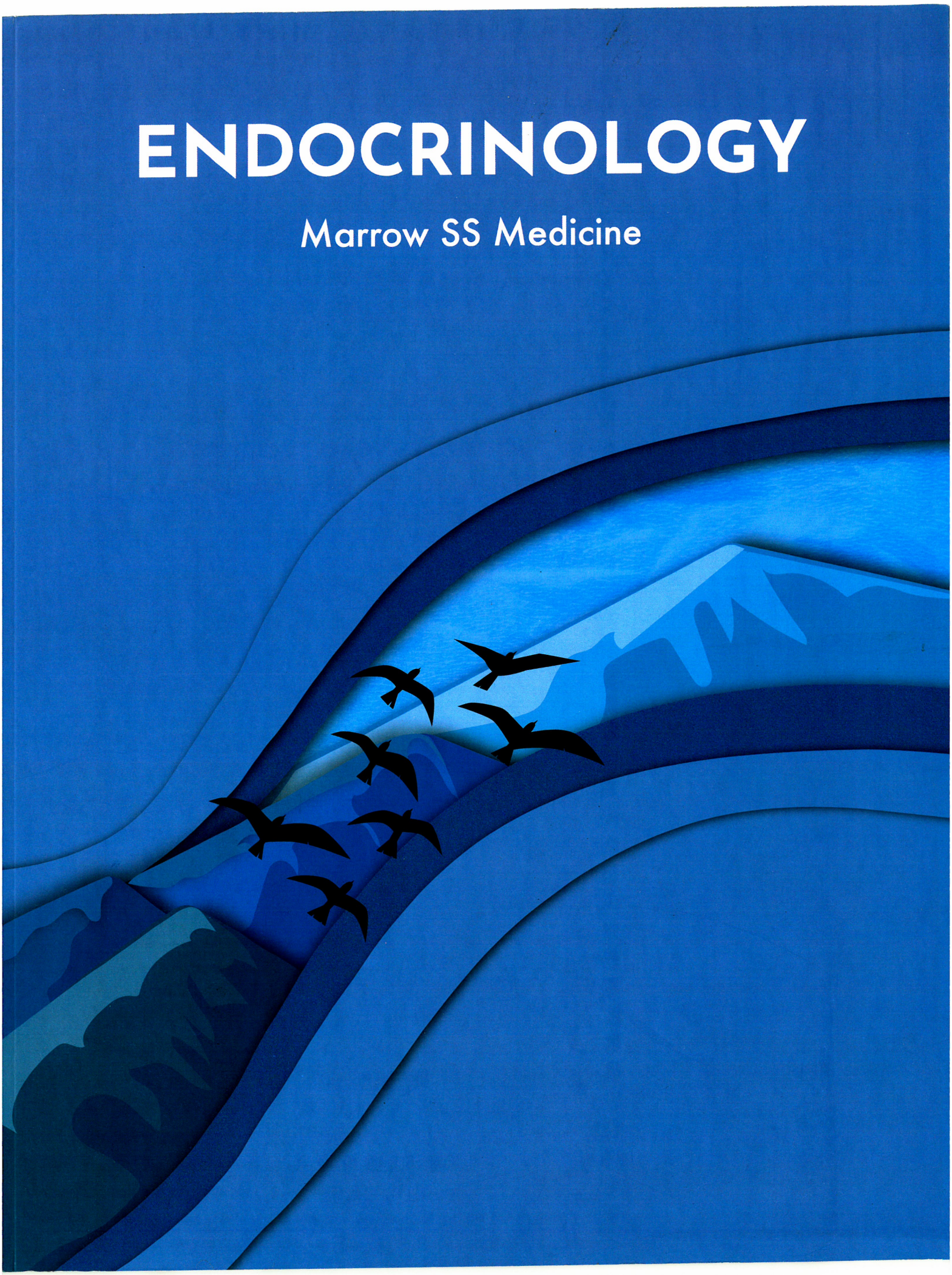
ENDOCRINOLOGY

Marrow SS Medicine



Dr. Mayur Agrawal

MBBS, MD, DM (Endocrinology)

A Gold Medalist in Medicine, Dr. Mayur Agrawal is the founder of the Hormone India Clinic and is a Consultant Endocrinologist. He completed his DM in Endocrinology from Sanjay Gandhi Post Graduate Institute, Lucknow and MD in General Medicine from Gandhi Medical College, Bhopal. With multiple book chapters and publications, he is an active organiser and participant in national level academic events and conferences.

Endocrinology

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- This set contains notes of all main videos published in the app until Jan 2025. You can find notes for any additional videos published after this date within the app under the videos section.

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PITUITARY TUMOR SYNDROMES

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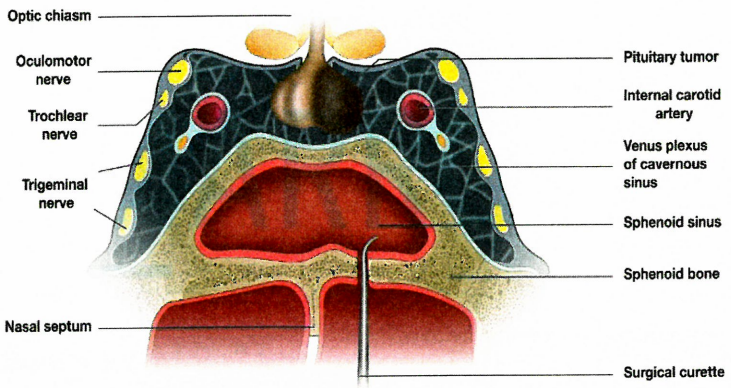
Clinical manifestations

00:00:20

Sellar masses may present with various clinical manifestations depending on :

- Anatomic location of the mass.
- Extension.
- Functionality.

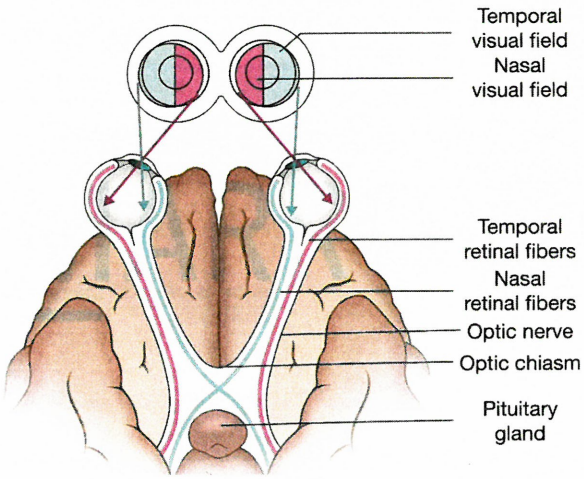


Pituitary tumor

Suprasellar extension :

Compression of optic chiasma :

- Dorsal sellar diaphragm → Area of least resistance → Suprasellar extension → Compression of optic chiasma.
- Leads to :
  - Loss of red perception.
  - Bitemporal hemianopia.
  - Superior or bitemporal field defect.
  - Scotoma.
  - Blindness.
- Ophthalmologic evaluation :
  - Visual acuity : Snellen chart.
  - Visual field : Bedside by confrontational testing, goldmann perimetry, Amsler grid, automated quantitative perimetry.



Pituitary gland

Headache :

- Due to ↑ intrasellar pressure which stretches the dural plate.
- Headache severity does not correlate with the size of the adenoma or the presence of suprasellar extension.

Invasion through palatal floor :

- Bony invasion may occur through the sellar floor to the sphenoid sinus.
- Aggressive tumors rarely invade the palate roof and cause nasopharyngeal obstruction, infection and CSF leakage.

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Pituitary stalk compression :

Pituitary stalk compression by intrasellar mass → Compress the portal vessels → Disrupting pituitary access to hypothalamic hormones and dopamine → Hyperprolactinemia (Even with a hormonally inactive mass) → Later, concurrent loss of other pituitary hormones.

Stalk section phenomenon :

Seen with trauma, whiplash injury with posterior clinoid stalk compression, skull base fractures.

Lateral mass invasion :

- Lateral mass invasion → may impinge on the cavernous sinus → Cranial nerve III, IV, VI, V-1 (Ophthalmic), V2 (maxillary) palsies.
- Diplopia, ptosis, ophthalmoplegia and decreased facial sensation.

Temporal and frontal lobe involvement :

Uncinate seizures, personality disorders and anosmia (Rare).

Hypothalamic involvement :

- Precocious puberty or hypogonadism.
- Diabetes insipidus (Adypsic).
- Sleep disturbances.
- Dysthermia.
- Appetite disorders.

Features of sellar mass lesions :	
Impacted structure.	Clinical impact.
Pituitary gland.	Hypogonadism.
	Hypothyroidism.
	Growth failure, adult growth hormone deficiency.
	Hypoadrenalism.
	Hyperprolactinemia (stalk compression).
Optic chiasma.	Loss of red perception.
	Bitemporal hemianopia.
	Superior or bitemporal field defect.
	Scotoma.
	Blindness.
Hypothalamus.	Temperature dysregulation.
	Appetite and thirst disorders.
	Obesity.
	Diabetes insipidus.
	Sleep disorders.
	Behavioral dysfunction.
	Autonomic dysfunction.
Cavernous sinus.	Ophthalmoplegia with or without ptosis or diplopia.
	Facial numbness.
Frontal lobe.	Personality disorder.
	Anosmia.
Brain.	Headache.
	Hydrocephalus.
	Psychosis.
	Dementia.
	Laughing seizures.

Neuroimaging

00:10:22

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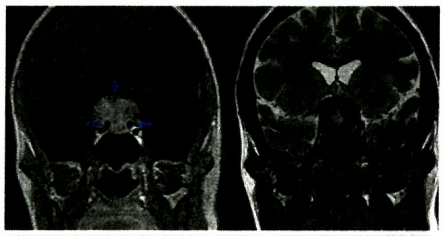
Gross features of pituitary gland :

- Pituitary gland height : 6 mm in children to 8 mm in adults.
- Pituitary gland may transiently enlarge during adolescence, pregnancy and postpartum.
- During pregnancy : 10 to 12 mm, and the stalk is 4 mm.
- Upper aspect : Flat or slightly concave.
- Stalk is midline and vertical.
- Empty sella or partial empty sella : Height <4 mm.



Pituitary macroadenoma on MRI

Features based on MRI :

- Choice of investigation : MRI sella with dynamic contrast.
- MRI taken before and after administration of gadolinium.
- Adenoma density is usually lower than that of surrounding normal tissue on T1-weighted imaging, and the signal intensity increases with T2-weighted images.
- Posterior pituitary lobe exhibits a discrete bright spot of high signal intensity on T1-weighted images, which declines with age.
- Slice thickness should be less than 3 mm to obtain a pixel of 1 mm.
- After gadolinium injection, microadenomas usually appear hypointense due to compromised microadenoma vasculature.
- Flip flop phenomena : Due to compromised vasculature, gadolinium washout is delayed, hence, delayed hyperintensity is seen when rest of the gland appears hypointense.
- CT scan : To assess extent of bony erosion or the presence of calcification.
- Thickened stalk : Seen in hypophysitis, granuloma, germinoma or chordoma.
- Meningiomas often are associated with bony hyperostosis, craniopharyngiomas may have calcifications and are usually hypodense on T2-weighted images.
- Gliomas are hyperdense on T2-weighted images.

Significance of CT scan in pituitary adenoma :

- Visualization of bony structures, including the sellar floor and clinoid bones and identifies bony invasion.
- Recognizes calcifications that characterize craniopharyngiomas, meningiomas and rarely aneurysms that are not evident on MRI.
- Hemorrhagic lesions, metastatic deposits, chordomas and evidence of calcification.

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Receptor imaging :

Radiolabeled D2 receptor antagonist by using 123I-iodobenzamide single-photon emission scanning :

- Prolactinomas express dopamine 2 (D2) receptors.
- Hence, used to differentiate between non functioning pituitary adenoma (NFPA) and prolactinoma.

Radiolabeled indium-pentetreotide scan :

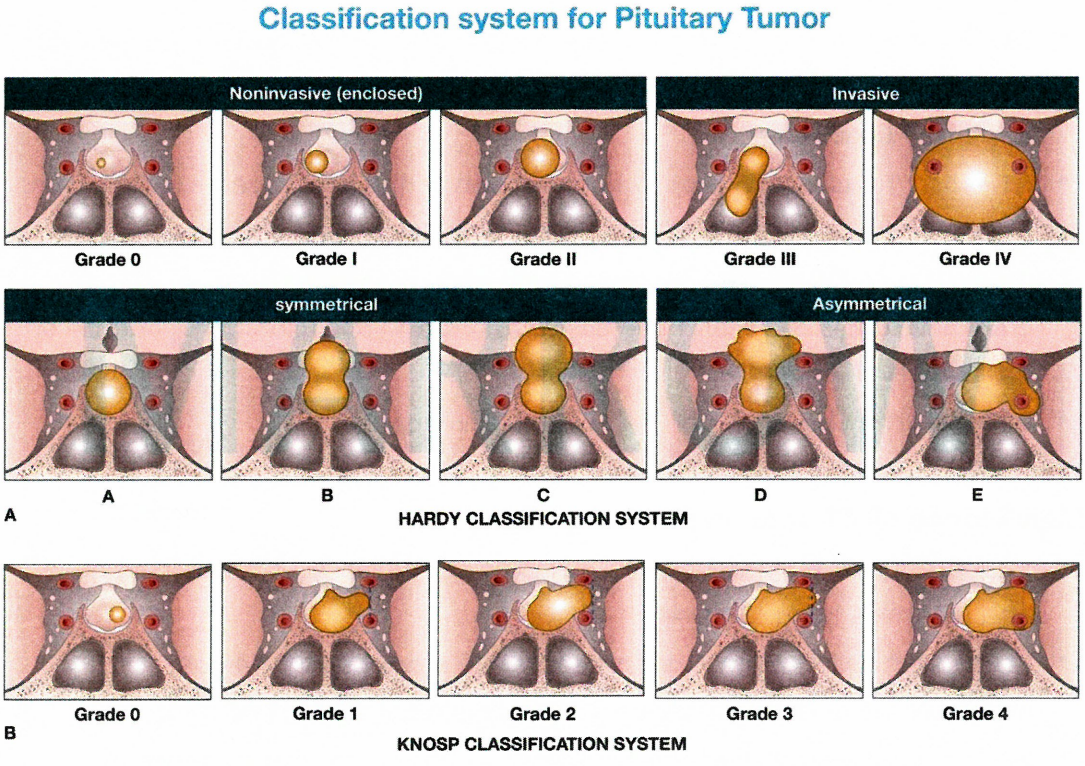
- Most pituitary adenomas express somatostatin receptor subtypes to a varying degree.

Single-photon emission CT (SPECT) :

- Sensitivity is about 1 cm, and it also detects normal pituitary.
- Hence limited for pituitary tumor detection, but it may be helpful for ectopic ACTH-secreting tumors.

Classification of pituitary tumors 00:19:58

Hardy's : Sellar and suprasellar extension.
Knosp's : Cavernous sinus invasion.
Elster.



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Hardy classification :

Non-invasive vs invasive :

Grade 0 : Tumor within the sella and contour maintained.

Grade I : Within the sella but slight bulge (+).

Grade II : Enlarged but confined to the sella.

Grade III : Localised invasion.

Grade IV : Diffuse destruction.

Based on suprasellar extension :

A : Extension towards the suprasellar skull.

B : Extension upto the 3rd ventricle.

C : Entire 3rd ventricle is involved.

D : Intracranial extradural involvement.

E : Extracranial extradural involvement.

Knosp's classification :

With respect to cavernous sinus invasion.

Grade 0 : No invasion.

Grade 4 : Encasement of internal carotid artery.

Note :

Encasement : Internal carotid artery involved $\geq 180^{\circ}$.

Abutment : Internal carotid artery involved $\leq 180^{\circ}$.

Evaluation 00:24:16

Ophthalmologic evaluation :

- Bitemporal hemianopia :
  - more common.
  - more pronounced superiorly.
  - D/t compression of the ventral optic chiasma, nasal ganglion cell fibres.
- Homonymous hemianopia : Postchiasmal compression.
- Monocular temporal field loss : Prechiasmal compression.

Laboratory investigation :

To assess functionality and deficiency :

- Serum prolactin (PRL)/basal prolactin.
- 8 AM cortisol/ 24-h urinary free cortisol (UFC) and/or overnight oral dexamethasone (1 mg) suppression test.

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- Thyroid function tests : T4, TSH.
- Na/K.
- Insulin-like growth factor (IGFI).
- LH/FSH.

Screening Tests for Functional Pituitary Adenomas		
	TEST	COMMENTS
Acromegaly	Serum IGF-1 Oral glucose tolerance test with GH obtained at 0, 30, and 60 min	Interpret IGF-1 relative to age- and sex-matched controls Normal subjects should suppress growth hormone to <1 µg/L
Prolactinoma	Serum PRL	Exclude medications MRI of the sella should be ordered if PRL is elevated
Cushing's disease	24-h urinary free cortisol Dexamethasone (1 mg) at 11 P.M. and fasting plasma cortisol measured at 8 A.M. Late night salivary cortisol ACTH assay	Ensure urine collection is total and accurate Normal subjects suppress to <5 µg/dL Distinguishes adrenal adenoma (ACTH suppressed) from ectopic ACTH or Cushing's disease (ACTH normal or elevated)
Gonadotropinoma	Baseline FSH, LH, free α subunit, ovarian hyperstimulation, estrogen (females), testosterone (males) TRH stimulation test with assays for LH, FSH, free α subunit, free LHβ, free FSHβ subunits	Rare; more commonly nonfunctioning adenomas Consider screening for hypopituitarism; Some gonadotropinomas exhibit an inappropriate gonadotropin response to TRH
TSH-producing adenoma	Free T_4, free T_3, TSH, free α subunit	Key feature is an inappropriately normal or high TSH in the setting of elevated free T_4 and T_3

Histologic evaluation :

Immunohistochemical staining after transsphenoidal surgery for :

- Hormones : Hormone studies are equivocal and in cases of clinically non-functioning tumors.
- Cell-type specific transcription factors.

Treatment 00:30:45

Usually pituitary adenomas are benign and slow growing tumors.

Goals :

- Normalization of hormone secretion.
- Amelioration of symptoms and signs.
- Shrinkage of tumor masses.
- Relief of adjacent structure compression.
- Restoration of pituitary function.
- Prevention of recurrence.

Treatment options :

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- Transsphenoidal surgery.
- Stereotactic radiotherapy.
- Novel therapeutic agents.

Transsphenoidal surgery :

- Desired surgical approach for pituitary tumors.
- Transcranial approaches : For invasive suprasellar mass surrounding the frontal or middle fossa or the optic nerves or invading posteriorly behind the clivus.
- Intraoperative microscopy helps in visual distinction between adenomatous and normal tissue.
- Surgical decompression and resection done in cases of :
  - Expanding pituitary mass.
  - Asymptomatic/headache.
  - Progressive visual field defects.
  - Cranial nerve palsies.
  - Hydrocephalus.
  - Intrapituitary hemorrhage/apoplexy.
- Whenever possible, the pituitary mass lesion should be selectively excised.
- Total hypophysectomy may be indicated if :
  - No hypersecreting mass lesion is clearly discernible.
  - multifocal lesions are present.
  - Remaining non-tumorous pituitary tissue is necrotic.

Complications :

- Operative mortality rate is ~1%
- Transient diabetes insipidus and hypopituitarism : Occur in up to 20%.
- Cranial nerve damage.
- Nasal septal perforation.
- Visual disturbances.
- CSF leaks occur in 4%.
- Less common complications : Carotid artery injury, hypothalamic damage and meningitis.

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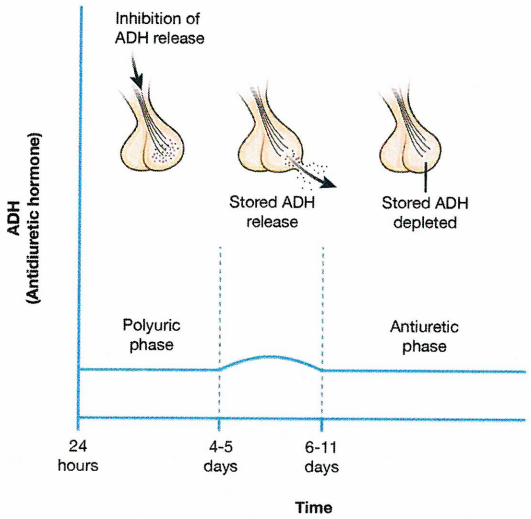
Post operative diabetes insipidus (DI) :

Transient DI (25%)	Permanent (20%)	Triphasic
• Within 24-48 hours. • Resolves in few days. • Due to axonal shock. • Temporary dysfunction.	• High stalk injury. • Closer the lesion to the magnocellular cell bodies in the hypothalamus, the more likely that the hypothalamic cell bodies will degenerate.	• Complete transection of tract. • 1st phase of DI : 5-7 days due to axonal shock. • 2nd phase : Antidiuretic phase of SIADH lasts for 2 days to 2 weeks. • 3rd phase of chronic DI : After the AVP stores are depleted.

Tri-phases of Central Diabetes insipidus after severe damage to hypothalamus or supraopticohypophyseal region



Radiation therapy :

- Primary therapy/adjunct to surgery or medical therapy.
- Because of its relatively slow onset of action, radiation therapy is usually reserved for post surgical management.
- Types :
  a. Conventional radiation : Total of <50 Gy (5000 rad) is given as 180-cGy (180- rad) fractions divided over ~6 weeks.
  b. Stereotactic radiosurgery : Large single high-energy dose from a cobalt-60 source (Gamma Knife), linear accelerator or cyclotron.

Complications :

- Transient nausea, weakness, alopecia, loss of taste and smell.
- ≥50% of patients develop loss of GH, ACTH, TSH and/or gonadotropin secretion within 10 years, usually due to hypothalamic damage.

- Optic neuritis : Approximately 2% cases.
- Risk of developing a secondary tumor after conventional radiation is 1.3% after 10 years and 1.9% after 20 years.

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medical management :

- Prolactinomas : Dopamine agonists.
- Acromegaly : Somatostatin receptor ligands (SRLs) and GH receptor antagonist.
- TSH-secreting tumors : SRLs and occasionally dopamine agonists.
- ACTH-secreting tumors : SRLs, adrenal-directed therapy.

Sellar masses 00:39:23

In hypothalamic regions :

- Anterior and preoptic hypothalamic regions : Paradoxical vasoconstriction, tachycardia and hyperthermia.
- Ventromedial hypothalamic nuclei involved : Hyperphagia and obesity seen.
- Preoptic nuclei : Central osmoreceptors → Polydipsia and hypodipsia.
- Central hypothalamus : Stimulate sympathetic neurons → ↑Catecholamine and cortisol levels → Cardiac arrhythmias, hypertension and gastric erosions.

Craniopharyngiomas :

- Benign, locally invasive, suprasellar cystic masses.
- Often large, cystic, and locally invasive.
- Derived from Rathke's pouch.
- Partially calcified : Seen on skull x-ray and CT images.
- Over 60% arise from within the sella, and others arise from parasellar cell rests.

Epidemiology :

- more than half of all patients present <20 years.
- Bimodal peak :
  - 5-14 years of age.
  - Later at 50-74 years.
- 80-90% of all pituitary tumors in children : Craniopharyngioma.
- Comprises of 15% of all intracranial tumors in children.

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Clinical features :

- Hypopituitarism (90% cases).
- Diabetes insipidus (10%).
- About half of affected children present with growth retardation.
- When intra-sellar, can be distinguished from pituitary adenomas by separate visible rim of normal pituitary tissue.
- Cystic mass filled with cholesterol-rich viscous fluid which may leak into the CSF → Aseptic meningitis.

Types :

i. Adamantinomatous form :
   - WNT/ beta catenin mutation.
   - Seen in children.

ii. Papillary forms :
   - BRAF mutation.
   - Seen in adults.

Investigations :

- MRI head with contrast :
  - Neuroimaging of choice.
  - MRI is generally superior to CT for evaluating cystic structure and tissue components of craniopharyngiomas.
- CT scan : To define calcifications and invasion into surrounding bony structures and sinuses.

Treatment :

- Transcranial or transsphenoidal surgical resection followed by postoperative radiation of residual tumor.
- In the absence of radiotherapy, 75% of craniopharyngiomas recur and 10-year survival is <50%.
- BRAF inhibitors (Dabrafenib or vemurafenib) either alone or in combination with MEK inhibitors (Trametinib or cobimetinib).
  Craniopharyngiomas (Particularly papillary) are associated with activated BRAF V600E mutations.

Post operative complications :

- Hyperphagia and obesity post surgery.
- Narcolepsy.

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- Diabetes insipidus, adipsic hypernatremia.
- Recurrence (20%).

Rathke's cysts :

- Developmental failure of Rathke's pouch obliteration.
- Usually anterior and intermediate lobes are involved.
- Small (<5 mm) cysts entrapped by squamous epithelium and are found in ~20% at autopsy.
- Do not grow usually.
- Often diagnosed incidentally.
- 1/3rd present in adults with compressive symptoms : Diabetes inspidus/ hyperprolactinemia.

Pituitary metastases :

- Blood-borne metastatic lesions.
- Usually from breast cancer (m/c), lung, gastrointestinal, primary or metastatic lymphoma, leukemias and plasmacytomas.
- Almost exclusively in the posterior pituitary → Leads to DI.
- Diagnosis : Histologic examination of excised tumor tissue.

Hypothalamic hamartomas :

- From astrocytes, oligodendrocytes, and neurons.
- May overexpress GnRH, GHRH, CRH.
- C/F :
  - Laughing-associated seizures (Gilastic seizure).
  - Pallister-Hall syndrome :
    Craniofacial abnormalities, imperforate anus, cardiac, renal, and lung disorders, and pituitary failure.
    Mutations in the carboxy terminus of the GLI3 gene.

Germinomas or GCT :

- Extra sellar tumors arising from pineal and neurohypophysis region.
- Infancy, 2nd decade.
- Clinical features :
  - DI.
  - Short stature.
  - Puberty or movement disorders.
  - Serum HCG, CSF HCG, AFP ↑.

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- Treatment :
  - Radiotherapy.
  - Radiotherapy + Chemotherapy.
- Associations : ↑HCG leads to gonadotropin independent isosexual puberty (GISP) in males.
- Any enlargement in pineal gland after 1 year should arise suspicion of pineal mass lesion.

One liners :

- Sella chordomas : Bony clival erosion, local invasiveness and calcification.
- Arachnoid cysts : Isointense with CSF.
- Meningiomas : Isodense on T1 & T2 + Calcification or bony erosion.
- Histiocytosis X : DI, exophthalmos, and punched out lytic bone lesions (Hand Schüller-Christian disease) with characteristic axillary skin rash.
- Hypothalamic gliomas : 1/3rd associated with neurofibromatosis.
- Germinomas, embryonal carcinomas, teratomas and choriocarcinomas : Arise in parasellar region and produce hCG.
- Pituitary infections : Acute pituitary abscesses and perisellar arachnoiditis seen as isointense central cavity with surrounding ring enhancement.
- Pituicytoma :
  - Benign central noninvasive suprasellar glial cell tumor.
  - Stains for vimentin, S100 protein, and glial fibrillar acidic protein.
- Hemochromatosis and hemosiderosis : Predominantly gonadotroph cell damage.

Hypophysitis :

- Pituitary stalk thickening.
- Clinical features :
  - Headache, visual field impairment, hyperprolactinemia and pituitary deficiency.
  - Secondary hypoadrenalism (ACTH deficiency).
  - Followed by hypothyroidism, hypogonadism, and GH or PRL deficiency.
- MRI reveals a pituitary mass, often indistinguishable from an adenoma.
- Treatment :
  - High dose glucocorticoids is the mainstay, often resolving the sellar mass and improving endocrine dysfunction.
  - Recurrences are reported in over 40%.