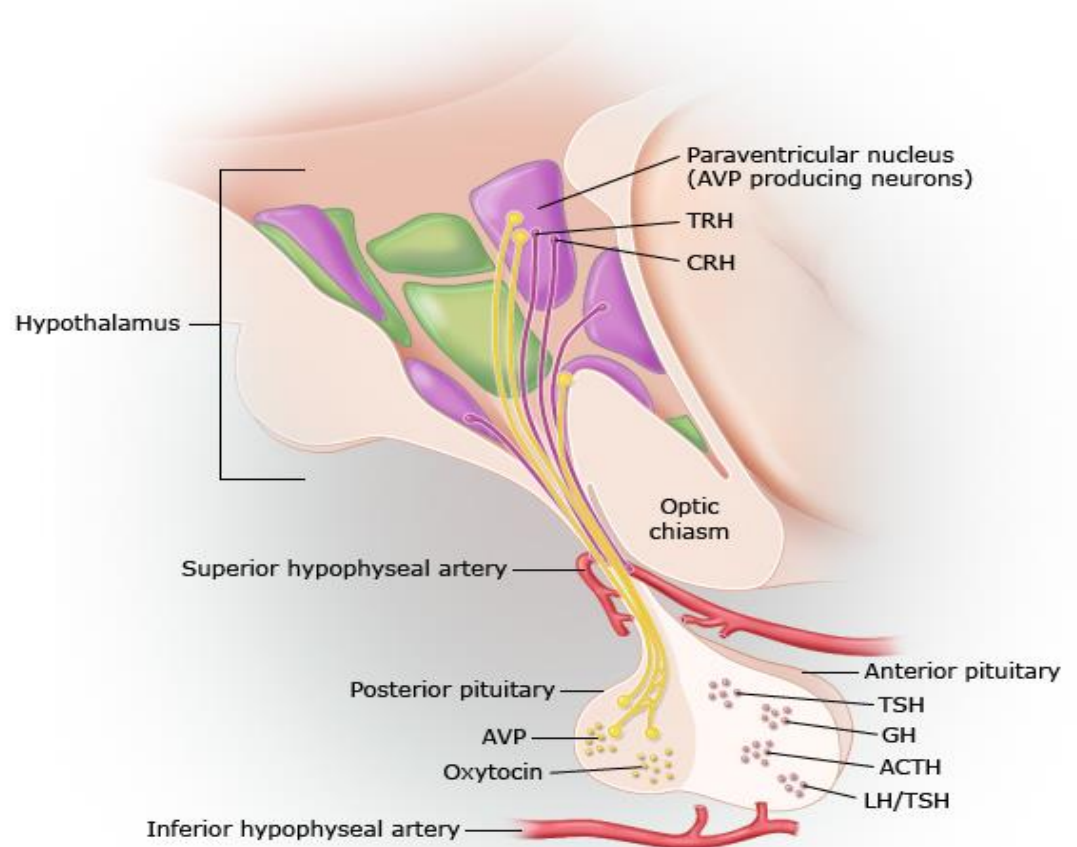


Acromegaly, SIADH, Diabetes Insipidus

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medicine



Acromegaly

- Acromegaly is the clinical syndrome that results from excessive secretion of **growth hormone (GH)**
- Excess GH stimulates hepatic secretion of **insulin-like growth factor-1 (IGF-1)**, which causes most of the clinical manifestations of acromegaly.
- The mean age at diagnosis is 40 to 45 years.

Pathophysiology

- Growth hormone is produced by the **anterior pituitary** gland.
- The most common cause of unregulated growth hormone secretion is a **pituitary adenoma**.
- This adenoma can be microscopic or a significantly sized tumour that causes compression of local structures.

Familial syndromes

Multiple endocrine neoplasia type 1 (GH-cell adenoma)

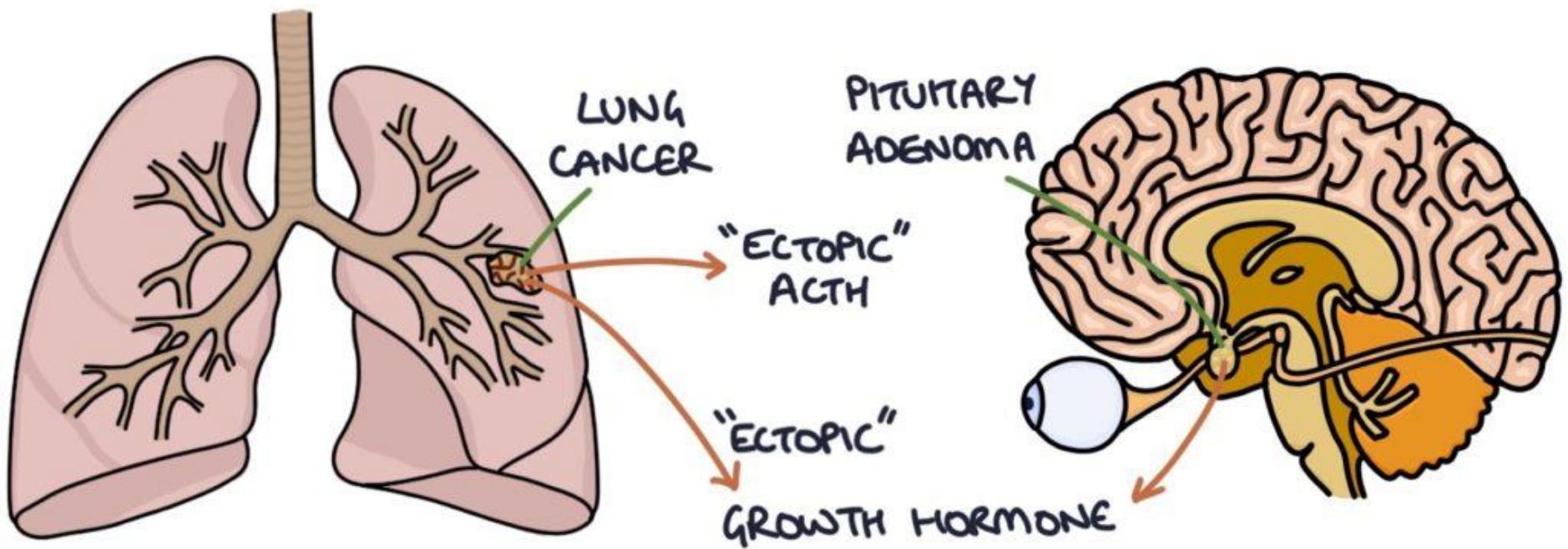
Familial acromegaly

McCune-Albright syndrome (rarely adenoma)

Carney's syndrome

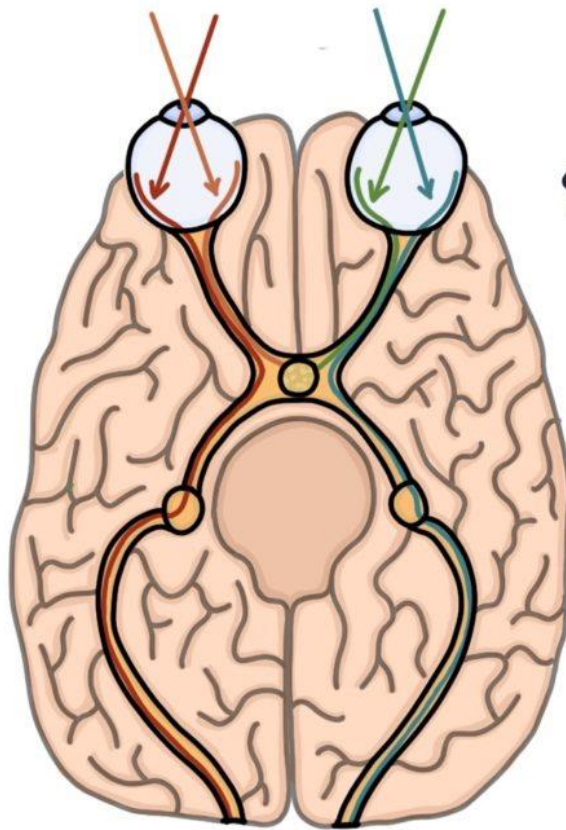
ectopic

- Acromegaly can also be secondary to cancer, such as lung or pancreatic cancer, with a tumour that secretes ectopic growth hormone-releasing hormone (GHRH) or growth hormone (GH).
- This is a **paraneoplastic syndrome**, meaning that it occurs alongside (para-) the neoplasm (tumour).
- *Bronchial carcinoid, pancreatic islet-cell tumor, small cell lung cancer, adrenal adenoma, medullary thyroid carcinoma, pheochromocytoma*

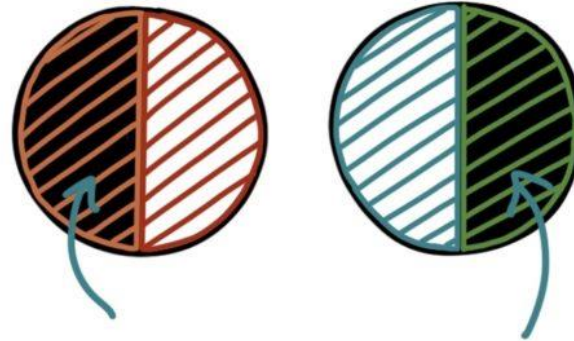


Clinical features

- A pituitary tumour of sufficient size can press on the **optic chiasm**.
- Pressure on the optic chiasm leads to a stereotypical **bitemporal hemianopia** visual field defect
- a loss of the outer half of the vision in both eyes.
- The inner half of the vision is spared, as this does not cross at the optic chiasm and stays on the same side of the head.



BITEMPORAL HEMIANOPIA



LOSS OF VISION
OUTER HALF

Clinical presentation

- ✓ Headache
- ✓ Visual field defect (bitemporal hemianopia)
- ✓ Excess growth hormone causes tissue growth
- ✓ Prominent forehead and brow (**frontal bossing**)
- ✓ Coarse, sweaty skin
- ✓ Large nose
- ✓ Large tongue (macroglossia)
- ✓ **Large hands and feet**
- ✓ Large protruding jaw (**prognathism**)



Additional features

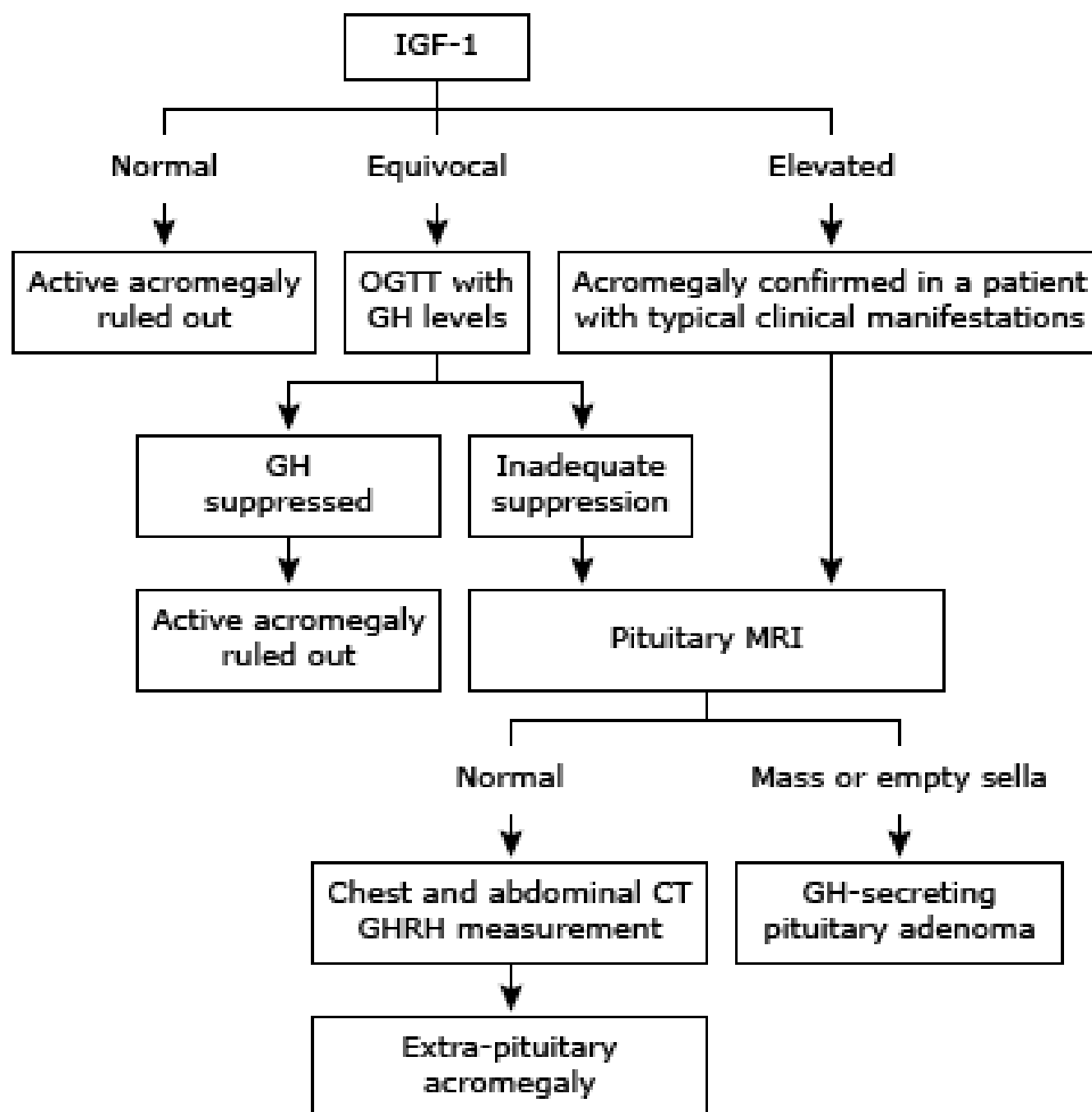
- LV Hypertrophy
- Hypertension
- Type 2 diabetes
- Carpal tunnel syndrome
- Arthritis
- Colorectal cancer

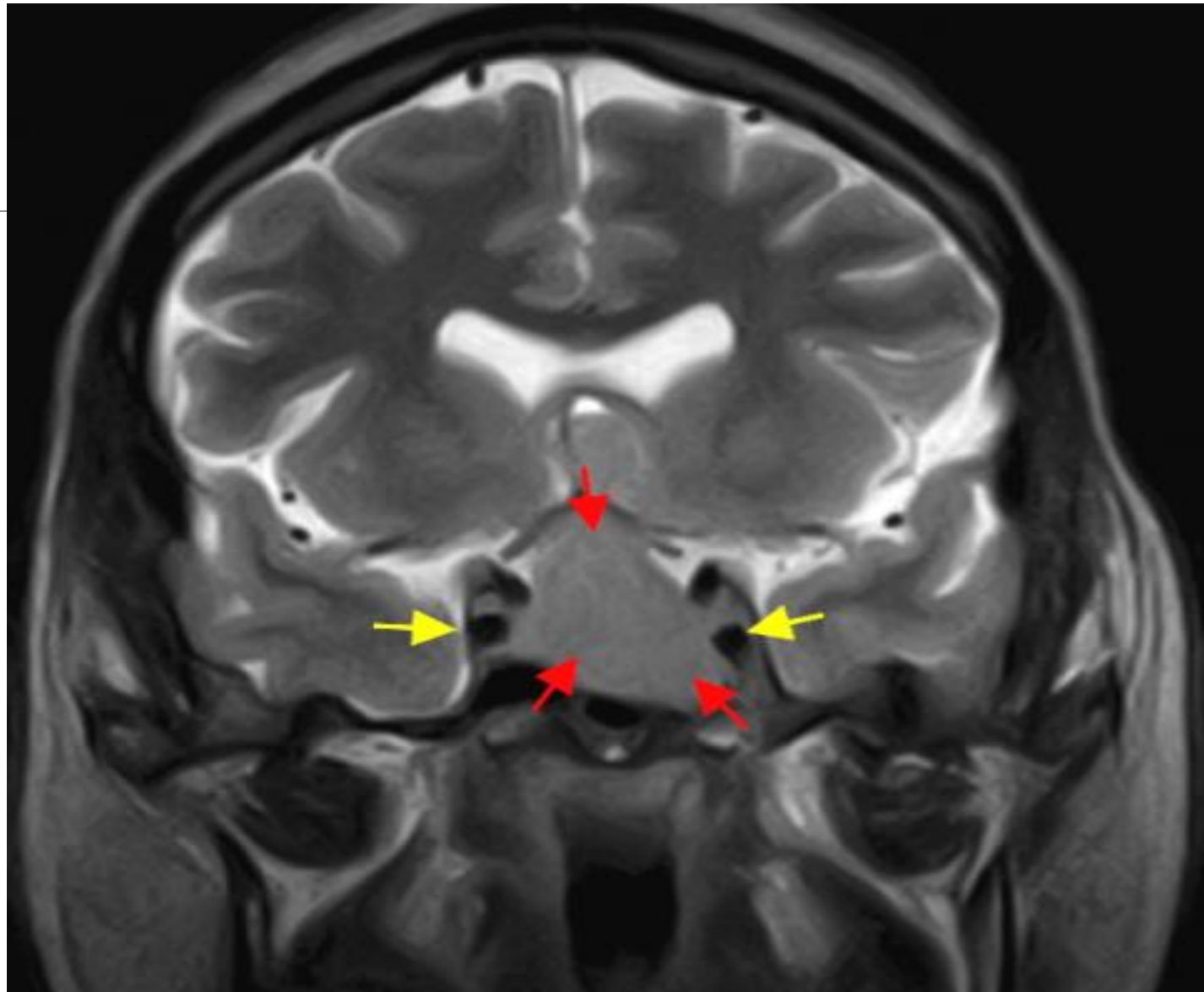
investigations

➤ IGF -1

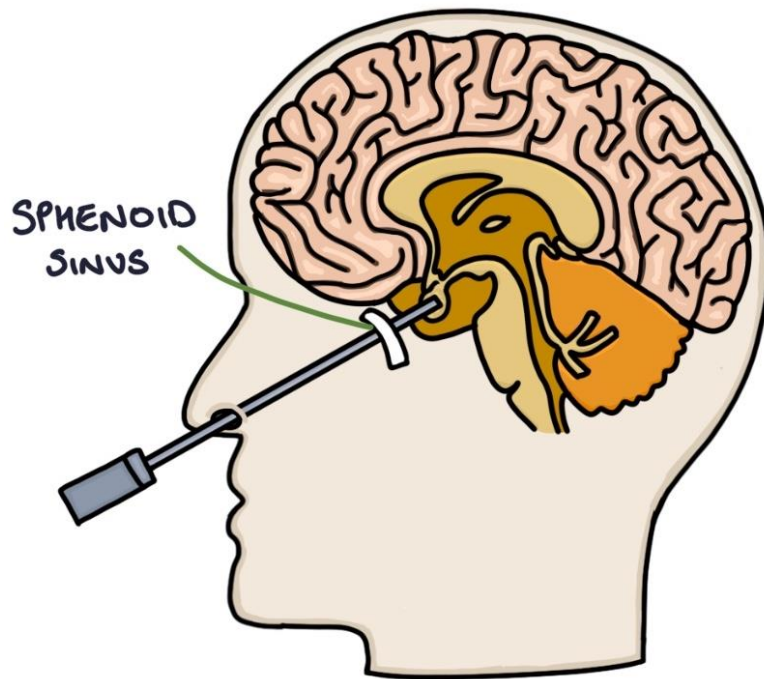
➤ Growth Hormone Suppression test(75g glucose drink with growth hormone levels at baseline and 2 hours following the drink, the glucose should suppress the growth hormone level) if $> 1 \text{ ng/ml}$ s/o acromegaly

➤ PITUITARY MRI





TREATMENT



- Pituitary Adenoma: **Trans-sphenoidal surgery**
- Radiotherapy
- **Pegvisomant** is a growth hormone receptor antagonist given daily by a subcutaneous injection
- Somatostatin analogues (e.g., **octreotide**) block growth hormone release
- Dopamine agonists (e.g., **bromocriptine**) block growth hormone release
-

Acromegaly vs gigantism

GH excess that occurs before fusion of the epiphyseal growth plates in a child or adolescent is termed pituitary gigantism.

ADH

- Antidiuretic hormone (ADH) is produced in the hypothalamus and secreted by the posterior pituitary gland.
- It is also known as vasopressin.
- ADH stimulates water reabsorption from the collecting ducts in the kidneys.

SIADH

➤ The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a disorder of impaired water excretion caused by the **inability to suppress the secretion** of antidiuretic hormone (ADH)

Excess ADH

There are two potential sources of excessive ADH:

- Increased secretion by the **posterior pituitary**
- **Ectopic** ADH, most commonly by small cell lung cancer

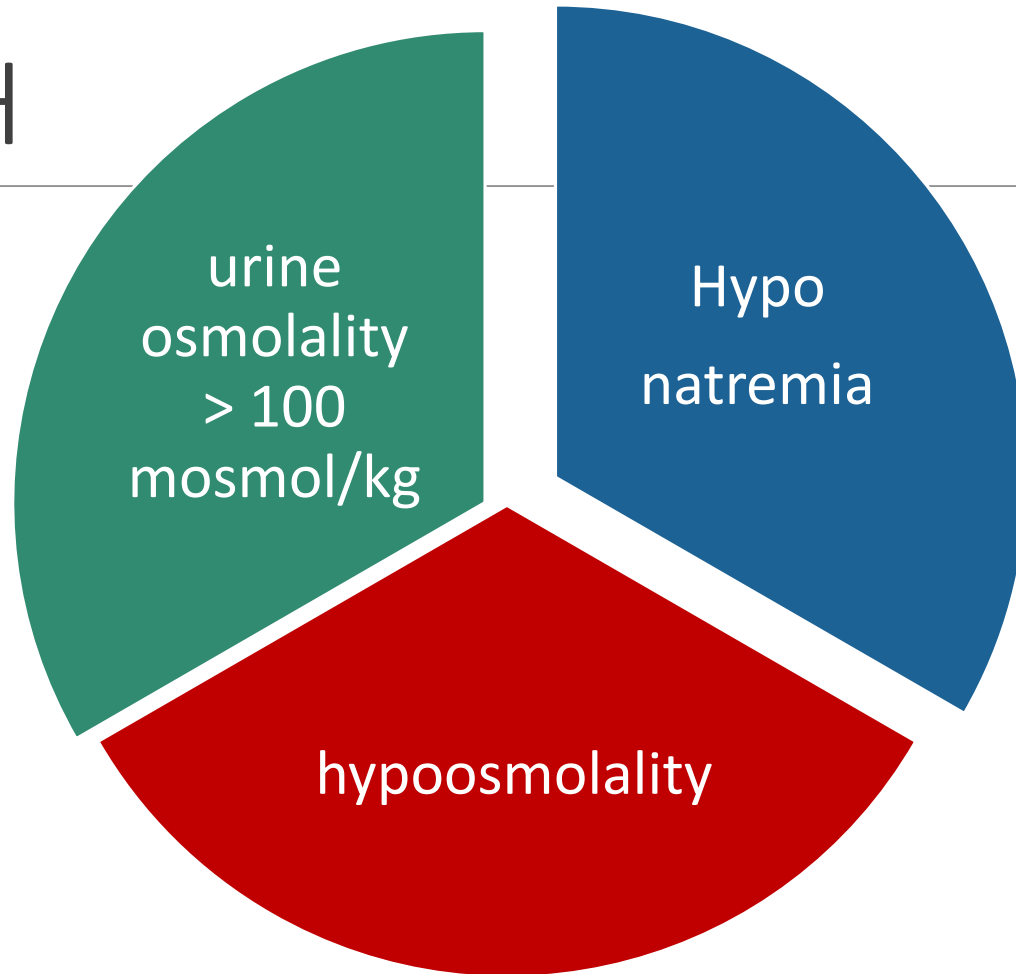
hyponatremia

- Excessive ADH results in **increased water reabsorption** in the collecting ducts, diluting the blood. This excess water reduces the sodium concentration (**hyponatremia**).
- The extra water is not usually significant enough to cause fluid overload.

Euvolaemic hyponatraemia

- SIADH results in euvolaemic hyponatraemia.
- Euvolaemic means normal (eu-) volume (-vol-) of blood
- The urine becomes more concentrated as the kidneys excrete less water.
- Therefore patients with SIADH have high **urine** osmolality and high urine sodium.

SIADH



CLINICAL PRESENTATION

- The symptoms of SIADH relate to low sodium (hyponatraemia).
- Depending on the sodium level and how rapidly it occurs, they may be asymptomatic or present with non-specific symptoms:
 - ✓ Headache
 - ✓ Fatigue
 - ✓ Muscle aches and cramps
 - ✓ Confusion
 - ✓ Severe hyponatraemia can cause seizures and reduced consciousness.

Causes

- Post-operative after major surgery
- Lung infection, particularly atypical pneumonia and lung abscesses
- Brain pathologies, such as a head injury, stroke, intracranial haemorrhage or meningitis
- Medications (e.g., SSRIs and carbamazepine)
- Malignancy, particularly small cell lung cancer
- Human immunodeficiency virus (HIV)

DIAGNOSIS

- Euvolaemia
- Hyponatraemia
- Low serum osmolality
- High urine sodium
- High urine osmolality
- RULE OUT OTHER CAUSES

OTHER CAUSES

- No history of diuretic use
- No diarrhoea, vomiting, burns, fistula or excessive sweating
- No excessive water intake
- No chronic kidney disease or acute kidney injury
- No heart failure or liver disease
- No adrenal insufficiency

MANAGEMENT

- Admission
- Treat underlying cause
- Fluid restriction – less than 800ml/day
- Hypertonic saline
- Oral salt tablets
- Oral urea
- Vasopressin receptor antagonist

Treat other causes

- ❖ Hormone replacement in adrenal insufficiency or hypothyroidism
- ❖ Treatment of infections such as meningitis, pneumonia, or tuberculosis
- ❖ Cessation of offending drugs, such as selective serotonin reuptake inhibitors or chlorpropamide

Hypertonic saline

- one liter of 3 percent saline contains 513 mEq of sodium
- For **acute** symptomatic cases- **bolus** of 100ml 3% saline is given , with monitoring, to raise Na at 1-3 mmol/hr
- For **chronic** cases , **slower** correction: 100 ml 3%saline at 15-30 cc/hr , with monitoring, to raise < 6-8 mmol in first 24 hrs and <6 mmol in the next24 hrs

Osmotic demyelination syndrome

- ❖ Osmotic demyelination syndrome is also known as :
central pontine myelinolysis (CPM).
- ❖ It is usually a complication of long-term severe hyponatraemia (e.g., under 120 mmol/L) **being treated too quickly** (e.g., more than a 10 mmol/L increase per 24 hour)

CPM

- ❖ First phase is due to the electrolyte imbalance. The patient presents as encephalopathic and confused. They may have a headache, vomiting and seizures.
- ❖ The second phase is due to the demyelination of the neurones, particularly in the **pons**. This occurs a few days after the rapid correction of sodium.
- ❖ This may present with spastic quadriparesis, pseudobulbar palsy and cognitive and behavioural changes.

ADH

- Antidiuretic hormone is produced in the hypothalamus and secreted by the posterior pituitary gland.
- It is also known as vasopressin.
- ADH stimulates water reabsorption from the collecting ducts in the kidneys.

DIABETES INSIPIDUS (AVP –D)

- It is a syndrome characterized by the excretion of abnormally large volumes of dilute urine
- With diabetes insipidus, the kidneys are unable to reabsorb water and concentrate the urine, leading to:
 - Polyuria (excessive amounts of urine)
 - Polydipsia (excessive thirst)

Diabetes insipidus

- ✓ A lack of antidiuretic hormone (**cranial** diabetes insipidus)
- ✓ A lack of response to antidiuretic hormone (**nephrogenic** diabetes insipidus)

Nephrogenic Diabetes Insipidus

Nephrogenic diabetes insipidus : when the collecting ducts of the kidneys do not respond to ADH. It can be idiopathic, without a clear cause, or it can be caused by:

- » Medications, particularly lithium (used in bipolar affective disorder)
- » Genetic mutations in the ADH receptor gene (X-linked recessive inheritance)
- » Hypercalcaemia (high calcium)
- » Hypokalaemia (low potassium)
- » Kidney diseases (e.g., polycystic kidney disease)

Cranial Diabetes Insipidus

the hypothalamus does not produce ADH for the pituitary gland to secrete.

It can be idiopathic, without a clear cause, or it can be caused by:

- » Brain tumours
- » Brain injury
- » Brain surgery
- » Brain infections (e.g., meningitis or encephalitis)
- » Genetic mutations in the ADH gene (autosomal dominant inheritance)
- » Wolfram syndrome (a genetic condition also causing optic atrophy, deafness and diabetes mellitus)

Presentation

- Polyuria (producing more than 3 litres of urine per day)
- Polydipsia (excessive thirst)
- Dehydration
- Postural hypotension

Investigations

- » Low urine osmolality (lots of water diluting the urine)
- » High/normal serum osmolality (water loss may be balanced by increased intake)
- » More than 3 litres on a 24-hour urine collection

The water deprivation test is the test of choice for diagnosing diabetes insipidus.

MRI BRAIN



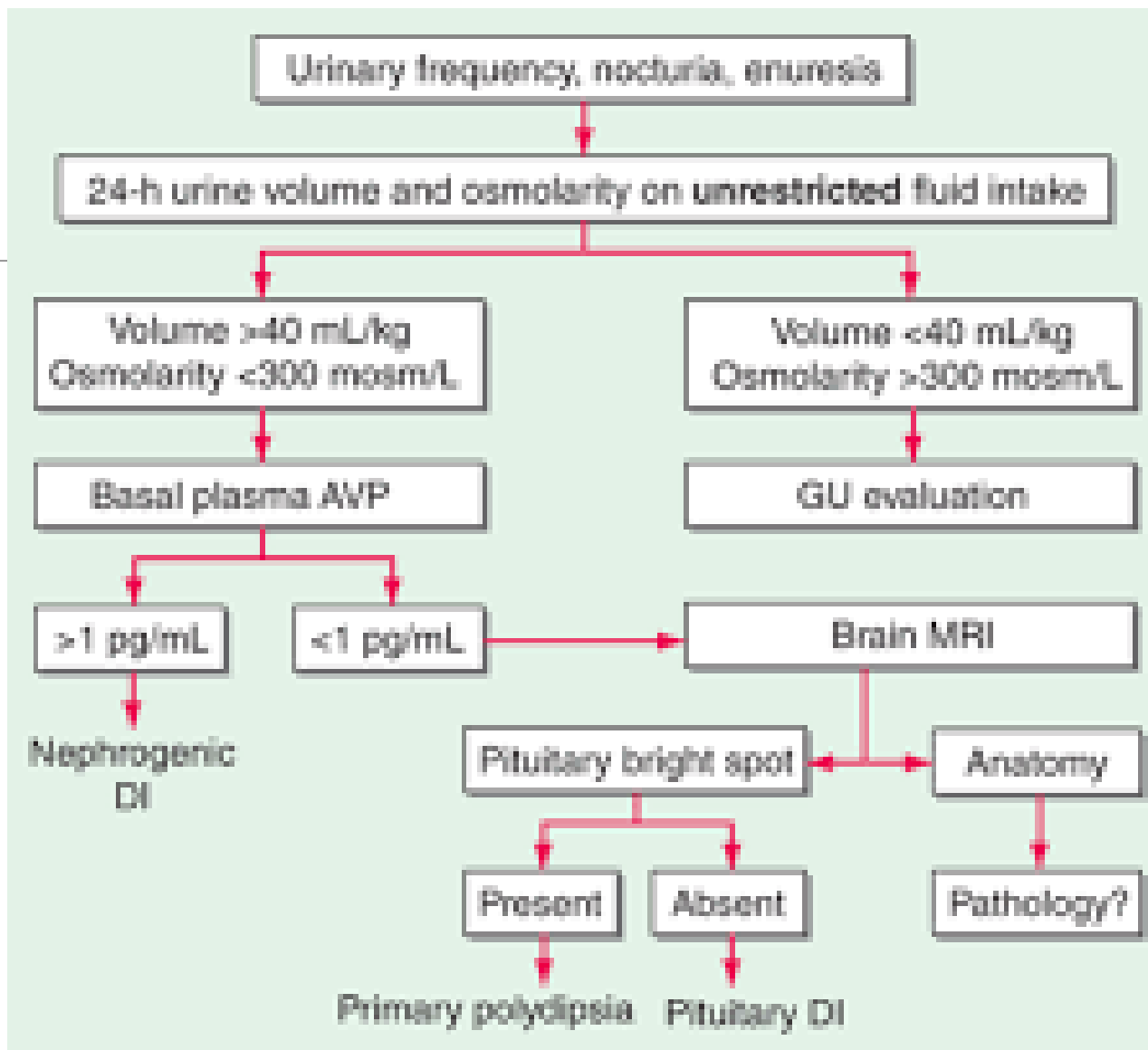
Loss of the pituitary
hyperintense spot or bright
spot on a T1-weighted MRI
image reflects the loss of
functional integrity of the
neurohypophysis

Water Deprivation Test

- The patient avoids all fluids for up to 8 hours before the test (water deprivation).
- After water deprivation, urine osmolality is measured.
- If the urine osmolality is low, synthetic ADH (desmopressin 2 mcg) is given.
- Urine osmolality is measured over the 2-4 hours following desmopressin.

Water Deprivation Test

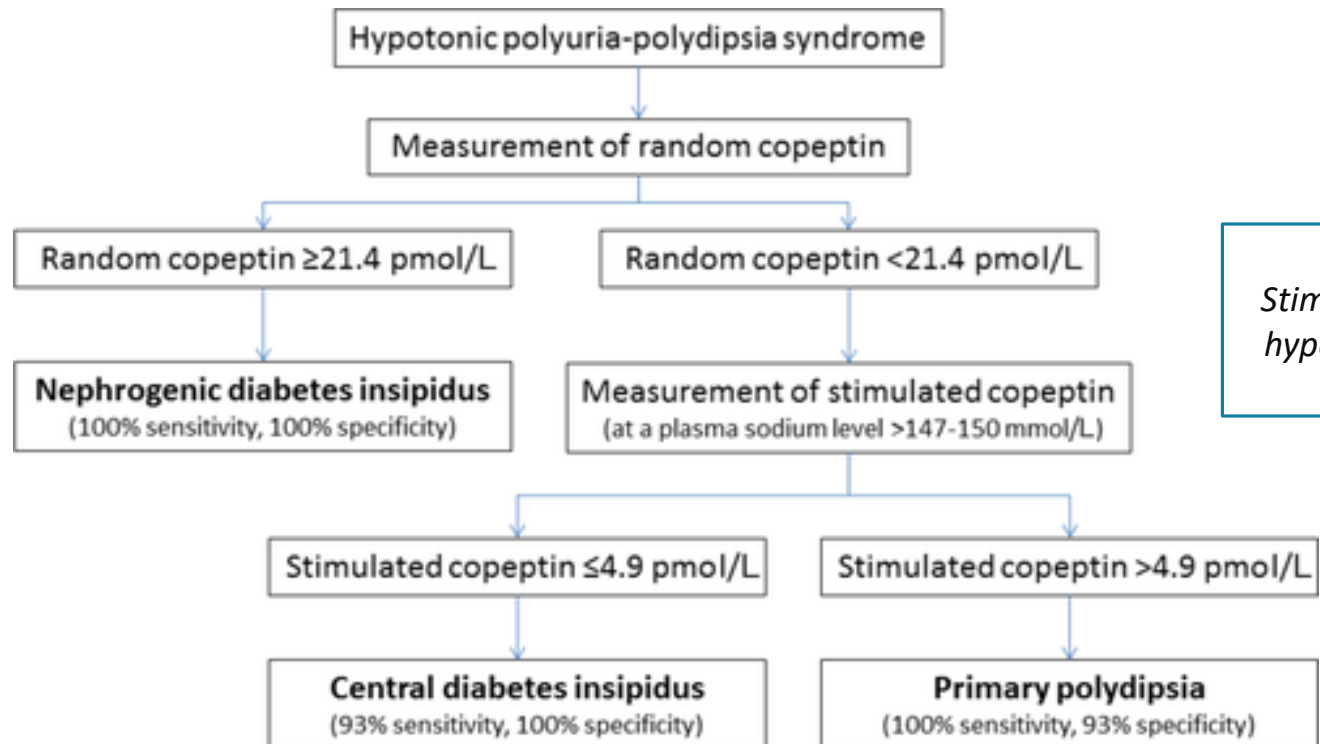
	Urine Osmolality After Water Deprivation	Urine Osmolality After Desmopressin
Primary Polydipsia	High	Not required
Cranial Diabetes Insipidus	Low	High
Nephrogenic Diabetes Insipidus	Low	Low



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition
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Copeptin assay

- copeptin (the C-terminal glycoprotein moiety of the AVP **prohormone** and therefore a surrogate marker of ADH)



Stimulated = give hypertonic saline

treatment

- ❖ The underlying cause should be treated (e.g., stopping lithium)
 - ❖ Mild cases may be managed conservatively.
 - ❖ **Desmopressin (synthetic ADH)** can be used in cranial diabetes insipidus to replace the absent antidiuretic hormone.
 - ❖ The serum sodium needs to be monitored, as there is a risk of hyponatraemia (low sodium) with desmopressin.
- Nephrogenic diabetes insipidus is less straightforward to treat.
 - Management options include:
 - Ensuring access to plenty of water
 - **High-dose desmopressin**
 - **Thiazide diuretics**
 - **NSAIDs**

SUMMARY

ACROMEGALY

SIADH

DI