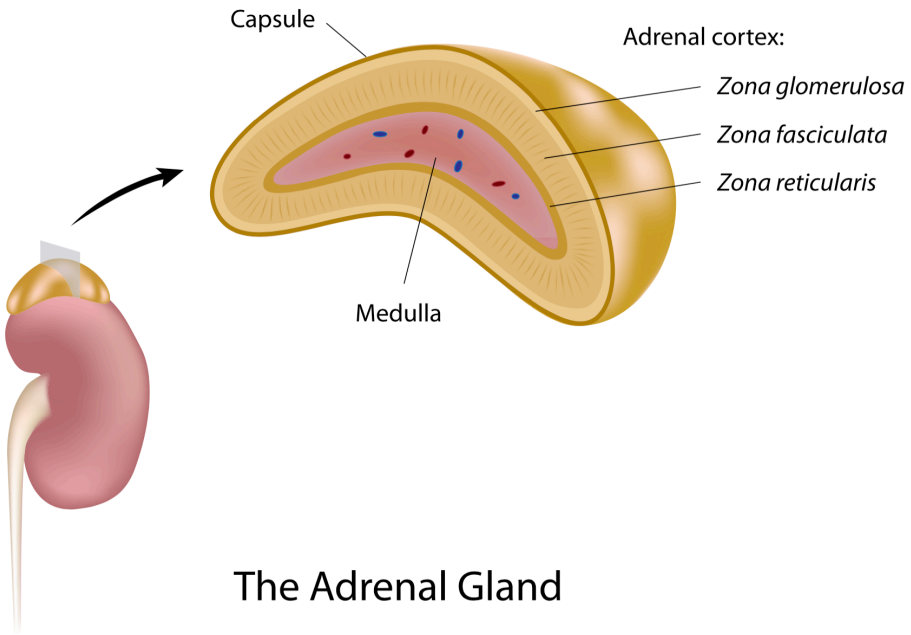
B Pathophysiology



The Adrenal Gland

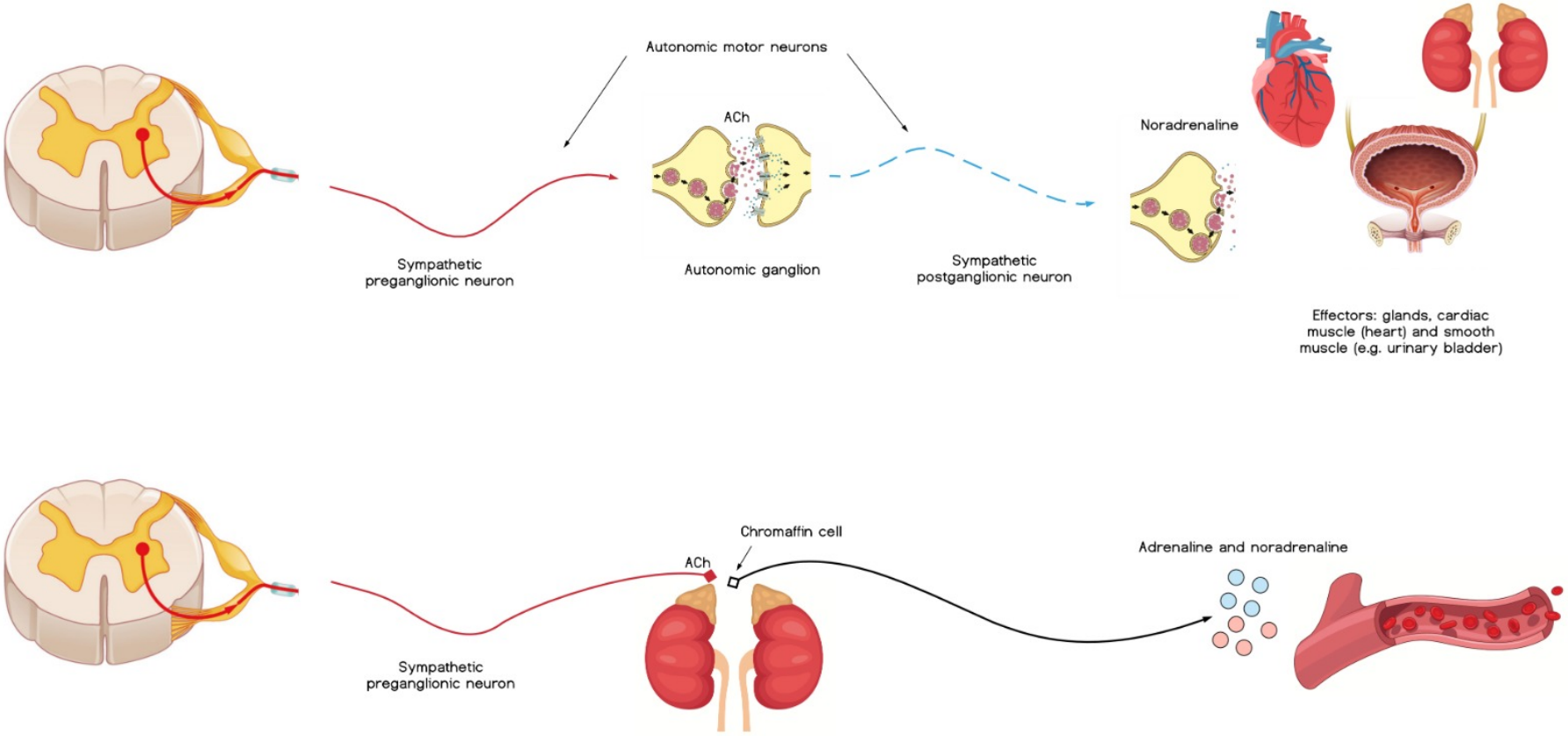
Adrenal cortex is split into 3 layers:

- Zona **g**lomerulosa = mineralocorticoids
- Zona **f**asciculata = glucocorticoids
- Zona **r**eticularis = sex steroid hormones

Adrenal medulla is composed of catecholamine-secreting cells (**chromaffin cells**)

- Adrenaline (predominantly)
- Noradrenaline

B Pathophysiology



B Pathophysiology

Definition: (usually) benign tumours of the chromaffin cells of the adrenal medulla; referred to as paragangliomas if extra-adrenal

Epidemiology

- 0.05% of all hypertensive patients
- Typical presentation is between 30-50 years of age
- Linked to a number of genetic conditions, so phaechromocytomas tend to run in families

Risk factors

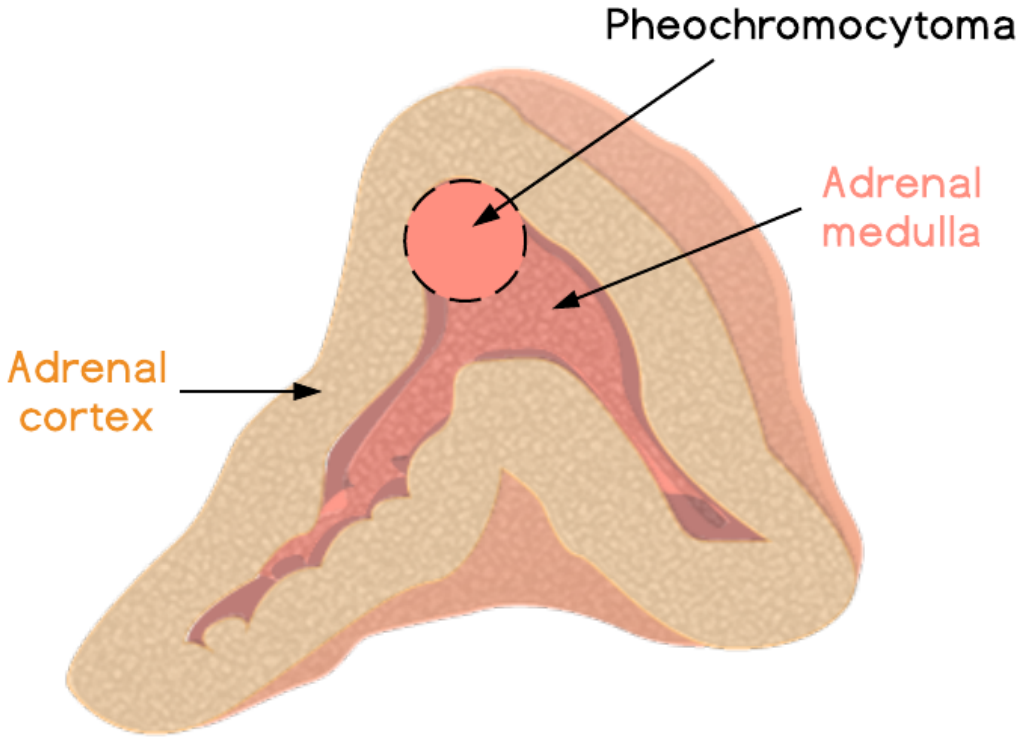
- Von-Hippel-Lindau syndrome
- Neurofibromatosis type 1
- MEN 2a
- MEN 2b

B Pathophysiology

Phaeochromocytomas are (usually) benign tumours of the chromaffin cells of the adrenal medulla

Rule of 10s:

- 10% extra-adrenal (paraganglioma)
- 10% bilateral
- 10% malignant
- 10% familial



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Clinical features

Symptoms	Signs
Episodic headache	**Hypertension**
Palpitations	Tachycardia
Anxiety	Hypertensive retinopathy
Diaphoresis (sweaty)	

B Investigations

Bedside

- **ECG**
- **24h urinary metanephrine collection:** first line along with plasma metanephrines

Bloods

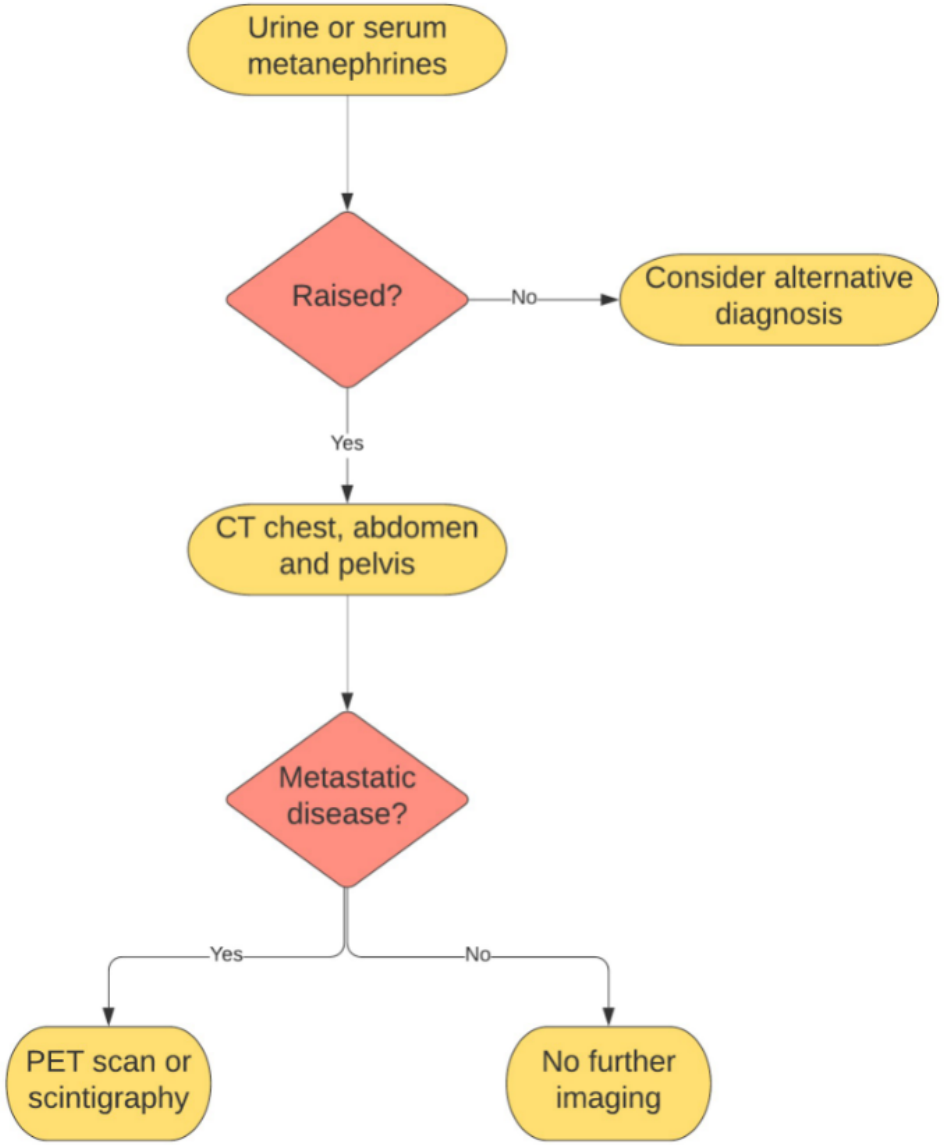
- **Plasma-free metanephrines**
- **Bone profile**

Imaging

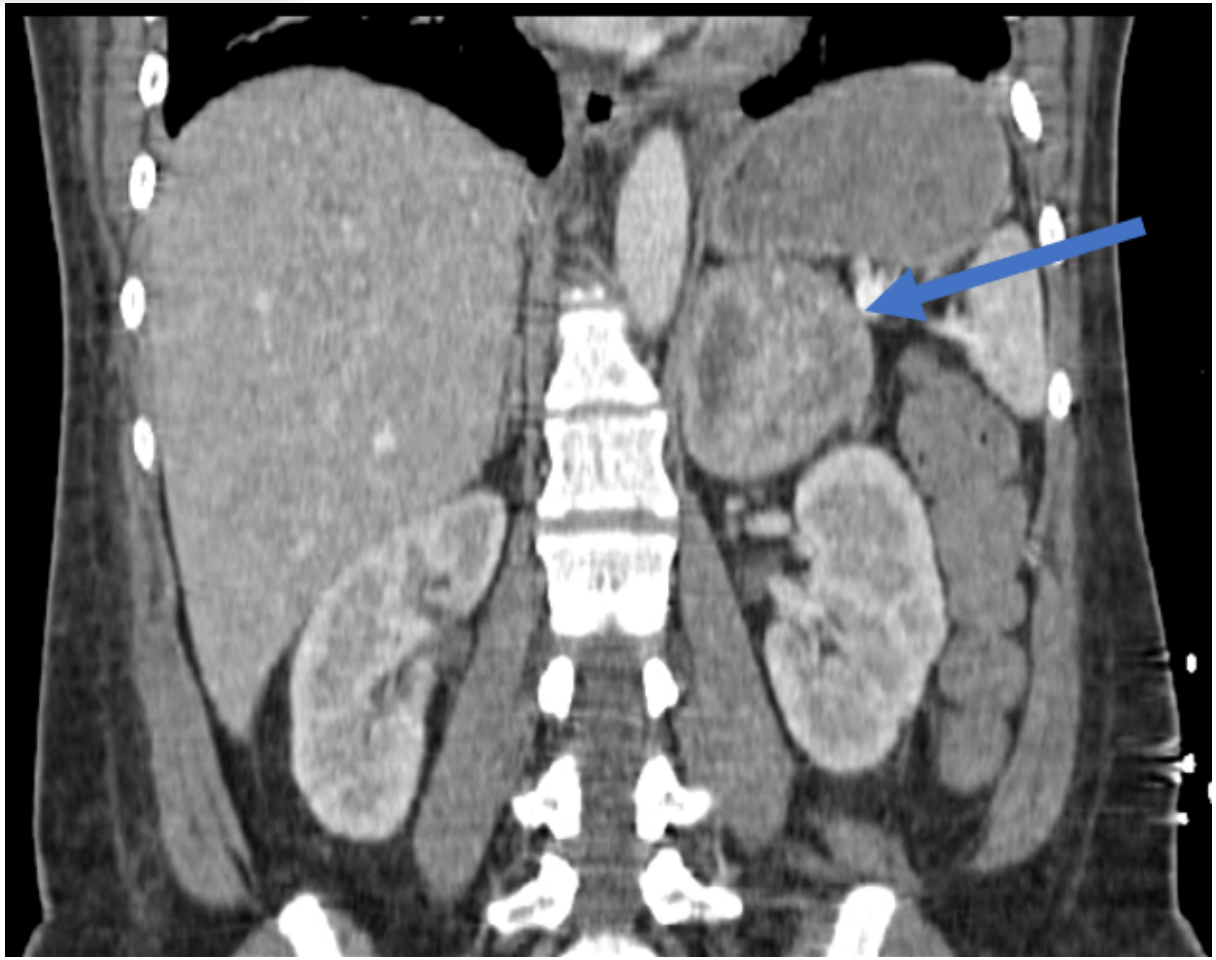
- **CT abdomen and pelvis:** if there is biochemical evidence of a phaeochromocytoma, look at the adrenal for evidence of a tumour
- **PET scan:** used if metastatic disease suspected

Special tests

- **I-123 MIBG scintigraphy:** radionucleotide incorporates itself into the phaeochromocytoma, which helps localise metastatic tissue
- **Genetic testing**


Urine or serum metanephrines
Raised?
No
Consider alternative diagnosis
Yes
CT chest, abdomen and pelvis
Metastatic disease?
Yes
No
PET scan or scintigraphy
No further imaging

B Investigations



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B Management

First line

Peri-operative:

- Initial alpha blockade (e.g. phenoxybenzamine) followed by beta-blockade (e.g. propranolol).
- Commencing beta-blockers first can lead to **unopposed alpha stimulation** and subsequent vasoconstriction

Surgical:

- Definitive management with laparoscopic adrenalectomy

Second line

Medical:

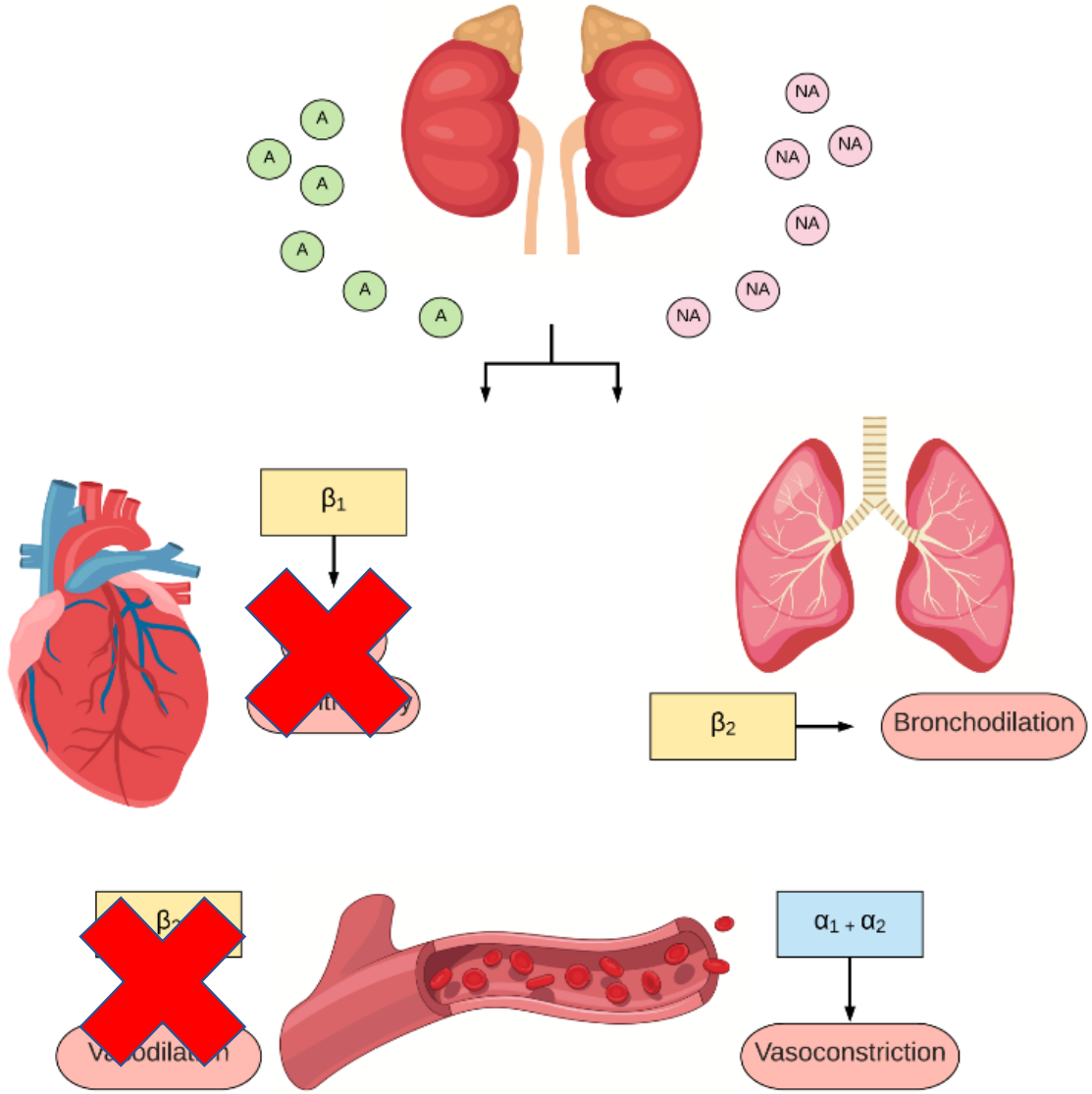
- Patients not suitable for surgery should be treated with long term anti-hypertensive agents

B Management

Peri-operative:

- Initial alpha blockade followed by beta-blockade

- Commencing beta-blockers first can lead to **unopposed alpha stimulation** and subsequent vasoconstriction



B Complications

Complications	Management
Hypertensive crisis • Encephalopathy • Myocardial infarction • Arrhythmia • Renal Failure	IV labetalol
Post-operative hypotension	IV fluids

Recap

- Phaeochromocytoma is a **neuroendocrine tumour** arising from chromaffin cells of the adrenal medulla
- First line investigation is with serum or urinary metanephrines
- Management involves **peri-operative alpha blockade, followed by beta-blockade**
- Definitive management comprises a **laparoscopic adrenalectomy**
- Rarely, a phaeochromocytoma can be extra-adrenal, where they are referred to as paragangliomas

Case 2

History

A 42-year-old male presents to his GP complaining of tunnel vision. Last month he crashed his car driving down a one-way street. He is a known asthmatic, requiring a MART inhaler. Despite his asthma, he has a 20 pack-year history.

On examination he is noted to have a cushingoid habitus, moon face and inter-scapular fat deposits.

Observations

HR 87, BP 148/94 mmHg, RR 14, SpO2 97%, Temp 36.8

B Pathophysiology

Definition: Cushing's syndrome describes a state of hypercortisolism

Epidemiology

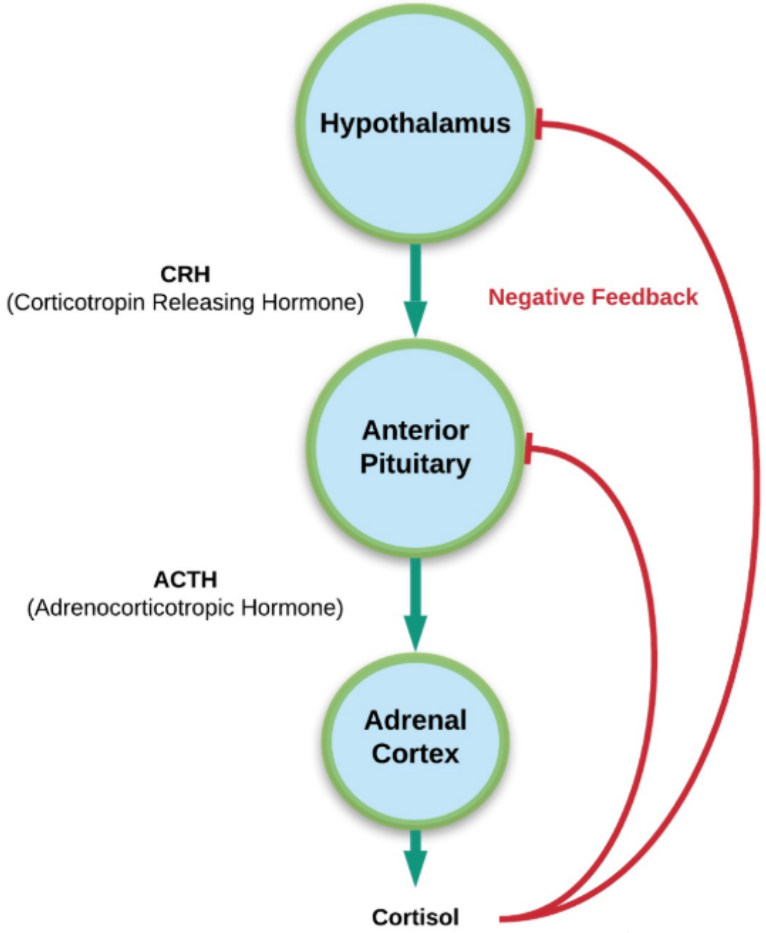
- Cushing's syndrome is uncommon, with an estimated incidence of 1-10 per million per year

Risk factors

- Long term steroid use
- Adrenal adenoma
- Pituitary adenoma
- Small cell lung cancer
- Neuroendocrine tumours

B Pathophysiology

	Causes of hypercortisolaemia
ACTH dependent	Pituitary tumor **(Cushing's disease)**
	Ectopic tumour
ACTH independent	Adrenal tumour
	Iatrogenic

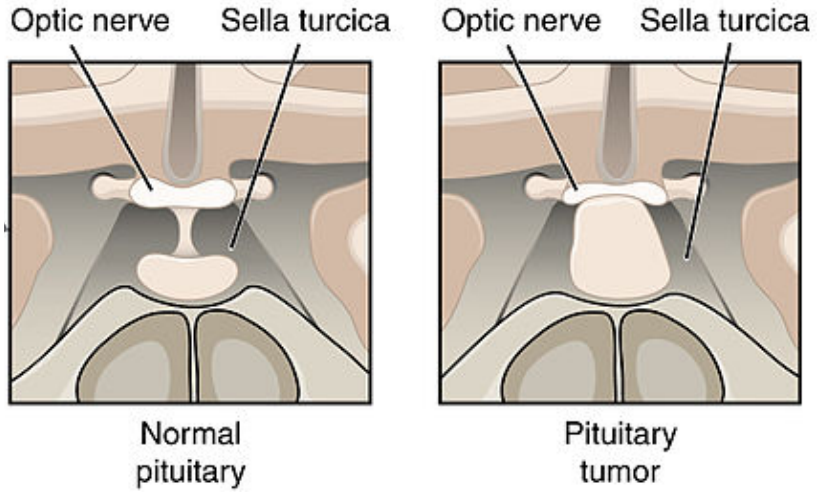


B Pathophysiology

Cushing's disease

Pituitary gland tumours can cause a triad of effects:

1. **Increase in hormone** e.g. ACTH or prolactin
2. **Mass effect:** decrease in other hormones produced by the pituitary gland (hypopituitarism)
3. **Mass effect:** tumour growth affects local structures, including the optic chiasm



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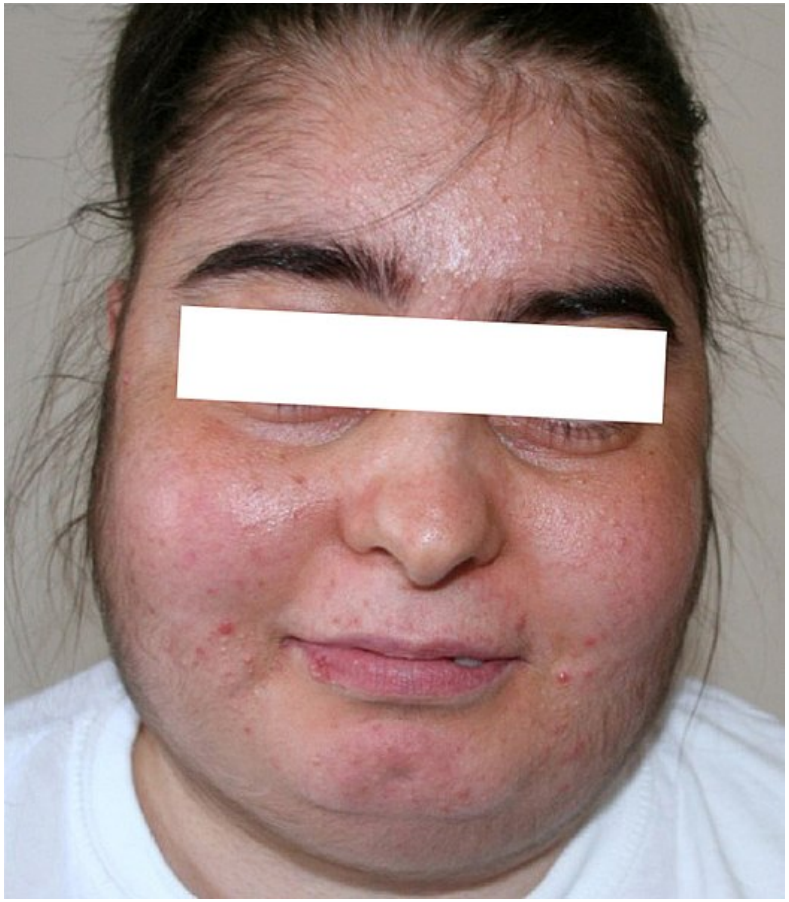
B Clinical features

Symptoms	Signs
Bloating and weight gain	Hypertension
Mood change	Moon face
Menstrual irregularity	Buffalo hump
Easy bruising	Central adiposity
Tunnel vision (Cushing's disease only)	Violaceous striae
	Proximal myopathy

B Clinical features



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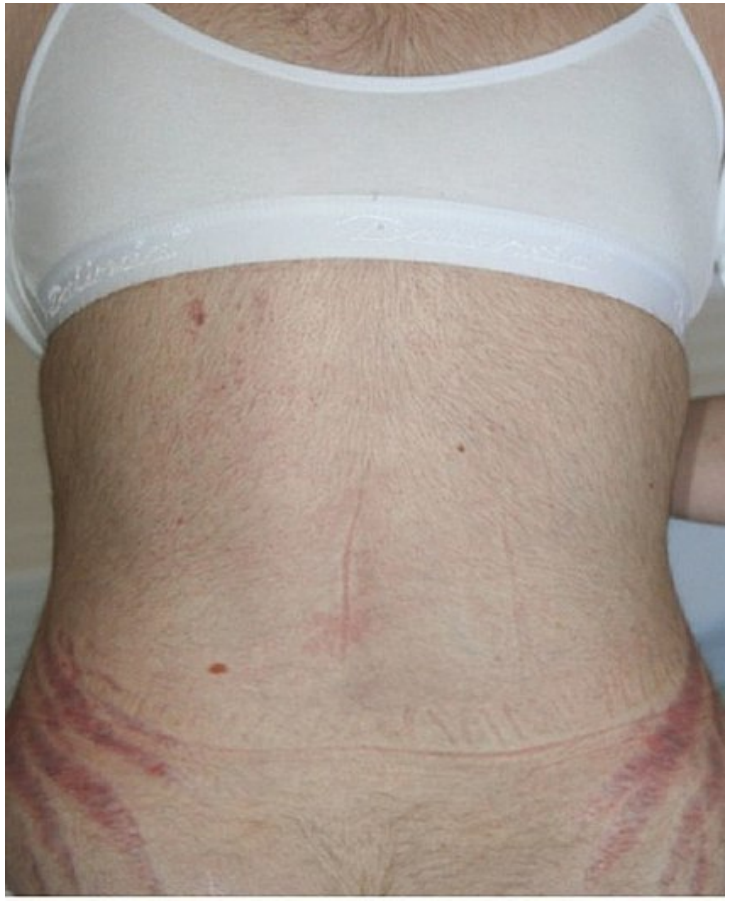

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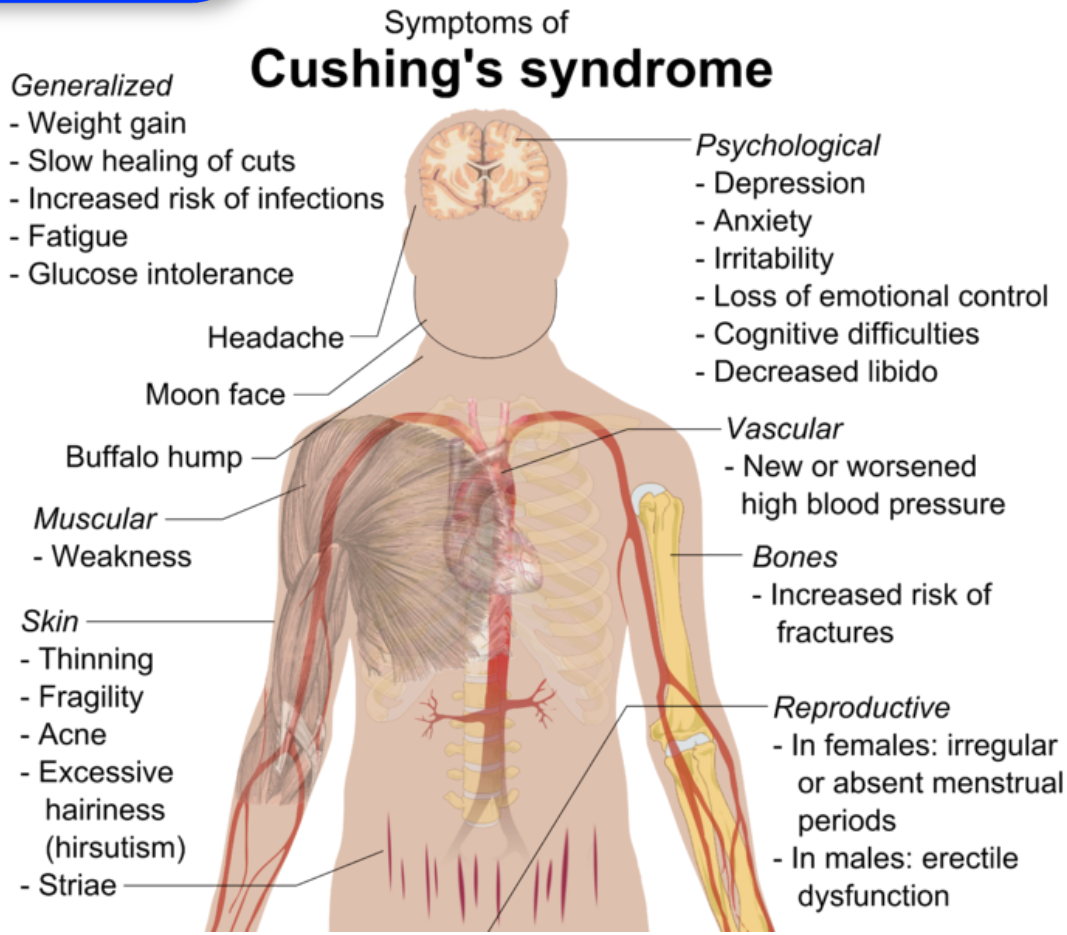
B Clinical features



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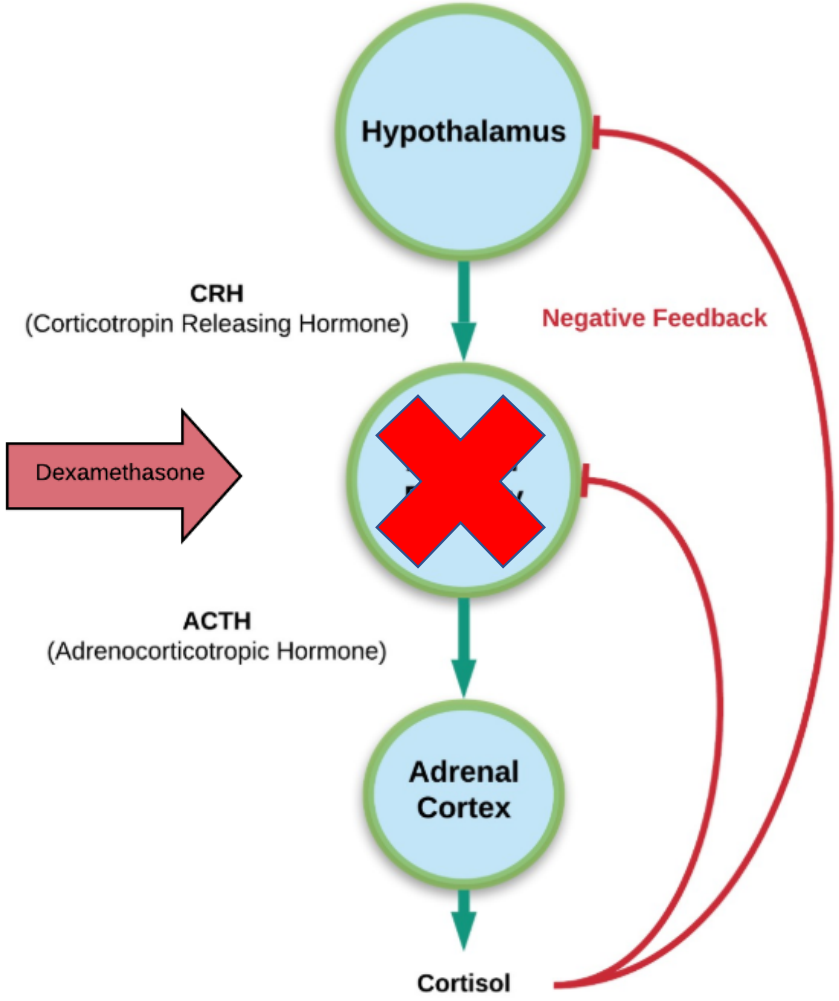
B Investigations

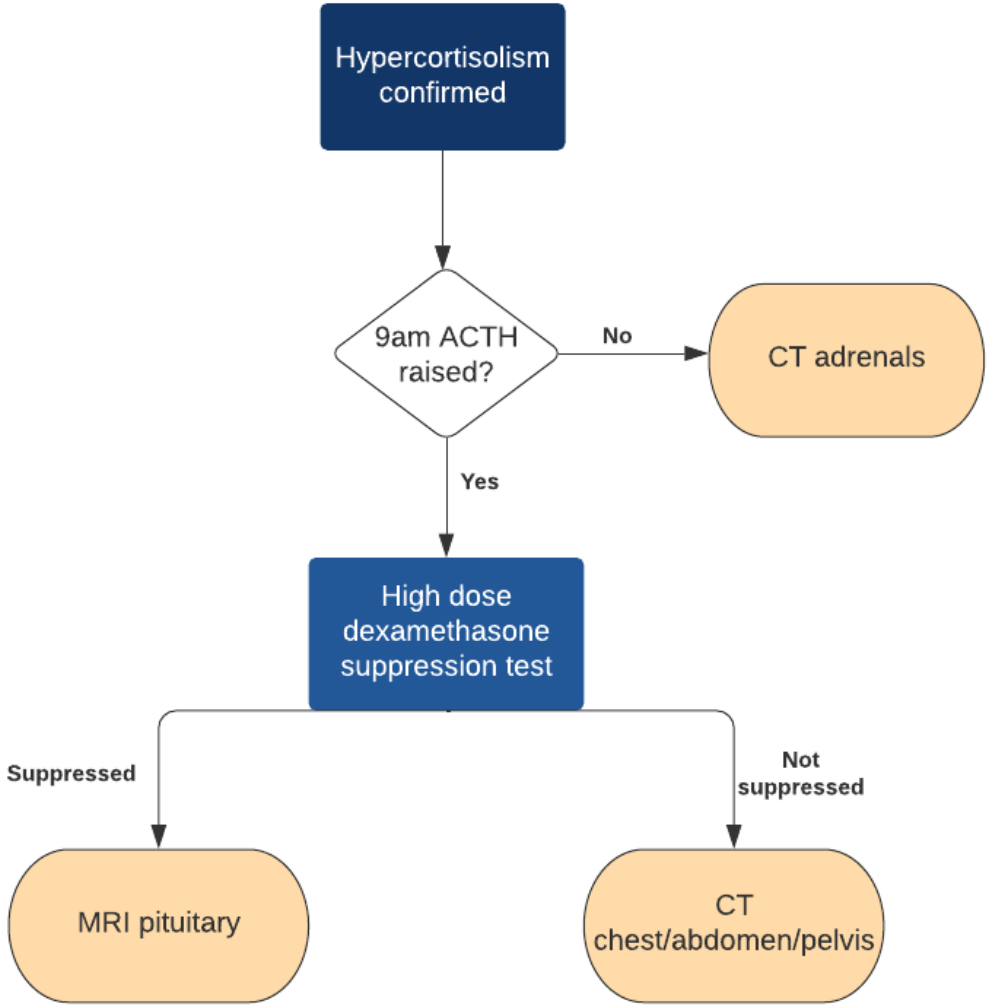
Step 1 – confirm hypercortisolism

- 24-hour free urinary cortisol
- Late-night salivary cortisol
- Overnight dexamethasone suppression test
- Low dose dexamethasone suppression test

Step 2 – localise the source of the hypercortisolism

- 9am ACTH
- High dose dexamethasone suppression test
- CT adrenals

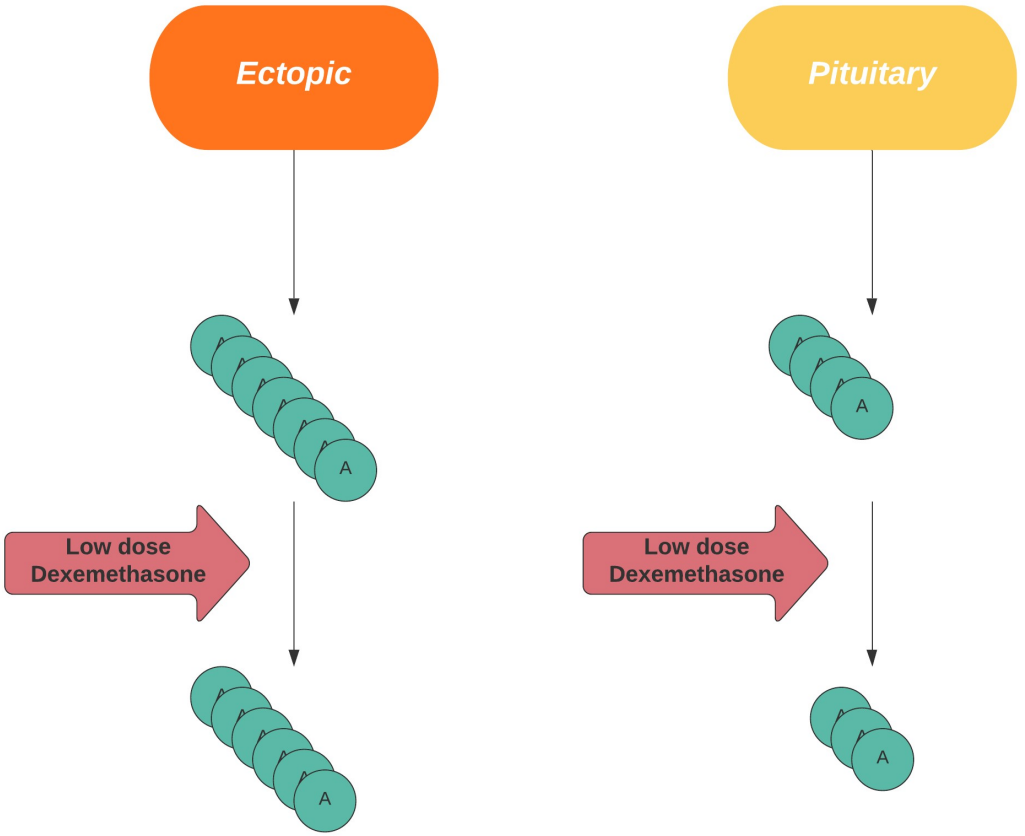


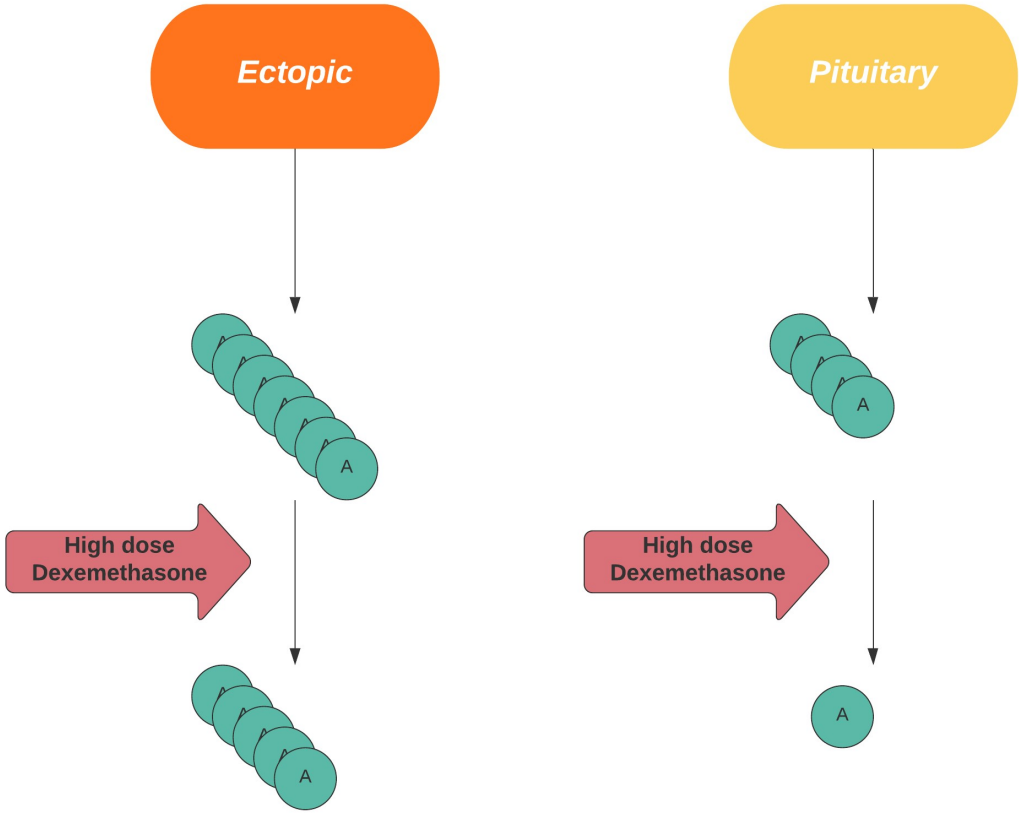

Hypercortisolism confirmed
9am ACTH raised?
No
CT adrenals
Yes
High dose dexamethasone suppression test
Suppressed
Not suppressed
MRI pituitary
CT chest/abdomen/pelvis

B Investigations

	Low dose DST	High dose DST
Pituitary tumour	Not suppressed	Suppressed
Ectopic source	Not suppressed	Not suppressed

B


Ectopic
Pituitary
A
Low dose
Dexemethasone
A
Low dose
Dexemethasone
A
A


Ectopic
Pituitary
A
High dose
Dexemethasone
A
High dose
Dexemethasone
A
A

B Management

ACTH dependent causes:

- **Pituitary adenoma (Cushing's disease)**
  - **First-line:** treatment is with **trans-sphenoidal resection** of the pituitary gland
  - **Second line:** medical therapy (e.g. glucocorticoid antagonists) or radiotherapy if surgery fails

- **Ectopic ACTH source:** treatment of underlying cancer

ACTH independent causes:

- **Iatrogenic:** review the need for medication and try weaning if possible

- **Adrenal tumour:** tumour resection or adrenalectomy

B Complications

Complications	Management
Cardiovascular	HTN Ischaemic heart disease
Endocrine	T2DM
Musculoskeletal	Osteoporosis
Infection	Immunosuppressed

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