

# Pituitary Disease Factfile



*The Pituitary Foundation Information Booklets*

The  
**Pituitary**  
FOUNDATION

*Working to support pituitary patients, their carers & families*



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## Introduction - about this factfile

These Factsheets were written in response to requests by General Practitioners and their pituitary patients for more information on pituitary disease. The Pituitary Foundation has already produced an excellent set of patient booklets explaining how pituitary disease can affect patients' lives, the kind of treatments available and general advice on how to cope with particular problems. This Factfile includes more detailed information, specifically written for the GP. Each Factsheet gives background information on the condition, how it is investigated and possible treatments. Since many of the investigations and treatments may be used for several different syndromes, the information on the sheets is extensively

cross-referenced. Resources are provided on each Factsheet and an additional separate list, including organisations, is also included.

## Abbreviations

<b>ACTH</b>	Adrenocorticotrophic hormone
<b>AVP</b>	Vasopressin (ADH)
<b>ADH</b>	Antidiuretic hormone
<b>CSF</b>	Cerebrospinal fluid
<b>CT</b>	Computed tomography
<b>DDAVP</b>	Desmopressin
<b>DI</b>	Diabetes insipidus
<b>FSH</b>	Follicle-stimulating hormone
<b>GH</b>	Growth hormone
<b>LH</b>	Luteinising hormone
<b>GnRH</b>	Gonadotrophin-releasing hormone
<b>PRL</b>	Prolactin
<b>MRI</b>	Magnetic resonance imaging
<b>TSH</b>	Thyroid-stimulating hormone

## Helpline:

for general patient support enquiries  
**0117 370 1320**  
Monday to Friday 10:00am to 4:00pm

## Endocrine Nurse Helpline:

**0117 370 1317** Mondays 6:00pm to 9:00pm and Thursdays 9:00am to 1:00pm

**[helpline@pituitary.org.uk](mailto:helpline@pituitary.org.uk)**  
**[www.pituitary.org.uk](http://www.pituitary.org.uk)**

## **Acknowledgements**

We would like to thank the many specialists in the world of endocrinology who have written these sheets including Stephanie Baldeweg, Peter Bayliss, Claire Blessing, Peter Clayton, Jurgen Honneger, Trevor Howlett, Stafford Lightman, John Monson, John Newell-Price, Peter Trainer and John Wass. They, alongside patients and GPs, read and made valued contributions to achieve this updated Factfile. © 1999, 2006, 2011 and 2014 to be reviewed June 2016.

## **Disclaimer:**

Every care has been taken in the compilation of this Factfile to ensure it reflects current practice (as at publishing date). Knowledge and clinical practice continually evolve. The reader is therefore advised to check with a specialist endocrinologist or with a product manufacturer if they have any concerns. The publishers and authors are not responsible for any errors or omissions or for any consequences from the application of the information presented in this Factfile.

# A Guide to Pituitary Apoplexy

**Bleeding or reduced blood flow in the pituitary gland can result in pituitary damage. This is called pituitary apoplexy. If there is only reduced blood flow with no bleeding, this condition is also called pituitary infarction. It usually happens in people with pre-existing pituitary tumours. The Greek word 'apoplexy' literally means sudden brain dysfunction.**

The pituitary gland is situated in a bony hollow and is surrounded by important structures, such as the nerves responsible for vision. In apoplexy the gland swells suddenly and this can cause pressure in the surrounding brain structures. The swelling can also cause the pituitary gland to stop producing one or more of the pituitary hormones.

Up to 5% of patients with pituitary tumours may develop apoplexy at some point. In fact, studies have shown that bigger tumours (macroadenomas) carry a higher risk of apoplexy compared with smaller ones (microadenomas). High or low blood pressure, head injury, certain medications such as warfarin, cardiac surgery and very rarely certain endocrine dynamic tests may increase the risk of apoplexy.

It is important that pituitary apoplexy is diagnosed and treated. If it remains untreated, apoplexy may cause seriously ill health and even death. The most common symptoms are headache, nausea or vomiting, changes in eye-sight, such as double vision, restriction in eye movement and drowsiness. These symptoms are not unique in apoplexy but may occur in other conditions such as meningitis, subarachnoid haemorrhage or (rarely) migraine, from which pituitary apoplexy has to be distinguished. The best way to diagnose pituitary apoplexy is a Magnetic Resonance Imaging (MRI) scan.

The bleeding or pituitary infarction may not show on a Computerised Tomography (CT) scan. Blood tests are also important to check if the hormones produced by the pituitary gland are adequate.

In the event of pituitary apoplexy urgent treatment is required. This consists of intravenous fluids, corticosteroids and close monitoring. Surgery may be required to relieve the pressure and swelling around the pituitary gland. This usually can be done by making a small incision inside the nostril (transsphenoidal surgery). With treatment, the majority of patients recover and if the vision was affected it often gradually improves. If the vision was severely affected at the beginning, it may not fully recover. If the pituitary gland does not function properly after recovery patients may need hormone replacement therapy. Patients will need regular check ups at a specialist endocrine clinic to monitor the condition.

In 2010, a national working group developed guidelines for the management of pituitary apoplexy, to increase awareness amongst doctors and to standardise and improve the treatment of this rare, but potentially life-threatening condition.

## Indicative References

1. Murad-Kejbou S, Eggenberger E. Pituitary apoplexy: evaluation, management, and prognosis. *Current Opinion in Ophthalmology* 2009; 20:456-61.
2. Nawar R, AbdelMannan D et al. Pituitary Tumor Apoplexy: A Review. *Journal of Intensive Care Medicine* 2008; 23(2): 75-90.
3. Randeva HS, Schoebel J et al. Classical pituitary apoplexy: clinical features, management and outcome. *Clin Endocrinology (Oxf)* 1999; 51:181-188.

# Non-functioning pituitary tumours

The most common type of pituitary tumour is non-functioning (i.e. it does not cause excessive hormone production). Tumours of this type most commonly become apparent when the patient has visual symptoms or headaches due to pressure on the optic nerve and it is often the optician who refers the patient with abnormal visual fields to the GP (in which case the GP would want to refer to an ophthalmologist who, in turn, is likely to refer to an endocrinologist). The tumour may also damage the adjacent, normal pituitary gland (causing hypopituitarism - factsheet 6) or occasionally compress the pituitary stalk, causing hyperprolactinaemia (factsheet 5).

Please see 'Who and When to Refer' (factsheet 15).

## Presenting symptoms

- visual disturbance
- oligomenorrhoea or amenorrhoea in women
- tiredness and lack of energy
- reduced libido and potency in men
- headache

## Investigations

An MRI scan will be carried out to determine the size and site of the tumour. Visual field tests are used to determine the degree of functional impairment of the visual pathway. Blood tests will be needed to assess pituitary function.

## Treatment possibilities

### In the absence of pressure signs/symptoms

Patients may not need treatment, but will be monitored closely using MRI scans and visual field checks at intervals of 6 or 12 months. Alternatively surgery or, rarely, radiotherapy may be advised.

### In the presence of pressure signs/symptoms

Patients will usually need transsphenoidal surgery (factsheet 10), which may be followed by radiotherapy to prevent recurrence (factsheet 11). If pituitary hormones are deficient, pituitary hormone replacement therapy will be given (factsheet 12).

## Patient management

### Post-operative

Most patients will have improved, or at least stabilised, visual fields. Removal of the nasal packing, if this method used, is often the only part of the procedure that patients find uncomfortable. Some patients may find that their frequency of headaches changes. Other complications, such as Cerebral Spinal Fluid (CSF) leaks can occur, although rarely, and need to be treated by a further small operative procedure (factsheet 10).

### Long-term

Regular visual field assessments may be needed. MRI scans are usually repeated within the first post-operative months and follow-up scans are initially carried out at increasing intervals from 6 months to 5 years.

### Radiotherapy

Pituitary radiotherapy (factsheet 11) may be used after surgery to reduce the risk of regrowth of the tumour. Since radiotherapy can cause hypopituitarism at variable times after treatment, patients should be tested for pituitary function on a regular basis, probably at 6 months, 1 year, 2 years and then bi- or triennially.

## Watchpoints

### Urgent - refer to hospital

- Deterioration of vision
- Clear fluid dripping down the back of the throat or through the nose soon after surgery (CSF leak - factsheet 10)

### Non-urgent (but still very important)

- If the patient is on hydrocortisone, ensure that replacement therapy is increased when seriously ill or under major physical or psychological stress (factsheet 6)
- Treat headaches and migraine
- Ask about erectile function
- General wellbeing - consider whether the patient is growth hormone deficient e.g., if energy lacking, otherwise for replacement therapy
- Menstrual cycle loss – consider whether the patient needs hormone replacement therapy

## Questions patients may ask

### Why do I bump into objects?

The pituitary normally sits under the optic apparatus. When the pituitary enlarges, visual problems caused by compression of the visual pathway are often the first symptom. Visual acuity (vision that can be corrected by wearing spectacles) may not be changed, but visual fields are reduced, firstly in the upper outer quadrant, then the whole temporal field (the field of vision on both left and right sides of the head as opposed to central vision).

### Will my sight return after treatment?

The chances of at least partial recovery are

good if the tumour is treated promptly. Treatment is effective in stopping any further visual loss in almost all cases.

### Why have my periods stopped?

The tumour may prevent the pituitary from being able to secrete the hormones that control menstruation and fertility.

### Have I inherited this, will my children get it?

In all but very exceptional circumstances there is no hereditary link.

## Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

## Patient information booklets

- *The Pituitary Gland: its conditions & Hormones explained*
- *Pituitary Surgery & Radiotherapy*

Other information and resource links available at [www.pituitary.org.uk](http://www.pituitary.org.uk).

## For GPs

Endotext.org 'Your Endocrine Source'  
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The Pituitary Foundation website  
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H Turner and JAH Wass (Eds).

**More specialist resources**

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(Second Edition), Editors and authors Michael P. Powell, Stafford L. Lightman and Edward R. Laws. Humana Press, Totowa, New Jersey

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*The Diagnosis and Treatment of Pituitary Insufficiency (1997)*

Lamberts SWJ (Ed) Bristol, UK: BioScientifica

*Endocrinology (1997) Levy*

A & Lightman SL

New York: Oxford University Press

*The Epidemiology, Pathogenesis and Management of Pituitary Tumours*

(1998) Webb SM (Ed) Bristol, UK: BioScientifica

# Acromegaly

**Incidence:** 4-6 new cases per million per year

**Prevalence:** 60 per million

**Acromegaly is the result of growth hormone (GH) hypersecretion by a pituitary macro- or microadenoma. Many of the actions of GH are mediated by insulin-like growth factor-1 (IGF-1), which is secreted from the liver and other organs under the regulation of GH. GH levels fluctuate over the day. Plasma IGF-1 levels, in contrast, fluctuate little during the day and can be used, along with GH, as a measure of disease activity. Up to a third of tumours co-secrete prolactin.**

Acromegaly most often occurs in adults aged 30-50 years. Presentation before the growing ends of bones have fused (usually around 18 years of age) is rare and is the cause of pituitary gigantism. Elevated GH levels are associated with changes in appearance, headaches, sweating and tiredness. Acromegaly affects a number of body systems and is associated with a two-fold increase in mortality, particularly from cardiovascular disease.

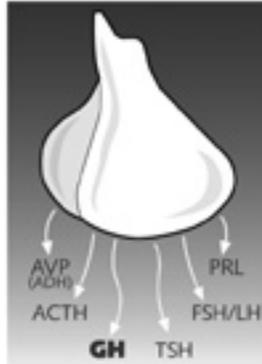
## Presenting symptoms

Excessive GH secretion produces a gradual change in appearance (not usually noticed by those living or working with the patient) due to its effects on cartilage and soft tissues. Symptoms have often been present for a decade before the diagnosis is made. The patient may notice enlargement of the hands and feet and may experience growth of the jaw. Nerve compression

symptoms may occur, particularly carpal tunnel syndrome. Premature osteoarthritis of the weight-bearing joints is also characteristic. Obstructive sleep apnoea may be present, especially in men, leading to daytime sleepiness.

## The main features are:

- coarsening of facial features
- enlarged hands and feet
- carpal tunnel syndrome
- excessive sweating and oily skin
- headaches
- vision disturbance
- sleep apnoea
- general tiredness



There should be a low threshold for referral for any patient with any suspicion of acromegaly as the greatest challenge in the diagnosis of acromegaly is thinking of the disease. Once suspected, biochemical confirmation or exclusion of the disease is usually straightforward. We strongly recommend that all referrals be to an endocrinologist rather than neurosurgeon or others. Please see 'Who and When to Refer' (factsheet 15).

## Investigations

Investigations will include a GH series and an analysis of the GH response to a glucose load (Glucose Tolerance Test), as well as measurement of prolactin and other pituitary function tests. An MRI scan will be carried out and visual field tests may be performed to determine the size and position of the adenoma.

## Treatment possibilities

Epidemiological evidence suggests that with

normalisation of GH and IGF-1 levels, life expectancy can be restored to normal. The treatment recommended by the consultant will depend on the size and activity of the adenoma and also on the age of the patient. Transsphenoidal surgery is the treatment of choice in most cases and can be dramatically effective, especially for microadenomas. However, some patients may need medical treatment or radiotherapy after surgery to reduce GH levels. Some GH-secreting adenomas are treatable by long-term medical therapy with or without radiotherapy. The consultant may offer the patient a choice between long-term medical treatment, involving injections, or surgery.

### Medical therapy

Some patients may need long-term medical treatment to maintain acceptable GH and IGF-1 levels. High levels of GH, even when the patient has no symptoms, are associated with a 2-3-fold increase in mortality.

Stabilisation of GH may be achieved with a dopamine agonist, particularly if the tumour also secretes prolactin. Cabergoline, is effective, potent and causes few side effects. However, the somatostatin analogues octreotide and lanreotide, which act by inhibiting GH release from the pituitary, are much more effective in reducing GH and IGF-1 to acceptable levels. Octreotide/Lanreotide are available as long-acting preparations that require to be injected monthly, (Sandostatin LAR and Lanreotide Autogel). Normalisation of GH and IGF-1 can be achieved in between half and two-thirds of patients. Somatostatin analogues also cause tumour shrinkage in most cases, when they may improve surgical results. Some patients suffer gastrointestinal side effects with these drugs

and there is some risk of developing gallstones. Pegvisomant is a GH receptor antagonist that blocks GH action by preventing GH from binding to its receptor. Unlike other forms of treatment, it does not attempt to inhibit GH release from the pituitary and as GH levels do not fall with treatment, disease activity is judged by measuring IGF-1.

Patients may develop hypopituitarism (factsheet 6) after surgery, or several years after radiotherapy. Hormone replacement therapy will then be needed (factsheet 12).

### Watchpoints

#### Urgent - refer to hospital

- Deterioration of vision
- Clear fluid dripping down the back of the throat or through the nose soon after surgery (CSF leak - factsheet 10 Surgery)

#### Non-urgent (but still very important)

- If the patient is on hydrocortisone, ensure that replacement therapy is increased when seriously ill or under major physical or psychological stress
- Treat headaches
- Treat depression
- Treat carpal tunnel syndrome
- Treat osteoarthritis: refer for hip/knee replacement if required
- Ask about erectile function, 70% have problems. Treat this, reassure that it is part of the disease and that it can be treated
- The patient is likely to have obstructive apnoea and to snore very loudly. It can be helped by treatment to lower GH, and by continuous positive airways pressure (CPAP)
- Ask about change in bowel habit as some increased risk of colonic polyps and colonic carcinoma

## Questions patients may ask

### Why do my hands hurt?

Growth can occur in the connective tissue of the carpal tunnel compressing the median nerve.

### Why do I wake up tired?

Growth hormone causes hypertrophy of the nasopharyngeal tissue and sleep apnoea (usually noticed by the partner). This can be treated

### Why am I getting headaches?

A large tumour may compress surrounding tissues.

### Why can't I get my wedding ring on?

Hypertrophy of the soft tissues of the joints causes enlargement of hands and feet.

### Why has my shoe size increased?

See above.

### Why does my jaw ache when I eat an apple?

Growth of the mandible disturbs dental occlusion and puts increased strain on the temporomandibular joints.

### Why do I keep biting my tongue?

GH promotes growth of the tongue.

### Why do I have backache?

Growth of cartilaginous tissues causes musculoskeletal abnormalities and degenerative changes.

### Why do I have such bad arthritis?

Growth and degenerative changes are common. One of the main aims of treatment is to prevent this.

### Why do I sweat so much?

Not known but when GH levels are normal the problem disappears.

### Have I inherited this, will my children get it?

In all but very exceptional circumstances there is no hereditary link.

## Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

### Patient Information Booklet

- *Acromegaly*

Other information and resource links available at [www.pituitary.org.uk](http://www.pituitary.org.uk)

### For GPs

Endotext.org 'Your Endocrine Source' [www.endotext.org](http://www.endotext.org) ([www.endotext.org/neuroendo/index.htm](http://www.endotext.org/neuroendo/index.htm))

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*Oxford Handbook of Endocrinology OUP (2009)*  
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**More specialist resources**

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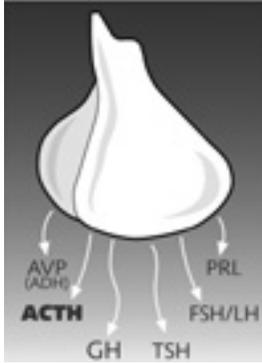
*The Diagnosis and Treatment of Pituitary Insufficiency* (1997) Lamberts SWJ (Ed) Bristol, UK: BioScientifica

*Endocrinology* (1997) Levy A & Lightman SL  
New York: Oxford University Press

*Acromegaly.* (2009) Wass JAH (Ed)  
BioScientifica, UK

# Cushing's disease

**Incidence:** 5-6 new cases per million per year



**Cushing's disease (i.e. an ACTH-secreting pituitary adenoma) is the most common cause of spontaneous Cushing's syndrome; other causes are an adrenal**

**tumour or an ectopic tumour secreting ACTH. Spontaneous Cushing's syndrome is caused by excessive circulating cortisol; it is rare but is associated with a significant increase in morbidity and mortality, even if treated. Cushing's syndrome may also be the unavoidable result of steroid treatment for allergy, asthma, arthritis or other life-threatening condition. Diagnosis and differential diagnosis of Cushing's syndrome is complex and referral to a specialist centre is recommended in all cases in whom the condition is suspected. The recommended route of referral is through an endocrinologist rather than neurosurgeon or others. Please see 'Who and When to Refer' (factsheet 15).**

## Presenting symptoms

- moon face - particularly filling in of the temporal fossa
- weight gain - central obesity
- muscle wasting and proximal myopathy (patients have difficulty standing from a seated position without use of arms)

- thin skin - tendency to bruise
- hirsutism (caused by androgen excess)
- violaceous striae
- hypertension
- diabetes
- osteoporosis and fractures
- psychiatric disturbance (often characterised by amplification of previous mood swings).

## Investigations

Overnight dexamethasone suppression test and/or 24-hour urinary cortisol measurements. If this indicates Cushing's syndrome further tests to confirm the diagnosis and to determine the source of excessive cortisol will be required.

Normal screening tests do not always exclude the diagnosis - if clinical suspicion is high then specialist referral may still be necessary. During diagnosis and differential diagnosis further dynamic endocrine tests, chest X-ray and pituitary, adrenal and lung/abdomen MRI or CT scans may be required.

## Treatment possibilities

Transsphenoidal surgery is usually the recommended treatment if the condition is due to a pituitary tumour. In cases where surgery is contra-indicated or fails to reduce cortisol levels, adrenalectomy and/or pituitary radiotherapy may be necessary. Some patients may need bilateral adrenalectomy to control disease when pituitary surgery is not effective.

## Patient management post-operative

Patients in remission normally undergo substantial changes immediately after surgery which, apart from welcome changes in physical appearance and resolution of other symptoms and signs, may initially involve depression.

This is the result of the profound change in steroid status. No further treatment may be required except monitoring for recurrence of Cushing's and regrowth of the tumour. However, most patients will require hydrocortisone therapy, some on a long-term basis and patients need strong reassurance that feeling worse after surgery is usual, but that in the long run things improve. If the patient needs hydrocortisone for more than one year postoperatively, the outlook for long-term remission is excellent. If surgery results in hypopituitarism, long-term hormone replacement therapy will be required (factsheet 12).

### Long-term

Patients require close follow up on a long-term basis. Pituitary hormone replacement therapy will be required after surgery in some cases, and requires careful specialist monitoring. Advice should be given regarding the dose of steroid to be taken during intercurrent illness (factsheet 12).

Long-term effects of radiotherapy may also include the development of partial or complete hypopituitarism. Patients may need help to follow a suitable diet and encouragement to take regular exercise to control weight gain.

### Watchpoints

#### Urgent - refer to hospital

- Deterioration of vision
- Clear fluid dripping down the back of the throat or through the nose soon after surgery (CSF leak - factsheet 10)

#### Non-urgent (but still very important)

- If the patient is on hydrocortisone, ensure that replacement therapy is increased when seriously ill or under major physical or psychological stress

- Patients may have major mood swings after successful treatment to lower circulating corticosteroids. This can last for many months, so reassurance and treatment for depression may be necessary
- Obesity is often the aspect of Cushing's disease that female patients find most distressing. Weight reduction following successful treatment is often slow
- Patients will need exercises to restore muscle strength and possibly further treatment for osteoporosis

### Questions patients may ask

#### Why am I putting on weight?

Increased cortisol causes accumulation of fat deposits and a redistribution of fats to the face, neck and abdomen.

#### Why am I getting hairy?

ACTH stimulates increased secretion of androgens from the adrenal cortex causing hirsutism.

#### Why do I feel so weak?

Hypersecretion of cortisol causes the increased breakdown of tissue proteins. One effect of this is muscle wasting, which mainly affects the muscles of the upper arms and thighs. This can make it difficult to climb stairs, or stand after sitting.

#### Why am I so moody?

The excess steroid produced by the tumour has a direct effect on the brain. It tends to produce dramatic mood swings.

**Why do I bruise so easily?**

Increased breakdown of tissue proteins causing weakening of capillaries.

**Why have I developed stretch marks?**

Increased breakdown of skin proteins makes the skin more fragile

**Why do I have backache?**

As above - the back muscles are weakened by the steroids and the extra weight which you gain also puts a strain on them. The steroids also affect the bones of the back.

**Have I inherited this, will my children get it?**

In all but very exceptional circumstances there is no hereditary link.

**Resources for patients**

available from The Pituitary Foundation Helpline or our website **www.pituitary.org.uk** or our Endocrine Nurse Helpline

**Patient Information Booklet**

- *Cushing's*

Other information and resource links available at **www.pituitary.org.uk**

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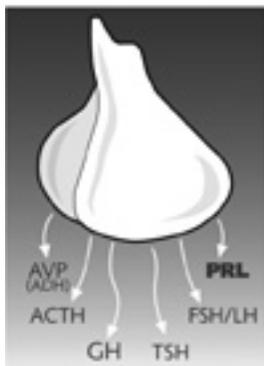
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Bristol, UK: BioScientifica

*Oxford Textbook of Endocrinology OUP* (2002)  
JAH Wass & S Shalet (Eds)

# Hyperprolactinaemia

**Incidence:** Most common secreting adenoma. They are more common in women and macroprolactinomas are more **common in men**.



**Prolactin levels are normally high during pregnancy and lactation. Abnormally high levels of prolactin at other times may be caused by a prolactin-secreting**

**pituitary tumour or by a non-secreting pituitary tumour that prevents dopamine (prolactin release-inhibiting hormone) from the hypothalamus reaching normal prolactin-producing cells (lactotrophs) of the pituitary. Raised prolactin levels are also sometimes found in Cushing's syndrome, hypothyroidism and polycystic ovarian disease. A number of drugs increase prolactin levels by blocking the action of dopamine, e.g., metoclopramide, domperidone, some anti-depressants and the phenothiazines. Stress raises prolactin levels so the very act of venepuncture can result in high levels.**

The behaviour of prolactin-secreting tumours is defined by their size at presentation. Microprolactinomas (less than 10mm in diameter) rarely expand to become macroprolactinomas. In men, prolactinomas tend to present late, because reduced potency and loss of libido - the hormonal effects of raised prolactin levels - are subtle and develop

slowly. In women, absent periods and/or inappropriate production of breast milk often allow the diagnosis to be made early.

There should be a low threshold for referral for any patient with any hyperprolactinaemia, as the greatest challenge in the diagnosis of hyperprolactinaemia is thinking of the disease. Once suspected, biochemical confirmation or exclusion of the disease is usually straightforward. See 'Who and When to Refer' (factsheet 15).

## Presenting symptoms

- galactorrhoea
- oligomenorrhoea or amenorrhoea
- reduced libido
- erectile dysfunction
- pressure effects (e.g., headache and visual disturbance) with macroadenomas

## Investigations

Useful GP screening tests include basal prolactin, thyroid function tests, a careful drug history and exclusion of pregnancy. If prolactin (normal range <400 mU/l) is mildly elevated (400 – 1000 mU/l) it should be repeated before referral.

Dynamic prolactin stimulation tests such as the TRH test have no part in the investigation of hyperprolactinaemia. Measurement of serum prolactin on three separate occasions (at least 2 hours after rising and when patient rested) provides all the information necessary.

A prolactin level >5000 mU/l usually indicates a true prolactinoma rather than a functionless tumour causing a raised prolactin. Specialist tests include pituitary imaging (preferably MRI) and visual field testing if indicated (macroadenomas) and assessment of pituitary function.

Macroprolactin is a biologically inactive form of prolactin that causes no clinical problem, other than being detected in prolactin assays resulting in spurious elevation of serum prolactin levels. Macroprolactin should be suspected in any patient with an elevated prolactin but no associated signs or symptoms. Most laboratories can test for macroprolactin.

Please see 'Who and When to Refer' (factsheet 15).

### Treatment objectives and possibilities

Osteoporosis is a concern in any patient with hypogonadism – manifest clinically as amenorrhoea or erectile dysfunction. In any patient with one year of hypogonadism a bone density scan should be performed and a major goal in the treatment of hyperprolactinaemia is the prevention of osteoporosis.

In addition, treatment should stop galactorrhoea and restore oestrogen levels in women, and hence menstruation, fertility, libido and vaginal lubrication to normal. In men, treatment of high prolactin should normalise testosterone levels, and hence erectile function and libido.

For macroprolactinomas, an additional objective is to shrink the tumour in order to reduce any pressure effects, such as visual failure.

### Patient management

Most patients are treated medically with the dopamine agonists cabergoline, or bromocriptine, both of which reduce prolactin levels, allow oestrogen or testosterone levels to rise and greatly reduce the size of the tumour. Surgery to reduce tumour size, and radiotherapy to reduce the chance of recurrence, are rarely required.

Medical treatment with cabergoline, quinagolide, or bromocriptine controls prolactin and symptoms in the majority of patients, but needs to be continued long term. In patients with microprolactinomas an attempt to withdraw the medication can be made after 3 years. These drugs can be associated with some dizziness and nausea. This can be limited by taking the medicine in the middle of meals or last thing at night and by starting at low dose.

Cabergoline is the most widely prescribed treatment for prolactinoma as it is more potent and associated with fewer side-effects. However, recent guidance suggests that patients taking cabergoline should have regular examination of the heart (echocardiography) and watch out for shortness of breath as cabergoline can cause (at higher dosage) fibrosis of the lungs and heart valves. There had been concern about fibrosis etc, but that recent large UK data suggest no excessive risk. Any monitoring will be advised by an endocrinologist.

### Pregnancy and prolactinomas

Patients should be followed during pregnancy by an endocrinologist. Ideally it is advisable for patients to have discussed pregnancy with their endocrinologist prior to conception.

Most women are advised to cease taking dopamine agonists for the duration of pregnancy and during lactation. However, many thousands of babies have been born to mothers taking bromocriptine and there is no evidence of an increased incidence of malformation or miscarriage. Cabergoline treatment appears to be safe during pregnancy. During pregnancy, there is a slight risk of tumour enlargement, particularly in patients with macroadenomas. Any patient who experiences severe headaches

or visual disturbances should be seen urgently by their specialist.

## Watchpoints

### Urgent - refer to hospital

- Deterioration of vision

### Non-urgent (but still very important)

- Remember that successful treatment usually results in restoration of fertility (particularly in microprolactinomas)
- Patients may be predisposed to problems related to osteoporosis
- Ask about erectile function. Reassure that it is part of the disease and that it can be treated

## Questions patients may ask

### Why do I have a discharge from my breasts?

Prolactin is normally required to initiate and maintain lactation. The secretion of prolactin from a pituitary tumour may have the same effect.

### Will a microprolactinoma grow into a macroprolactinoma?

In the vast majority of cases, no. This very rarely happens.

### Have I inherited this, will my children get it?

In all but very exceptional circumstances there is no hereditary link.

### Do all patients with prolactinomas need treatment?

Most do. If you have infertility problems,

problems with lack of interest in sex (low libido) or impotence, excessive milk production or a large tumour causing pressure symptoms, then there is a clear case for treatment. If not, then the need may not seem so clear. However, prolonged sex-hormone deficiency (particularly oestrogen in women) causes thinning of the bones, or osteoporosis. Therefore, most doctors believe that women without regular periods should receive treatment. The same applies to men with low testosterone levels.

### How long will I have to take tablets for prolactinoma?

You will probably need to take these tablets for a relatively long time, with interruption during pregnancy as described earlier. If you have a microprolactinoma, many specialists withdraw treatment for a trial period every three years or so; in some patients the problem seems to disappear during prolonged tablet treatment. If you have a large tumour, your treatment courses may last several years; tumour control is maintained and side-effects during long-term treatment are not usually a problem.

### What are my fertility prospects as a man with prolactinoma?

Tablet treatment alone may improve your sperm count and lead to the return of normal fertility, although this may take several months. Additional treatment with hormone injections (FSH and LH)

may also be necessary. Fertility is usually attainable.

### **Is tablet treatment better than surgery for prolactinomas?**

Tablet treatment is the accepted form of treatment. Occasionally (5-10%) patients have either severe side effects or do not respond to cabergoline. In these patients surgery may be advised although it is not always curative (70- 80%) and the operation may cause hypopituitarism.

### **Resources for patients**

available from The Pituitary Foundation Helpline or our website **www.pituitary.org.uk** or our Endocrine Nurse Helpline

### **Patient Information Booklet**

- *Prolactinoma*

Other information and resource links available at [www.pituitary.org.uk](http://www.pituitary.org.uk)

### **For GPs**

Endotext.org 'Your Endocrine Source'  
**www.endotext.org** ([www.endotext.org/neuroendo/index.htm](http://www.endotext.org/neuroendo/index.htm))

The Pituitary Foundation Website  
**www.pituitary.org.uk**

*Oxford Handbook of Endocrinology OUP* (2009)  
H Turner & JAH Wass (Eds).

### **More specialist resources**

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London: Royal College of Physicians

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*Endocrinology* (1997) Levy A & Lightman SL  
New York: Oxford University Press

*The Epidemiology, Pathogenesis and Management of Pituitary Tumours* (1998) Webb SM (Ed)  
Bristol, UK: BioScientifica

# Hypopituitarism



**Hormone deficiency caused by the inadequate secretion of one or more of the hormones normally secreted by the pituitary, is known as**

**hypopituitarism. It may commonly be caused by compression of the normal pituitary tissue by an enlarging pituitary tumour, by pituitary surgery, or radiotherapy.**

If hypopituitarism is caused by tumour compression, function may be partially or fully recovered after surgery or medical therapy to reduce the size of the tumour. Pituitary surgery may cause hypopituitarism in a minority of cases and improve pituitary function in others, and deficiencies can be transient (particularly diabetes insipidus). Detailed post-operative endocrine assessment is therefore essential.

Hypopituitarism after treatment of a pituitary tumour by radiotherapy typically develops slowly and progressively over a period of several years.

## Presenting symptoms

Deficient hormone	Symptoms
<b>GH</b> (growth hormone)	Growth retardation in children Adults: excessive tiredness, muscle weakness, lack of drive, impaired quality of life scores
<b>FSH/LH</b> (>secondary hypogonadism)	Hypogonadism – In men: reduced facial and body hair, low libido, impotence; in women: amenorrhoea, reduced libido, dyspareunia and hot flushes
<b>TSH</b> (>secondary thyroid deficiency)	Weight gain, decreased energy, sensitivity to cold, constipation, dry skin
<b>ACTH</b> (>secondary adrenal deficiency)	Pale appearance, weight loss, low blood pressure, dizziness, tiredness, ‘collapse’ during intercurrent illness
<b>AVP/ADH</b> (argine vasopressin or Anti-Diuretic Hormone)	Thirst, polyuria and nocturia – diabetes insipidus

**Acute hypopituitarism (e.g., pituitary apoplexy)** - sudden headache, collapse, hypothermia, hypoglycaemia and hypotension - may be a life-threatening emergency. Prompt

steroid replacement is required for ACTH deficiency presenting acutely and during intercurrent illness in established ACTH deficiency.

## Investigations

Tests for hypopituitarism should be performed under the guidance of an endocrinologist. Please see 'Who and When to Refer' (factsheet 15).

**Growth hormone** GH deficiency in children will require referral to a paediatric endocrine centre. Adult GH deficiency requires specialist assessment.

**Gonadal function** FSH, LH, prolactin, oestradiol and testosterone are assessed by serum levels. Testosterone in men should be measured at 9am to avoid falsely low results due to the circadian rhythm. In women with periods, bloods are normally performed in the follicular phase – but measurement of a Day 21 progesterone may be used to confirm ovulation.

If fertility is desired, then a different approach to hormone replacement will be needed and a full assessment of both partners will be carried out.

**Thyroid function** In pituitary-dependent hypothyroidism circulating thyroid hormone levels are low or low-normal but TSH can be low, normal or even slightly elevated. Laboratories must be asked for free thyroxine (free T4) as well as TSH, and thyroid hormone replacement adjusted on the basis of free thyroxine level (many laboratories will now only provide TSH measurements routinely unless free T4 is specifically requested and discussed)

**Adrenal function** ACTH stimulated secretion of cortisol is assessed using the short synacthen or the insulin stress test. A basal 9am cortisol gives limited information but low levels (<200nmol/L) should prompt early (and <100nmol/L urgent) referral.

**Diabetes insipidus** The diagnosis and cause is usually obvious and if so may be confirmed by measurement of basal serum and urine

osmolalities but sometimes a water deprivation test is required.

## Treatment possibilities

(for full details see factsheet 12)

**GH** - Synthetic GH replacement is given to children. The treatment of adults with GH replacement is clinically effective for many (though not all) patients with GH deficiency. NICE has issued guidelines to identify patients in whom treatment is indicated.

**ACTH** - Treatment is usually with hydrocortisone (= cortisol), typically 3 times daily. Prednisolone or dexamethasone is occasionally used. Increased doses are required during acute stress including intercurrent illness or surgery. Fludrocortisone is not normally required in pituitary deficiency.

**TSH** - Treatment with levothyroxine. Free T4 levels must be used for monitoring since TSH levels are not informative.

**FSH/LH** - Treatment with oestrogen in women (and progestogen in women with a uterus). Testosterone replacement in men given intramuscularly (i.m. every 2-4 weeks or 3-monthly depot), transdermally (usually via gel), orally or by implant. For fertility, treatment with gonadotropins is required which should only be performed at a specialist centre which provides effective monitoring.

**AVP/ADH** - Treatment with desmopressin (DDAVP) by intranasal spray, tablets or Melts.

## Patient management

Management of patients with hypopituitarism on multiple hormone-replacement therapy (which The Foundation believes) is best achieved by life-long supervision by a specialist endocrine outpatient clinic. The time interval

for specialist monitoring will vary with the patient and the treatment received, but will probably be at intervals of 2-6 months immediately post treatment, to annual or biennial in the longer term. Patients may need help with managing hydrocortisone therapy (factsheet 12).

## Watchpoints

### Urgent - refer to hospital

- Deterioration of vision
- Clear fluid dripping down the back of the throat or through the nose soon after surgery (CSF leak - factsheet 10)
- As emergency if unable to take increased oral steroid replacement during acute intercurrent illness (e.g., vomiting)

### Non-urgent (but still very important)

- If the patient is on hydrocortisone, ensure that replacement therapy is increased when seriously ill or under major physical or psychological stress
- Watch for gradual deterioration in endogenous pituitary function and provide replacement therapy as required

## Questions patients may ask

### Will I have to take tablets in the long term?

If the pituitary tumour or treatment for it has affected the function of the normal pituitary, its function does not usually recover and will need to be replaced in the long term.

### Will I need regular check-ups?

Yes, but pituitary tumours are usually well

controlled and, if they regrow at all, grow very slowly. Outpatient appointments are usually made 12 months to 2 years apart.

### Will I need regular scans?

Perhaps, but again, these too are carried out several years apart.

### Will I still be able to have a family?

Yes, if the reason for infertility is pituitary disease. The effects of pituitary tumours on fertility can be treated, although some treatments are not currently paid for by the NHS (factsheet 12).

### If I take replacement therapy, will I feel exactly the same as I did before my pituitary tumour developed?

Replacement therapy is unable to fully match the body's natural, intricate hormone balance. Every patient is different and, whilst many return to fairly normal life, the main object of replacement therapy is to achieve as good a quality of life as possible for patients.

### Have I inherited this, will my children get it?

In all but very exceptional circumstances there is no hereditary link.

## Resources for patients

available from The Pituitary Foundation  
Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk)  
or our Endocrine Nurse Helpline

## Patient Information Booklet

- *The Pituitary Gland; Its conditions and hormones explained*

Other information and resource links available  
at [www.pituitary.org.uk](http://www.pituitary.org.uk)

## For GPs

Endotext.org 'Your Endocrine Source'  
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*Oxford Handbook of Endocrinology and Diabetes*  
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Wass (Eds).

*Oxford Textbook of Endocrinology and Diabetes*  
2nd Edition OUP (2010) JAH Wass & PM  
Stewart (Eds)

NICE guidance of growth hormone in adults  
<http://www.nice.org.uk>  
Adults: <http://guidance.nice.org.uk/TA64>  
Children: <http://guidance.nice.org.uk/TA42>  
NICE service guidance on Brain and other  
CNS Tumours [http://guidance.nice.org.uk/  
CSGBraincns](http://guidance.nice.org.uk/CSGBraincns)

# Craniopharyngioma

**Incidence:** 9% approx of all childhood intracranial tumours

**Craniopharyngiomas are benign tumours accounting for approximately 9% of all intracranial tumours in childhood, and are the most common peripituitary tumour in this age group. In adults, craniopharyngiomas account for 1% of brain tumours. Their behaviour is unpredictable and their origin is not fully understood. They are usually situated close to the pituitary gland and hypothalamus. The tumour consists of solid parts, sometimes calcified, and cysts, which may be filled with a dense oily fluid.**

## Presenting symptoms

Craniopharyngiomas can cause symptoms at any age, but those presenting in childhood are relatively fast growing, have a more aggressive course and can be more difficult to treat.

Symptoms have usually been present for some time before diagnosis. They are usually associated with raised intracranial pressure and possibly anterior and posterior pituitary failure.

Symptoms and signs at presentation may include:

- Headaches (typically in the morning), nausea and vomiting (commoner in children).
- Visual field defect (typically bilateral temporal hemianopia - poor vision to both sides - but complete loss of vision in one or both eyes can occur).
- Slow growth during childhood.
- Delayed or arrested puberty, and very occasionally precocious puberty.
- Thirst and passing large volumes of dilute urine (diabetes insipidus).

- Tired, difficulty recovering from minor illness (ACTH, cortisol deficiency).
- Tired, cold intolerance, constipation, slow pulse, dry skin (TSH/T4 deficiency).
- Changes in behaviour.

Please see 'Who and When to Refer' (factsheet 15).

## Investigations

An MRI or CT scan determines the precise size and position. Additional tests that form part of the evaluation include assessments of biochemical, endocrine (especially an assessment of hypothalamic-pituitary axis), psychological and visual function.

## Treatment possibilities

Because of the position of the tumour, transcranial, subfrontal surgery is almost always required. However some small craniopharyngiomas may be approached by the transsphenoidal route. Complete excision is rare. In most patients, partial removal is followed by radiotherapy. Prior to the operation, or if the tumour re-grows, insertion of a CSF shunt may be required if hydrocephalus (excessive accumulation of CSF in the ventricular system) is present.

## Patient management

All patients require long-term follow up, to allow early detection of any tumour re-growth and to treat the effects of the lesion on hypothalamic and pituitary function. Recurrence after surgery alone is common, but is less likely when radiotherapy is also given. Following surgery, at approximately 2-3 months, a further assessment of hypothalamic-pituitary axis is required. Many patients will be panhypopituitary (factsheet 6), and it is relatively common for diabetes insipidus (factsheet 8) to develop.

Children with panhypopituitarism may need long-term GH (factsheet 12), cortisol, thyroid and sex hormone replacement. Annual MRI or CT scans to check for re-growth are especially important in the first 3 years after treatment.

Other common problems post-op are increased or decreased appetite (resulting in weight problems) and reduced powers of concentration and short-term memory loss.

## Watchpoints

### Urgent - refer to hospital

- Deterioration in vision and/or recurrent headache. These may indicate regrowth and/or cyst recurrence.
- Intercurrent illness, in particular vomiting and diarrhoea in patients on cortisol replacement. Hydrocortisone replacement will need to be increased, and may need to be given by injection. Families should have hydrocortisone injections available for emergency use.
- CSF leak (very rare in children) Clear fluid dripping down the back of the throat or through the nose soon after surgery (factsheet 10)

### Non-urgent (but still very important)

- Depression, psychological difficulties and problems in school are relatively common in children treated for craniopharyngioma.

## Questions patients may ask

### How likely is it that the craniopharyngioma will re-grow?

If this is going to occur then the majority of cases are within 3 years, but it may recur many years later. Partial removal results in a higher chance of the tumour increasing

in size. This risk is considerably reduced by postoperative radiotherapy.

### How will I know if the craniopharyngioma is re-growing?

There may be no symptoms. Regular MRI scans are essential.

### Will my child be able to continue at school?

Most children remain in mainstream schooling without experiencing any difficulties. Difficulties may include sight problems, psychological and educational difficulties.

### Are my other children likely to develop this?

No, it is not hereditary or familial.

### Will it be possible for my child to have children?

With appropriate treatment at the time fertility is required, the young person should have a good chance of achieving fertility.

### Why is my child so sleepy?

As these tumours tend to occur above the pituitary, the part of the brain that deals with the organization of sleep and wakefulness is sometimes disturbed as the tumour grows, or by the surgical treatment. Damage to this part of the brain is often associated with increased somnolence.

### Why has my child's appetite increased?

The part of the brain that deals with feeling full after eating is sometimes disturbed for the same reasons.

## Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

## Patient Information Booklet

- *Craniopharyngioma* - Available from The Child Growth Foundation, for contact details go to factsheet 16.

Other information and resource links available at [www.pituitary.org.uk](http://www.pituitary.org.uk)

## For GPs

Endotext.org 'Your Endocrine Source'  
[www.endotext.org](http://www.endotext.org) ([www.endotext.org/neuroendo/index.htm](http://www.endotext.org/neuroendo/index.htm))

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*Oxford Handbook of Endocrinology OUP* (2002)  
JAH Wass & H Turner (Eds).

## More specialist resources

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Editors and authors Michael P. Powell, Stafford L. Lightman and Edward R. Laws. Humana Press, Totowa, New Jersey

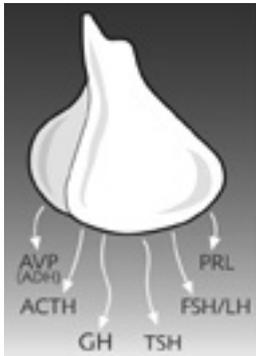
*Pituitary Tumours. Recommendations for service provision and guidelines for management of patients.* Consensus statement of a working party (1997) RN Clayton & JAH Wass (Eds)  
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*Endocrinology* (1997) Levy A & Lightman SL  
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*The Epidemiology, Pathogenesis and Management of Pituitary Tumours* (1998) Webb SM (Ed)  
Bristol, UK: BioScientifica

# Diabetes insipidus



The condition **diabetes insipidus (DI)** is characterised by the passage of large volumes of urine (>3 litres/24hrs), and persistent thirst. It is distinguished from diabetes

mellitus (sugar diabetes) by 'insipid' urine, i.e., lacking taste, in contrast to the 'sweet tasting' urine of diabetes mellitus. A common cause of DI is inadequate secretion of vasopressin, the antidiuretic hormone, from the posterior pituitary. However, some patients suffer from renal conditions in which the kidneys fail to respond correctly to vasopressin; this is nephrogenic DI.

Trauma, infection, granulomatous disease (e.g., sarcoidosis) or tumours in the region of the hypothalamus or pituitary may reduce vasopressin secretion. Pituitary surgery not infrequently causes DI which is usually transitory lasting a few hours or days; occasionally it may be permanent and be accompanied by loss of other pituitary hormones. Pituitary surgery also causes other forms of hypopituitarism which are covered elsewhere (factsheet 6).

## Presenting symptoms

- Polyuria, in excess of 3 litres/24hrs in adults
- Thirst and polydipsia (excessive drinking)
- Tiredness, lethargy and reduced concentration (often the result of lack of sleep due to night-time visits to the toilet)

## Investigations

The diagnosis is suggested by copious volumes of dilute urine with normal or slightly raised serum sodium. A water-deprivation test for up to 8 hours with measurements of serum sodium, blood and urine osmolalities and urine volume at 2-hour intervals followed by observation of urinary responses to desmopressin (DDAVP - an artificial vasopressin), can differentiate DI from other causes of polyuria (i.e., persistent excessive drinking or nephrogenic DI). An MRI scan of the pituitary region to include the hypothalamus and posterior pituitary is necessary.

## Treatment

Mild cases of DI (urine output 3-4 litres/24 hrs) can be managed by ingestion of water to quench thirst. Others require desmopressin (DDAVP) which can be given orally, intranasally or parenterally. It is essential to avoid chronic overdosage which will cause hyponatraemia (low serum concentration of sodium). Very occasionally, patients with extensive lesions affecting the hypothalamus may have lack of thirst as well, and this presents a particular challenge to management with the need for daily weights and fixed fluid intakes.

## Long-term management

Because of the risk of hyponatraemia, occasional (1-3 monthly) measurements of serum sodium are advised until patients are on stable therapy, when most will only need biochemical monitoring every 6-12 months.

## Questions patients may ask

### Why am I so thirsty?

Lack of the normal vasopressin secretion, means that the kidneys are unable to concentrate the urine. This results in a high sodium level in the blood which stimulates thirst.

### Why do I have to visit the toilet so often?

Lack of vasopressin reduces the kidneys ability to concentrate the urine resulting in the production of large volumes of urine.

### Why do I have headaches?

This can happen after your DI is treated and it is important to balance the dose of desmopressin and the amount of fluid you drink so as not to retain too much water and develop hyponatraemia (low sodium).

### Will I recover from DI?

DI can be caused by surgical trauma or accident and may in some cases be transitory, but patients may require treatment for life.

### Is it harmful to miss a dose of DDAVP?

Generally speaking it is safer to miss a dose of DDAVP than to take an extra dose. You will simply notice that your thirst will be greater than normal, and you should drink more.

## Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

## Patient Information Booklet

• *Diabetes Insipidus* Other information and resource links available at [www.pituitary.org.uk](http://www.pituitary.org.uk)

## For GPs

Endotext.org 'Your Endocrine Source'  
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 Bristol, UK: BioScientifica

*Disorders of the Posterior Pituitary.* Newell-Price and Besser. In *The Oxford Textbook of Medicine* (Warrell, D.A., Cox, T.M., Firth, J.D. eds), 2002

# Traumatic brain injury and hypopituitarism

**Brain injury may cause damage to the hypothalamus and/or pituitary gland. Although the true incidence of brain injury and hypopituitarism remains unclear, the poor outcome for patients who go unrecognised could be devastating, with morbidity and the potential for mortality.**

Therefore, it is important to raise awareness of this issue amongst primary health care professionals. Most patients recover quickly from their head injury and experience no long-term problems. However, some patients can develop problems after a few weeks, months or sometimes, years.

## Presenting symptoms

Deficient hormone	Symptoms
<b>GH</b> (Growth Hormone)	Children: Growth retardation Adults: Excessive tiredness, muscle weakness, lack of drive, impaired quality of life scores
<b>FSH/LH</b> ( >secondary hypogonadism)	Hypogonadism – In men: reduced facial and body hair, low libido, impotence. In women: amenorrhoea, reduced libido, dyspareunia and hot flushes
<b>TSH</b> (> secondary thyroid deficiency)	Weight gain, decreased energy, sensitivity to cold, constipation, dry skin
<b>ACTH</b> (> secondary adrenal deficiency)	Pale appearance, weight loss, low blood pressure, dizziness, tiredness; ‘collapse’ during intercurrent illness
<b>AVP/ADH</b> (arginine vasopressin or Anti-Diuretic Hormone)	Thirst, polyuria and nocturia – diabetes insipidus

## Investigations

Tests for hypopituitarism should be performed under the guidance of an endocrinologist. Please see ‘Who and When to Refer’ (factsheet no: 15) Please also see ‘Hypopituitarism’ Factsheet no: 6 for explanation of hormone investigations, treatment possibilities, management and watchpoints.

## Resources for patients

available from The Pituitary Foundation Helpline or

## Hypopituitarism

Hormone deficiency caused by the inadequate secretion of one or more of the hormones normally secreted by the pituitary, is known as hypopituitarism. It may commonly be caused by compression of the normal pituitary tissue by an enlarging pituitary tumour, by pituitary surgery, or radiotherapy. It should, however, be emphasised that documented combined hypopituitarism after head injury is uncommon, and if it does occur it may have been associated with very significant head injury.

our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline Other information and resource links available at [www.pituitary.org.uk](http://www.pituitary.org.uk)

**For GPs** Endotext.org ‘Your Endocrine Source’

[www.endotext.org](http://www.endotext.org) ([www.endotext.org/neuroendo/index.htm](http://www.endotext.org/neuroendo/index.htm)) The Pituitary Foundation Website [www.pituitary.org.uk](http://www.pituitary.org.uk) *Oxford Handbook of Endocrinology and Diabetes* 2nd Edition OUP (2010) JAH Wass & PM Stewart (Eds) *NICE guidance of growth hormone in adults* <http://www.nice.org.uk>

# Pituitary Surgery

**Tumours vary in size and activity. If surgery is recommended it may be for one of three reasons:**

- to remove hormone-producing tissue (typically in acromegaly or Cushing's disease)
- to reduce the volume of a tumour that is compressing the optic chiasm or other structures
- to reduce the volume of, or excise, non hormone-producing tissue that is likely to threaten surrounding structures in the future; for example, in a relatively young patient, in whom continued growth of the tumour is suspected or has been proven by sequential scans.

Transsphenoidal surgery is the most usual method but transcranial surgery is required in some tumours with major intracranial extension. The transsphenoidal approach allows the surgeon a clear, direct view of the tumour (through an operating microscope) and avoids a craniotomy (making a hole in the skull) with its associated slight risks of damage to the brain and epilepsy.

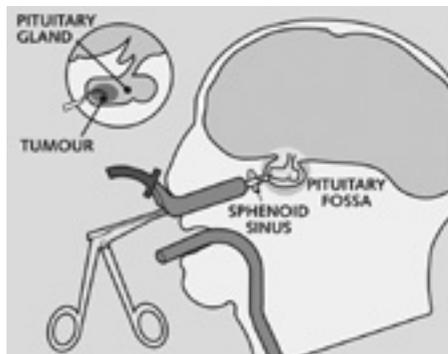
Endoscopic surgery is becoming the main approach in many centres. Fine tubes (endoscopes) are pushed through the back of the nose.

MRI and/or CT scans will give the surgeon information on the size and position of the tumour.

Successful outcome of this surgery is very dependent on the experience of the surgeon.

## Patient management prior to surgery

The Pituitary Foundation recommends that the initial point of referral is an endocrinologist who will arrange for essential preliminary tests (including blood tests, MRI and visual fields) to be performed before surgery.



## Follow-up

The patient will be referred to an endocrinologist for post-operative pituitary function assessment at about 5-8 weeks and back to the surgeon at about 12 weeks (for MRI and visual field assessment). In some cases additional replacement pituitary hormones will be needed. These appointments should, ideally, be combined to cause minimal inconvenience to the patient.

## Diabetes insipidus (factsheet 8)

If the patient suffers from new onset polyuria and nocturia after surgery, it is likely that they have developed a degree of diabetes insipidus (DI). This is unusual after transsphenoidal surgery, but in all cases is highly amenable to treatment. In most cases DI is temporary and disappears within a few months, but in 1-2% of patients, especially after removal of prolactinoma and Cushing's tumours, it may be permanent but remain treatable.

## Cerebrospinal fluid leak

It is possible to develop a CSF leak from the nose in the post-operative period (this is rare). This is associated with a risk of meningitis, and

is an inconvenience for the patient. Any flulike symptoms or discharge of water-like fluid from the nose should be treated with a view to this possibility. Patients need to be referred back to the surgeon for treatment urgently.

### **Sinusitis**

This is not uncommon after this operation, particularly for patients with acromegaly. Symptoms usually clear given time, but occasionally need further treatment or an ENT referral.

### **Stitches**

Depending on the surgical technique, stitches are inserted in the upper gum or in the nostril. They are usually soluble. The wound itself will be completely healed in 3 weeks. Complete absorption of stitches can take 3 months and loose ends may need to be removed/snipped away. There may be some numbness around the front teeth; this may occasionally be permanent.

### **Weight gain**

A major problem for many patients is weight gain. These patients are likely to need some encouragement to follow a suitable diet and take regular exercise. This may be particularly difficult after a period of illness and hospitalisation. However, including more exercise into their lifestyle should also improve the patient's general feeling of well-being.

The adrenal glands and cortisol are responsible for fat cell development. If cortisol levels are high due to having Cushing's then weight is usually gained around the trunk and in the face. If taking hydrocortisone as a replacement and the dose is too much, then weight can be gained.

It is essential that all pituitary hormones are at satisfactory levels, as even small deficiencies in testosterone, thyroid hormone and growth hormone can make it more difficult to lose weight. Regular monitoring with an endocrinologist is important to establish that hormone levels are satisfactory, but also an opportunity to discuss any weight gained.

### **Emotional impact**

Surgical treatment which involves the head has a strong emotional impact for some patients. Please see 'Psychological Issues' (factsheet 14).

### **Questions patients may ask**

#### **Why do I need an operation?**

A benign tumour of the pituitary gland may be compressing the optic nerve (which lies just above it) and affecting your sight or you may have a tumour that is producing excessive amounts of hormone which could cause you problems.

#### **Is it cancer?**

No, the vast majority of tumours are benign.

#### **Will my eyesight improve after the operation?**

Once the optic nerve is no longer compressed most patients will notice an improvement, this will carry on improving for 6 months after the operation. However, if your eyesight was very poor before the operation, it may not recover so much.

### How long will I be in hospital?

This varies between treatment centres, but may be 3-9 days.

### When will I be able to go back to work?

Depending on the job and circumstances, it is usually wise to plan for about 4-6 weeks off and reassess after that time. Some patients may take longer to recover.

### Have I inherited this, will my children get it?

In all but very exceptional circumstances there is no hereditary link.

### Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

### Patient Information Booklet

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# Radiotherapy

## Indications for radiotherapy (Rt) use in pituitary adenoma:

### Following surgical resection

- If tumour persists outside pituitary fossa on post-op scan.
- For functioning adenoma: if hormone levels do not fall to normal post-op and/or medical therapy is not subsequently controlling hormone secretion.
- Consider for patients with recurrent disease (+/- following second operation - especially if chiasm is compressed).
- Patients with small volume functioning adenoma away from the optic chiasm or recurrence following conventional radiotherapy can be considered for single fraction radiotherapy (also called radio surgery).

### For inoperable disease

- If patient is fit enough to receive RT (e.g., when tumour is pressing on chiasm).

Radiotherapy was once regarded as a routine treatment for pituitary adenomas, especially those at higher risk of relapse (tumour >1cm in size).

Many factors have led to a reduction in the routine use of radiotherapy following surgery over the past 20 years:

- Patients with functioning adenomas can frequently be treated with medical therapy if hormone levels remain elevated post op, and some centres now reserve RT for those failing medical therapy e.g., in Acromegaly somatostatin analogue therapy may be used first line and RT reserved for cases where growth hormone fails to reach safe levels on treatment.
- Changes in tumour size can now be monitored with sequential MR imaging.
- Half of patients with normal pituitary function pre RT will develop

hypopituitarism within 20 years of radiotherapy, necessitating regular endocrine follow up.



*A clear plastic mask made specially for each patient's head, holds the patient's head still during the brief treatment. The targeting marks are lined up against the cross-beams of a laser set into the walls of the radiotherapy room. The radiotherapy treatment is delivered to the target area from three directions.*

## Benefits of radiotherapy

- Controls disease in 94% of cases at 10 years and 88% at 20 years.
- Reduces local recurrence from 60% with surgery alone to 5% (surgery + RT).
- Reduces hormone secretion in 90% cases of acromegaly, median 4 ½ years to normalisation of hormone levels.

- 55% of patients with impaired visual fields or acuity notice improvement following surgery and RT.

*Note:* because of the possibility of loss of normal pituitary function several years after RT, it is essential that all patients have regular follow-ups with an endocrinologist.

## Radiotherapy delivery

### Planning

In order to reduce the amount of normal brain irradiated, the patient's head should be firmly immobilised on to the radiotherapy treatment couch, thus reducing movement. This allows the radiotherapist to minimise the margins for movement added to the tumour target volume. Three techniques can be employed to immobilise the patient:

- A mask can be made in one session using a thermoplastic mesh drawn down over the patient's face, which is then attached to a firm baseboard.
- Or a perspex mask is moulded from a plaster of Paris cast of the patient's face. This requires two hospital visits. A hole in the Perspex mask is made for mouth and nostrils. Patients with a beard will be asked to shave to give a firm fit of the mask. Accuracy for both mask systems is 5-10mm.
- A stereotactic ring frame can be fitted using skull vault screws (for a single fraction treatment-radiosurgery) or using patient specific dental and occipital impressions to allow repeat usage for multiple treatments. This ring is then fixed to the treatment couch with 1-3mm accuracy.

A CT scan is performed with the patient in the immobilisation device and the radiotherapist and physicist define a treatment volume and

patient specific customised plan in order to treat this volume. Usually three or four treatment fields are used on a daily basis. Patient specific shielding blocks or blocking leaflets in the machine treatment head are used to reduce the volume of normal tissue irradiated. The planning process can take 1 – 3 weeks.

### Treatment

Radiotherapy is usually given in small doses, every working day, for 5-6 weeks giving a typical total dose of 45Gy in 25 fractions dose of 45 – 50 Gy. Each treatment, which is painless, lasts for 10 – 15 minutes – the actual radiotherapy about 2 minutes. Treatments are delivered using a Linear Accelerator (LINAC) machine. Lining up markers on the mask with laser beams embedded in the walls of the treatment room confirms the absolute position of the patient relative to the treatment machine, and thus safe delivery of treatment. Using the stereotactic immobilisation ring ensures slightly higher precision than the mask systems. But is more time consuming to deliver and requires specific equipment and expertise, which is not available in all departments and its benefit is still being evaluated.

Single fraction radiotherapy (radiosurgery) is increasingly used for pituitary adenomas in the specific indications outlined above. This is delivered using either a LINAC or Gamma Knife® (an array of cobalt sources around the patient's head). A dose of 100 Gy to the tumour centre is delivered in a single treatment. A steep dose gradient beyond the tumour edge aims to reduce the dose to surrounding critical structures.

Stereotactic radiosurgery appears safe and effective with numerous studies confirming

this over the last few years. Patient selection is critical to success and depends in great part on the anatomy of the tumour to be treated and previous treatment given. The main determinant is the proximity to the optic apparatus as this tolerates radiation less well.

## **Adverse effects of radiotherapy**

### **Transient side effects:**

- Skin erythema, irritation and transient hair loss occurs at the sites of beam entry and exit. The hair almost always re-grows within a few months.
- Headache – treat symptomatically, avoid steroids if possible.
- Tiredness, which can last for a few months.

### **Long term, permanent side effects:**

- Hypopituitarism. In those patients with normal function before RT, 30% of patients by 10 years, 50% by 19 years develop hypopituitarism. They will need endocrine follow up with annual pituitary function tests.
- Optic nerve damage. <1% of cases show some visual deterioration.
- 2nd tumour. 1.9% at 20 years. However, techniques for RT have improved in the last 20yrs.
- CVA. Relative risk of 4 compared with normal population.

## **Questions patients may ask**

### **How long will it take?**

The treatment itself only takes about 10-15 minutes, but radiotherapy has to be given in small doses over a long period (usually 5 weeks), so you will need to attend the radiotherapy clinic each working day during the treatment period.

### **Will I lose my hair?**

Generally, no. A small amount of hair is lost at the sites of radiation entry and exit (i.e., the temples, above the forehead and the nape of the neck typically in front of each ear), but this almost always re-grows within a few months.

### **Will it hurt?**

Treatment is much the same as having an X-ray - it is quite painless.

### **What are the possible side effects?**

Tiredness starts during or after the end of the treatment schedule and can last for several weeks. Some patients occasionally experience nausea, mild headache or some reddening of the skin, but this is unusual. Rarer longer-term side effects will be discussed in more detail by the radiotherapist, however impaired pituitary function is seen in half of patients with functioning pituitaries before RT. This can occur after years. It is important the patient attends regular endocrine follow up for many years.

### Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

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# Hormone Replacement Therapy

**Patients may need hormone replacement therapy for a number of reasons. Pituitary tumours are the most common cause of hypopituitarism. The tumour may have compressed or damaged the pituitary tissue and patients found to have hypopituitarism should be referred to a specialist endocrinologist.**

Surgery to remove the tumour may cause temporary or permanent damage and radiotherapy may (over a period of several years) also irreversibly affect pituitary function. After treatment, long-term monitoring of pituitary function is required, which should be carried out by a specialist endocrinologist. The time interval between endocrine assessments will vary with the patient and the treatment received, but will probably be at intervals of 6-12 months immediately post-treatment, increasing to annual or biennial in the longer term.

The correct route of referral is through an endocrinologist rather than neurosurgeon or others. Please see 'Who and When to Refer' (factsheet 15).

## **GH**

GH replacement is required in children with low GH levels and slow growth rate. GH also has important effects in adult tissues such as bone, fat and muscle, and lack of GH may increase mortality rates from heart disease. Until recently, the lack of widely available supplies of GH has restricted this therapy to children. However human recombinant growth hormone is now available, which is free from risk of Creutzfeldt-Jacob disease (CJD), and has been shown to be clinically effective. Adults who suffer from biochemically documented GH

deficiency, and who exhibit excessive tiredness, muscle weakness, weight gain, anxiety and depression, may benefit from GH therapy. GH is administered by daily subcutaneous injection. The dose for adults is considerably lower than that required for children (women require more GH than men). The reported side effect of GH therapy is fluid retention but this is rarely a problem with carefully titrated therapy in current practice. The evidence suggests that GH therapy is clinically effective; it may also improve bone mineral density in adults with GH deficiency. Replacement therapy with GH has been approved by NICE in patients selected on the basis of a quality of life deficit.

## **FSH & LH**

FSH and LH secreted by the pituitary gland stimulate the production of oestrogen, progesterone and testosterone. If FSH and LH are no longer produced, because of pituitary damage, sex hormone replacement with oestrogen and progesterone or testosterone is usual, unless fertility is required. In the longer term, sex hormone replacement reduces the risk of osteoporosis and cardiovascular disease in both men and women. Testosterone can be given as a gel, intramuscularly, by implant, buccal SR and patches. Oestrogen/progesterone can be given as skin patches or as pills.

For fertility, treatment with gonadotrophins is required at a specialist centre which provides effective monitoring. The human recombinant gonadotrophins available are free from possible risk of new variant CJD. The objective is a singleton pregnancy and a multiple pregnancy should be considered as a failure of treatment. The specialist centre should have high-resolution ultrasonography available.

HRT is safe for women of pre-menopausal age, in whom the benefits of maintaining bone strength outweigh the deficits, and breast cancer has not been shown to be a problem.

## ACTH

ACTH deficiency is treated by prescribing hydrocortisone or alternatively prednisolone (not recommended for children). The average dose requirement of hydrocortisone is 20 mg split over the day (e.g. 10/5/5mg a day) and most patients feel better if they have 3 doses – on waking, midday and early evening (5 – 6pm). In normal health, the lowest levels of cortisol are between 6pm and 6am. Patients will need to learn the situations in which a higher dose of steroid should be taken. Examples are:

- Infections
- Dental treatment
- Hospital treatment e.g., operations

Supplies of tablets and a steroid card should always be carried and wearing a Medic Alert or similar bracelet is important in case of accident. Learning the skill of self-injection of hydrocortisone (or encouraging another member of the family to do so) can be potentially life saving, particularly if patients wish to travel to areas where medical care is not readily available. Full instruction on intramuscular injection technique should be provided by hospital clinic or general practice. Urgent injection of hydrocortisone is indicated in emergency situations especially when intake of tablets is compromised e.g., by vomiting.

## TSH

In the absence of the normal production of TSH by the pituitary gland, patients require Thyroxine. Thyroxine has a relatively long half

life (several days), so that if a tablet is forgotten no action is required.

## AVP (ADH)

Diabetes insipidus may be a transient effect of surgery or a long-term result of damage to the hypothalamus or posterior pituitary. AVP (ADH) is replaced by giving desmopressin (referred to as DDAVP) provided as tablets, nasal spray or melts. Patients should be warned not to drink too much and a sensible precaution may be to leave out one treatment each week to prevent water overload. DI may disappear spontaneously. The only way to check this is to stop the treatment.

## Prolactin (PRL)

No replacement formulation is available or necessary under normal circumstances. The absence of prolactin may lead to an inability to breast-feed.

### Questions patients may ask

#### Will I have to take tablets in the long term?

If, as often happens, the pituitary tumour or its treatment have caused hypopituitarism, this does not usually recover and the patient will need long term replacement therapy.

#### Will I need regular check-ups?

Yes, but as pituitary tumours are usually well controlled and grow very slowly, if at all, outpatient appointments are usually made 12 months to 2 years apart.

**Will I need regular scans?**

Perhaps, but again, these too are carried out years apart.

**Have I inherited this, will my children get it?**

There is ongoing research into familial incidence e.g. in Gigantism, but the majority of cases are sporadic.

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# Male Hypogonadism

**Male hypogonadism is a state of testosterone deficiency which may result from either testicular or pituitary/ hypothalamic diseases. Males can be affected at any age and present with clinical features which differ according to the timing of disease onset in relation to puberty.**

## Presenting symptoms

In pre-pubertal onset of testosterone deficiency, sexual development will be absent or incomplete e.g., lack of genital enlargement, lack of pubic/ axillary hair and beard growth, lack of muscle development, lack of sexual interest and failure of the voice to break. Spermatogenesis will not be initiated and infertility is the general rule.

In post-pubertal onset of testosterone deficiency, the established secondary sexual characteristics are poorly maintained. Symptoms include tiredness, reduced libido and sexual functioning, reduced body and facial hair and muscle mass, infertility and a lack of general well-being including depression. Flushing and sweating, similar to female menopausal symptoms, may occur.

Common to both presentations, testosterone deficiency is associated with reduced bone mass, increased risks for osteoporotic fractures and mild anaemia.

## Classification of hypogonadism

**Primary hypogonadism:** When androgen deficiency is the result of testicular diseases, the condition is described as primary hypogonadism or hypergonadotrophic hypogonadism. The latter is so-called because of high LH and FSH levels from the pituitary which makes a vain attempt to stimulate the failing or absent gonads to secrete more testosterone.

## Causes of primary hypogonadism

- Klinefelter's syndrome (47 XXY)
- Bilateral cryptorchidism (un-descended testes)
- Bilateral anorchia (no testicular tissue present)
- Testicular torsion and orchitis
- Testicular tumour
- Orchiectomy
- Chemotherapy or radiotherapy (affects fertility more than testosterone production)

**Secondary hypogonadism:** When androgen deficiency is the result of diseases of the pituitary/ hypothalamus, the condition is described as secondary hypogonadism or hypogonadotrophic hypogonadism due to the low levels of LH and FSH. When there is no other concurrent pituitary hormone deficit, the condition is usually called isolated hypogonadotrophic hypogonadism. This may be due to a congenital deficiency in hypothalamic gonadotrophin releasing hormone (GnRH)

## Causes of secondary hypogonadism:

- Pituitary tumour (factsheet 3)
- Suprasellar tumour i.e., craniopharyngioma (factsheet 8)
- Isolated hypogonadotrophic hypogonadism
- Kallmann's syndrome (isolated hypogonadotrophic hypogonadism associated with an absent or impaired sense of smell)
- Iron overload (haemochromatosis or frequent blood transfusions)
- Systemic diseases – acute and chronic
- Glucocorticoid treatment
- AIDS
- Gross obesity

Overall, pituitary tumours are the commonest causes of hypogonadism, followed by Klinefelter's syndrome.

## Clinical examination

Physical examination is important to confirm the clinical diagnosis of hypogonadism and to elucidate the underlying cause. Important points include:

- assess pubertal progress and stature in late adolescent patients
- body, facial and pubic hair growth
- body habitus (i.e., eunuchoidal limb proportions, muscle bulk, feminine fat distribution, gynaecomastia)
- testicular examination (assess size, position, consistency i.e., very small and firm in Klinefelter's)
- visual field assessment which may highlight a pituitary lesion (classically a bitemporal hemianopia resulting from chiasmal compression)
- sense of smell (absent in Kallmann's syndrome)

## Investigations

**To confirm testosterone concentration is subnormal** a single 9am measurement of total testosterone usually suffices. In men over 50, particularly overweight patients, SHBG-corrected free testosterone is important.

**To differentiate primary from secondary hypogonadism** a single measurement of LH and FSH will support the biochemical diagnosis of either primary or secondary hypogonadism.

**To identify the underlying cause and assess severity of testosterone deficiency**

- prolactin, 9am serum cortisol and thyroid function as a baseline assessment of pituitary function
- MRI scanning of the pituitary should be arranged if hypogonadotrophic

hypogonadism is confirmed

- karyotyping (Klinefelter's syndrome - 47XXY (80% of cases), mosaics, 48XXXY etc.)
- haemoglobin
- bone mineral density
- ultrasound of the testes

## Treatment

Any potentially reversible underlying cause should be treated prior to commencing replacement therapy.

Referral to a specialist Endocrinology centre for investigation and subsequent management is recommended. Please see 'Who and When to Refer' (factsheet 15).

Androgen replacement can be administered in the following modalities

- Oral testosterone undecanoate (Restandol) can be given. Disadvantages include unreliable absorption requiring a twice or three times daily dosage and therefore inconsistent testosterone replacement. This is not a reliable form of replacement for adult men.
- Testosterone esters (Sustanon 100 and 250) are administered as a deep intramuscular injection usually every 2-3 weeks. They provide reliable replacement with a good safety record for over 50 years. The main side effect is limited to relatively short duration, localised pain at the injection site. Nebido is the main injectable form of testosterone used; this formulation requires only 3-monthly injections in to the muscles of buttocks, and provides constant testosterone levels for up to 14 weeks. Testosterone levels begin to rise within 24 hours of the injection.
- Testosterone gel is frequently used for replacement therapy. Average doses are

50mg per day, but this needs titration by an endocrinologist initially. Single sachet and multiple dose preparations are available. It is applied once daily to the skin surface over the shoulders, upper arms and abdomen will deliver stable physiological blood levels of testosterone.

- A buccal testosterone preparation called Striant SR. This is a twice daily mucoadhesive tablet which adheres to the gum and is placed above the incisors. Physiological levels of testosterone are achieved in most patients. Side effects are infrequent and are usually local, including gum irritation, gingivitis and a bitter taste.

Infertility resulting from secondary hypogonadism is usually amenable to treatment. In this situation there is dormant testicular tissue which should respond to gonadotrophin treatment with human chorionic gonadotrophin (hCG) and FSH self-administered subcutaneously twice to thrice weekly over 6-12 months. Primary hypogonadism including Klinefelter's syndrome are synonymous with irreversible and permanent infertility.

The psychological impact of infertility can be great and counselling may be required. See 'Psychological Issues' (factsheet 14) for basic information.

### **Initiation and monitoring treatment: assessing response**

Initial treatment will depend upon the age of the patient and the underlying cause of the hypogonadism. Younger patients are often androgen-naïve and will benefit from lower starting doses and gradual increase over 2-3 years to the full adult replacement dose of testosterone. This is particularly desirable for maximising

linear growth potential. Older men should ideally be treated with shorter acting preparations in case of aggravating undetected androgen-responsive diseases e.g., prostate cancer. Adult men may have a preference for longer acting preparations such as testosterone implants.

The aim should be to maintain plasma testosterone within the physiological range. It is good practice to ascertain that this has been achieved in the first 3-6 months of initiating treatment by dose titration. Thereafter, an annual pre-dosing check of testosterone should be more than sufficient.

The clinical response should be apparent within the first few weeks and best judged by the patient's own observations. Physical changes such as genital, hair and muscle growth are generally observed within 3-6 months. Bone mineral density changes may be used as a more long-term parameter of responses and compliance to testosterone.

In older patients, monitoring the haematocrit, prostate size (digital rectal examination) and function (PSA) constitute sensible clinical practice.

Counselling in accepting the invariably life-long testosterone treatment, subfertility or infertility is important.

Side effects may include gynaecomastia, exacerbation of prostatic disease, fluid retention in those with pre-existing cardiac or renal disease, exacerbation of pre-existing liver dysfunction, obstructive sleep apnoea, polycythaemia and exacerbation of premorbid behavioural problems.

### **Watchpoints**

#### **Urgent - refer to hospital**

- back pain or urinary obstruction – may indicate prostate cancer and metastatic disease

- testicular mass
- deterioration of vision (suggesting secondary hypogonadism)

## Questions patients may ask

### Will my sex life improve?

Testosterone treatment will increase your sex drive. Sexual functioning is more complicated and is dependent on several factors in addition to testosterone. Testosterone will not help erectile impotence with normal sex drive

### Will I be able to have children?

If the underlying cause is due to a testicular problem then invariably the patient will be infertile. With secondary causes hCG/FSH treatment is successful in up to 70% of cases.

### Will it make me more aggressive?

Not in an antisocial sense but it will make you have more self-confidence and be more assertive.

### Have I inherited this, will my children get it?

In all but very exceptional circumstances there is no hereditary link.

## Resources for patients

available from The Pituitary Foundation Helpline or our website [www.pituitary.org.uk](http://www.pituitary.org.uk) or our Endocrine Nurse Helpline

## Patient Information Booklet

- *Male Hormones & Infertility*

Klinefelter's Syndrome Association  
13 York Rise, Orpington, Kent, BR6 8PR

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# Psychological Issues

**Pituitary disorders require life-long treatment. As with other chronic conditions, many problems may arise which often require the difficult task of disentangling the physiological, social and psychological aspects.**

In considering the psychological impact of pituitary disease, there are a number of common problems and patients will need sympathetic help in dealing with them.

- The emotional impact of neurosurgery
- The need to adapt to altered body image
- The feeling of 'cure'
- Social interactions and the effects of chronic illness on family

## **Emotional impact of neurosurgery**

Surgical treatment for pituitary disease may be perceived as threatening and often produces a slower than hoped for improvement in the condition. Some patients may experience severe symptoms similar to post traumatic stress disorder after treatment. Patients will be concerned that some of the tumour remains in situ and may regrow. A full recovery undoubtedly takes a considerable time and building up unrealistic expectations before treatment impedes rather than helps recovery.

## **The need to adapt to altered body image**

*Acromegaly* can have a profound effect on physical appearance causing Body Dysmorphic Disorder (BDD). In acromegalics there are facial changes and enlargement of hands and feet, which, although slow to develop, are not always reversible. Some patients regard themselves as 'freaks', and learning to cope with this may take years rather than months. Intervention programmes exist to help with

these problems, contact Changing Faces (factsheet 16 - Resources).

*Cushing's* patients usually suffer from truncal obesity. Increased glucocorticoids in Cushing's affect weight and body fat distribution. They are also associated with muscle weakness, reduced capacity for physical activity and decreased glucose tolerance. GH therapy may help some patients (factsheet 12).

Altered body image is particularly stressful for women, and can be a major cause of depression when it affects relationships.

## **Feeling 'cured'**

Treatment, even if effective in regulating hormonal levels to what is regarded as normal, may not be followed by a 'feeling of cure'. Some patients who have pituitary insufficiency may still feel that they have diminished overall capacity even when they are receiving what is regarded as adequate hormone replacement therapy.

## **Social interactions and the effects of chronic illness on Family**

Hormonal imbalance has many consequences. The effects of depression, tiredness, snoring and reduced or absent sexual function are some of the aspects of pituitary disease which may lead to social or family problems.

Restoring hormonal balance should remove or improve many of these symptoms.

## **Resources for patients**

available from The Pituitary Foundation  
Helpline or our website

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Helpline

## **Patient Information Booklet**

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of booklets including *Psychological Impact of  
Diagnosis & Treatment* and *Relationships &  
Communication with Yourself and with Others*

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Psychotherapy and Psychosomatics 67

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Press, Totowa, New Jersey (This contains  
a "patient's eye view" chapter written by a  
patient.)

# Referrals: When should you refer and to whom

## Diagnosis of pituitary disease is not straightforward.

There is a wide range of symptoms, reflecting the various conditions caused by a pituitary tumour. Some are specific and obvious but many are vague and may not point to the pituitary.

Most GPs see only one or two cases in their whole careers, which compounds the problem.

The following tables list symptoms associated with various tumour types: more details are included in the specific sheets.

Whilst you would not want to send every patient with a headache to an endocrinologist, those with high circulating thyroxine and high TSH should be referred. To this end a list of basic tests is also included.

For acromegaly & prolactinoma especially, there should be a low threshold for referral for any patient with any suspicion of these conditions as the greatest challenge in their diagnosis is thinking of the disease. Once suspected, biochemical confirmation or exclusion of the disease is usually straightforward.

## Who should you refer to?

Ideally to a specialist endocrinologist or a local physician with a special interest in endocrinology.

It is better to see an endocrinologist first rather than a surgeon as the surgeon will need to refer the patient to an endocrinologist in any case. In some cases surgery is not recommended.

The endocrinologist can arrange all the specialist diagnostic tests to be completed prior to surgery enabling accurate monitoring of treatment to take place.

## Life-long relationship

Life-long specialist monitoring will be required after initial treatment to ensure the appropriate and optimum balance of hormones is achieved. Many patients will be on life-long hormone replacement. In most cases a shared care protocol is established between the specialist and the patient's GP.

## Presenting symptoms

These are the main symptoms; see individual sheets for additional information.

Main symptoms common to various tumour types	Associated with:
Visual disturbance	Non-functioning (NF), acromegaly, hyperprolactinaemia, craniopharyngioma
Oligomenorrhoea or amenorrhoea	NF, hyperprolactinaemia, hypogonadism
Reduced libido in men & women, and reduced potency in men	NF, hyperprolactinaemia hypogonadism
Headache	NF, acromegaly, hyperprolactinaemia, craniopharyngioma
Tiredness and lack of energy	NF, acromegaly, hypopituitarism (especially loss of GH and/or ACTH).

Main symptoms specific to one or two types of tumour	Associated with:
Coarsening of facial features	Acromegaly
Enlarged hands and feet, growth of the jaw	Acromegaly
Carpal tunnel syndrome	Acromegaly
Excessive sweating and oily skin	Acromegaly
Sleep apnoea	Acromegaly
Moon face - particularly filling in of the temporal fossa	Cushing's
Weight gain - central obesity	Cushing's
Muscle wasting and proximal myopathy (patients have difficulty standing from a seated position without use of arms)	Cushing's
Thin skin - tendency to bruise	Cushing's
Hirsutism (caused by androgen excess)	Cushing's
Violaceous striae	Cushing's
Hypertension	Acromegaly, Cushing's
Diabetes	Acromegaly, Cushing's
Osteoporosis and fractures	Cushing's
Psychiatric disturbance (often characterised by amplification of previous personality traits)	Cushing's
Galactorrhoea	Hyperprolactinaemia
Growth retardation in children.	Any pituitary tumour causing hypopituitarism and Growth Hormone Deficiency (GHD), craniopharyngioma
In adults: excessive tiredness, muscle weakness, lack of drive, impaired quality of life	Hypopituitarism - GH deficiency
Tired, difficulty recovering from minor illness	Hypopituitarism - (ACTH, cortisol deficiency), craniopharyngioma
Weight gain, decreased energy, sensitivity to cold, constipation, dry skin	Hypopituitarism - TSH deficiency.
Pale appearance, weight loss, low blood pressure, dizziness, tiredness, 'collapse' during intercurrent illness	Hypopituitarism – ACTH deficiency

Main symptoms specific to one or two types of tumour	Associated with:
Thirst, polydipsia, polyuria and nocturia	Hypopituitarism - AVP deficiency - diabetes insipidus, craniopharyngioma
Delayed or arrested puberty, and very occasionally precocious puberty.	Craniopharyngioma
Dyspareunia and hot flushes in women	Hypogonadism
Absence of or incomplete sexual development: <ul style="list-style-type: none"> <li>- lack of genital enlargement</li> <li>- lack of pubic/ axillary hair and beard growth</li> <li>- lack of muscle development</li> <li>- lack of sexual interest</li> <li>- failure of the voice to break.</li> <li>- spermatogenesis will not be initiated and infertility is the general rule.</li> </ul>	Pre-pubertal onset of testosterone deficiency - male hypogonadism
Poorly maintained established secondary sexual characteristics: - tiredness - reduced libido and sexual functioning - reduced body and facial hair and muscle mass, infertility	Post-pubertal onset of testosterone deficiency – male hypogonadism

# Resources: Information and Support

## For patients

Publications produced by The Pituitary Foundation, available both as printed matter and via our website [www.pituitary.org.uk](http://www.pituitary.org.uk)

### Patient information booklets

- *The Pituitary Gland; Its conditions and hormones explained*
- *Acromegaly*
- *Cushing's*
- *Diabetes Insipidus*
- *Prolactinoma*
- *Male Hormones & Infertility Issues*
- *Pituitary Surgery & Radiotherapy*
- *Psychological Issues in Pituitary Disease (Series)*
- *Employment*
- *Weight Control & Nutrition*
- *Hydrocortisone Advice for Adults*
- *Hydrocortisone Advice for Parents*
- *Pituitary Patients Handbook*

### Proceedings of several Pituitary Foundation conferences

These proceedings include many aspects of pituitary disease such as articles on growth hormone, new aspects of surgery, visual problems and reports of workshops on acromegaly, Cushing's, diabetes insipidus, hypopituitarism, prolactinoma, psychological problems, self image and patient-consultant communication.

### **Pituitary Life: The Pituitary Foundation's magazine**

These contain useful articles on all aspects of pituitary disease written by both medical specialists and patients. Examples include information on taking steroids, experiences of testosterone therapy, etc.

## For GPs

Endotext.org 'Your Endocrine Source'  
[www.endotext.org](http://www.endotext.org)  
 (www.endotext.org/neuroendo/index.htm)

The Pituitary Foundation Website  
[www.pituitary.org.uk](http://www.pituitary.org.uk)

*Endocrinology* (1997) Levy A & Lightman SL  
 New York: Oxford University Press  
*Treating Acromegaly*. (1994) Wass JAH (Ed) Bristol, UK: Society for Endocrinology

*The Epidemiology, Pathogenesis and Management of Pituitary Tumours* (1998) Webb SM (Ed)  
 Bristol, UK: BioScientifica

*Emotional aspects of pituitary disease* (1998)  
 Weitzner MA, Sonono N & Knutzen R (Eds).  
 Psychotherapy and Psychosomatics 67

*Endocrinology* (1997) Levy A & Lightman SL.  
 New York: Oxford University Press  
*Clinical Endocrinology* (1998) Grossman AB Oxford: Blackwell Science

*Treating Acromegaly* (1994) Wass JAH (Ed)  
 Bristol, UK: Society for Endocrinology

# Resources: Information and Support

This information is correct at time of publication

Name of organisation	Website	Phone number
<b>Addison's Disease Self Help Group</b>	<a href="http://addisons.org.uk">addisons.org.uk</a>	
<b>British Society for Paediatric Endocrinology and Diabetes</b>	<a href="http://bsped.org.uk">bsped.org.uk</a>	
<b>British Thyroid Foundation</b>	<a href="http://btf-thyroid.org">btf-thyroid.org</a>	0870 770 7933
<b>Diabetes UK</b>	<a href="http://diabetes.org.uk">diabetes.org.uk</a>	0345 123 2399
<b>Congenital Adrenal Hyperplasia</b>	<a href="http://cahisus.co.uk">cahisus.co.uk</a>	
<b>Carers UK</b>	<a href="http://carersuk.org">carersuk.org</a>	0808 808 7777
<b>Changing Faces</b>	<a href="http://changingfaces.org.uk">changingfaces.org.uk</a>	0300 012 0275
<b>Child Growth Foundation</b>	<a href="http://childgrowthfoundation.org">childgrowthfoundation.org</a>	0208 995 0257
<b>Contact a Family</b>	<a href="http://cafamily.org.uk">cafamily.org.uk</a>	0808 808 3555
<b>Headway</b>	<a href="http://headway.org.uk">headway.org.uk</a>	0808 800 2244
<b>Sexual Advice Association</b>	<a href="http://sda.uk.net">sda.uk.net</a>	
<b>Kallmann's Syndrome</b>	<a href="http://hypohh.net">hypohh.net</a>	
<b>Medic Alert</b>	<a href="http://medicalert.org.uk">medicalert.org.uk</a>	01908 951045
<b>Multiple Endocrine Neoplasia</b>	<a href="http://amend.org.uk">amend.org.uk</a>	
<b>National Osteoporosis Society</b>	<a href="http://nos.org.uk">nos.org.uk</a>	01761 471 771
<b>Premature Menopause</b>	<a href="http://daisynetwork.org.uk">daisynetwork.org.uk</a>	
<b>Pre-menstrual Syndrome</b>	<a href="http://pms.org.uk">pms.org.uk</a>	0844 815 7311
<b>Polycystic Ovary disease</b>	<a href="http://verity-pcos.org.uk">verity-pcos.org.uk</a>	
<b>RNIB</b>	<a href="http://rnib.org.uk">rnib.org.uk</a>	0303 123 9999
<b>Tall Persons Club</b>	<a href="http://tallclub.net">tallclub.net</a>	07000 825 512
<b>Turners Syndrome Support Society</b>	<a href="http://tss.org.uk">tss.org.uk</a>	0300 111 7520
<b>Other useful contacts site</b>	<a href="http://self-help.org.uk">self-help.org.uk</a>	



**The Pituitary Foundation**

**86-88 Colston Street,**

**Bristol, BS1 5BB**

**[www.pituitary.org.uk](http://www.pituitary.org.uk)**

Helpline: 0117 370 1320

Administration Line: 0117 370 1333

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86 Colston Street

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*Working to support pituitary patients, their carers & families*