

Pituitary Gland Disorders — Hypothalamic–Pituitary–Thyroid Axis (HPT- Axis), Pituitary Sellar Masses, Pituitary Apoplexy and Sheehan’s Syndrome

[See online here](#)

The pituitary gland/hypophysis is in the Sella turcica/pituitary fossa which is a part of the sphenoid bone and forms the cranial fossa. The gland is divided into the posterior and the anterior pituitary. The most common cause of these disorders is pituitary tumors which are mostly benign (Adenomas) in nature. Diagnosis in most cases is made with MRI, CT imaging and laboratory work-ups. Treatment approaches for pituitary gland disorders involve various methods including medication and surgery. Prognosis depends on the diagnosis.



Introduction of Pituitary Gland Disorders

The pituitary gland/hypophysis is in the Sella turcica/pituitary fossa which is a part of the sphenoid bone and forms the cranial fossa. The gland is divided into:

- **Anterior pituitary or adenohypophysis** which has its origin from the ranthkes pouch during embryological development. It begins as a dorsal evagination of the stomodeum and comprises of endocrine cells that secrete hormones that exert functions on other body organs.
- **The posterior pituitary or neurohypophysis** is mainly made up from the infundibulum which is a nervous extension of the hypothalamus. It mainly secretes hormones from the hypothalamus such as oxytocin and vasopressin.

The anterior pituitary

The anterior pituitary is a **master gland that secretes hormones to control other organs** in the body in the maintenance of homeostasis. These hormones are secreted based on the various cell types that exist in the gland, and based on the part of the pituitary gland involved:

1. **Thyrotropes** secrete a thyroid-stimulating hormone that stimulates the thyroid gland to produce and release the thyroid hormone thyroxine.
2. **Corticotropes** produce adrenocorticotropic hormone which acts on the adrenal glands.
3. **Gonadotrophs** release follicle-stimulating hormone and luteinizing hormone which act on the reproductive system.
4. **Somatotrophes** release growth hormone.
5. **Lactotrophs** release prolactin hormone.

The posterior pituitary

The posterior pituitary, on the other hand, **releases hormones that are from the hypothalamus** via the neurological connection between the two parts. These hormones include oxytocin and vasopressin.

The intermediate part of the pituitary gland is not fully functional in humans, but it is thought to be responsible for melanin synthesis and the maintenance of skin color.

Structures in connection with the pituitary gland

Structures in close association with the pituitary gland are affected by its enlargement and thus form **part of the pathological presentation** of these diseases when affected. These relations include:

- The hypothalamus.
- The optic chiasma and other cranial nerves that control extraocular eye movement.
- The cavernous sinus system and vessels that supply the midbrain.

The hypothalamus-pituitary-thyroid axis (HPT axis)

It is also known as the **thyrotrophic feedback mechanism** and it **controls the body's metabolism by regulating the release of thyroid hormones** from the thyroid gland.

In a normal status, the hypothalamus releases thyrotropin-release hormone that stimulates the pituitary gland to release thyroid stimulating hormone.

The thyroid stimulating hormone **induces the thyroid hormone biosynthesis at all stages and its release into circulation as triiodothyronine and tetraiodothyronine (T3/T4)**. The level of circulating thyroid hormones regulate the amount of thyrotropin release hormone secreted from the hypothalamus via a negative feedback mechanism in that, when the level of T3 and T4 is low in circulation, there is an increase release of thyrotropin release hormone and TSH that induces an increase in thyroid hormone synthesis and vice versa.

Hyperthyroidism

In hyperthyroidism, the hypothalamus is inhibited and the levels of thyrotropin and thyroid stimulating hormone fall. The axis is also influenced by a variety of other local

and neurohumoral factors.

Pituitary Gland Disorders

Disorders of the pituitary gland arise in:

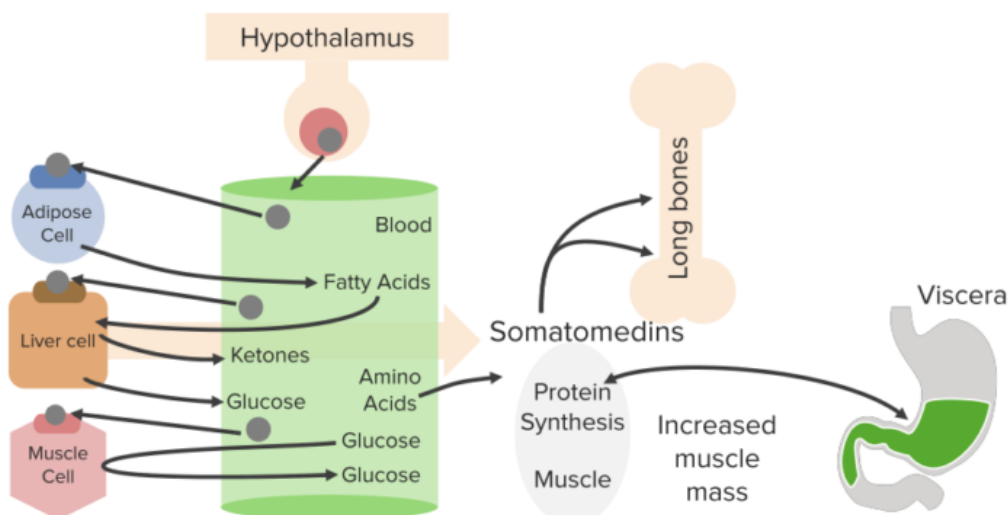
- **Hypersecretion** of pituitary gland hormones.
- **Hyposecretion** of the pituitary gland hormones.
- Pituitary gland **enlargement** and resulting mass effects on nearby organs.
- **Ischemic injury** of the gland leading to hyposecretion.
- **Surgery and radiotherapy** induce hyposecretion.
- **Genetic mutations** of the genes leading to development of the gland.
- **Idiopathic causes.**

The most common cause of these disorders is **pituitary tumors** which are **mostly benign** (Adenomas) in nature.

Certain syndromes arise from the deranged hormone state and its effects. These states include:

- **Excessive growth hormone** leads to gigantism and acromegaly in adults, while **reduced secretion of growth hormone** leads to dwarfism in children and premature ageing in adults.
- **Secretion of excessive ACTH** leads to Cushing's disease, while reduced secretion leads to Addison's disease.
- **Low levels of thyroid stimulating hormone** lead to cretinism, while **hypersecretion of thyroid stimulating hormone** leads to goiter and Graves' disease.
- **Hypersecretion of prolactin** causes amenorrhea, galactorrhea, and sub-fertility states.
- **Hypersecretion of FSH and LH** leads to disturbed menstrual and reproductive cycles, while **hyposecretion** causes amenorrhea and impotence.
- **Excessive ADH** from the posterior pituitary leads to a syndrome of inappropriate ADH secretion (**SIADH**), while **reduced secretion** of the hormone leads to diabetes insipidus.

Target Organs: The Effects of Growth Hormone



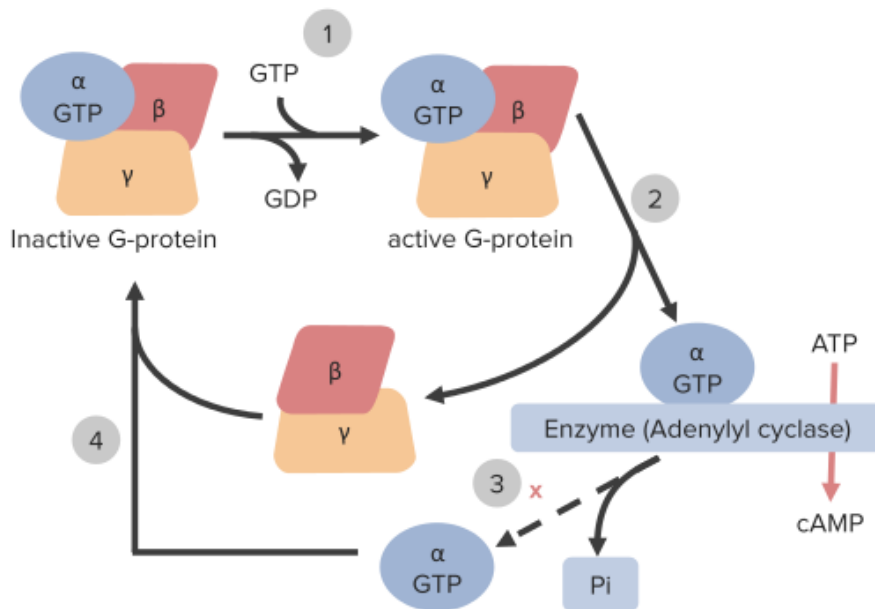
Pituitary sellar masses

Pituitary gland masses are mostly **adenomas** that are **benign and slow growing** masses. They mostly involve the anterior pituitary gland; however, they may involve any part of the gland and they may also be cancerous.

Etiology of pituitary sellar masses

It is traced and named from the cells of origin as follows:

- Craniopharyngiomas and germ cell tumors arise from developmental cells.
- Meningiomas are those that arise from the protective brain coverings.
- Metastatic tumors.
- Those from supporting structures of the brain.
- Pituitary hyperplasia.
- Abscesses.



Classification of pituitary sellar masses

They are classified **based on size** as:

- **Microadenomas** which are less than 1 cm in size.
- **Macroadenomas** which are equal to or more than 10 cm in size.

They can also be classified **based on staining characteristics** as:

- **Chromophobic** masses which do not take up the stain.
- **Chromophilic** masses that take up the stain.

Epidemiology of pituitary sellar masses



Adenoma

They represent 10–15% of all diagnosed tumors and 90% of these are adenomas.

Prolactinomas are mostly seen with women.

They are diseases of adults representing the 4th–5th decade of life as the most commonly affected group.

Pathophysiology of pituitary sellar masses

Pituitary tumorigenesis studies have suggested that pituitary tumor development has a **strong genetic link**. Some of the identified genetic mutations that lead to pituitary tumor development include mutations in Ras protein, p53 protein and pituitary tumor transformation gene (PTTG-1).

These mutations are thought to be carried down in an **autosomal dominant inheritance** pattern, thus anyone with the mutation and have environmental trigger factors for pituitary tumorigenesis is at an increased risk of developing a sellar/pituitary mass.

Presentation of pituitary sellar masses

They present with features of:

	Hypofunctional adenoma	Hyperactive functional adenoma
Growth hormone	Obesity Reduced muscle strength, hypoglycemia Increase in cholesterol levels	Gigantism Acromegaly Hirsutism Frontal bossing
Gonadotropin hormones	Diminished libido Impotence Shrunken testis Breast atrophy Delayed puberty	
Thyrotropin hormone	General body malaise Weight gain Cold intolerance Constipation	Myxedema Proptosis Lid lag Lid retraction
Corticotropin hormone	Secondary adrenal insufficiency features	Cushing syndrome of pituitary origin

The patients may also present with features of mass effects:

- Seizures
- Hydrocephalus
- Visual disturbances
- Headaches

- Diplopia

Investigations of pituitary sellar masses

MRI

MRI of the brain offers the **best soft tissue study**, more so to the pituitary region, thus, it is the imaging method of choice.

CT

CT scan of the head offers an additional assessment, especially when there is a **hemorrhagic event in the Sella turcica or erosion of nearby bone** as seen with craniopharyngiomas.

Laboratory work-ups

Laboratory work-ups for hormonal assays to determine the functionality of the specific mass such as:

- GH and IGF-1 assays.
- Free T3 and T4 levels and TSH levels.
- Cortisol levels and dexamethasone suppression tests.

Treatment of pituitary sellar masses

The most immediate attention should be **controlling the levels of hormones in circulation**, i.e., the replacement in deficiency and inhibition of hypersecretion.

Replacement therapy

- Glucocorticoid replacement therapy in hypoadrenalism.
- Steroid replacement therapy in reduced prolactin states.

Inhibition of hypersecretion

- Dopamine agonists to reduce secretion of prolactin hormone and growth hormone receptor antagonists such as pegvisomant and inhibition of adrenal steroidogenesis by ketoconazole and metyrapone.

Surgical removal of large masses with mass effect via a Transphenoidal approach.

Radiotherapy to reduce the growth of a pituitary mass.

Chemotherapy with temozolamide, carboplatin and etoposide reducing growth of the mass.

Prognosis of pituitary sellar masses

The conditions are associated with a **predicted course** with avoidance of symptoms and surgery to control complications.

Pituitary apoplexy and Sheehan syndrome

Pituitary apoplexy

Pituitary apoplexy is a disease of **sudden pituitary gland impairment of vascular**

supply leading to the development of headaches, blurring of vision, and altered mental status. This is a **vascular accident** that may arise from **acute hemorrhage or infarction of the gland**.

Sheehan syndrome

Sheehan syndrome/post infarction hypopituitarism is a **rare** entity of **pituitary hypofunction** that arises from **hypovolemic shock** during and/or after childbirth.

Etiology of pituitary apoplexy and Sheehan syndrome

Whereas the cause of **Sheehan syndrome is mainly hypovolemic shock**, **pituitary apoplexy** is also associated with:

- Head trauma
- Endocrine stimulation tests
- Radiation exposure

Epidemiology of pituitary apoplexy and Sheehan syndrome

Pituitary apoplexy

Pituitary apoplexy occurs in 10% of pituitary adenomas and is mostly seen in the post-operative period of management. It has a slight male preponderance in a 2:1 male to female ratio and it is more common in the 4th–6th decade of life.

Sheehan syndrome

Sheehan syndrome is a rare disease seen **exclusively in pregnancy and the postpartum period**.

Pathophysiology of pituitary apoplexy and Sheehan syndrome

The pituitary gland is supplied by a low-pressure system that enters via the hypophyseal stalk that lacks a well-defined collateral blood supply making it very sensitive to minute changes in demand-supply mismatch and mechanical compression episodes.

Pituitary apoplexy

Pituitary apoplexy arises from **massive and rapid enlargement** of a gland located in a small cavity that compresses its own blood supply **leading to ischemia and death**. The enlargement may also induce a rupture damaging the unique blood vessel supply to the remaining part of the gland causing apoplexy.

Sheehan syndrome

Sheehan syndrome results from a **pregnancy-induced hypertrophy and hyperplasia** of the pituitary lactotrophs in preparation for the upcoming period of lactation. However, this **enlargement is not accompanied by the needed increase in blood supply** and, worse still, the enlargement may be accompanied by blood loss and hypovolemic shock during childbirth, leading to low blood supply and ischemic injury to the gland.

This is a rare entity exclusively seen in pregnancy and the postpartum period.

Presentation of pituitary apoplexy and Sheehan syndrome

Pituitary apoplexy presents with:

- Headaches
- Visual disturbances
- Nausea and vomiting

The patients with **Sheehan syndrome** present with:

- Amenorrhea
- Agalactorrhea
- General body malaise
- Hypothyroidism features (weight gain, hair loss, cold intolerance)
- Dilutional hyponatremia
- Hypotension
- Hypoglycemia

Investigations of pituitary apoplexy and Sheehan syndrome

MRI

MRI of the brain offers the **best soft tissue study**, more so to the pituitary region, thus, it is the imaging method of choice. It can view minor bleeds missed by CT scans.

CT

CT scan of the head is the imaging of choice in cases of **trauma or hemorrhage**, but may miss minute bleeds in this region.

Laboratory work-ups

Laboratory work-ups for pituitary hormonal assays to determine the functionality of the remnant gland.

Histology shows necrosis of the gland in hemorrhagic regions.

Treatment of pituitary apoplexy and Sheehan syndrome

Medical therapy

- Involves the administration of high dose steroids to control the intracranial pressure, as well as rapid correction of the hormonal and electrolyte abnormalities that have set in.

Surgical therapy with emergency decompression of the accumulating bleed and control of further damage.

Complications of pituitary apoplexy and Sheehan syndrome

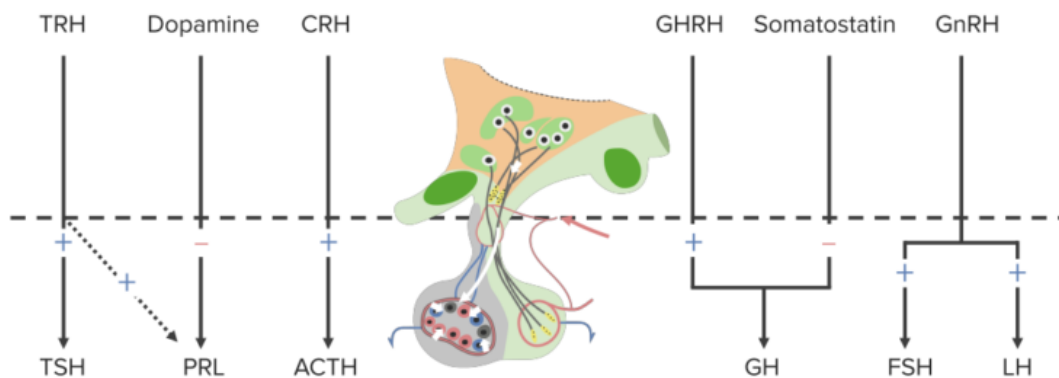
The conditions are associated with:

- Extraocular muscle **paralysis** and permanent **loss of eye function** leading to ptosis.
- Raised **intracranial pressure** and **altered mental status**.
- **Adrenal crisis**.
- **Menstrual irregularities**.

Hyperprolactinemia

It is a condition of an **elevated level of pituitary prolactin hormone** in circulation (>30 ng/ml). The hormone is responsible for breast development and lactation.

Prolactin (PRL)



Etiology of Hyperprolactinemia

Some **common causes of pathological hyperprolactinemia** include:

- **Lactotroph adenomas** that represent 40% of the causes of hyperprolactinemia.
- **Drugs** such as dopamine antagonists (phenothiazines, risperidone and pimozide).
- **Reduced dopaminergic inhibition**.
- **Idiopathic**.

Causes of physiological hyperprolactinemia include:

- Pregnancy
- Breast feeding
- Nipple stimulation
- Stress
- Estrogen
- Hypothyroidism
- Chest wall injury

Epidemiology of Hyperprolactinemia

Hyperprolactinemia occurs in **less than 1%** of the general population and in association with galactorrhea and amenorrhea.

It has a slight female preponderance and, when it occurs in men, it attacks early and in a more dramatic way.

Presentation of Hyperprolactinemia

In **women**, the disease presents with:

- Oligorrhea
- Amenorrhea
- Infertility
- Galactorrhea due to its effect on lactotrophs

In **men**, it presents with:

- Sexual disturbances
- Visual field defects and other visual disturbances
- Reduced testosterone
- Hypogonadism

Investigations of Hyperprolactinemia

MRI

MRI of the brain offers the **best soft tissue study**, more so to the pituitary region, thus, it is the imaging method of choice.

CT

CT scan of the head offers an **additional assessment for Sella turcica masses**, especially when there is erosion of nearby bone as seen with craniopharyngiomas.

Laboratory work-ups

Laboratory work-ups for prolactin levels which should be greater than 200 ng/ml in hyperprolactinemia.

Thyroid function tests to rule out associated hypothyroidism.

Pregnancy testing due to similar feature in pregnancy.

Visual field testing to assess for any complications.

Treatment of Hyperprolactinemia

Treatment approaches involve various methods such as:

- **Withdrawal of causative drugs** such as phenothiazines and dopamine antagonist drugs.
- **Medical treatment** with bromocriptine and cabergoline is the treatment of choice, especially for patients with mild elevation of hormones. Dopamine agonists reduce secretion of prolactin hormone.
- **Surgical removal of large tumors** with mass effects. The preferred method is the transphenoidal approach.
- **Radiotherapy** to reduce the growth of a pituitary mass. This is associated with a risk of bleeding and pituitary apoplexy formation.

Complications of Hyperprolactinemia

Hyperprolactinemia is associated with:

- Extraocular muscle **paralysis** and permanent **loss of eye function** leading to ptosis and blindness as the end effect
- **Hemorrhage** and **pituitary apoplexy** formation
- **Osteoporosis**
- **Infertility**

Prognosis of Hyperprolactinemia

A **third of the patients have complete resolution** with treatment. The disease is associated with **high recurrence rates** of up to 80% if managed surgically, thus necessitating the need for **long-term medical treatment** to avoid recurrence.

References

Barrett, K. E., & Ganong, W. F. (2012). *Ganong's review of medical physiology*. New York: McGraw Hill Medical.

Boon, N. A., Walker, B. R., Colledge, N. R., & Davidson, S. (2010). *Davidson's principles and practice of medicine*. Edinburgh: Churchill Livingstone.

Harrison, T. R., Fauci, S. A., Kasper, L. D., Longo, L. D., Hauser, S. L., & Jameson, J. L. (2012). *Harrison's Principles of Internal Medicine*. 18th edition. New York: McGraw Hill.

Ortiga-Carvalho, T. M., Chiamolera, M. I., Pazos-Moura, C. C., & Wondisford, F. E. "Hypothalamus-Pituitary-Thyroid Axis." *Comprehensive Physiology*. 2016 ;6(3):1387-428. doi: 10.1002/cphy.c150027. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27347897>

Snyder, P. J., & Cooper, D. S. (2017, July 24). "[Causes, presentation, and evaluation of sellar masses.](#)" Available at: <https://www.uptodate.com/contents/causes-presentation-and-evaluation-of-sellar-masses>

Vaphiades, M., & Roy, H. (2015, May 23). "[Pituitary Apoplexy.](#)" Available at: <http://emedicine.medscape.com/article/1198279-overview>

Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).

Notes