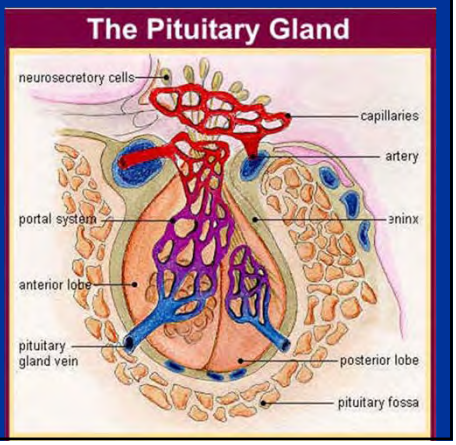
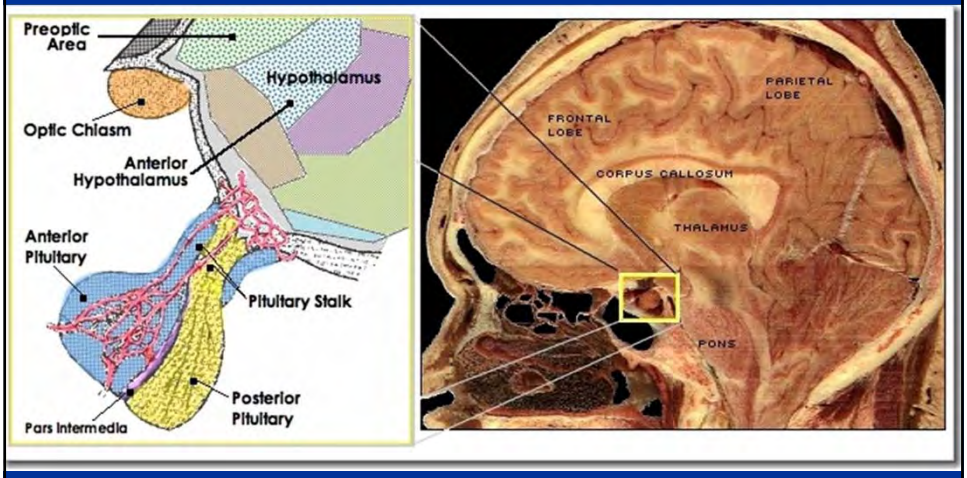
Hypopituitarism
Diabetes Insipidus
Pituitary tumours (1)

Dr T Kemp

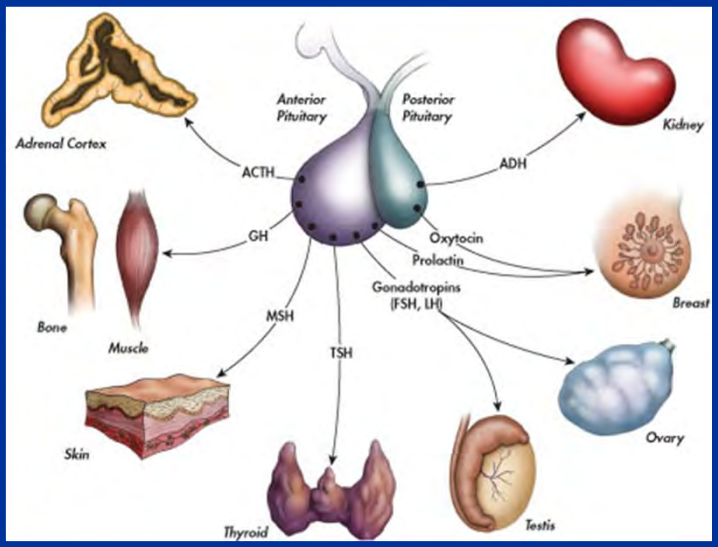
- Endocrinology and Metabolism Unit
- Steve Biko Academic Hospital



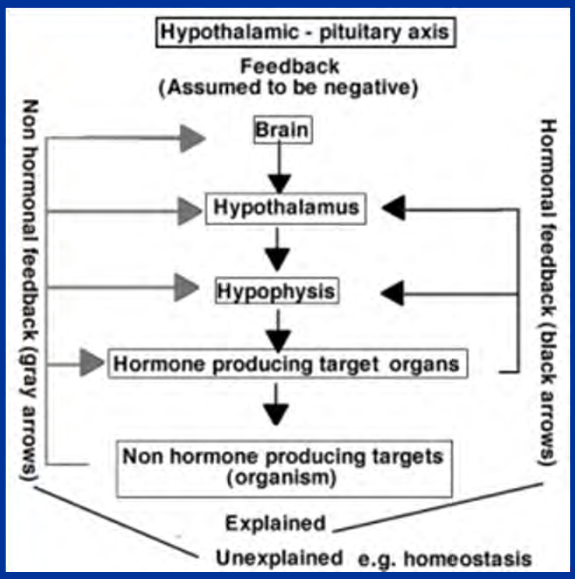
Pituitary anatomy



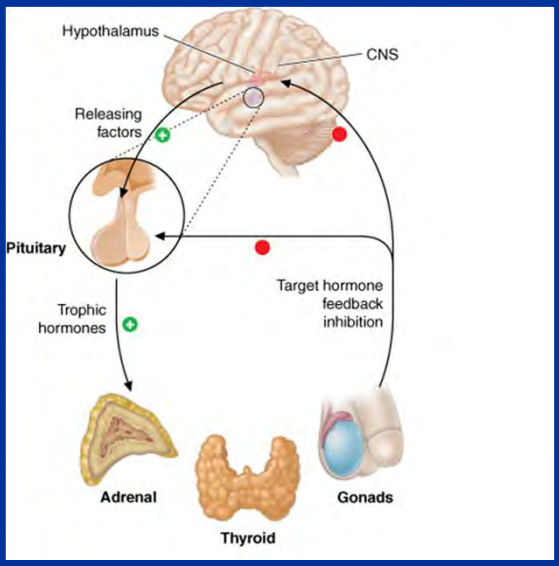
Target organs of the pituitary gland



Pituitary axis



Negative feedback



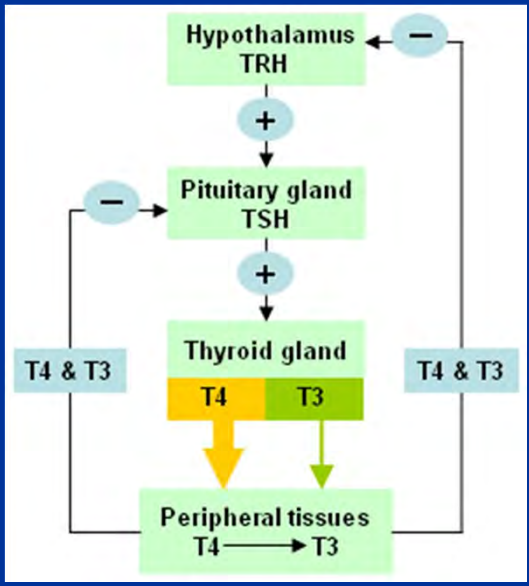
Pituitary axis

Hypothalamus:
-CRF (Corticosteroid releasing factor)
-DA (Dopamine)
-GHRH (Growth hormone releasing hormone)
-GnRH (Gonadotropin releasing hormone)
-TRH (Thyroid releasing hormone)

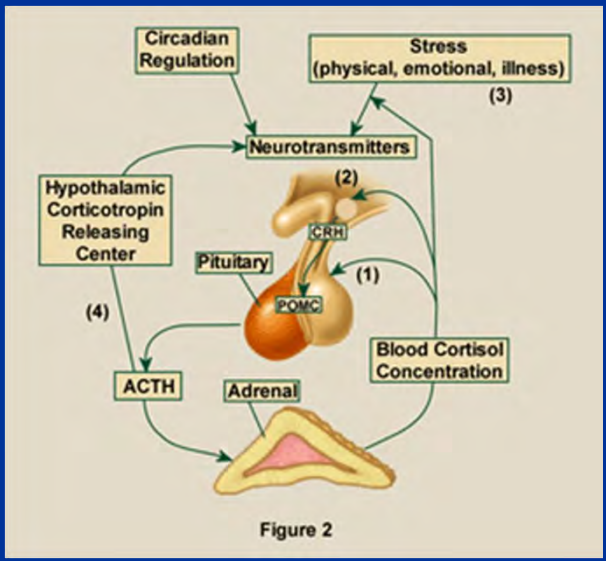
Anterior pituitary:
-ACTH (Adrenocorticotrophic hormone)
-PRL (Prolactin)
-GH (Growth hormone)
-LH (Luteinizing hormone)
-FSH (Follicle stimulating hormone)
-TSH (Thyroid releasing hormone)

Posterior pituitary:
-ADH (Antidiuretic hormone)
-Oxytocin

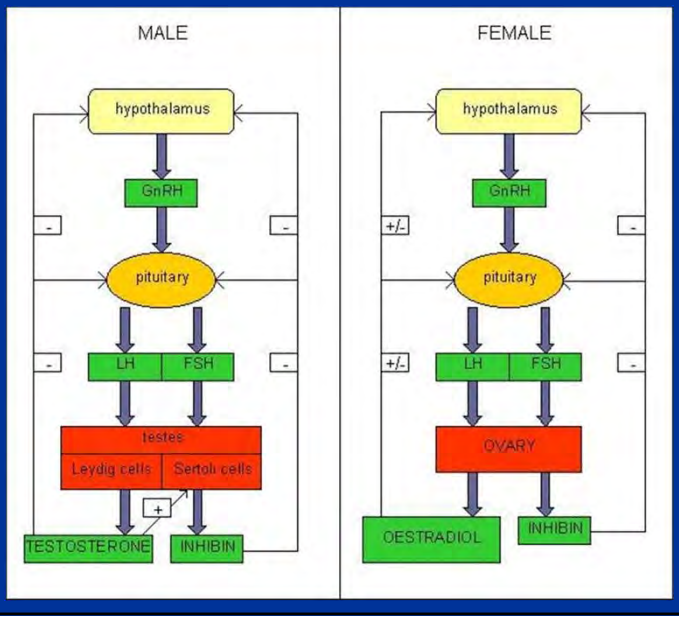
Hypothalamus-Pituitary-Thyroid axis



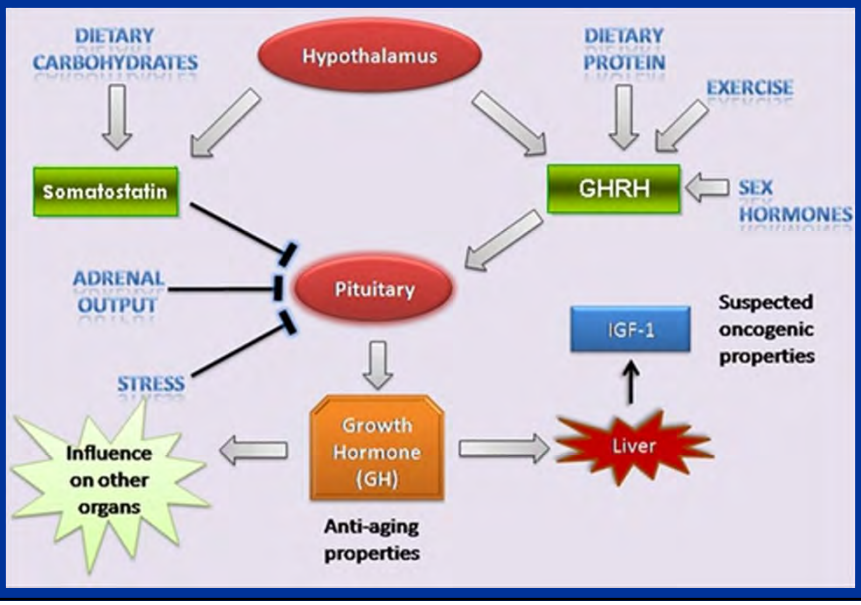
Hypothalamus-Pituitary-Adrenal axis



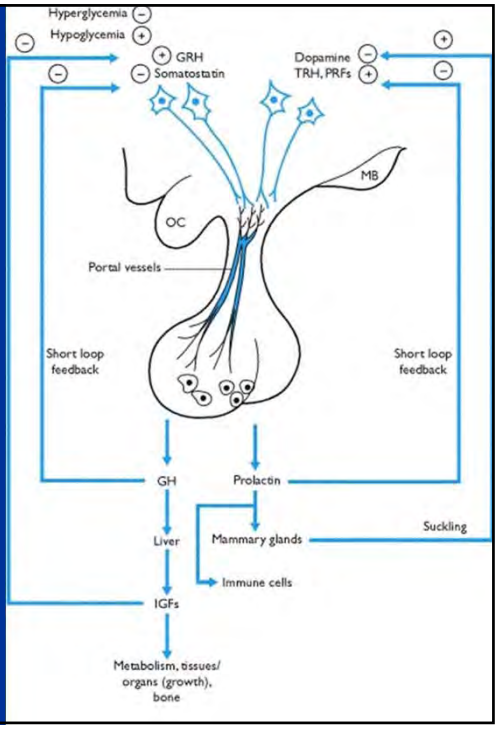
Hypothalamus-Pituitary-Gonadal axis



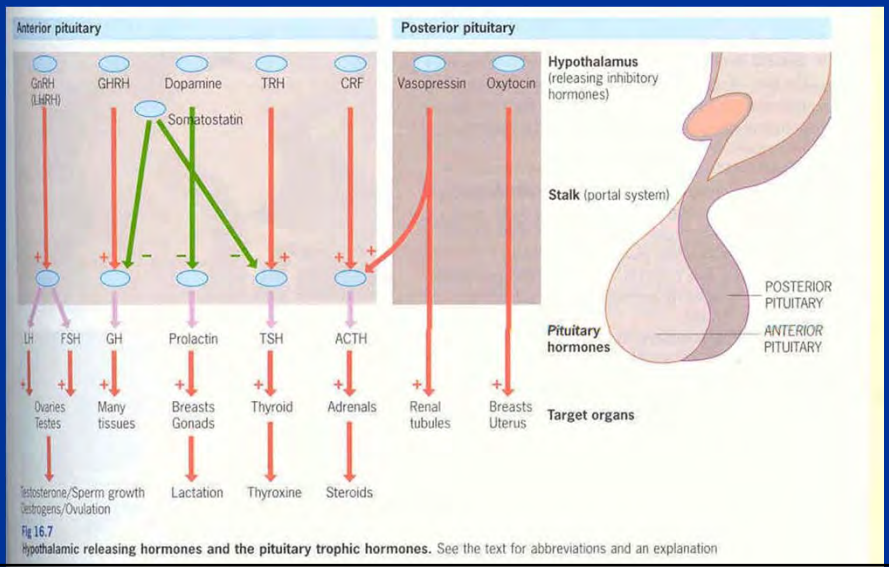
Growth Hormone axis



Prolactin axis



Hypothalamic and Pituitary Hormones (summary)



Hypothalamic or Pituitary Diseases

- Hormone excess
- Hormone deficiency
- Hormone resistance
- Non-functioning tumours

- Hormone = A substance, usually a peptide or steroid, produced by one tissue and conveyed by the bloodstream to another to effect physiological activity, such as growth or metabolism

How to investigate patients with suspected pituitary hypothalamic disease

- Identify pituitary hormone deficiency
- Identify hormone excess
- Establish the anatomy and diagnosis

Principles of testing pituitary function

- For suspected hormone deficiency, do a stimulatory test for diagnosis
- For suspected hormone excess, do a suppression test for diagnosis
- To evaluate for a deficiency, usually test the hormone when it should be at its highest (eg 8h00 cortisol for suspected adrenal insufficiency)
- To evaluate for hormone excess, can be helpful to test the hormone when it should be at its lowest level (eg midnight cortisol for suspected Cushing's)

(1) Hypopituitarism

Hypopituitarism

Common Causes:

- Surgical hypophysectomy
- Compression by tumour
- Pituitary radiotherapy
- Sheehan syndrome
- Empty sella syndrome
- Metastatic tumours / granulomas

FSH / LH / GH
↓
TSH
↓
ACTH
↓
ADH

Aetiology:

- **9 I's**
  - **Invasive**
  - **Infarction**
  - **Infiltrative**
  - **Injury**
  - **Immunologic**
  - **Iatrogenic**
  - **Infectious**
  - **Isolated**
  - **Idiopathic**

- Invasive
  - Pituitary adenoma
  - Craniopharyngioma
- Infarction (vascular)
  - Pituitary apoplexy
  - Sheehan's Syndrome
- Infiltrative
  - Sarcoidosis
  - Haemochromatosis
- Immunologic
  - Autoimmune

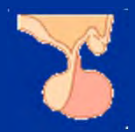
- Iatrogenic
  - Pituitary surgery
  - Radiation therapy
- Infectious
  - TB
- Isolated (e.g. Gonadotrophin deficiency)
  - Congenital – Kallman's Syndrome
  - Anorexia nervosa
- Injury
  - Trauma
- Idiopathic

Hypopituitarism

- Decreased or absent secretion of one or more pituitary hormones
- Macro-adenomas are the most common cause (followed by vascular causes)
- Remember pressure effects
- Decreased function of the rest of the pituitary gland
- Often more than one axis
- Classic fallout pattern

Gonadal
GH
Thyroid
ACTH
} Hypofunction

Hypofunction



➡ Regulators and hormones *LOW*

Hypogonadotrophic hypogonadism

Growth Hormone deficiency

Hypothyroidism

Hypoadrenalism

Prolactin (↑↓)

- Hypogonadotrophic hypogonadism
  - ⇩ LH, FSH, oestradiol, testosterone
  - ♀ Amenorrhoea
  - ♂ Erectile dysfunction, decreased libido

- Hypogonadotrophic hypogonadism
  - ↓ LH, FSH, oestradiol, testosterone
  - ♀ Amenorrhoea
  - ♂ Erectile dysfunction, decreased libido
- GH deficiency
  - GH
  - ↓ Growth retardation
  - Dwarfism

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  - Dwarfism
- Hypothyroidism
  - TSH low/normal, T3 + T4 low
  - Secondary Hypothyroidism

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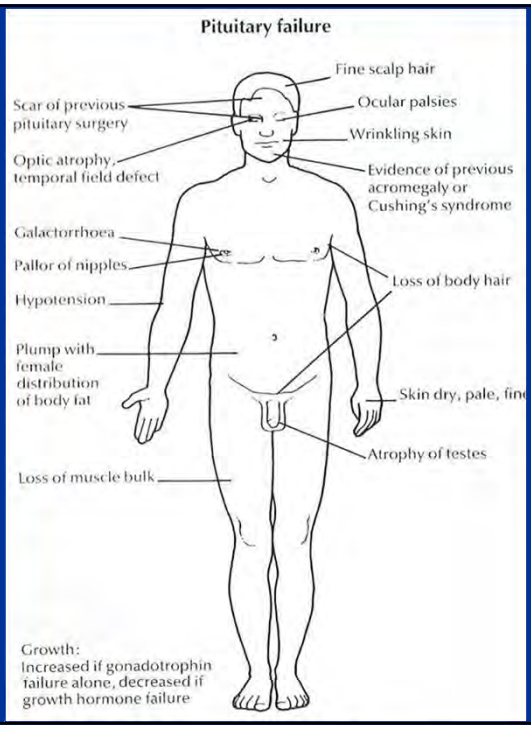
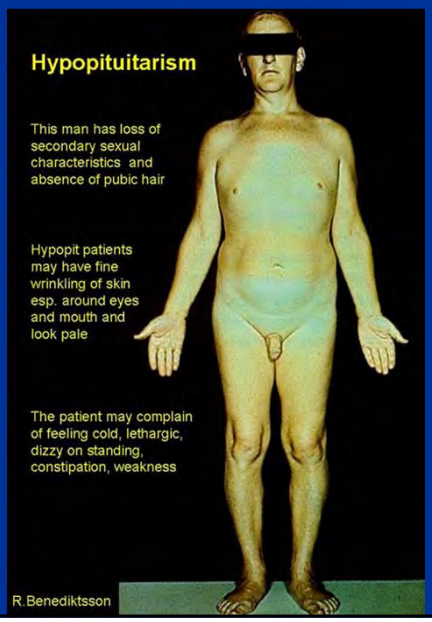
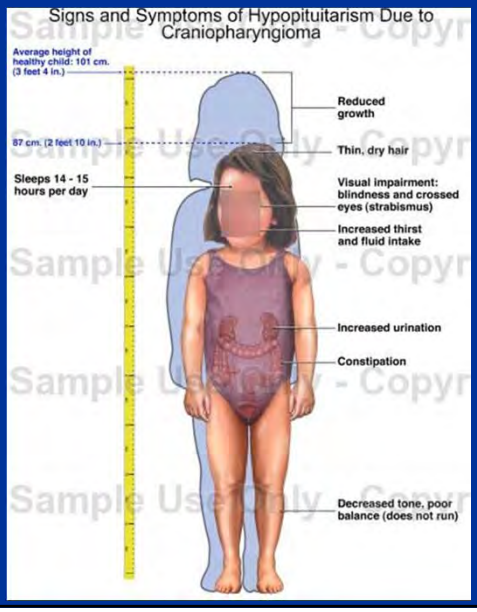
- GH deficiency
  - GH
  - ↓ Growth retardation
  - Dwarfism
- Hypothyroidism
  - TSH low/normal, T3 + T4 low
  - Secondary Hypothyroidism
- Hypoadrenalism
  - ↓ ACTH, ↓ cortisol
  - Secondary hypoadrenalism



Panhypopituitarism



Stunted growth / dwarfism



Central hypothyroidism

Testing for anterior hypopituitarism

- ACTH deficiency

- short ACTH stimulation test / insulin tolerance test

- LH/FSH deficiency

- serum LH/FSH/testosterone/oestradiol

- TSH deficiency

- random serum T4, TSH (but TSH can be ↑/↓/N)

- Growth hormone deficiency

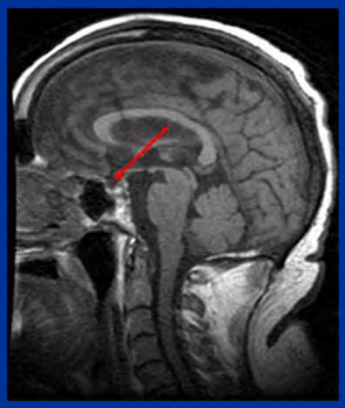
- only investigate if GH replacement is considered

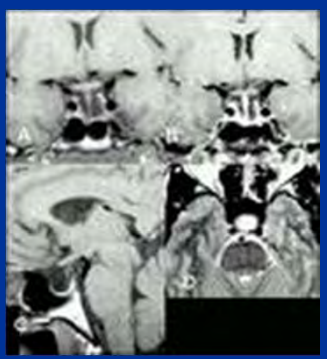
- exercise / other stimulatory tests

Special situations:
(1) EMPTY SELLA SYNDROME

- Occurs when the subarachnoid space extends into the sella turcica, partially filling it with cerebrospinal fluid
- This causes remodelling and enlargement of the sella and flattening of the pituitary
- Can be congenital; or secondary to Sheehan's syndrome, or pituitary radiation/surgery, or after pituitary adenoma infarction
- Usually normal pituitary function (but must exclude hormone insufficiency or hypersecretion)

Empty sella tursica

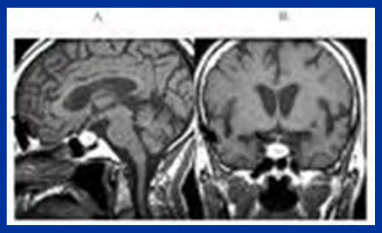


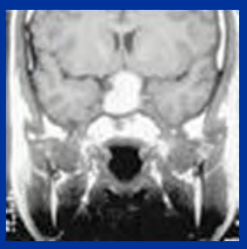


(2) PITUITARY APOPLEXY

- = rare but frightening syndrome of violent headache, visual and cranial nerve disturbances, and mental confusion/coma/death, resulting from haemorrhage or infarction of the pituitary gland
- Usually in a patient with a pituitary tumour, but can occur in DM, head trauma, anticoagulation therapy
- Diagnosed on MRI findings
- Treatment: high-dose dexamethasone, trans-sphenoidal pituitary decompression
- Evaluate afterwards: often multiple pituitary hormonal deficiencies

Pituitary apoplexy





(3) SHEEHAN'S SYNDROME

- = postpartum pituitary necrosis
- Preceded by obstetric haemorrhage leading to circulatory collapse
- Severe hypotension predisposes the enlarged pituitary to ischaemia
- Usually sparing of the posterior pituitary
- Clinically: commonly failure to lactate
- Also loss of axillary and pubic hair; hypothyroidism; hypocortisolism
- Damage is variable

Treatment of hypopituitarism:

Always replace with *Cortisol* before *Eltroxin!!*

Table 16.10
Replacement therapy for hypopituitarism

Axis	Usual replacement therapies
Gonadal	
Male	Testosterone intramuscularly, orally, as patch or implant
Female	Cyclical oestrogen/progestogen orally or as patch/implant
Fertility	HCG plus FSH (purified or recombinant) to produce testicular development, spermatogenesis or ovulation Pulsatile LHRH also used
Breast (Prolactin inhibition)	Dopamine agonist as replacement inhibition (e.g. bromocriptine 3–15 mg daily)
Growth	Recombinant human GH used routinely to achieve normal growth in children Also advocated for replacement therapy in adults where GH has effects on muscle mass and well-being
Thyroid	Thyroxine 100–150 µg daily
Adrenal	Hydrocortisone 15–40 mg daily (divided doses) or prednisolone 5–10 mg daily (Normally no need for mineralocorticoid replacement)
Thirst	Desmopressin (DDAVP) 10–20 µg one to three times daily by nasal spray or orally 100–200 µg thrice daily Carbamazepine and thiazides are rarely used in mild diabetes insipidus

(2) Diabetes Insipidus

Diabetes Insipidus

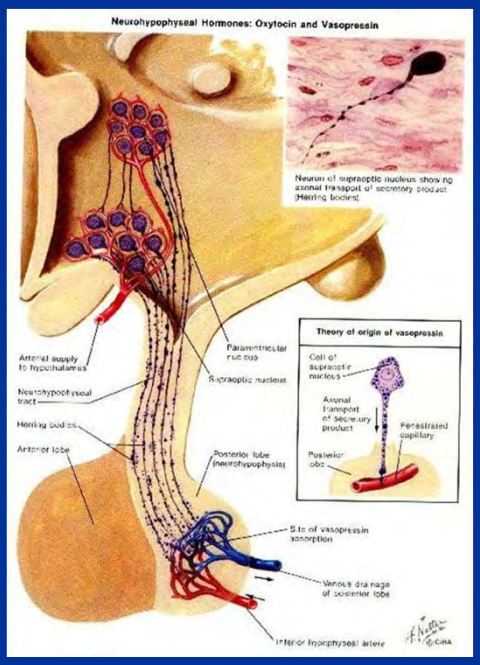
Diagnosis

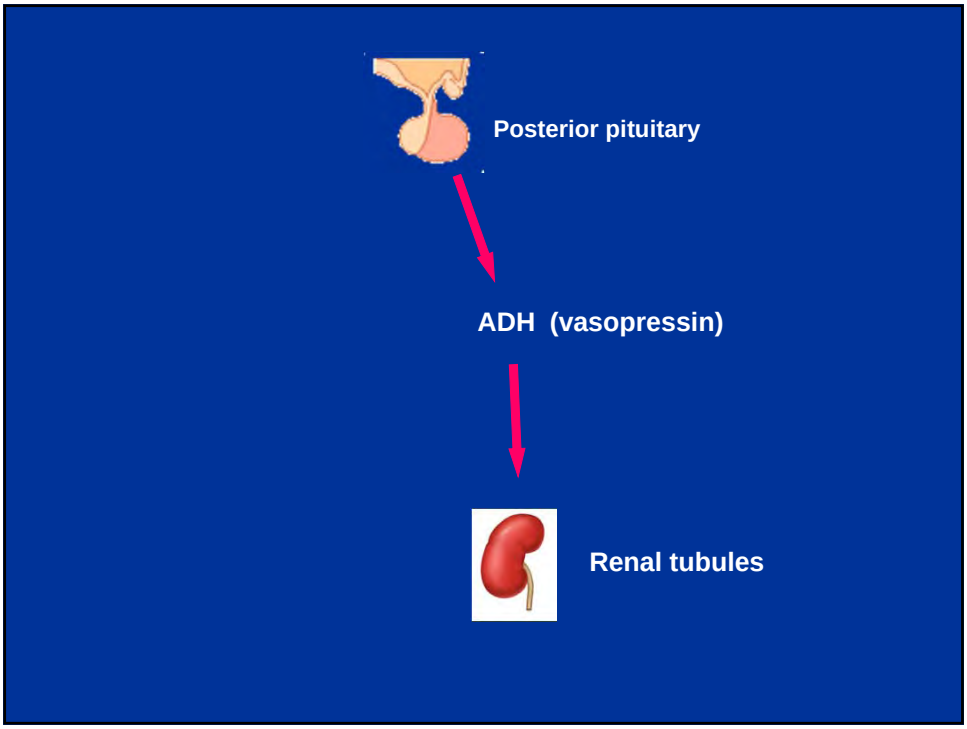
- Polyuria, polydipsia
- Urine SG < 1.006
- Vasopressin reduce urine output
- Hyperuricaemia

Causes

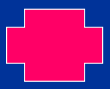
- Familial
- Idiopathic
- Damage to hypothalamus
- Pituitary stalk damage by tumour, anoxic encephalopathy, trauma, infection, histiocytosis

Treatment: Desmopressin


Neurohypophyseal Hormones: Oxytocin and Vasopressin
Theory of origin of vasopressin
Arterial supply to hypothalamus
Neurohypophyseal tract
Herring bodies
Anterior lobe
Paraventricular nucleus
Supraoptic nucleus
Posterior lobe neurohypophysis
Site of vasopressin absorption
Venous drainage of posterior lobe
Inferior hypophyseal artery
Cell of supraoptic nucleus
Axonal transport of secretory product
Fenestrated capillary
Posterior lobe


Posterior pituitary
ADH (vasopressin)
Renal tubules

THIRST



- ↑ osmolality
- Hypovolaemia
- Hypotension
- Nausea
- Hypothyroidism
- Angiotensin II
- Adrenaline
- Cortisol
- Nicotine
- Antidepressants

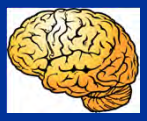
- ↓ osmolality
- Hypervolemia
- Hypertension
- Ethanol
- Alpha-adrenergic stimulation

Diabetes Insipidus is…

- A disorder resulting from deficient ADH action
- Characterized by large amounts of very dilute urine
- Types:
  - Central (neurogenic) DI
    (posterior pituitary hypofunction)
  - Nephrogenic DI

- **Central DI**
  - ➡ failure of the posterior pituitary gland to secrete adequate quantities of ADH
- **Nephrogenic DI**
  - ➡ kidney fails to respond to circulating ADH

Causes



- Traumatic
  - Surgery
- Tumours
- Infections
  - TB
- Infiltrations
  - Sarcoidosis
- Idiopathic
- Vascular
- Congenital

- Chronic renal disease, RTA
- Hypokalemia
- Hypercalcemia
- Drugs
  - Lithium
  - Demeclocycline
  - Glibenclamide
- Idiopathic
- Congenital

ΔΔ Polyuria + Polydipsia

- Diabetes mellitus
- Hypercalcaemia
- Psychogenic polydipsia
  (compulsive H_2O drinking)

Diagnosis of DI

- Patients with DI cannot concentrate urine – low urine osmolality
- Screening
  - Plasma osmolality 275 – 290 mosm/kg
  - Urine osmolality > 600 mosm/kg

Suggests good concentration and DI unlikely

Diagnosis of DI

	Central DI	Nephrogenic DI	Psychogenic polydipsia
Random serum osmolality	↑	↑	↓
Random urine osmolality	↓	↓	↓
Plasma Sodium	↑	↑	↓
Urine osmo during water deprivation test	No change	No change	↑
Recovery with vasopressin	Yes	No	Yes/no

Diagnosis of DI

- Exclude other causes of polyuria and polydipsia
- Confirm diagnosis of DI
- Look for the underlying cause *(NB refer)*
  - ✓ Central DI – MRI scan
  - ✓ Nephrogenic DI
  - ✓ Psychogenic polydipsia – psychiatric management

Treatment

- **Central DI**

  - Desmopressin, DDAVP
    - Intranasally 1- 3 times per day depending on severity
    - Subcutaneously or orally if cannot tolerate intranasal preparation
  - Monitor serum osmolality and serum sodium at regular intervals

- **Nephrogenic DI**
  - Drugs that sensitize renal tubules
    - thiazides, carbamazepine, chlorpropamide

Treatment

- **NB:**

Episodes of decreased level of consciousness very dangerous

MEDIC ALERT BRACELET !!!