Hypopituitarism
Diabetes Insipidus
Pituitary tumours (2)

Dr T Kemp

- Endocrinology and Metabolism Unit

- Steve Biko Academic Hospital

(3) Pituitary tumours

- Pituitary microadenoma
  - intrasellar adenoma < 1cm in size
- Pituitary macroadenoma
  - intrasellar adenoma > 1cm in size

Relative incidence

- Prolactinomas = 60%
- GH hypersecretion = 20%
- ACTH excess = 10%
- Nonfunctional tumours = 10%
- Hypersecretion of TSH or gonadotropins = very rare

Clinical presentation

- Hypersecretion of anterior pituitary hormones = functional pituitary tumour
- Hyposecretion of anterior pituitary hormones = hypopituitarism
- Local / pressure effects
- Incidentiloma

Consequences of pituitary tumours

- Hormone production: ⬆⬇
- Effects on surrounding structures:

Optic tracts
- visual field fallout
- optic atrophy

Cavernous sinuses
- cranial nerve 3,4,6

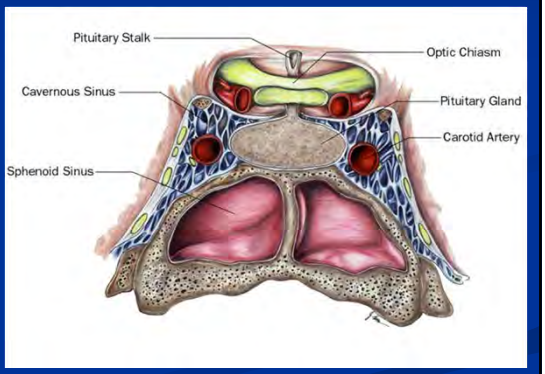
3rd ventricle
- hydrocephalus

Meninges
- headache

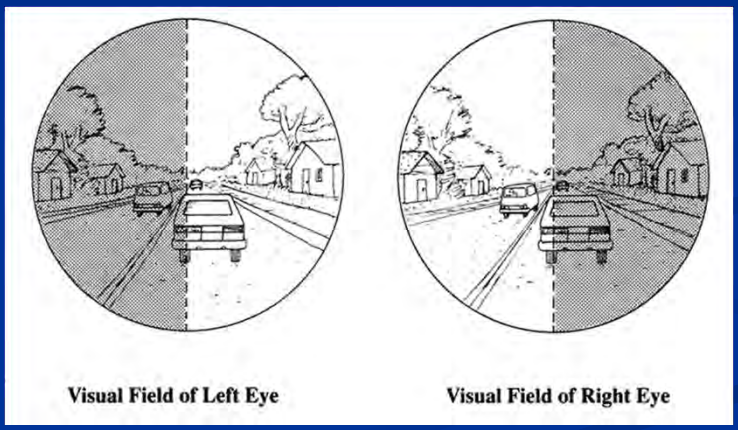
Sphenoid sinus
- CSF rhinorrhoea

Bony structures - erosion

Hypothalamus - appetite, thirst



Visual field loss – *homonymous hemianopia*



Special investigations

- Blood tests
  - NB: prolactin
  - rest of pituitary axis (LH/FSH, testosterone/oestradiol; GH/IGF-1; TFT; ACTH/cortisol)
- Eye fields
- Imaging: - skull X-rays
  - CT-scan
  - MRI (definitive test)

Imaging

- For micro-adenomas: need a MRI of the pituitary fossa!
- Macroadenomas can be detected on CT-scans (occasionally even on skull-X-rays: erosion)

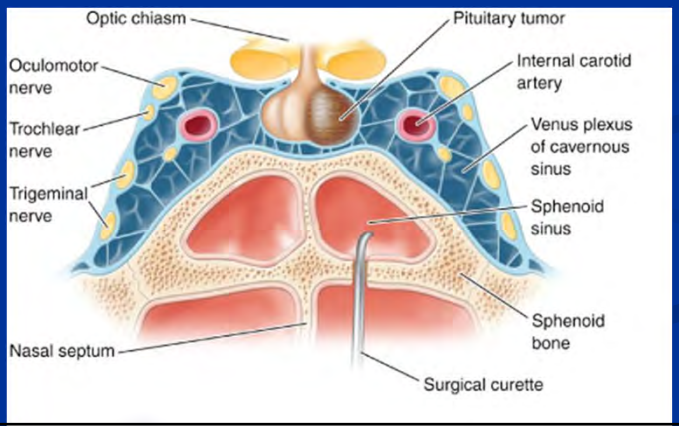
Treatment

Aims:

- To correct hypersecretion of anterior pituitary hormones
- To preserve normal secretion of other pituitary hormones
- To remove or suppress the adenoma itself

Surgery

- Transcranial
- Trans-sphenoidal



Radiotherapy

- Conventional radiotherapy
- Gamma knife radiosurgery or proton beam radiation

Medical therapy

- Always first option for prolactinomas
  - Bromocriptine (dopamine agonist)
  - very effective even for macroprolactinomas
- Somatostatin analogues
  - used for acromegaly or TSH-secreting adenomas
  - not very effective
- Nonfunctional microadenoma
  - can just observe

Non-functioning Pituitary Tumours

- Non-functional pituitary adenomas makes up a third of pituitary tumours
- Craniopharyngiomas / meningiomas / metastatic tumours can resemble adenomas, and can cause hypopituitarism or pressure effects
- Present late as large tumours with pressure on nearby structures
  - Headache
  - Pressure on optic chiasm or tracts
  - Extend into cavernous sinuses with pressure on N. III, IV, VI

Functioning Pituitary Adenomas

- Prolactinomas
- Growth hormones secreting tumours
  - Acromegaly / Gigantism
- ACTH-secreting tumours
  - Cushing's disease
- Other:
  - LH / FSH-omas
  - TSH-secreting tumours

Prolactinomas

Micro-adenoma

- < 10 mm, normal fossa
- Amenorrhoea, infertility, galactorrhoea
- Less obvious in males thus seldom diagnosed
- Random serum prolactin ↑

Macro-adenoma

- > 10 mm, spread beyond or distort fossa
- More frequently in men
- S-prolactin ↑↑
- Be aware a large tumour compressing the pituitary stalk can ↑ prolactin

Causes of Hyperprolactinaemia

Physiological

- Exercise
- Pregnancy
- Suckling
- REM sleep

Pharmacological

- Cimetidine / Ranitidine
- Methyldopa
- Metoclopramide
- Phenothiazines
- Protease inhibitors
- SSRI
- TAD
- Verapamil

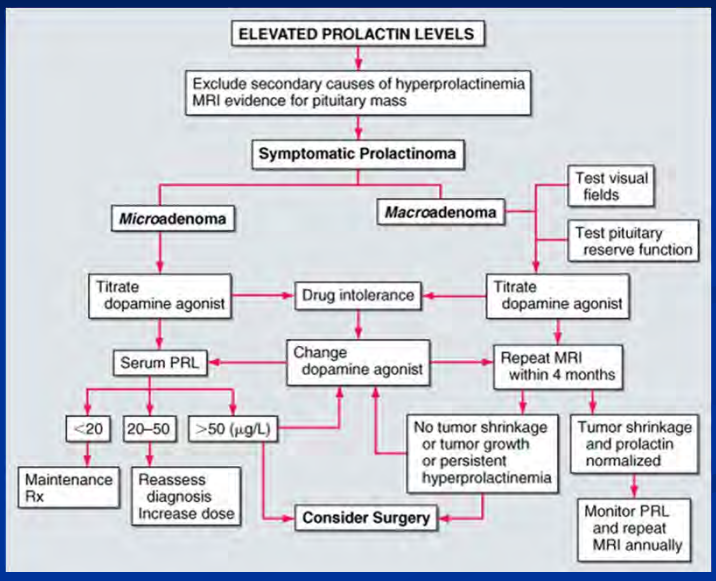
Pathological Causes

- Acromegaly
- Chronic chest wall stimulation e.g. herpes zoster, nipple rings etc.
- Cirrhosis
- Hypothyroidism
- Pituitary stalk section
- Convulsions
- MS
- Hypothalamic disease
- SLE

Prolactinoma Treatment

- Dopamine agonists
  - Bromocriptine
  - Pergolide
- Transsphenoidal surgery – seldom needed

Approach to Hyperprolactinaemia



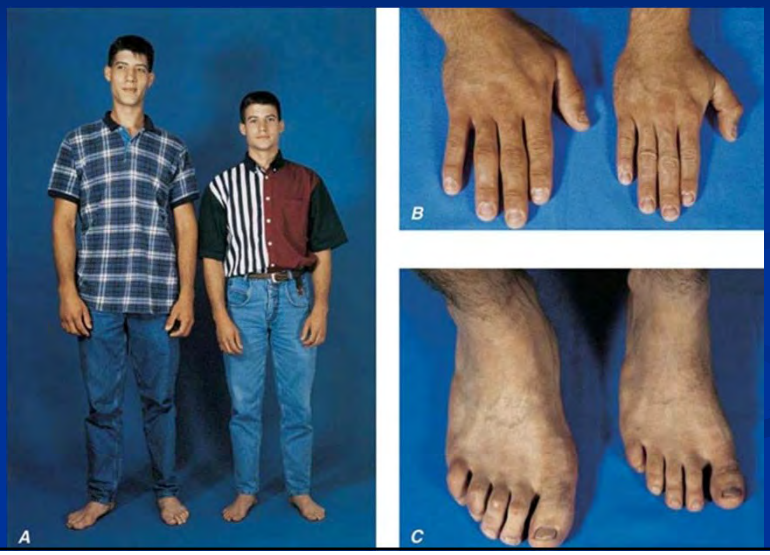
Acromegaly / Gigantism

- Caused by a pituitary Growth hormone (GH) secreting tumour
- Mostly macro-adenomas with local invasion in the cavernous sinus
- GH stimulates hepatic production of IGF-1 (the mediator of growth)
- If GH hypersecretion occurs before puberty, then patient develops gigantism
- Most often develops in adulthood; acromegaly develops

Clinical features

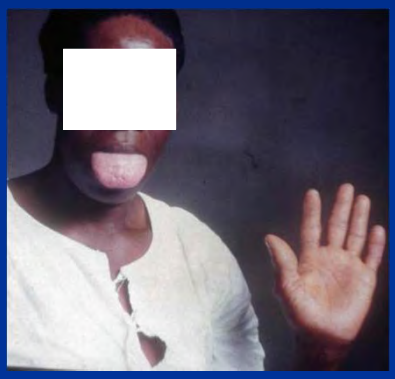
- Change in appearance (may be very slow; old photos are helpful)
- Visual field defects/headache: 25%
- Excess sweating is a common complaint
- Often DM and/or hypertension
- Proximal myopathy; carpal tunnel syndrome; arthropathy
- May have associated symptoms of hypopituitarism:
  - amenorrhoea, galactorrhoea, impotence

Gigantism
Spade-like, large hands and feet

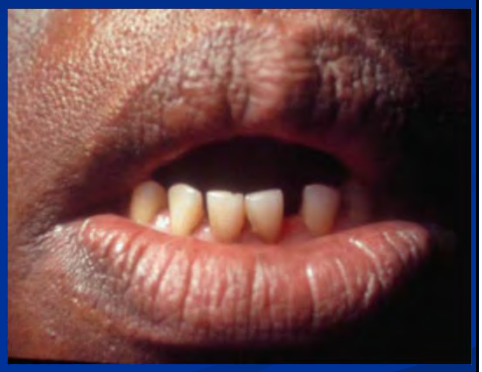


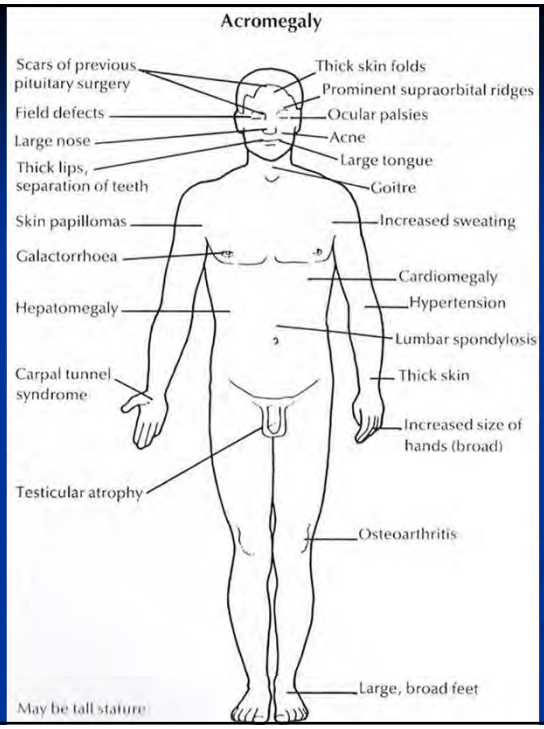
Broad nose, prominent supra-orbital ridge, prognatism

Large tongue with tooth marks on it



Gaps between teeth





Acromegaly & Gigantism

Indicators of disease activity

- Increase in ring and shoe size
- Excessive sweating
- Skin tags
- Glycosuria
- Hypertension
- Increasing loss of visual fields

Complications

- Untreated: premature death
- Coronary artery disease (2-3 x ↑)
- Hypertension
- IGT (25%) / DM type 2 (10%)
- Cardiac failure / cardiomyopathy
- Increased incidence of neoplasms eg colon cancer (2-3 x ↑)
- Visual defects
- Arthritis
- Hypopituitarism
- Quality of life: cosmetic, hyperhydrosis

Acromegaly & Gigantism

Diagnosis

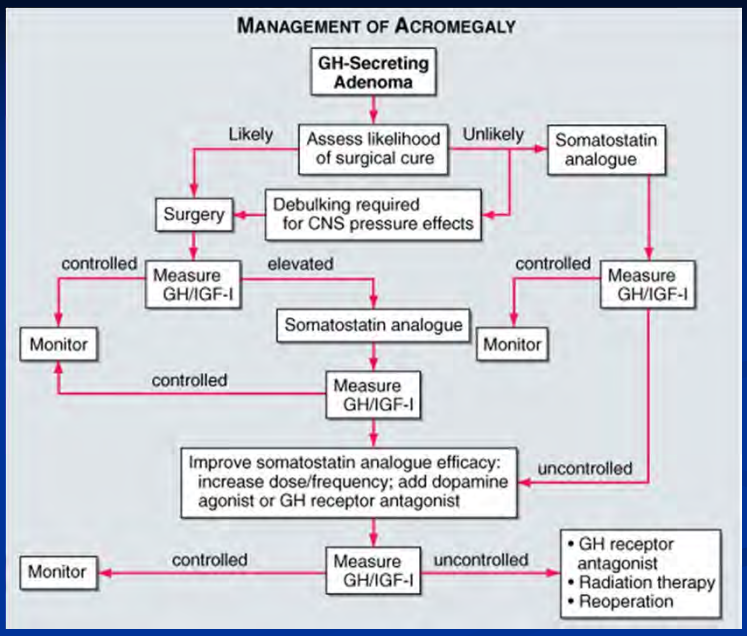
- Non-suppression of GH after 100 g glucose (GTT); can even paradoxically rise
- Normal people: suppress to <2mU/L
- IGF-1 elevated
- Prolactin ↑ in 30%
- NB: 1st biochemical confirmation before imaging!

Treatment

- Trans-sphenoidal or transcranial surgery: 1st line therapy (curative or debulking)
- Radiotherapy: 2nd line therapy (if acromegaly persist / to stop tumour growth)
- Problems with radiotherapy:
  - GH levels fall slowly over years
  - hypopituitarism can develop
- Radiotherapy and medical therapy used in combination if tumour inoperable

Medical therapy:

- Used for persistence of acromegaly after surgery
- Rarely used as primary therapy (pre-op or instead of surgery)
- Can be stopped after years if patient received radiotherapy
- Octreotide: somatostatin analogues
- GH receptor antagonist: pegvisomant
- Dopamine agonists: bromocriptine/cabergoline (especially if prolactin also increased)



Cushing's Syndrome

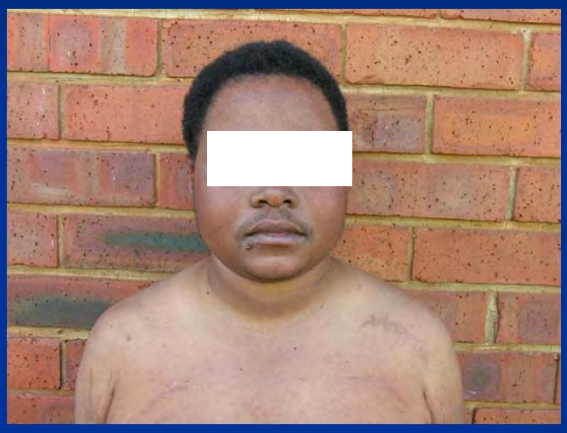
Cushing's syndrome

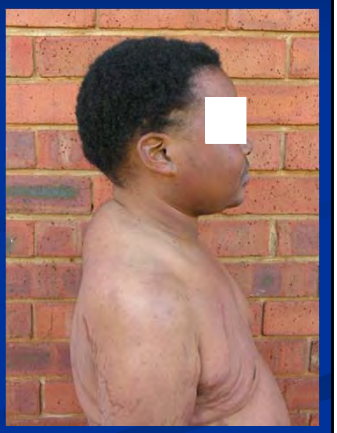
- Caused by excessive activation of glucocorticoid receptors
- Aetiology:
- Iatrogenic (most common cause!)
- Endogenous causes:
  - Pituitary Cushing's: +- 80% of patients
  - Adrenal Cushing's: benign (or malignant) adrenal tumour
  - Ectopic Cushing's: ACTH producing tumour outside the pituitary (usually lung cancer): rare

Classification of Cushing's syndrome

- ACTH-dependent
  - pituitary adenoma secreting ACTH ("Cushing's disease"; usually microadenoma)
  - ectopic ACTH syndrome
- Non-ACTH-dependent
  - iatrogenic
  - adrenal adenoma / carcinoma
- Pseudo-Cushing's syndrome
  - alcohol abuse / major depression / obesity

Moon facies; buffalo hump

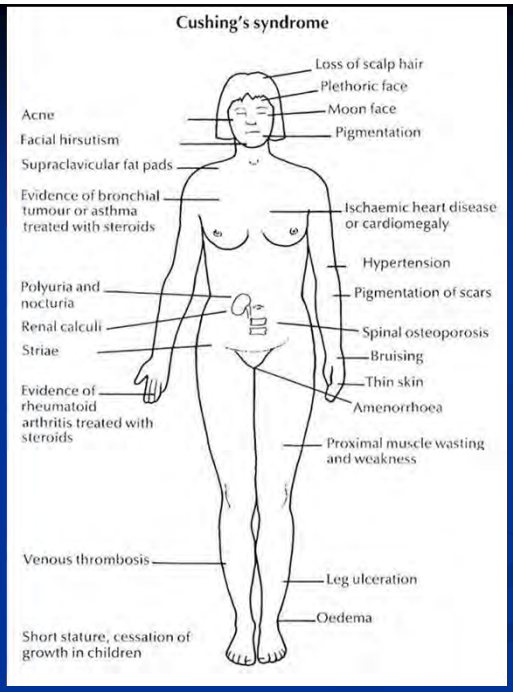




Striae; central obesity with thin arms and legs

- Weight gain
- Central obesity
- Striae (purple)

Figure 4-18B, Page 4.10



Complications

- Diabetes
- Hypertension
- Infections
- Bone: osteoporosis
- Muscle: proximal myopathy
- Psychological manifestations: psychosis, depression

Red flags for possible ectopic Cushing's

- Very high cortisol and ACTH
- Marked pigmentation
- Severe myopathy, severe hyperglycaemia
- No residual negative feedback
- Hypokalaemia
- If malignant (especially small cell lung CA): weight loss / cachexia / rapid onset

Diagnosis

- First exclude iatrogenic causes! (even topical or inhaled steroids)
- Several tests are usually combined to make the diagnosis
- 1st line tests: to confirm diagnosis
- 2nd line tests: to fing the cause
- NB: 1st biochemical confirmation before imaging!

Confirming the diagnosis

- Overnight Dexamethasone suppression test
  - 1mg orally at midnight; do plasma cortisol 8h00-9h00 (can give Dexa- or Bethamethasone)
  - if cortisol < 50nmol/L: excludes Cushing's
- 24h urine free cortisol (do at least two)
- Diurnal rhythm of plasma cortisol (in Cushing's: evening level >75% of morning level)
- Low-dose Dexamethasone suppression test
  - 0.5mg 6hourly x 48h

Finding the cause

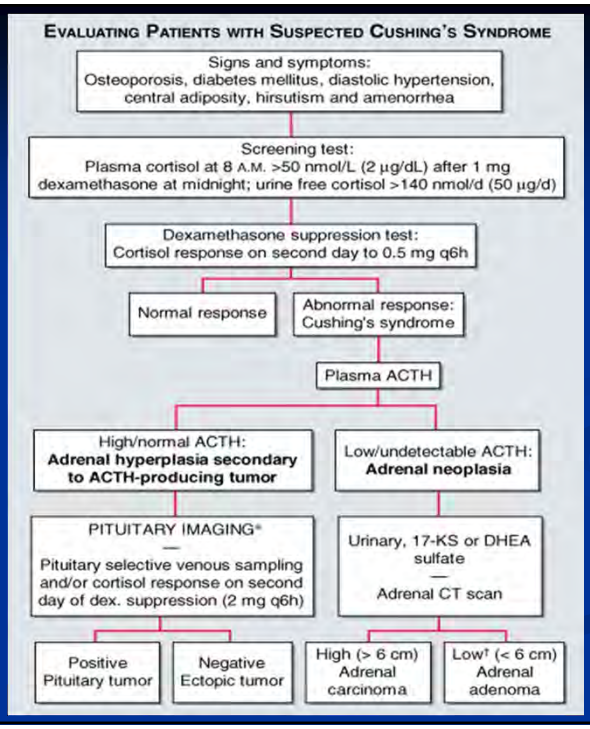
- Plasma ACTH
- If low ACTH:

- CT-scan adrenals

- If high ACTH:

- Inferior petrosal sinus sampling
- High-dose Dexamethasone suppression test (ectopic suppress < 50%)

- Pituitary source: pituitary MRI scan
- Ectopic source: chest & abdomen CT-scan



Treatment

- Untreated: 50% 5-year mortality
- Pituitary: removal of tumour (trans-sphenoidal or trans cranial surgery); medical therapy pre-op (ketokonazole / metyrapone)
- If not cured or unresectable:

  bilateral adrenalectomies & radiotherapy

  to prevent Nelson's syndrome
- Adrenal: laparotomy, removal of tumour
- Ectopic: ?chemotherapy / radiotherapy / surgery

Others

- Central hyperthyroidism
  - very rare
- LH/FSH-omas
- - precocious puberty
  - paediatrics