Pituitary disorders: an overview for the general physician

The pituitary gland is responsible for the production of the trophic hormones that control normal homeostasis. The hyper- or hypofunction of one or more of these may result in a distinct pathological clinical presentation, particularly in the presence of macroadenoma. Most pituitary disorders, however, present with non-specific signs and symptoms. This review gives an overview of pituitary disorders, their causes, clinical presentation, diagnosis and management.

The pituitary gland lies at the base of the skull in the pituitary fossa, formed by the sphenoid bone called the sella turcica. It measures approximately 15x10x5 mm and weighs about 750 mg. It may double in size in pregnancy. It is composed of the anterior pituitary, adenohypophysis, originating from Rathke's pouch, and the posterior lobe, neurohypophysis, arising from the ventral hypothalamus. The gland is connected to the hypothalamus by the stalk. The optic chiasm lies anterior to the pituitary stalk and the cavernous sinuses are located lateral to the gland. These are vulnerable to pituitary enlargement.

The anterior pituitary secretes distinct trophic hormones in a pulsatile manner: pro-opiomelanocortin, which is cleaved to form adrenocorticotrophic hormone (ACTH), growth hormone (GH), thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin. The secretion of anterior pituitary hormones is under hypothalamic control (*Table 1*).

Table 1. Pituitary hormones and their functions

Anterior pituitary hormones	**Function**
Adrenocorticotrophic hormone	Stimulates adrenal steroid synthesis
Follicule-stimulating hormone	Promotes follicular development in females Promotes spermatogenesis in males
Luteinizing hormone	Stimulates sex steroid production Maintains corpus luteum
Growth hormone	Promotes growth Multiple metabolic effects on protein synthesis, lipolysis and carbohydrate utilization
Prolactin	Promotes milk production
	Inhibits gonadotrophin secretion
Thyroid-stimulating hormone	Promoted thyroid hormone synthesis and secretion
Posterior pituitary hormones	
Antidiuretic hormone	Osmoregulation, regulation of extracellular volume
Oxytocin	Promotes uterine contraction and milk let down

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The posterior gland is neural tissue consisting of distal hypothalamic axons. The axon terminals contain neurosecretory granules filled with oxytocin and vasopressin, otherwise known as antidiuretic hormone (ADH). The synthesis and secretion of ADH is regulated by plasma osmolality and, to a much lesser extent, by volume and pressure arterial receptors.

An expanding pituitary mass may be asymptomatic and may be discovered incidentally during cranial imaging for other medical conditions or may cause destruction of the pituitary fossa and invasion and/or compression of the surrounding structures, including the functioning pituitary gland itself. Because of the proximity of the optic chiasm, suprasellar extension may result in the loss of temporal vision, starting superiorly, and eventually leading to the nasal fields also being affected, causing blindness. Lateral extension leads to the invasion and compression of the cavernous sinus, affecting the cranial nerves within it and resulting in ophthalmoplegia. Downward expansion will eventually cause CSF leak with possible CNS infection.

Functioning pituitary masses are rare but present with a characteristic array of symptoms and signs, which are discussed in this review. Large pituitary masses may lead to pituitary hypofunction.

The majority of pituitary masses are adenomas, benign tumours originating in the pituitary gland.

Pituitary incidentalomas

Incidence and prevalence

As cranial imaging has become widely available, pituitary radiological abnormalities have become more evident. About 10% of healthy adults will have pituitary adenomas on magnetic resonance imaging (MRI) or post mortem (Molitch and Russell, 1990; Hall et al, 1994; Buurman and Saeger, 2006). The incidence of hormone-secreting adenomas is extremely small. Most pituitary incidentalomas are of no clinical importance. Nevertheless, all patients with an incidentally found pituitary lesion should be referred to an endocrinologist for work-up.

Pathology

Adenomas are benign monoclonal neoplasms that account for 90% of all pituitary masses. They are divided into microadenomas, measuring less than 1 cm in diameter, and macroadenomas, measuring more than 1 cm in diameter. They may secrete a target trophic hormone and/or invade or compress neighbouring structures, thus leading to their varied clinical manifestation. Thirty per cent of pituitary adenomas are non-functioning.

Other sellar and parasellar masses include Rathke's cysts and craniopharyngiomas. Meningiomas and malignant primary and secondary neoplasms are occasionally encountered in this location. Pituitary infections with abscess formations and pituitary granulomatous disease are very rare.

Investigations

The initial evaluation of any pituitary mass requires a search for hormone hypersecretion, and in the case of a macroadenoma, for pituitary hypofunction. In addition larger tumours are likely to present with compressive symptoms, such as visual disturbance, headache, dizziness and behavioural problems. Cranial nerve abnormalities and visual field defects are relatively common.

High resolution imaging of the pituitary gland, hypothalamus and adjacent structures is offered by MRI which can pick up microadenomas measuring as little as 1 mm.

Ophthalmological examination, with formal visual field assessment, is indicated in patients with pituitary macroadenomas which abut the optic tract or invade cavernous sinuses.

Treatment

Treatment depends on the nature of the adenoma and may include medical treatment, surgery or irradiation alone or in combination. The aim of therapy is to correct hormone hypersecretion or deficiencies, prevent tumour growth, relieve compressive symptoms and preserve normal pituitary function.

In the hands of an experienced pituitary surgeon, the resection of pituitary masses, using a transsphenoidal approach, is associated with minimal morbidity and mortality. It allows for a short hospital stay and avoids the manipulation of brain tissue. Possible complications include CNS infection, CSF leak and total or partial hypopituitarism (Barker et al, 2003).

Pituitary irradiation is used as an adjunct to surgery, or in patients in whom surgery is contraindicated or not tolerated. Hypopituitarism following radiotherapy is common (Darzy and Shalet, 2005). Some investigators report an increased risk of secondary tumours and cognitive dysfunction (Minniti et al, 2005).

Hypopituitarism

Incidence and causes

The annual incidence of hypopituitarism is 4 in 100 000. An impaired production of pituitary hormones may occur for a variety of reasons. Acquired pituitary insufficiency remains the most common cause of hypopituitarism. Damage to the hypothalamus, developmental and genetic causes of pituitary hypofunction are rare.

Pituitary hypofunction can be caused by direct damage to the pituitary gland as a result of pituitary adenomas, head injury, surgery or cranial irradiation for primary pituitary tumours or metastatic deposits. The differential diagnosis further includes vascular accident, profound hypotension secondary to sepsis, pituitary ischaemic damage post-partum (Sheehan's syndrome), pituitary inflammation – hypophysitis; and infiltration, as in the case of sarcoidosis and haemochromatosis. Transient pituitary (and hypothalamic) hypofunction as a result of starvation, excessive exercise and critical illness are the most common reversible causes of hypopituitarism.

Clinical picture

The clinical picture of hypopituitarism depends on several factors, such as the degree of hormone deficiency, the actual hormone deficiency and, most importantly, the speed of onset of the deficiency (*Table 2*).

A slowly growing tumour, infiltrative process or radiation would classically initially affect GH secretion. Symptoms of GH deficiency are very non-specific, including fatigue, lack of energy and poor memory.

Gonadotrophs are next affected, presenting in men with various degrees of sexual dysfunction, eunuchoid appearance and fatigue; and in women with menstrual disturbance or amenorrhoea, reduced wellbeing and occasionally with frank menopausal symptoms. A prolonged deficiency of GH (De Boer et al, 1995) and gonadotrophs (Finkelstein et al, 1989) has a negative effect on cardiometabolic risk, body composition and bone mass (Mukherjee et al, 2004).

Symptoms of ACTH deficiency are non-specific: fatigue, loss of weight, weakness, nausea and abdominal pain. Acute deficiency, however, may present as a medical emergency with profound hypotension and cardio-

Table 2. Signs and symptoms of hypopituitarism (in adults)

Anterior pituitary hormones	Signs and symptoms
Adrenocorticotrophic hormone	Non-specific: lethargy, anorexia, weight loss Addisonian crisis: shock, acute abdomen, fever, confusion, hypoglycaemia, hyperkalaemia
Follicule-stimulating hormone and luteinizing hormone	Decreased libido, impotence and infertility Amenorrhoea and menopausal symptoms Change in body composition
Growth hormone	Decreased quality of life; lethargy, depression Increased cardiovascular risk; change in body composition
Thyroid-stimulating hormone	Hypothyroidism: lethargy, depression, hypothermia, bradycardia, hypotension, weight gain, constipation
Posterior pituitary hormone	
Antidiuretic hormone	Diabetes insipidus (polydipsia, polyuria, loss of weight) Dehydration

vascular collapse, hypoglycaemia, nausea and vomiting, and, in some cases, with headache and neurological deficit. If this not recognized, it can be life threatening.

TSH deficiency presents over the course of weeks to months, with the symptoms of hypothyroidism.

Cranial diabetes insipidus occurs after pituitary or hypothalamic surgery and following head trauma and is often transient. It is caused by an inability to synthesize ADH resulting in a large volume of diluted urine. This, usually, is not life threatening, unless access to fluid is restricted.

Investigations

Pituitary baseline assessment should take into account the diurnal variation of the evaluated hormones. Cortisol, LH, FSH, oestrogen or testosterone, prolactin, TSH and thyroxine (T4), and insulin-like growth factor-1 (IGF-1) levels should therefore be taken before 9 am (*Table 3*). Cortisol levels are at their highest on waking. A morning cortisol value below 100 nmol/litre indicates adrenal insufficiency. Cortisol values of 500 nmol/litre or greater are consistent with an intact hypothalamic–pituitary–adrenal axis. The values in between do not exclude secondary adrenal insufficiency and dynamic testing is therefore warranted (Arlt and Allolio, 2003).

Low LH and FSH, in the presence of low oestrogen or testosterone, point towards a pituitary or a hypothalamic cause. Low free thyroxine (free T4) and triiodothyronine (free T3) in the presence of low TSH confirms a pituitary problem.

Raised prolactin may be found in a prolactin-secreting adenoma, but also if there is damage to the pituitary stalk by a large tumour and the inhibitory action of dopamine on the lactotrophs is disrupted. High prolactin attenuates the gonadotrophs secretion, causing secondary hypogonadism.

GH secretion is stimulated by growth hormone-releasing hormone and inhibited by somatostatin and dopamine. GH has a short half-life and is secreted in a pulsatile fashion. Psychological or physical stress, acute illness, chronic liver and kidney disease and diabetes elevate GH levels. Hence, its single measurement is not useful. IGF-1 levels are used as a diagnostic tool and can be measured in the blood without great fluctuations throughout the day. IGF-1 has a longer half-life and is raised in acromegaly. IGF-1 levels are age and sex specific.

Table 3. Baseline pituitary tests
9am cortisol
Luteinizing hormone, follicle-stimulating hormone
Oestrogen or testosterone
Thyroid-stimulating hormone and free thyroxine
Prolactin
Insulin-like growth factor-1

Further assessment includes dynamic endocrine testing. The gold standard for assessing cortisol and GH reserve is the insulin tolerance test, during which symptomatic hypoglycaemia simulates a stress response and the levels of hormones are measured.

The simultaneous measurement of plasma and urine osmolarity in the presence of polyuria (and in the absence of osmotic diuresis and renal disease) will confirm diabetes insipidus. A water deprivation test followed by synthetic vasopressin administration can help to clarify the underlying cause.

Treatment

Steroid replacement is the most important constituent of replacement therapy. In an emergency, such as the first presentation of pituitary failure, postoperatively or in an acute illness hydrocortisone 100–200 mg over 24 hours is required. This can be tailed off on recovery to 20 mg in 24 hours given orally – 10 mg on waking, 5 mg around midday and 5 mg early in the afternoon. During a mild illness or in times of stress, e.g. exams, the dose can be doubled for a couple of days. Information gained from clinical symptoms and a cortisol day curve can be used to assess the adequacy of the replacement. Mineralocorticoid replacement is not indicated in pituitary failure. Patients on replacement glucocorticoid therapy should be carrying a steroid card.

Detailed information about hydrocortisone cover during illness or times of surgery can be found on the Pituitary Foundation website (www.pituitary.org.uk) (*Table 4*).

Thyroxine replacement should be commenced once cortisol treatment has started, as it accelerates cortisol metabolism and may precipitate an Addisonian crisis. As the TSH is not appropriately responding, clinical assessment and free thyroxine levels are used to optimize the replacement dose.

Sex hormone replacement is important for the normalization of sexual function, general wellbeing, body and bone composition. If fertility is desired gonadotrophin replacement may be required.

The benefit of GH replacement in adults can be difficult to assess. The National Institute of Clinical Excellence (2003) recommends that recombinant human GH should be used only in adults with confirmed severe deficiency and reduced quality of life, as confirmed by the Adult Growth Hormone Deficiency Questionnaire, and those who already receive replacement hormone treatment for any other pituitary hormone deficiency. Some authorities advocate the use of GH replacement for patients with cardiovascular risk (National Institute for Clinical Excellence, 2003; Koltowska-Haggstrom et al, 2005).

Diabetes insipidus is treated by oral or nasal vasopressin analogues.

Having discussed the approach to pituitary incidentalomas and their clinical consequences including hormone deficiency and compressive symptoms, this article will now look at hormone-secreting pituitary adenomas.

Prolactinoma

Incidence and cause

Prolactinomas are the most common benign neoplasms of the pituitary, with an annual incidence of 6 in 100 000. Prolactin is synthesized by lactotroph cells and stimulates milk production in pregnancy and lactation. Lactotrophs are under negative feedback control from dopamine. Prolactinaemia may be present as a result of lactotroph adenoma and stalk compression by a pituitary mass interrupting the negative feedback (the so-called stalk effect) from the hypothalamus.

Prolactinaemia is also commonly encountered in a multitude of other clinical scenarios. Pregnancy, stress and intercourse, as well as multiple medical conditions such as polycystic ovarian syndrome, chronic renal failure and cirrhosis could all cause elevated prolactin. The worst offenders, however, are drugs. Many antidepressants, antipsychotics, anti-emetics, some antihypertensives, opiates and oral contraceptives have been implicated, although there is no evidence use of the oral contraceptive pill increases the chance of developing prolactinomas (Pituitary Adenoma Study Group, 1983). Prolactin may be produced as a higher molecular mass form; so-called macroprolactin. Macroprolactin has no or minimal bioactivity. It does, however, interfere with prolactin assay. Most laboratories now routinely measure macroprolactin. Secondary causes of raised prolactin must be excluded.

Clinical picture

Hyperprolactinaemia usually presents with amenorrhoea, infertility and galactorrhoea in women and impotence, decreased libido and compressive symptoms in men – who often have larger tumours at presentation. Gynaecomastia and galactorrhoea in male patients are rare. Both men and women may have reduced bone density as a result of ensuing sex hormone deficiency (Schlechte, 2003).

A single measurement of prolactin may be enough to diagnose prolactinaemia. The level of the hormone is usually proportional to the size of the tumour. Occasional low prolactin in the presence of a large tumour may indicate an artefact in the assay called the 'hook effect'. This is the result of large quantities of antigen in an immunoassay system impairing antigen–antibody binding, resulting in low antigen determination.

Treatment

Medical treatment with dopamine agonists (e.g. bromocriptine and cabergoline) is the first-line therapy. The aim of this therapy is to alleviate gonadal dysfunctions, stop galactorrhoea, improve bone density and shrink the tumour to alleviate compressive symptoms and resume fertility. Bromocriptine is highly effective and restores fertility in over 90% of women with microadenomas (Molitch, 1999). Cabergoline is better tolerated and may work in patients resistant to treatment with bromocriptine (Colao et al, 1997).

Table 4. Advice to patient with intercurrent illness on hydrocortisone replacement therapy

Cortisol requirement increases during illness or surgery
If able to eat and drink during illness, the dose of hydrocortisone should be doubled (e.g. 20 mg, 10 mg, 10 mg), returning to a normal daily dosage once recovered
Patients with Addison's disease should keep at home a vial of 100 mg of hydrocortisone to be administered intramuscularly in an emergency
If unable to eat or drink, or vomiting occurs, hospital admission is necessary for intravenous or intramuscular hydrocortisone administration
For a moderate elective procedure or investigation hydrocortisone 100 mg intramuscularly should be administered before procedure
For major surgery or severe illness the patient should receive oral hydrocortisone 20 mg or hydrocortisone 100 mg intramuscularly. Hydrocortisone 50–100 mg should be administered 6-hourly until resolution of the illness
Patients should wear their MedicAlert bracelet or necklace and carry a steroid card

Once the prolactin levels have been stable for 2 years and the size of the adenoma has decreased by at least 50%, dopamine agonist withdrawal could be considered. The recurrence rate at 2–5 years was 31% for microprolactinomas and 36% for macroprolactinomas in one study (Colao et al, 2003).

Pituitary size increases in pregnancy. If pregnancy is desired, the usual advice for women with a microprolactinoma is to stop taking the dopamine agonist once a positive pregnancy test has been confirmed. There is no evidence, however, that dopamine agonists cause congenital malformations.

Dopamine agonists should be continued through pregnancy in women with macroprolactinomas. They require careful monitoring for tumour enlargement in pregnancy. Surgery should be discussed as a treatment option in patients with macroadenomas before conception, because the risk of tumour enlargement is 30% (Bronstein, 2005).

Transphenoidal surgery is indicated in patients with microadenomas who are unable to tolerate dopamine agonists or in those who are treatment resistant. It is also considered in patients with macroadenoma, especially if it extends beyond the sella, and patients with a significant psychiatric history, as depression and psychosis are contraindications for dopamine agonists.

Cushing's syndrome

Incidence and causes

Cushing's syndrome is a rare chronic state of glucocorticoid excess. Endogenous Cushing's syndrome can be divided into ACTH dependent and independent. The most common cause of Cushing's syndrome is excess production of ACTH from a corticotroph pituitary adenoma – otherwise known as Cushing's disease. It accounts for 70% of all cases and there are 0.1–1.0 new cases per 100 000 per year (Broscaro et al, 2001).

Ectopic ACTH secretion, particularly from bronchogenic carcinoma, accounts for about 10% of all cases. The rest of the cases represent Cushing's syndrome resulting from adrenal adenomas and carcinomas, and rarely, nodular adrenal hyperplasia. The most common cause of glucocorticoid excess is exogenous administration of corticosteroids in chronic lung and rheumatological disease.

Clinical picture

Glucocorticoid excess is characterized by the presence of certain clinical features – unfortunately none of them are diagnostic (Broscaro et al, 2001). Central obesity with supraclavicular and cervical fat pads, thin skin, purple stria over the trunk and abdomen, easy bruising, proximal muscle weakness and wasting are all considered to be 'classic' symptoms. Depression and other psychiatric disturbances are often observed. Hypertension and impaired glucose tolerance, as well as other biochemical abnormalities (e.g. hypokalaemic alkalosis) may be present.

Cushing's syndrome is associated with an increased morbidity and mortality of 30–50% at 5 years. This is related to the high incidence of cardiovascular complications, such as hypertension, in 75% of patients and diabetes in up to 50% of patients – exacerbated by obesity (Etxabe and Vazquez, 1994; Stewart, 2003).

Investigations

A series of laboratory investigations are used to confirm increased cortisol secretion. These include 24-hour urinary free cortisol collections, an overnight dexamethasone suppression test and midnight plasma or salivary cortisol (Arnaldi et al, 2003). False positive results occur in patients with depressive illness and alcoholism. The circadian pattern of cortisol release is also affected by major illness and trauma, chronic liver and kidney disease, and Cushing's syndrome.

A low dose dexamethasone suppression test is used to confirm the diagnosis of Cushing's syndrome of any aetiology. Raised ACTH, in the context of raised cortisol, points towards the pituitary or ectopic Cushing's syndrome. Further dynamic testing helps differentiate between the two.

A pituitary MRI with gadolinium enhancement should be performed in all patients with ACTH dependent Cushing's syndrome. Bilateral inferior petrosal sinus sampling for ACTH gradient may help to localize the microadenoma. Abdominal computed tomography (CT) can help to diagnose adrenal masses. Whole body CT or MRI scans are helpful to localize ectopic ACTH-secreting tumours.

Treatment

Transsphenoidal surgery is the first-line treatment offering around 70% remission rates (undetectable or <50 nmol/litre postoperative cortisol levels) in experienced hands with a higher cure rate in patients with microadenomas (Baldeweg et al, 2002; Rees et al, 2002; Yap et al, 2002).

Many drugs are used in the treatment of Cushing's syndrome. Some act at the level of the pituitary gland and some on the adrenal glands. The most commonly used are metyrapone and ketokonazole, which can be given in preparation for surgery, as an alternative to it or as adjuvant therapy in patients not cured by surgery.

Pituitary radiotherapy is the second-line treatment if surgery is unsuccessful.

Bilateral adrenalectomy can also be used as second- or third-line treatment. It can be complicated by Nelson's syndrome: generalized hyperpigmentation and signs of expanding pituitary mass.

Successful surgery and radiotherapy may require lifelong glucocorticoid replacement and, in the case of bilateral adrenalectomies, additional mineralocorticoid replacement. Treatment carries the risk of partial or complete hypopituitarism.

Acromegaly

Incidence and causes

Acromegaly is usually caused by GH secretion from pituitary adenoma and very rarely by secretion of IGF-1 by extrapituitary tumours. Acromegaly is rare, with an incidence of 3–4 cases per million per year. It often takes many years before a diagnosis is made; hence 70% of tumours are macroadenomas at presentation (Melmed, 2006).

Clinical picture

The clinical features at presentation are related to the trophic effects of GH and IGF-1. Patients may commonly exhibit coarse facial features, including frontal bossing, enlarged nose and tongue, increased intradental separation, enlarged hands and feet. The patient may complain of increased headaches, sweating, fatigue, symptoms consistent with carpal tunnel syndrome and obstructive sleep apnoea, visual and reproductive symptoms. On examination many are found to have hypertension, impaired glucose tolerance or frank diabetes mellitus, goitre, cardiomegaly and generalized organomegaly (Molitch, 1992).

Mortality analysis shows that 60% of patients die from cardiovascular disease and 25% from respiratory disease; 15% of patients are thought to succumb to malignancies (Colao et al, 2004). However, many researchers feel that GH and IGF-1, rather than inducing tumourgenesis de novo, may accelerate the growth of already existing neoplasms. Nevertheless, the mortality of the acromegalic population is 2–3 times that of a matched control group (Melmed, 2001; Renehan et al, 2003).

Investigations

This diagnosis is confirmed through an oral glucose tolerance test. A nadir GH level of greater than 1 μg/litre is diagnostic. A high IGF-1 level is highly specific to acromegaly and correlates well with disease activity. The liver is the main source of plasma IGF-1. A decline in its levels is seen in starvation and diseases associated with malnutrition, such as hepatic failure, inflammatory bowel disease and renal failure. It is also low in untreated hypothyroidism.

Treatment

The first-line treatment for pituitary adenoma causing acromegaly is transsphenoidal surgery. The success of surgery, determined by the rate of recurrence and compromise of other pituitary hormone secretion, depends on the size of the tumour. Up to 90% of patients with microadenomas are cured, compared with just half with macroadenomas (Fahlbusch et al, 1992; Baldeweg et al, 2003).

GH secretion is stimulated by growth hormone-releasing hormone and inhibited by somatostatin and dopamine. Somatostatin analogues, such as octreotide and lanreotide, are widely used to control GH secretion and to shrink tumours. Up to 80% of patients will achieve normal GH and IGF-1 levels (Merza, 2003). Dopamine agonists, such as cabergoline and bromocriptine, may be helpful in some patients. GH acts via GH receptors on the cell surface membrane. Pegvisomant, a GH receptor antagonist, blocks the generation of IGF-1 (Kopchick et al, 2002). It can be used in patients who have failed to respond to other treatments. The adenoma size must be monitored.

Primary and adjuvant radiotherapy is also useful, particularly in patients with extensive disease. Ten years after treatment gonadotrophic, thyrotrophic or corticotrophic deficiencies were observed in 80% of patients (Merza, 2003).

TSHomas and LH and FSH adenomas

TSH-secreting pituitary adenomas are very rare. They present with the signs and symptoms of hyperthyroidism and mass effect, as a majority of them are macroadenomas. The diagnosis is made on the basis of raised T4 and T3 in the presence of raised or inappropriately normal TSH and a pituitary mass. The treatment is surgical, with somatostatin analogues and antithyroid drugs used as adjuvant treatment.

LH and FSH gonadotroph adenomas account for up to 30% of non-functioning pituitary tumours. These are usually non-secretory and present with compressive signs and symptoms from enlarging macroadenoma and hypopituitarism. Functioning gonadotroph adenomas are not, as a rule, associated with specific endocrine abnormalities. Microadenomas may be followed up by serial MRI. Macroadenomas require resection and/or radiotherapy, followed by the treatment of hypopituitarism, if present.

Patient support group

The Pituitary Foundation is a national UK charity, which is working to provide information and support to those living with pituitary disorders, including patients, their relatives, friends and carers. It also offers useful information for the generalist and endocrinologist alike on its website (www.pituitary.org.uk).

Conclusions

It should be stressed that pituitary disease is rare but has a large impact on the morbidity and mortality of the affected patients. These patients often have non-specific symptoms and present themselves to a variety of specialties (*Table 5*). Endocrine emergencies resulting from pituitary disease are rare but potentially life threatening if unrecognized. Mimicking other emergency conditions pituitary disorders should be included in the differential diagnosis. Diagnostic procedures should not delay treatment but storage of the first blood sample will allow later assay. If in doubt ask for advice from specialist colleagues. A timely diagnosis is most important, as there are now many effective treatments at our disposal. BJHM

Conflict of interest: Dr Baldeweg is a trustee and member of the medical committee of the Pituitary Foundation.

Table 5. Differential diagnosis of non-specific manifestations of pituitary disorders

Symptom/sign	Pituitary disorder as part of the differential diagnosis
Sweating	Acromegaly
Obesity	Cushing's, secondary hypothyroidism
Fatigue	Cushing's, secondary hypothyroidism, secondary hypogonadism, prolactinoma
Flushing	Secondary hypogonadism
Hypotension	Hypocortisolaemia
Hypertension	Acromegaly, Cushing's
Glucose intolerance	Acromegaly, Cushing's

KEY POINTS

- Pituitary disease is relatively rare, but has a large impact on the morbidity and mortality of the affected patients.
- Symptoms suffered by patients are wide-ranging and non-specific, and may not be recognized for some years.
- Certain clusters of symptoms can give an indication of possible pituitary dysfunction. Patients may have chronic headache and visual symptoms, particularly deteriorating peripheral vision. There may be symptoms of primary hormone hypersecretion such as acromegaly, hyperprolactinaemia or Cushing's disease, or the symptoms may be much more general such as fatigue, amenorrhoea, loss of libido and erectile dysfunction associated with pituitary hypofunction.
- Endocrine emergencies caused by pituitary disease are rare but potentially life threatening if unrecognized. Mimicking other emergency conditions pituitary disorders should be included in the differential diagnosis. Diagnostic procedures should not delay treatment but storage of first blood sample will allow later assay. If in doubt ask for advice from specialist colleagues.
- For pituitary disease a timely diagnosis is most important, as there are now many effective treatments available.

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