

## THE HYPOTHALAMUS AND THE PITUITARY GLAND

### Functional anatomy:

The pituitary gland is enclosed in the sella turcica and bridged over by a fold of dura mater called the diaphragma sellae, with the sphenoidal air sinuses below and the optic chiasm above. The cavernous sinuses are lateral to the pituitary fossa and contain the 3rd, 4th and 6th cranial nerves and the internal carotid arteries. The gland is composed of two lobes, anterior and posterior, and is connected to the hypothalamus by the infundibular stalk, which has portal vessels carrying blood from the median eminence of the hypothalamus to the anterior lobe and nerve fibers to the posterior lobe.

### Classification of diseases of the pituitary and hypothalamus

20.55 Classification of diseases of the pituitary and hypothalamus		
	Primary	Secondary
<b>Hormone excess</b>		
Anterior pituitary	Prolactinoma Acromegaly Cushing's disease Rare TSH-, LH- and FSH-secreting adenomas	Disconnection hyperprolactinaemia
Hypothalamus and posterior pituitary	Syndrome of inappropriate antidiuretic hormone (SIADH; p. 436)	
<b>Hormone deficiency</b>		
Anterior pituitary	Hypopituitarism	GnRH deficiency
Hypothalamus and posterior pituitary	Cranial diabetes insipidus	(Kallmann's syndrome)
<b>Hormone resistance</b>	Growth hormone resistance (Laron dwarfism) Nephrogenic diabetes insipidus	
<b>Non-functioning tumours</b>	Pituitary adenoma Craniopharyngioma Metastatic tumours	

## **Hypopituitarism**

Hypopituitarism describes combined deficiency of any of the anterior pituitary hormones. The clinical presentation is variable and depends on the underlying lesion and the pattern of resulting hormone deficiency.

### **Causes:**

#### **A- Structural:**

- 1- Primary pituitary tumour: Adenoma
- 2- Craniopharyngioma
- 3- Secondary tumour (including leukaemia and lymphoma)
- 4- Meningioma.
- 5- Haemorrhage (apoplexy)

#### **B- Inflammatory/infiltrative**

- 1- Sarcoidosis
- 2- Infections, e.g. pituitary abscess, tuberculosis, syphilis, encephalitis
- 3- Haemochromatosis

#### **C- Congenital deficiencies**

E.g.: GnRH (Kallmann's syndrome)

#### **D- Functional**

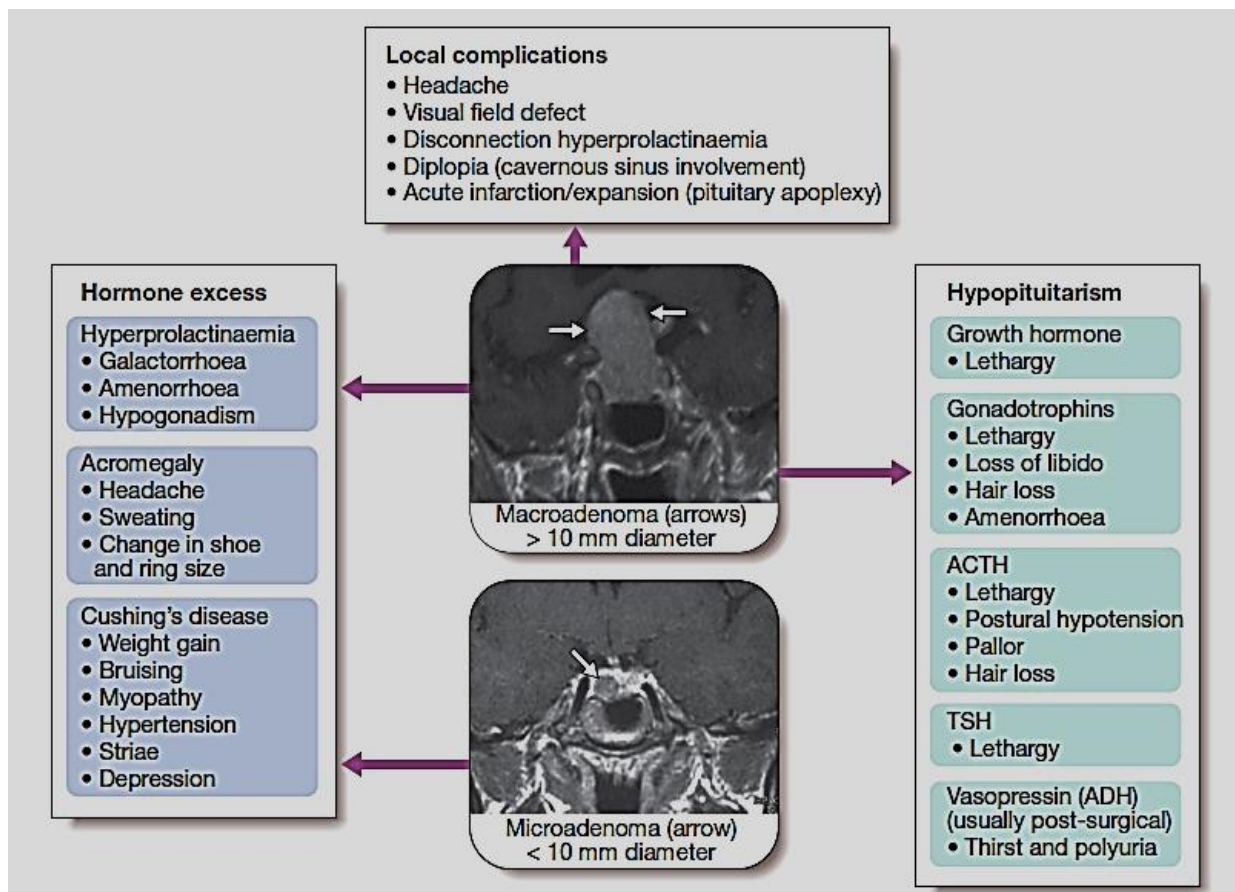
- 1- Chronic systemic illness
- 2- Anorexia nervosa
- 3- Excessive exercise

#### **E- Other**

- 1- Head injury
- 2- (Para)sellar surgery
- 3- (Para)sellar radiotherapy
- 4- Post-partum necrosis (Sheehan's syndrome)

### **Clinical assessment:**

The clinical feature of hypopituitarism related to hormonal deficiency, with feature of the cause either hormonal or local effect, for example patient with functional adenoma had feature of the hormone released by adenoma and feature of local compression on the surrounding, in addition to the feature of the hormonal deficiency of the rest of other hormone and as shown in the following figure:



The onset of hormonal deficiency varies according to type of hormone, the first hormone to be lost is growth hormone (which had nonspecific symptom such as lethargy, muscle weakness and increased fat mass), this followed by LH and FSH, and followed by ACTH, and the last hormone to be lost is TSH. (Don't forget: grow flat).

The onset of all of the above symptoms is notoriously insidious. However, patients sometimes present acutely unwell with glucocorticoid deficiency. This may be precipitated by a mild infection or injury, or may occur secondary to pituitary apoplexy.

## Investigation:

### *ACTH deficiency:*

- ✓ Short ACTH stimulation test
- ✓ Insulin tolerance test: only if there is uncertainty in interpretation of short ACTH stimulation test (e.g. acute presentation).

### *LH/FSH deficiency:*

- ✓ In the male, measure random serum testosterone, LH and FSH •

- ✓ In the pre-menopausal female, ask if the menses are regular •
- ✓ In the post-menopausal female, measure random serum LH and FSH (FSH normally  $> 30$  IU/L and LH  $> 20$  IU/L).

### ***TSH deficiency:***

- ✓ Measure random serum T4. Note that TSH is often detectable in secondary hypothyroidism.

### ***Growth hormone deficiency***

- ✓ Only investigate if growth hormone replacement therapy is being contemplated •
- ✓ Measure immediately after exercise •
- ✓ Consider other stimulatory tests arginine, glucagon and clonidine.

### ***Cranial diabetes insipidus***

- ✓ Only investigate if patient complains of polyuria/polydipsia, which may be masked by ACTH or TSH deficiency •
- ✓ Exclude other causes of polyuria with blood glucose, potassium and calcium measurements •
- ✓  
Water deprivation test or 5% saline infusion test Identify hormone excess •

### ***Others***

Measure random serum prolactin •

If there are clinical features establish the anatomy and diagnosis consider visual field testing •

Image the pituitary and hypothalamus by MRI or CT

### ***Management:***

Firstly we have to treat the cause.

In acute presentation we treat like that of adrenocortical insufficiency except that sodium depletion is not an important component to correct. Chronic hormone replacement therapies include:

## **Cortisol replacement**

Hydrocortisone should be given if there is ACTH deficiency.  
Mineralocorticoid replacement is not required.

## **Thyroid hormone replacement**

Levothyroxine 50–150 µg once daily should be given. Unlike in primary hypothyroidism, measuring TSH is not helpful in adjusting the replacement dose because patients with hypopituitarism often secrete glycoproteins which are measured in the TSH assays but are not bioactive. The aim is to maintain serum T4 in the upper part of the reference range. It is dangerous to give thyroid replacement in adrenal insufficiency without first giving glucocorticoid therapy, since this may precipitate adrenal crisis.

## **Sex hormone replacement**

This is indicated if there is gonadotrophin deficiency in women under the age of 50 and in men to restore normal sexual function and to prevent osteoporosis.

## **Growth hormone replacement**

Growth hormone (GH) is administered by daily subcutaneous self-injection to children and adolescents with GH deficiency and, until recently, was discontinued once the epiphyses had fused.

Some individuals remain lethargic and unwell in spite of treatment of other hormone.

These patients may feel better, and have objective improvements in their fat: muscle mass ratios and other metabolic parameters, if they are also given GH replacement. Treatment with GH may also help young adults to achieve a higher peak bone mineral density. The principal side-effect is sodium retention, manifest as peripheral oedema or carpal tunnel syndrome.

## **Pituitary tumour**

Pituitary tumours produce a variety of mass effects, depending on their size and location, most intrasellar tumours are pituitary macroadenomas (most commonly nonfunctioning adenomas), whereas suprasellar masses may be craniopharyngiomas. The most common cause of a parasellar mass is a meningioma.

**Clinical feature:**

Common but non-specific presentation is with headache, which may be the consequence of stretching of the diaphragm sellae. Although the classical abnormalities associated with compression of the optic chiasma are bitemporal hemianopia or upper quadrantanopia, any type of visual field defect can result. Lateral extension of a sellar mass into the cavernous sinus with subsequent compression of the 3rd, 4th or 6th cranial nerve may cause diplopia.

Occasionally, pituitary tumours infarct or there is bleeding into cystic lesions. This is termed 'pituitary apoplexy' and may result in sudden expansion with local compression symptoms and acute-onset hypopituitarism. Non-haemorrhagic infarction can also occur in a normal pituitary gland; predisposing factors include catastrophic obstetric haemorrhage (Sheehan's syndrome), diabetes mellitus and raised intracranial pressure.

**Investigations**

Patients suspected of having a pituitary tumour should undergo MRI or CT.

The definitive diagnosis is made on histology after surgery.

All patients with (para)sellar space-occupying lesions should have pituitary function test.

**Treatment:**

The treatment of pituitary tumor by surgery as first line and radiotherapy as second line and no role for medical treatment except in prolactinoma where the medical treatment (dopamine agonist) regard as first line, and in acromegaly as second line of treatment.

Urgent treatment is required if there is evidence of pressure on visual pathways, in which surgery is needed except if the prolactin is over 5000 mU/L, then the lesion is likely to be a macroprolactinoma and to respond to a dopamine agonist with shrinkage of the lesion, making surgery unnecessary.

All operations on the pituitary carry a risk of damaging normal endocrine function; this risk increases with the size of the primary lesion. Pituitary function should be retested 4–6 weeks following surgery, primarily to detect the development of any new hormone deficits.

Following surgery, usually after 3–6 months, imaging should be repeated and, if there is a significant residual mass and the histology confirms an anterior pituitary tumor, external radiotherapy may be given to reduce the risk of recurrence. Radiotherapy is not useful in patients requiring urgent therapy because it takes many months or years to be effective and there is a risk of acute swelling of the mass.

Fractionated radiotherapy carries a life-long risk of hypopituitarism (50–70% in the first 10 years) and annual pituitary function tests are obligatory. There is also concern that radiotherapy might impair cognitive function, cause vascular changes and even induce primary brain tumors.

Stereotactic radiosurgery, best delivered by the ‘gamma knife’, allows specific targeting of residual disease in a more focused fashion.

Non-functioning tumours should be followed up by repeated imaging.

**With best regard**