Hypopituitarism

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Objectives

01 Anatomy and Physiology of Pituitary Gland

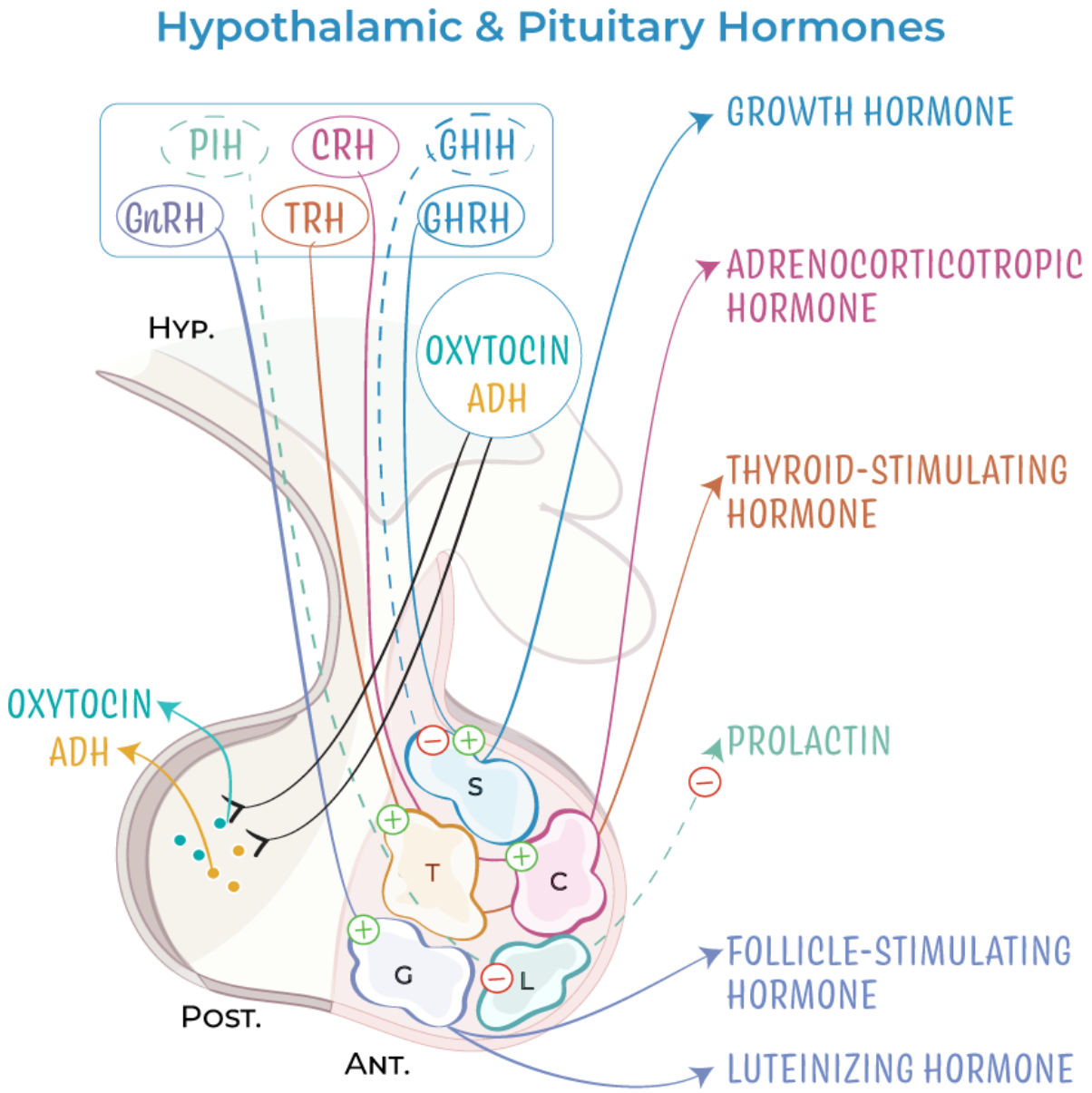
02 Hypopituitarism

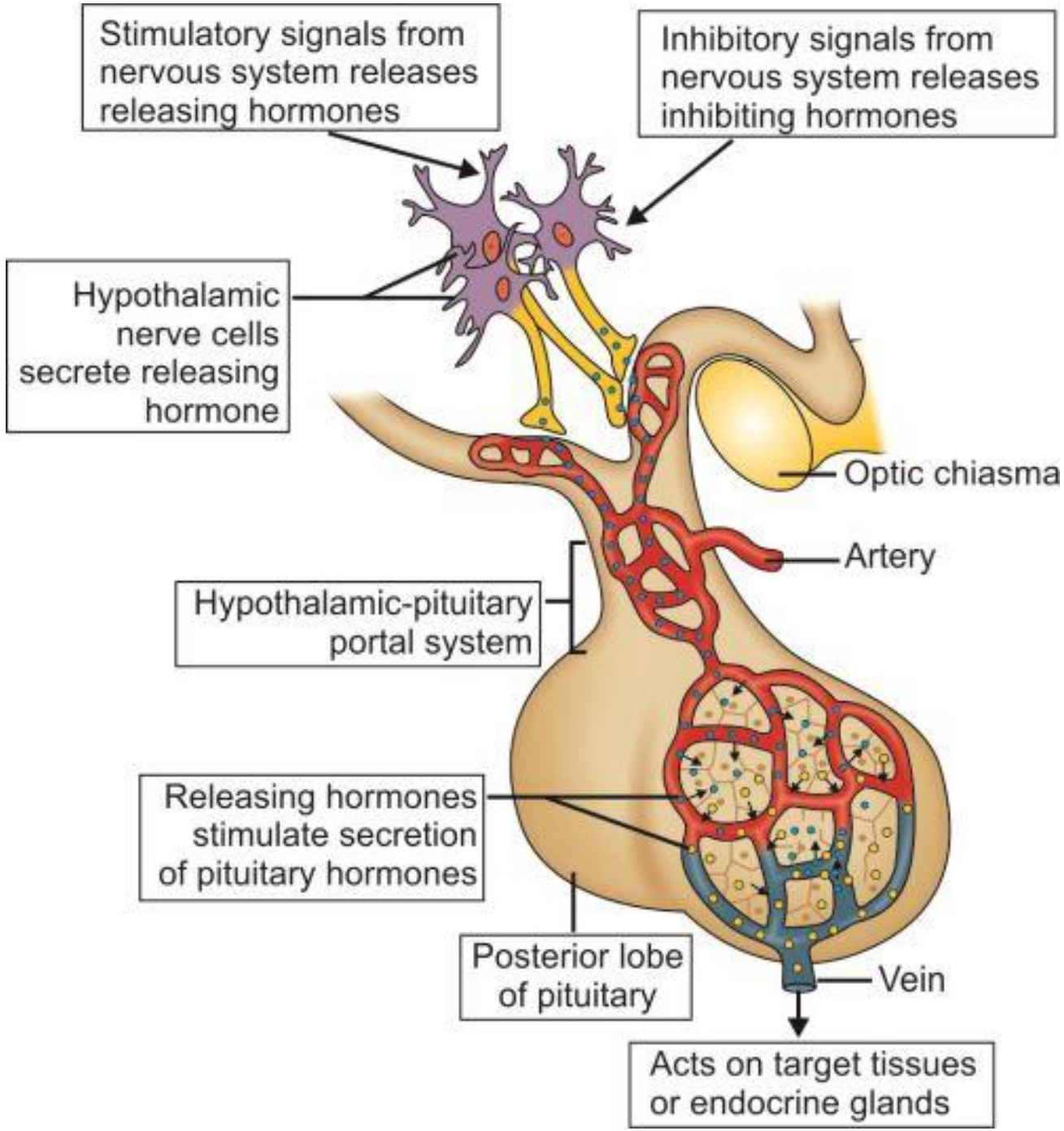
03 Investigation & Diagnosis of Hypopituitarism

04 Treatment of Hypopituitarism

Introduction

- The pituitary plays a central role in several major endocrine axes.
- The pituitary is considered the "Master Gland"
- Diseases of the hypothalamus and pituitary have an annual incidence of approximately 3 per 100,000 and a prevalence of 30–70 per 100,000.
- The gland is connected to the hypothalamus by the pituitary stalk (or infundibular stalk).

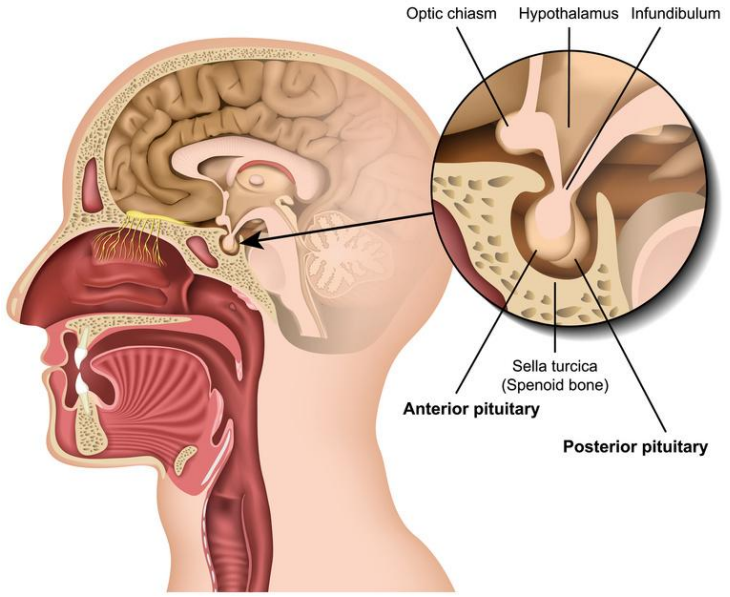



Stimulatory signals from nervous system releases releasing hormones
Inhibitory signals from nervous system releases inhibiting hormones
Hypothalamic nerve cells secrete releasing hormone
Optic chiasma
Artery
Hypothalamic-pituitary portal system
Releasing hormones stimulate secretion of pituitary hormones
Posterior lobe of pituitary
Vein
Acts on target tissues or endocrine glands

Anatomy of Pituitary Gland

Location and Bony Enclosure

- **The pituitary gland is enclosed within a small depression in the sphenoid bone, called Sella Turcica.**
- **It is bridged superiorly by the diaphragma sellae (a fold of dura mater).**

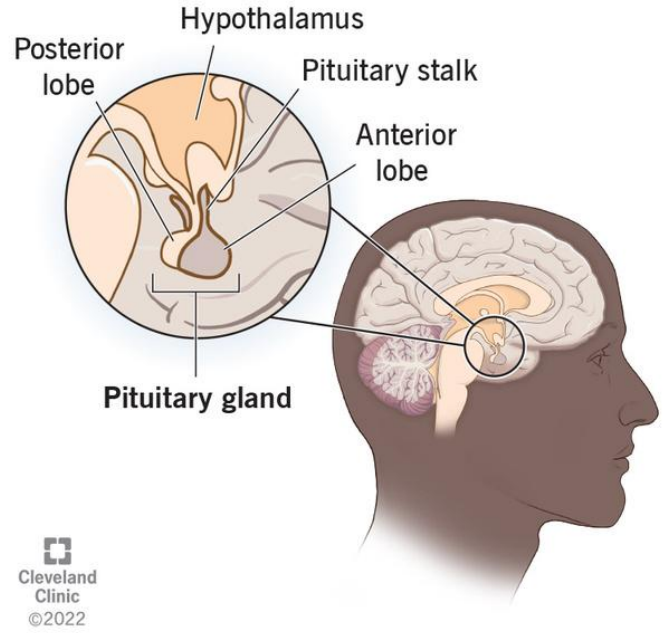


Relations to surrounding structures:

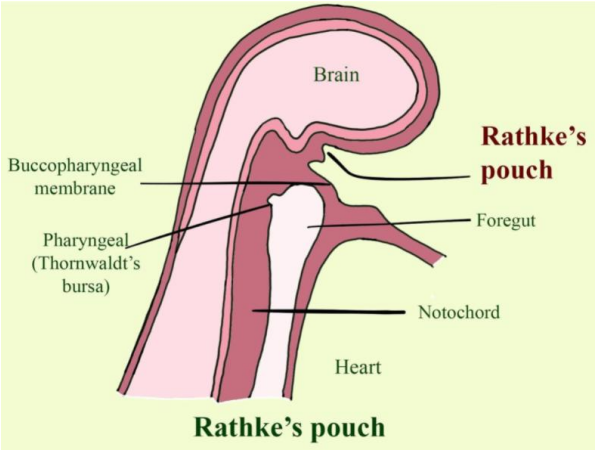
1. Superiorly: The optic chiasm is situated above the sella.

2. Laterally: The cavernous sinuses are lateral to the pituitary fossa.

- Contents: The 3rd, 4th, and 6th cranial nerves and the internal carotid arteries.



Pituitary Lobes



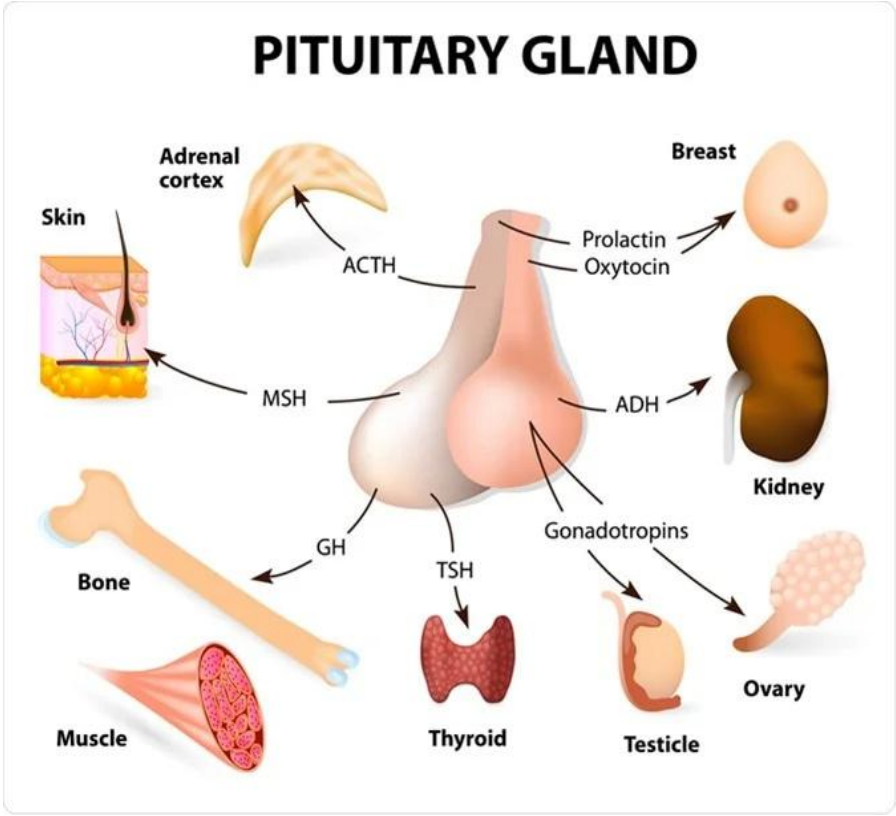
The Pituitary is divided into 2 lobes:

Anterior Lobe [Adenohypophysis] (80% of Pituitary):

- **Releases 6 Hormones, regulated by hypothalamic hormones transported via specialized portal vessels.**
  - **Derived from oral ectoderm, Rathke's Pouche.**

Posterior Lobe [Neurohypophysis]:

- **Stores & releases 2 hormones synthesized by hypothalamus, controlled by nerve fibers from the hypothalamus.**
  - **Derived from neuroectoderm**



Physiology of Pituitary Gland

Anterior Lobe Hormones:

Adrenocorticotropic Hormone (ACTH):

- Stimulates growth of adrenal cortex and secretion of its hormones.

Thyroid Stimulating Hormone (TSH):

- Stimulates growth of thyroid and secretion of T3 and T4 via cAMP

Growth Hormone (GH):

- Effects growth of skeletal muscles and long bones (linear growth).
- Helps to maintain blood sugar homeostasis.

Anterior Lobe Hormones:

Follicle Stimulating Hormone (FSH):

- Stimulates follicle development in ovaries in women. As they mature, they produce estrogen.
- Stimulates sperm development by the testes in men.

Lutenizing Hormone (LH):

- Triggers ovulation of an egg from the ovary in women.
- Stimulates testosterone production by the interstitial cells of testes in men.

Prolactin (PRL):

- Stimulates and maintains milk production by the mother's breasts after childbirth.

Physiology of Pituitary Gland

Posterior Lobe Hormones:

Oxytocin:

- Causes Uterine contractions.
- Breast Milk Secretion.

Vasopressin (ADH):

- Acts at renal collecting ducts on V2 receptors to cause insertion of aquaporin channels and increases water reabsorption thereby concentrating urine

Sequence of Hormone Loss in Hypopituitarism

Growth Hormone (GH) is affected first, followed by **Gonadotropins (LH/FSH)**, then **Thyroid-Stimulating Hormone (TSH)**, and finally **Adrenocorticotropic Hormone (ACTH)**.
Prolactin is usually preserved. Posterior pituitary hormones (**Oxytocin** and **AVP**) are spared unless the damage involves the hypothalamus or the pituitary stalk

Hypopituitarism

- Describes **combined deficiency** of any of the **anterior pituitary hormones**. The clinical presentation is variable and depends on the underlying lesion and the pattern of resulting hormone deficiency.
- The **posterior pituitary** is usually **spared** because it has a **separate blood supply**, a **neuroectodermal origin**, if affected, it can cause **diabetes insipidus** due to deficiency of **vasopressin (ADH)**.

Causes of Hypopituitarism

- By far the most common disorder is an **adenoma** of the anterior pituitary gland. Causes are broadly classified as **Structural**, **Inflammatory**, **Congenital**, or **Functional.**
- * = most common causes of pituitary hormone deficiency.

20.53 Causes of anterior pituitary hormone deficiency

Structural

- Primary pituitary tumour
- Adenoma*
- Carcinoma (exceptionally rare)
- Craniopharyngioma*
- Meningioma*
- Secondary tumour (including leukaemia and lymphoma)
- Chordoma
- Germinoma (pinealoma)
- Arachnoid cyst
- Rathke's cleft cyst
- Haemorrhage (apoplexy)

Inflammatory/infiltrative

- Sarcoidosis
- Infections, e.g. pituitary abscess, tuberculosis, syphilis, encephalitis
- Lymphocytic hypophysitis
- Haemochromatosis
- Langerhans cell histiocytosis

Congenital deficiencies

- GnRH (Kallmann syndrome)*
- GHRH*
- TRH
- CRH

Functional*

- Chronic systemic illness
- Anorexia nervosa
- Excessive exercise

Other

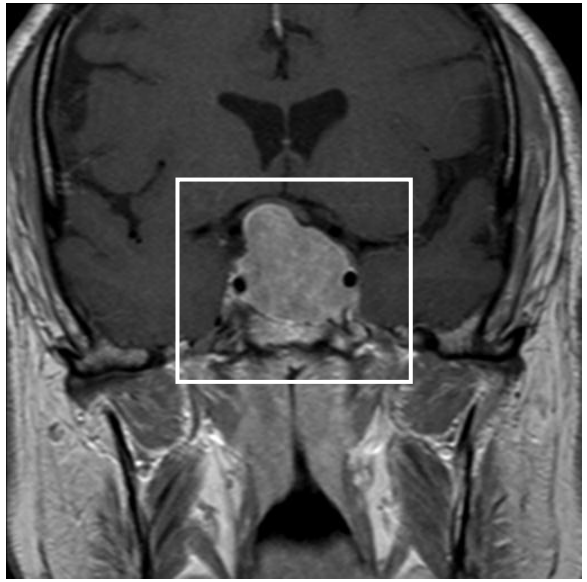
- Head injury*
- (Para)sellar surgery*
- (Para)sellar radiotherapy*
- Post-partum necrosis (Sheehan syndrome)
- Opiate analgesia

Pituitary adenomas “pituitary neuroendocrine tumors”

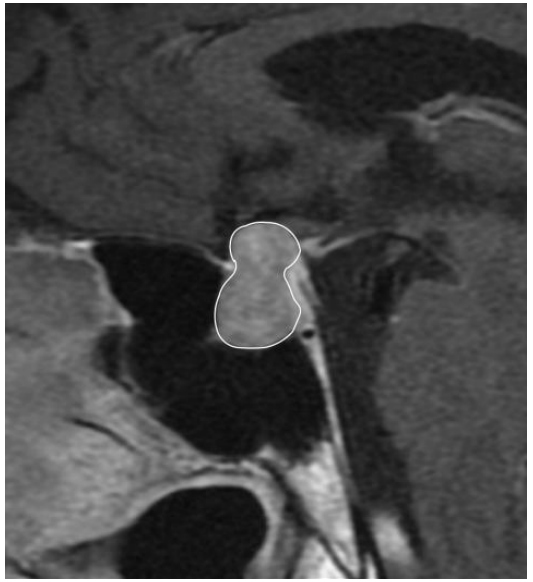
- **Benign tumors** that arise **sporadically** from the anterior pituitary gland. They are classified as either **microadenomas** (<10 mm diameter) or **macroadenomas** (>10 mm diameter) according to their **size**, and as either **secretory (functional)** or **nonsecretory (nonfunctioning)**.
- Peak incidence: **35–60 years** & some cases (~ 5%) have a genetic/familial association: Multiple endocrine neoplasia type 1 (**MEN1**)
- **Nonsecretory macroadenomas** can destroy the surrounding normal pituitary tissue, which results in **hypopituitarism**.
- Secretory adenomas produce the hormone of their cell type, causing hyperpituitarism (Prolactinoma being MC).

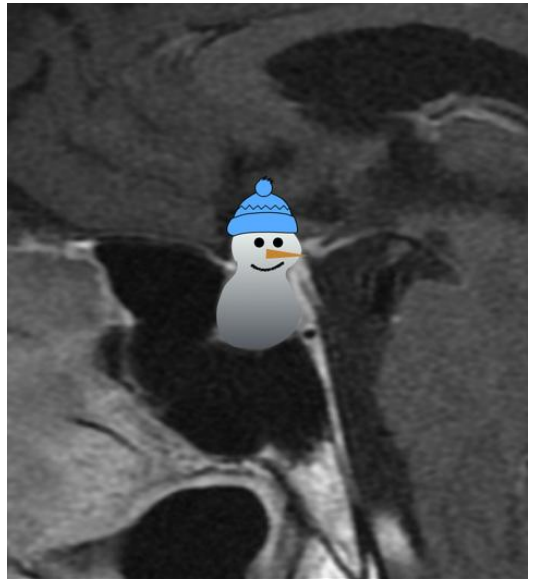
Nonsecretory Macroadenomas

- **Mass effects** (e.g., **headache**, **bitemporal hemianopsia** due to compression of the **optic chiasm**, **diplopia**).



- coronal T1-weighted MRI image
- **Severe compression** and elevation of the **optic chiasm**





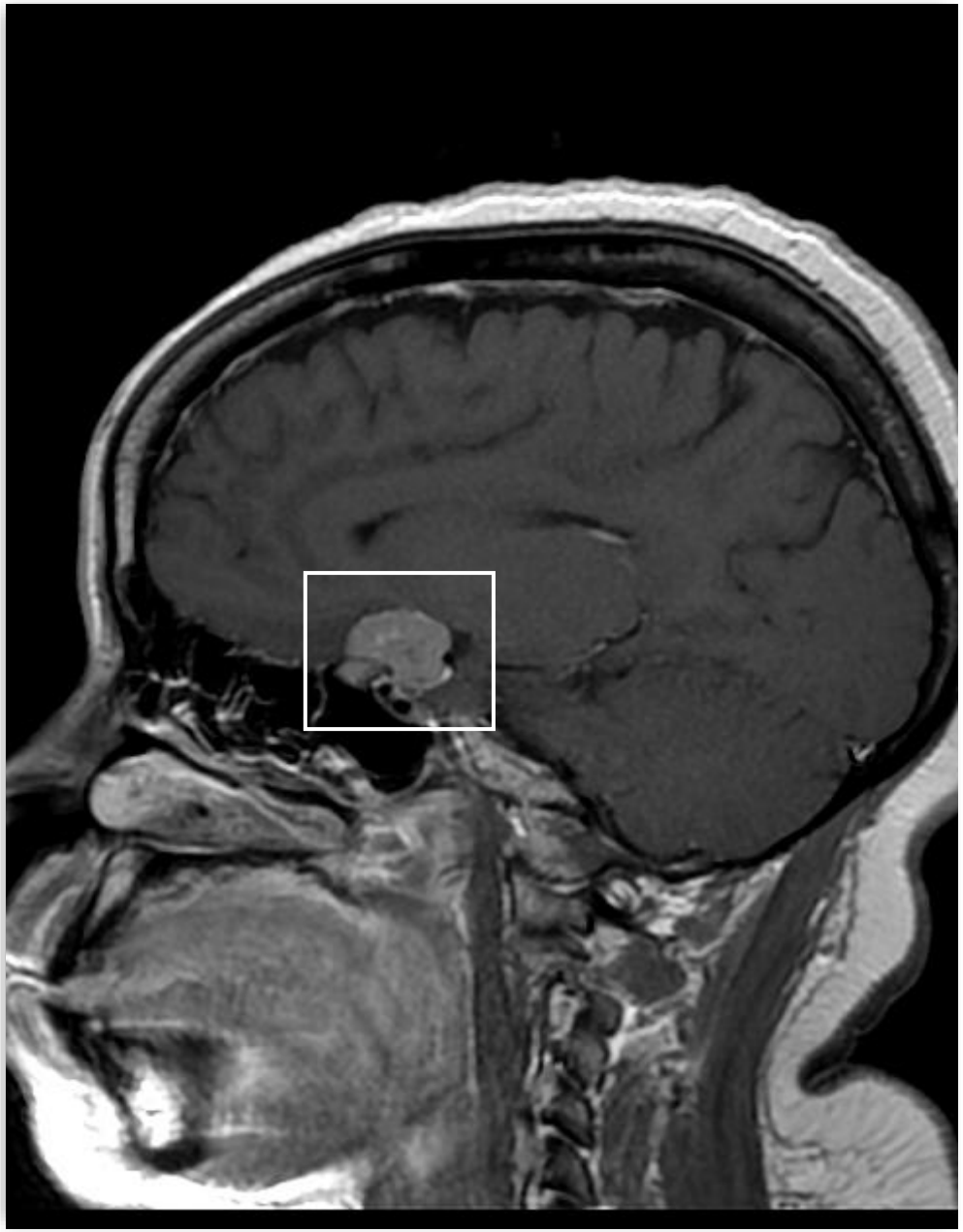
Mass may exhibit a "**figure-of-eight**" or "**snowman**“ shape

bitemporal hemianopsia

- Relating to the **temple side** (the outer half of the visual field)
- **Blindness** or loss of vision

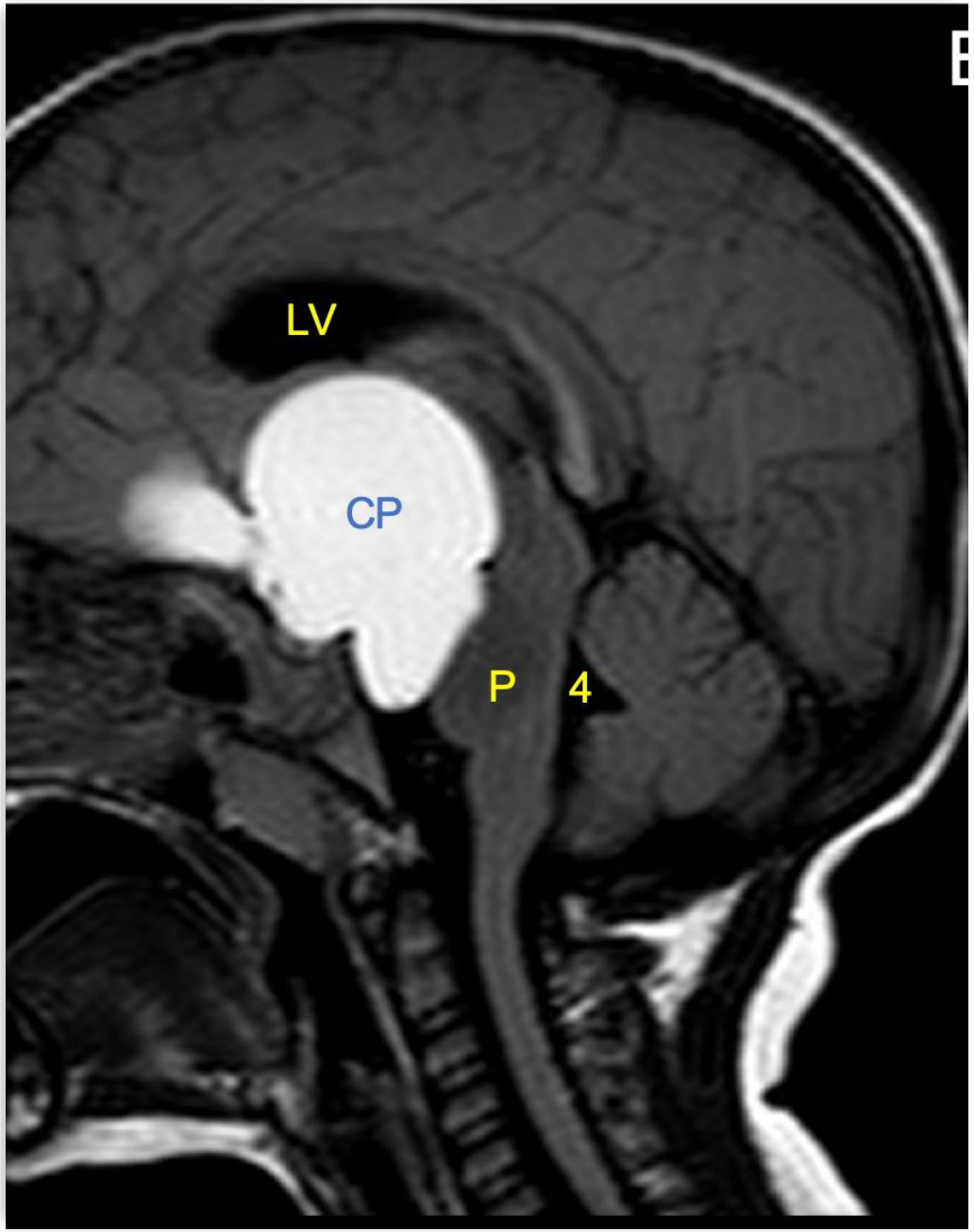
Meningiomas

- Almost always benign, **slow-growing** brain tumors.
- **Most common benign primary brain tumor** in adults
- **Compression of the Pituitary Gland (Mass Effect):** A growing meningioma that extends into the **sella or suprasellar region** can exert a direct pressure, causing **destruction** of anterior pituitary gland. The loss of these cells leads to a gradual, sequential **failure of hormone secretion**.
- **Compression of the Pituitary Stalk (Stalk Effect):** This action interrupts the flow of the **releasing and inhibiting hormones** that travel from the hypothalamus down to the anterior pituitary. The lack of hypothalamic stimulation is a major cause of **hormone deficiency (secondary hypopituitarism)**.



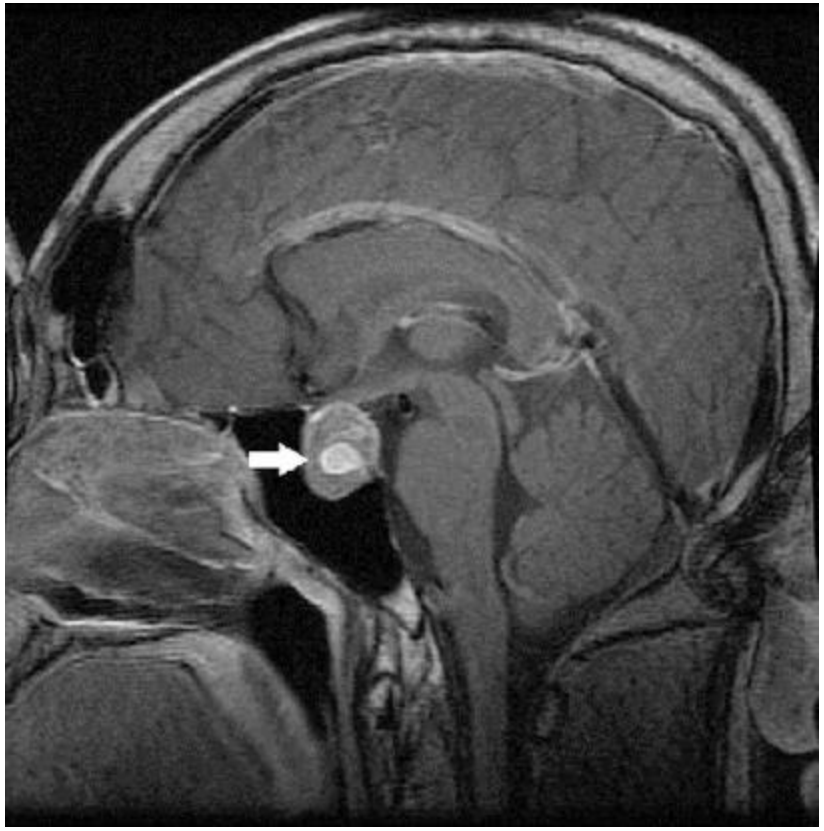
Craniopharyngioma

- **Benign dysontogenetic tumor** arising from a remnant of the **Rathke pouch**
- Tumor arises in the **suprasellar region** and can extend into the **intrasellar region** causing compression of the pituitary → **hypopituitarism**
- **Bimodal distribution**: 5–14 years; second peak at 50–75 years
- Generally **good prognosis** , with a 10-year survival rate of ~ 90%; however, the recurrence rate is high
- LV=Lateral ventricle, P=Pons, 4=Fourth ventricle



Pituitary apoplexy

- A clinical syndrome resulting from **sudden hemorrhage (bleeding)** and/or **infarction** within the pituitary gland.
- Almost always occurs within a pre-existing pituitary tumor (adenoma), which may have been previously undiagnosed.

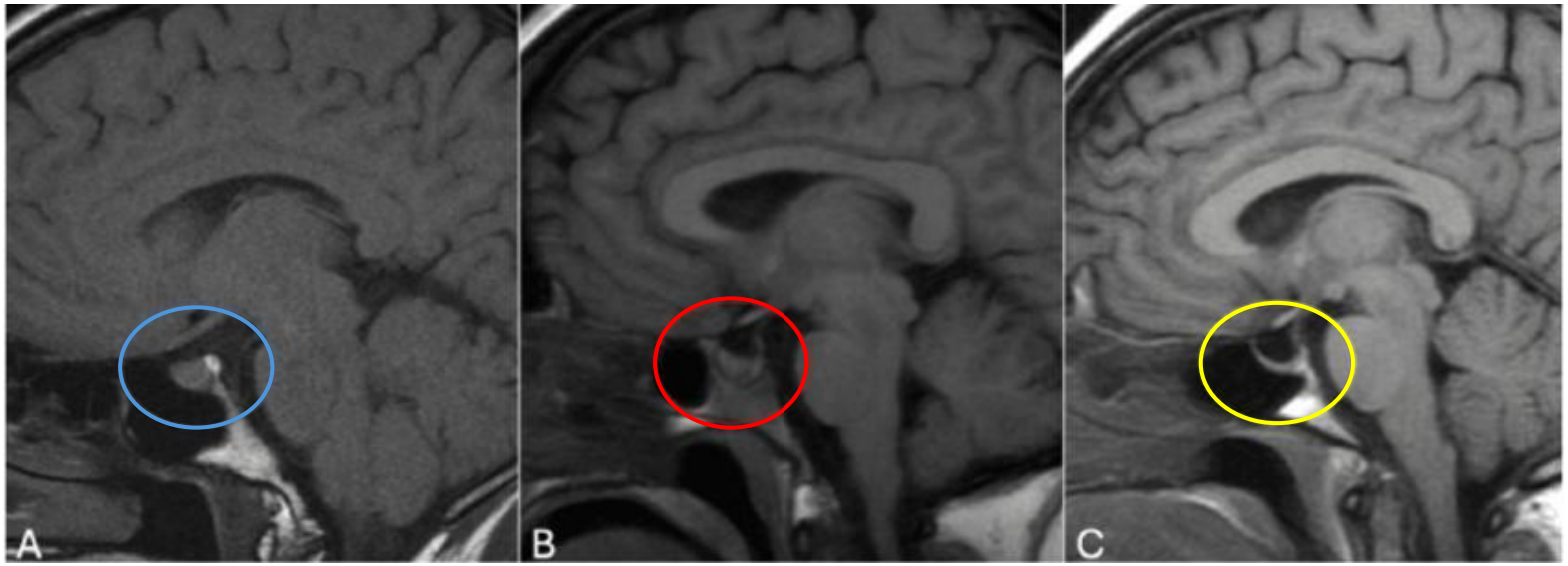


The Triad of Symptoms:

- **Sudden, Severe Headache** often described as **the worst of the patient's life**. The most common initial symptom (80-90% of cases).
- **Visual Impairment: Visual acuity loss** (decreased vision or blindness) and **visual field defects** (classically bitemporal hemianopia)
- **Ophthalmoplegia:** Paralysis of the eye muscles, often causing **diplopia (double vision)** and/or **ptosis (drooping eyelid)**, A key localizing sign of **sellar/parasellar pathology**.

Post-partum necrosis (Sheehan syndrome)

- Of the pituitary gland. Usually occurs following **postpartum hemorrhage** but can also occur even without clinical evidence of hemorrhage.
- During pregnancy, **hypertrophy** of prolactin-producing regions increases the size of the pituitary gland, making it **very sensitive** to ischemia.
- Blood loss during delivery/postpartum hemorrhage; **ischemia** of the pituitary gland → **empty sella turcica** on imaging



A. **normal** sella turcica (blue circle)
B. **partially** empty sella turcica (red circle)
C. **complete** empty sella turcica (yellow circle)

- Filled with **CSF** (Clear on imaging)

Kallmann syndrome

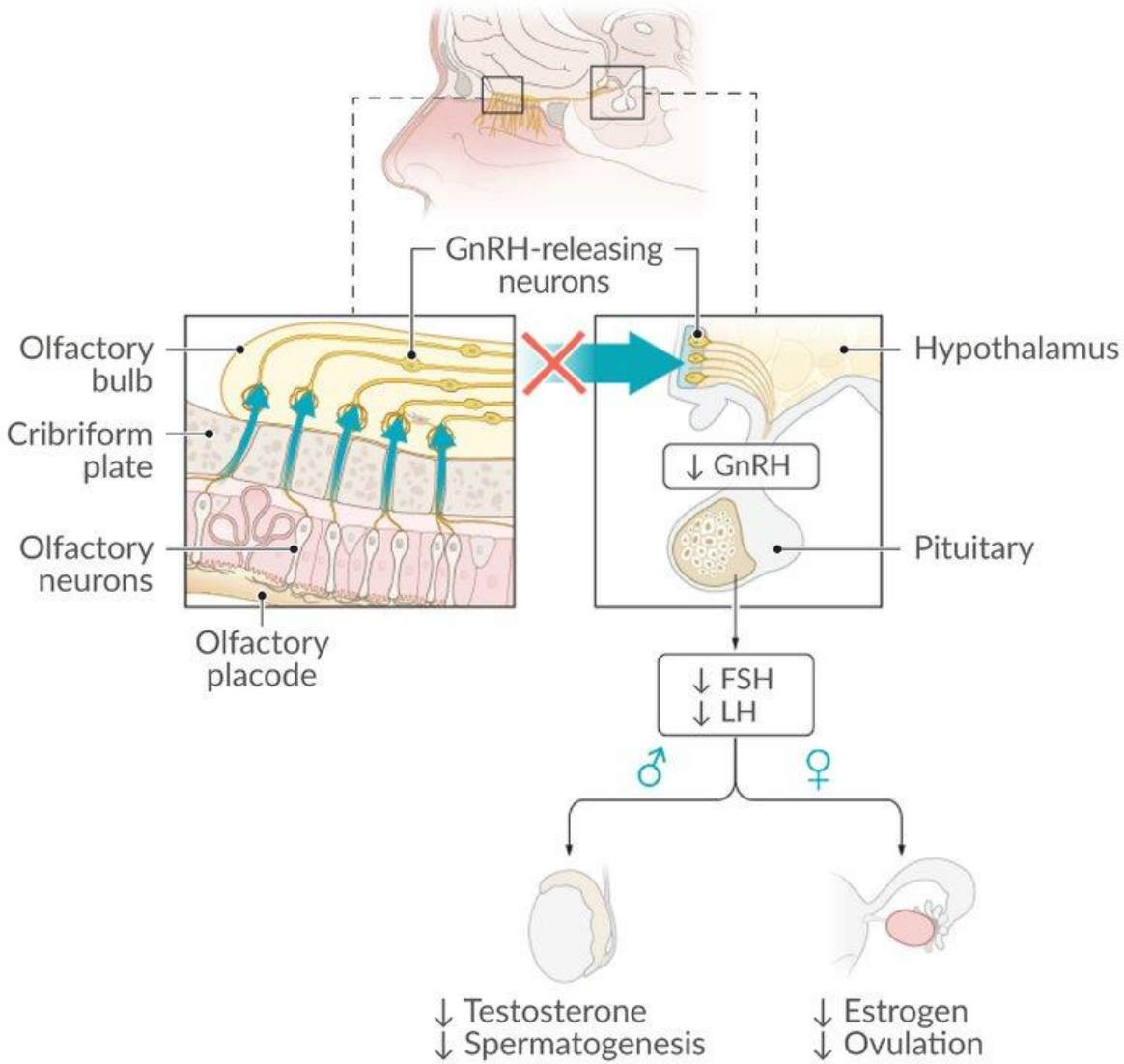
- A rare, complex genetic disorder characterized by the combination of two key features:

1. **Congenital Hypogonadotropic Hypogonadism (CHH)**: Failure to undergo or complete puberty due to a deficiency in the sex hormones.
2. **Anosmia** or **Hyposmia**: An absent or severely impaired sense of smell.

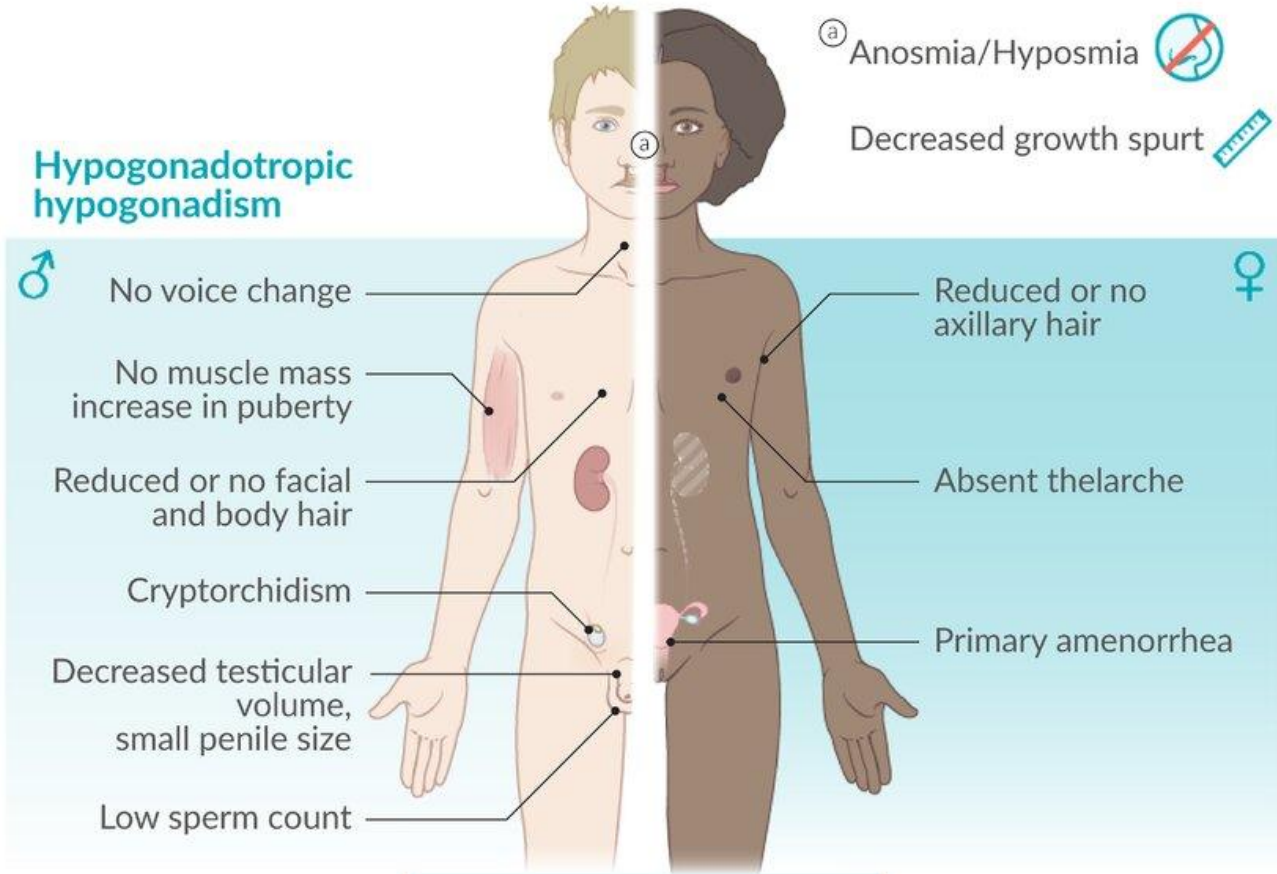
- Defective migration of **GnRH**-releasing neurons from the olfactory bulbs to the hypothalamic preoptic nuclei → ↓ GnRH secretion and underdevelopment of the olfactory bulbs
- ↓ GnRH → ↓ pituitary secretion of FSH and LH → **↓ testosterone** in male individuals and **↓ estrogen** in female individuals

Kallmann syndrome

Pathophysiology



Clinical features



Associated conditions for both genders

Cleft lip and palate
Renal agenesis

How to diagnose Hypopituitarism

What's our approach:

- To investigating pituitary disease is similar across most cases.

Anterior lobe deficiencies laboratory investigations:

- 1 . ACTH deficiency
- First line: morning cortisol level
- If its < 3 mcg/dL diagnosis of Al supported; serum
- ACTH values required to differentiate between primary and central Al.
  - High ACTH: supports primary Al
  - Low to normal ACTH: supports central Al
- 3-15 mcg/dL: Perform ACTH stimulation test.
- >15 mcg/dL: likely excludes Al

LH/FSH deficiency:

- Male: LH and FSH are decreased. Testosterone is decreased.
- Female: If the patient has a regular menstrual cycle there is no need to do extra diagnostic tests.
- But if the patient is presented with oligorrhea, amenorrhea or post menopause if we suspect secondary hypogonadism.
- LH/FSH are decreased.
- Estradiol is decreased.

GH deficiency:

*Before we do a simulation test we need to test for:

Serum IGF-I, typically it should be normal or high in response to GH but when it's low we can continue to do GH simulation test.

*It's procedure:

*Record baseline GH serum level.

*Administer stimulating agent (e.g., macimorelin).

*Repeat serum GH levels at set intervals.

If the level is low it supports GH deficiency.

TSH deficiency:

*T FT and free T4 are the first line tests in secondary hypothyroidism.

*But if there is uncertainty we do a TSH simulation test by administration TRH (IV) then we measure the TSH levels and if there is no response we can confirm TSH deficiency.

Prolactin deficiency:

There is no specific usage for it since it's very rare to occur and when it occurs panhypopitutarism like (Sheehan syndrome and pituitary apoplexy).
But to test it basal prolactin in the morning is sufficient. It's rarely to do dopamine simulation test.

Posterior Lobe Deficiencies:

ADH (Vasopressin) deficiency:

It is used to test for central diabetes insipidus. Initial testing are:

Collect a 24-hr urine sample:

Increased urine output, decreased urine osmolality.

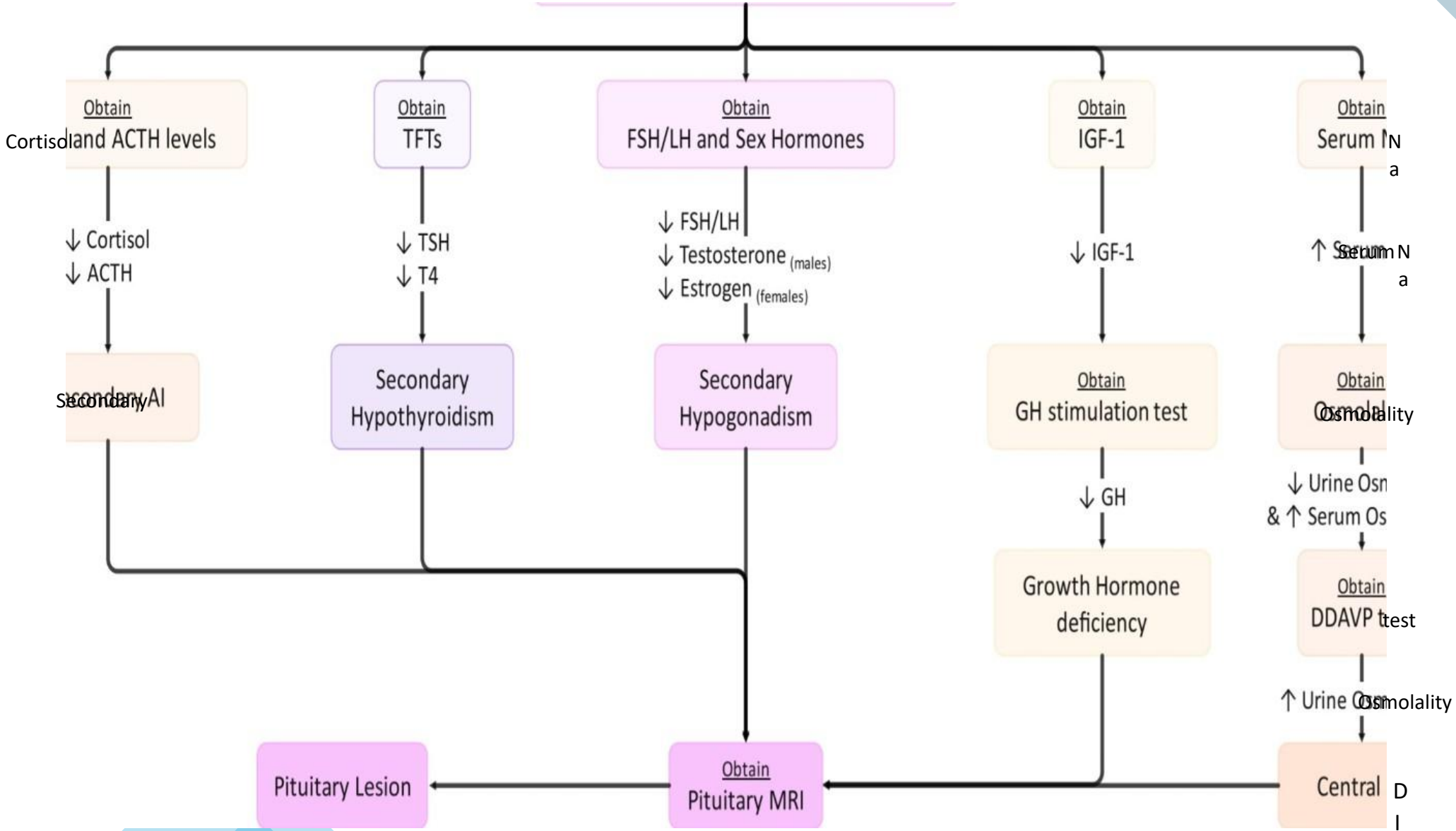
Normal or increased plasma osmolality. Normal or increased serum sodium

Water Deprivation test:

Initial deprivation causes no change to urine osmolarity

Following exogenous desmopressin administration causes Increse in Urine Osmolarity

Diagnostic Approach to Hypopituitarism



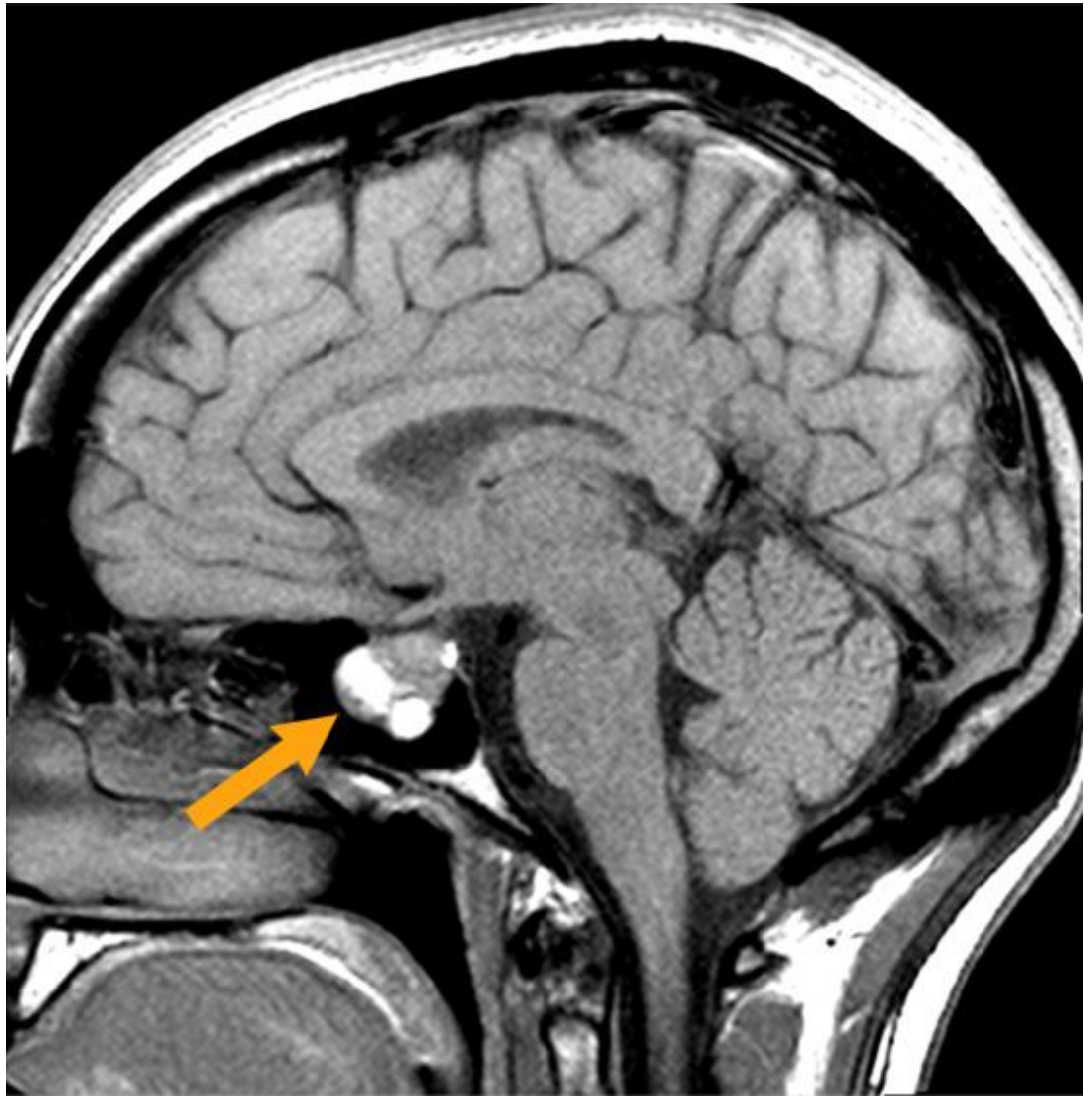
Imaging

*When hormone deficiency is identified cranial imaging (preferably MRI) is indicated to identify the cause (e.g. pituitary adenomas).

Brain MRI:

- Preferred imaging modality
- Findings depend on the underlying etiology and include pituitary adenomas (most common cause in adults), congenital malformations, and trauma.

CT Head (w/out IV contrast):
used if there are contraindications to MRI or in patients requiring rapid evaluation, e.g., after suspected TBI or SAH



Pituitary Gland Tumor

In emergency setting (e.g. adrenal crisis, myxedema coma) treatment is indicated prior to any biochemical testing.

*Adrenal crisis: is an acute severe glucocorticoid deficiency that requires immediate emergency treatment. (It can be caused by pituitary apoplexy).

*Myxedema coma: It's an extremely rare life threatening condition decompensation of preexisting thyroid hormone deficiency.

Hypopituitarism: Clinical Assessment & Emergency Management

• Hypopituitarism requires immediate recognition of life-threatening complications and systematic hormone replacement therapy. This guide covers emergency assessment, acute management, maintenance therapy, and long-term follow-up strategies.

Assess for Clinical Instability

Identify signs of hypopituitarism crisis or secondary adrenal crisis immediately:

Severe Hypotension

Shock not responding to fluid resuscitation resuscitation indicates adrenal crisis requiring requiring emergency intervention.

Gastrointestinal Symptoms

Weakness, vomiting, and abdominal pain pain signal acute hormonal deficiency.

Hypoglycemia

Low blood glucose from cortisol deficiency deficiency requires immediate glucose administration.

If any signs present: initiate emergency management immediately.

Emergency Management Protocols

For acute distress, immediate intervention precedes full diagnostic workup. Three critical emergencies require emergencies require specific interventions:

Hypernatremia

Severe hypernatremia from central diabetes insipidus is managed with desmopressin (DDAVP) to restore water balance.

Adrenal Crisis

Most immediate life-threatening emergency. Give IV hydrocortisone immediately without waiting for diagnostic confirmation in suspected suspected ACTH deficiency.

Myxedema Coma

In severe hypothyroidism (TSH deficiency), administer IV hydrocortisone **FIRST** before any thyroid hormone to prevent cardiovascular collapse.

Maintenance Hormone Replacement Therapy

Once stable, long-term replacement is tailored to specific deficiencies. All patients require treatment for secondary adrenal insufficiency, secondary hypothyroidism, hypogonadism, and diabetes insipidus. Growth hormone deficiency should be treated in all children and considered in adults. Prolactin, oxytocin, and MSH deficiency require no replacement.

Cortisol (ACTH axis)

- Secondary adrenal insufficiency
- Hydrocortisone 10–25 mg/day split doses
- Replace before thyroid; sick-day rules

Thyroid (TSH axis)

- Secondary hypothyroidism
- Levothyroxine; target free T4 upper-normal
- Start only after cortisol therapy

Gonadal (LH/FSH)

- Low testosterone/estrogen
- Testosterone or estrogen ± progesterone
- Use gonadotropins for fertility

Growth Hormone

- Reduced growth, muscle, bone density
- Daily recombinant GH
- Confirm deficiency; monitor IGF-1

ADH (Posterior)

- Diabetes insipidus
- Desmopressin nasal/oral/SC
- Monitor Na^+ to avoid hyponatremia

Treat Underlying Cause & Long-Term Management

Identify and treat the underlying cause of hypopituitarism. Common causes like pituitary macroadenoma may require transsphenoidal surgery. Treatment is typically lifelong, but with consistent hormone replacement and careful management, most patients control symptoms and lead full, active lives.

01

Regular Monitoring

Blood tests monitor hormone levels, ensuring accurate replacement doses replacement doses and avoiding under- or over-treatment.

02

Dose Adjustment

Adjust doses, especially glucocorticoids, during illness, surgery, or surgery, or major bodily stress using stress dosing protocols.

03

Patient Education

Educate patients on acute adrenal insufficiency signs and importance of importance of stress dosing and emergency protocols.

Critical Reminders for Safe Management

Success in hypopituitarism management depends on adherence to these essential principles:

Medical ID

Patients must carry emergency steroid card or bracelet for identification during crisis.

Cortisol First

Always replace cortisol before thyroid hormone to prevent adrenal crisis.

Treat Cause

Identify and treat underlying cause if reversible (e.g., pituitary tumor resection).

Lifelong Therapy

Most hormone replacements are lifelong; continuous follow-up is essential for safety and optimal outcomes.

THANK YOU