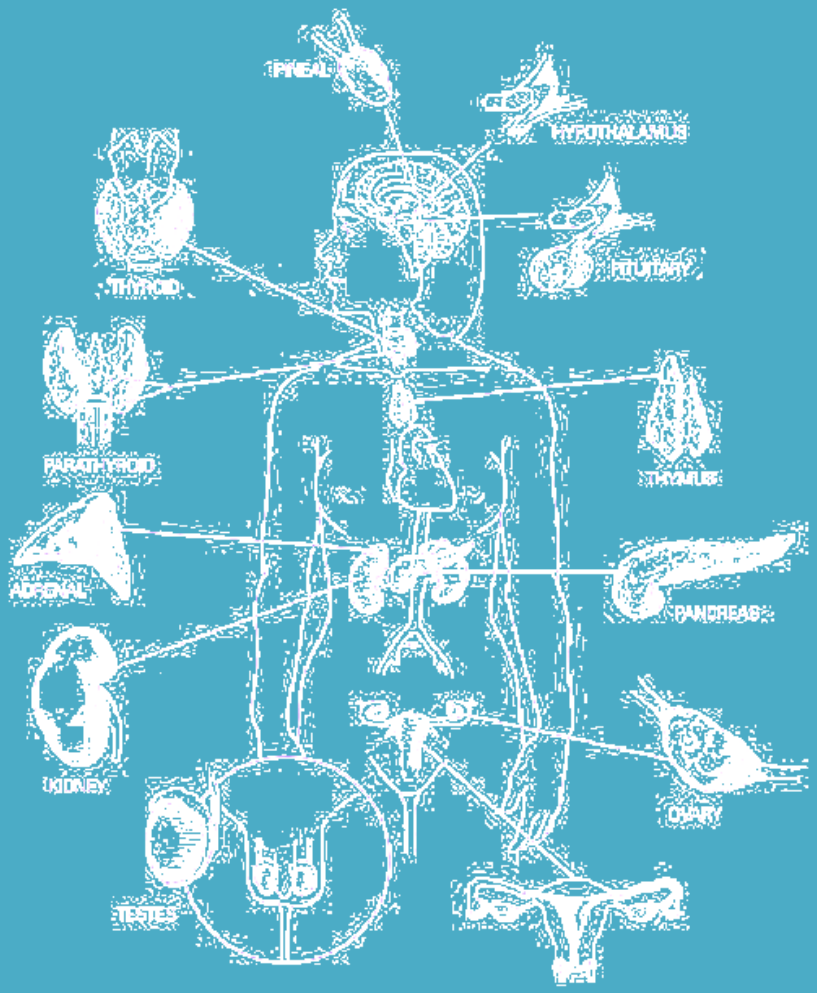
MEDICINE TEAM

431 – Endocrine Block - 2013



ANTERIOR PITUITARY INSUFFICIENCY

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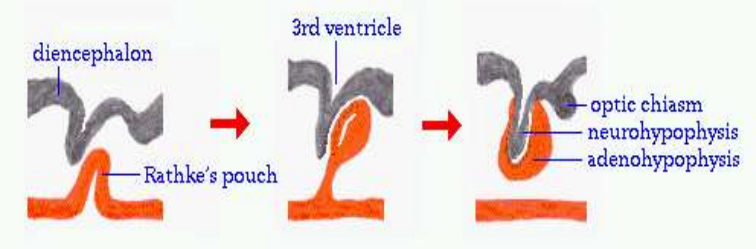
Anterior Pituitary insufficiency

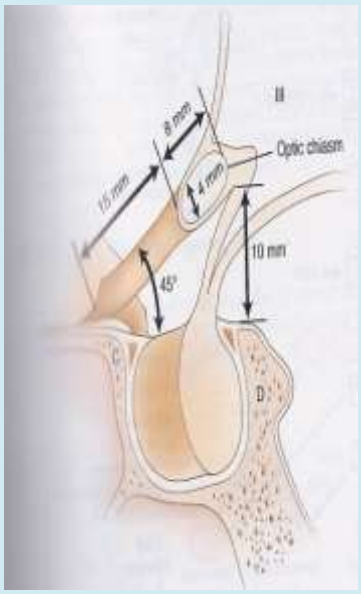
- Important
- Student's notes
- Notes was in the notes box in Doctors' slides

Objectives:

- ✓ Basic Embryology, Anatomy and physiology
- ✓ Non-functional pituitary tumours mass-effect
- ✓ Prolactin secreting cell disorder: prolactinoma
- ✓ Growth hormone secreting cell disorder: acromegaly
- ✓ ACTH secreting cell disorders: cushing's
- ✓ TSH secreting cell tumor: TSHoma
- ✓ Gonadotropin secreting cell disorder

Embryology	Anterior pituitary is recognizable by 4- 5th wk of gestation
	Full maturation by 20th wk
	• Anterior Pituitary developed from Rathke's pouch, Ectodermal evagination of oropharynx & Migrate to join neurohypophysis • Portion of Rathke's pouch →→ Intermediate lobe • Remnant of Rathke's pouch cell in oral cavity →→ pharyngeal pituitary • Posterior pituitary from neural cells as an outpouching from the floor of 3rd ventricle • Pituitary stalk in midline joins the pituitary gland with hypothalamus that is below 3rd ventricle  • Development of pituitary cells is controlled by a set of transcription growth factors like pit-1, Prop-1, Pitx2

Anatomy



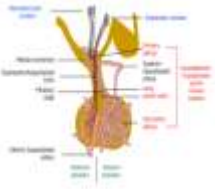
Lies at the base of the skull as sella turcica

Roof is formed by diaphragma sellae
* Diaphragma sella is formed by a reflection of dura matter preventing CSF from entering the sella turcica by this diaphragm

Floor by the roof of sphenoid sinus

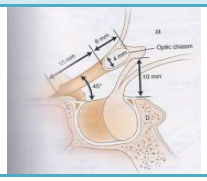
Pituitary stalk and its blood vessels pass through the diaphragm
*Normal pituitary stalk length 5- 7 mm , 2-3 mm in diameter

Pituitary gland measures 15 X 10 X 6 mm, weighs 500 mg but about 1 g in women
*Height is 5-7 mm and 10 mm lateral dimension, height is 10. superior, middle supply ant. Pituitary. Inferior supply stalk and post pituitary artery



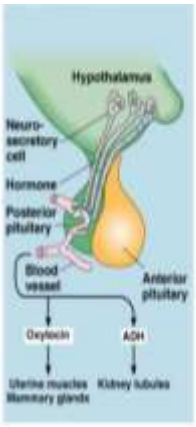
Blood supply : Superior, middle, inferior hypophysial arteries (internal carotid artery) running in median eminence from hypothalamus.

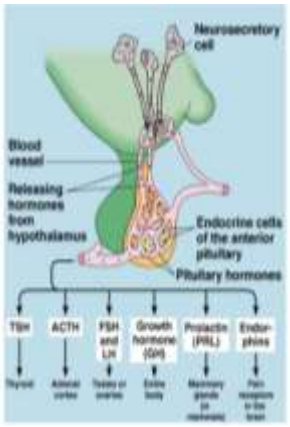
Venous drainage:
To superior and inferior petrosal sinsuses to jugular vein

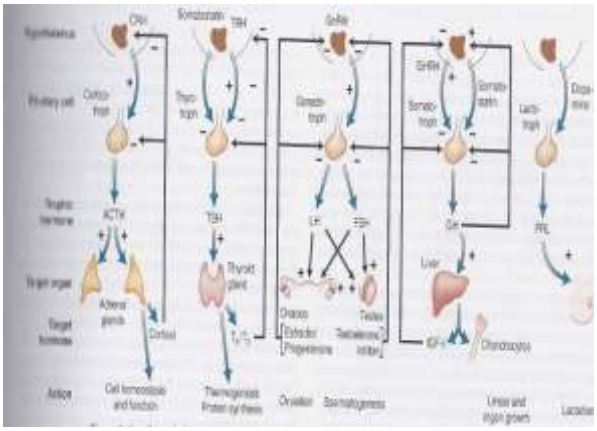


Optic chiasm lies 10 mm above the gland and anterior to the stalk

❖ Hypothalamic stimulatory hormones :





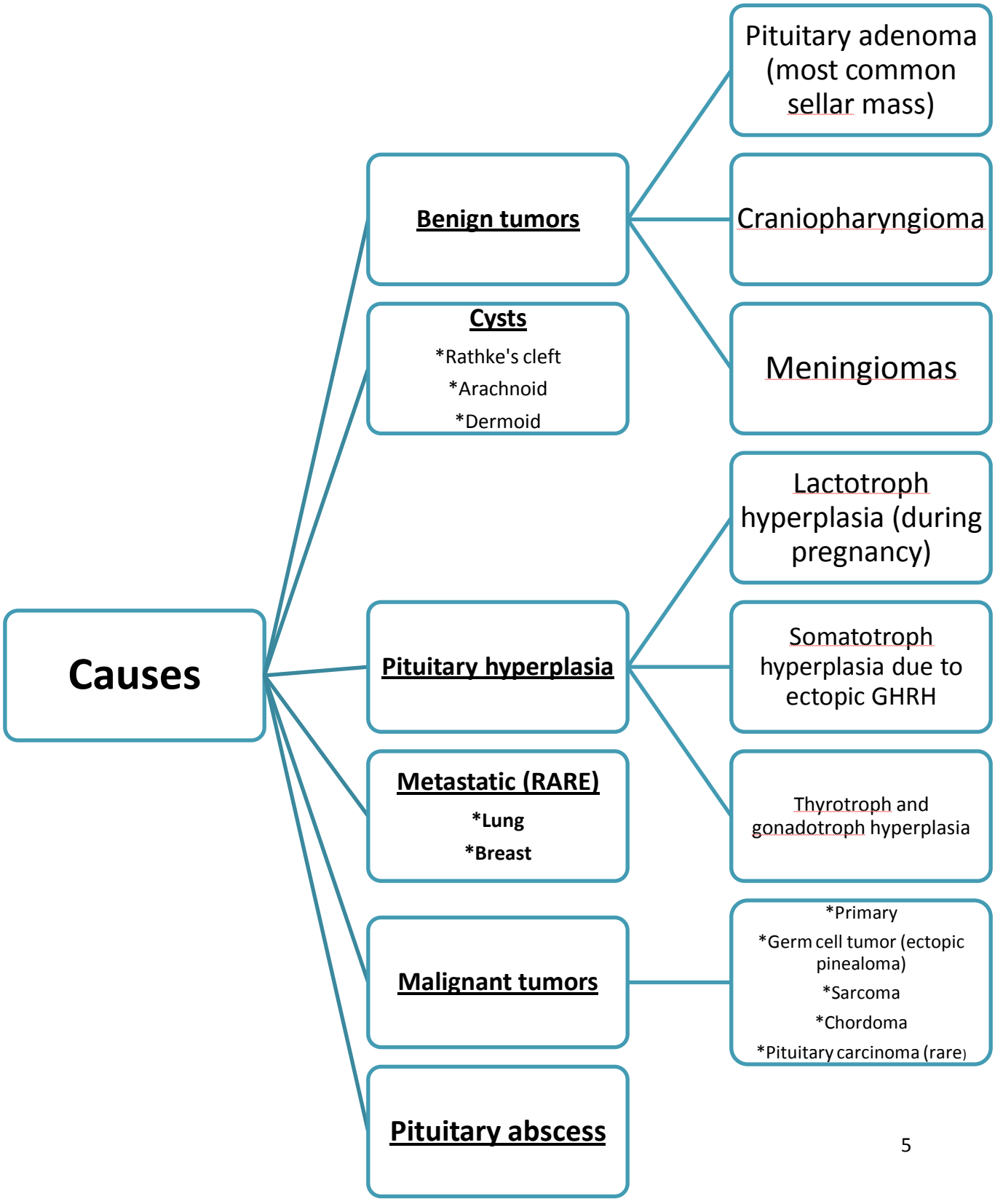


Corticotropin-releasing hormone - 41 amino acids; released from paraventricular neurons as well as supraoptic and arcuate nuclei and limbic system	**Adrenocorticotropic hormone -** basophilic corticotrophs represent 20 percent of cells in anterior pituitary; ACTH is product of proopiomelanocortin (POMC) gene
	Melanocyte-stim hormonee POMC product
	Endorphins - also products of POMC gene
Growth hormone-releasing hormone - two forms, 40 and 44AA	**Growth hormone** - acidophilic somatotrophs represent 50% of cells in anterior pituitary
Gonadotropin-releasing hormone - 10 amino acids; mostly released from preoptic neurons	**Luteinizing hormone and follicle-stimulating hormone** - gonadotrophs represent about 15 % of anterior pituitary cells
Thyrotropin-releasing hormone - three amino acids; released from anterior hypothalamic area	**Thyroid-stimulating hormone -** thyrotropes represent about 5 percent of anterior pituitary cells
Prolactin-releasing factors (serotonin acetylcholine, opiates, &estrogens)	**Prolactin - lactotrophs** represent 10 to 30 percent of anterior pituitary cells

❖ Hypothalamic inhibitory hormones :

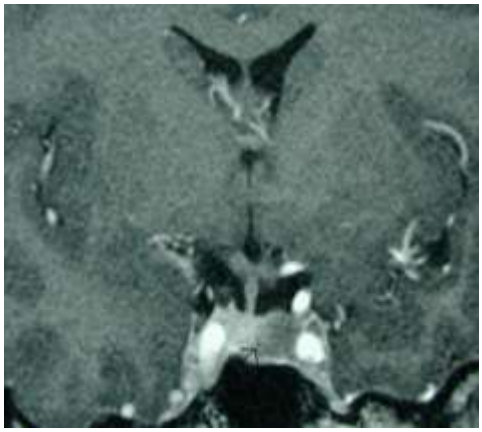
Somatostatin - 14 amino acids	**Inhibits the release of growth hormone**
Prolactin-inhibiting factors - includes dopamine	Major prolactin control is inhibitory

❖ Sellar mass :


Causes
Benign tumors
Pituitary adenoma (most common sellar mass)
Craniopharyngioma
Meningiomas
Cysts
*Rathke's cleft
*Arachnoid
*Dermoid
Pituitary hyperplasia
Lactotroph hyperplasia (during pregnancy)
Somatotroph hyperplasia due to ectopic GHRH
Thyrotroph and gonadotroph hyperplasia
Metastatic (RARE)
*Lung
*Breast
Malignant tumors
*Primary
*Germ cell tumor (ectopic pinealoma)
*Sarcoma
*Chordoma
*Pituitary carcinoma (rare)
Pituitary abscess

Other causes:

- **Neurologic symptoms (most common)**
  - ✓ Visual impairment
  - ✓ Headache
  - ✓ Other (including diplopia, seizures, and CSF rhinorrhea)
- **Incidental finding**
  - ✓ When an imaging procedure is performed because of an unrelated symptom
- **Hypopituitarism**
  - ✓ Biochemical evidence (most common)
  - ✓ Clinical symptoms (less common, but include oligomenorrhea or amenorrhea in women, decreased libido and/or erectile dysfunction in men)



← Left side microadenoma post contract

❖ Evaluation of Pituitary mass :

- Pituitary adenoma: 10 % of all pituitary lesions
- Genetic-related
- MEN-1, Gs-alpha mutation, PTTG gene, FGF receptor-4
- Pituitary incidentaloma: 1.5 -31% in autopsy (prevalence)
  - 10 % by MRI most of them < 1 cm

*Guanine nucleatide stimulatory protein gene found in 40 % of somatotroph adenoma/ inactivation mutation in tumor supressing gene in men 1.

❖ Assessment of pituitary function :

* Baseline: TSH, FT4, FT3, LH, FSH, Prolactine, GH, IGF-I, Testosterone, Estradiol
* MRI brain (most important assessment)
* Neuropthalmic evaluation of visual field

1. Non-Functional Adenoma.

- No signs and symptoms of hormonal **<u>hypersecretion</u>**
- 25 % of pituitary tumour
- Needs evaluation either micro or macroadenoma
- Average age 50 – 55 yrs old, more in male

❖ **Presentation of NFPA**:

- As incidentaloma by imaging
- Symptoms of mass effects (mechanical pressure)
- Hypopituitarism (mechanism)
- Gonadal hypersecretion

*Mass effect tumour expansion lateral compressing cavernous sinus causing cranial nerve palsy like double vision, stretching meninges causing headache, or pushing temporal lobe causing seizure, pushing optic chiasm or headache from apoplexy. Hypopituitarism from suprasellar mass pushing stalk and cutting portal blood supply and hypothalamus signal to pituitary

Table 2
Clinical characteristics of NFPA patients.

	Nomikos et al[15]	Losa et al[16]	Chang et al[17]	Ferrante et al[53]	Total
Number of patients	721	491	663	295	2170
Mean age	54.2 ± 19	–	53 (median)	50.4 ± 14.1	
Gender (M/F)	401/320	276/215	394/269	161/134	1232/938 (56.7% M)
Incidental finding	57 (7.9%)	57 (11.6%)	49 (7.4%)	–	163/1875 (8.7%)
Headaches	70 (9.7%)	–	212 (32%)	122 (41.4%)	404/1679 (24%)
Visual deficits	222 (30.8%)	287/486 (59.1%)	327 (49%)	200 (67.8%)	1036/2170 (47.7%)
Pressure on cranial nerves	–	22 (4.5%)	26 (3.9%)	–	48/1154 (4.2%)
Apoplexy	27 (3.7%)	48 (9.8%)	24 (3.6%)	–	99/1875 (5.3%)
Symptoms of Hypopituitarism	345 (47.8%)	–	342 (51.6%)	118 (40%)	805/1679 (48%)
Documented Hypopituitarism	614 (85%)		–	183 (62%)	797/1016 (78.4%)
Hypogonadism	512/659 (77.7%)	335/474 (70.7%)		128 (43.3%)	975/1261 (77.3%)
Hypoadrenalism	230 (31.9%)	115/478 (24.1%)		77 (26.2%)	422/1494 (28.2%)
Hypothyroidism	129/658 (19.6%)	116/462 (25.1%)		72 (24.5%)	317/1415 (22.4%)
Hyperprolactinemia	199 (27.6%)	251/462 (54.3%)	–	82 (27.6%)	532/1478 (35.9%)

Treatment of non-functional pituitary adenoma

Surgery	* Recurrence rate 17 % if gross removal, 40 % with residual tumour * Predictors of recurrence: young male, cavernous sinus invasion, extent of suprasellar extention of residual tumor, duration of follow up, marker; Ki-67
Observation	with annual follow up for 5 years and then as needed, visual field

	exam Q 6-12 month if close to optic chiasm. Slow growing tumour
Adjunctive therapy	Radiation therapy, Dopamine agonist and somatostatin analogue

***Tumour greater than 2 cm, visual field defect, optic chiasm compression or touching by tumor with no visual field defect, headach, suprasellar/parasellar tumor extension**

2. Functional Adenoma (Hormonal secreting).

Clinical Disease and medical therapy

Clinical disease	Hormone produced by tumor	Estimated frequency (%)	Medical therapy
Acromegaly	Growth hormone	5-10	Somatostatin analog (octreotide), growth hormone receptor blocker
Cushing's disease	ACTH	10-15	Ketoconazole (Blocks cortisol synthesis)
Gonadotroph	FSH, LH	5	None
Prolactinoma	Prolactin	20-30	Dopamine agonist (Bromocriptine, Cabergoline, Pergolide)
Null cell	None	20-25	None
Thyrotropic	TSH	<3	Somatostatin analog (Octreotide), Propylthiouracil
Other (Including mixed cell adenoma)	None	20	None

EFFECT OF PITUITARY TUMOR

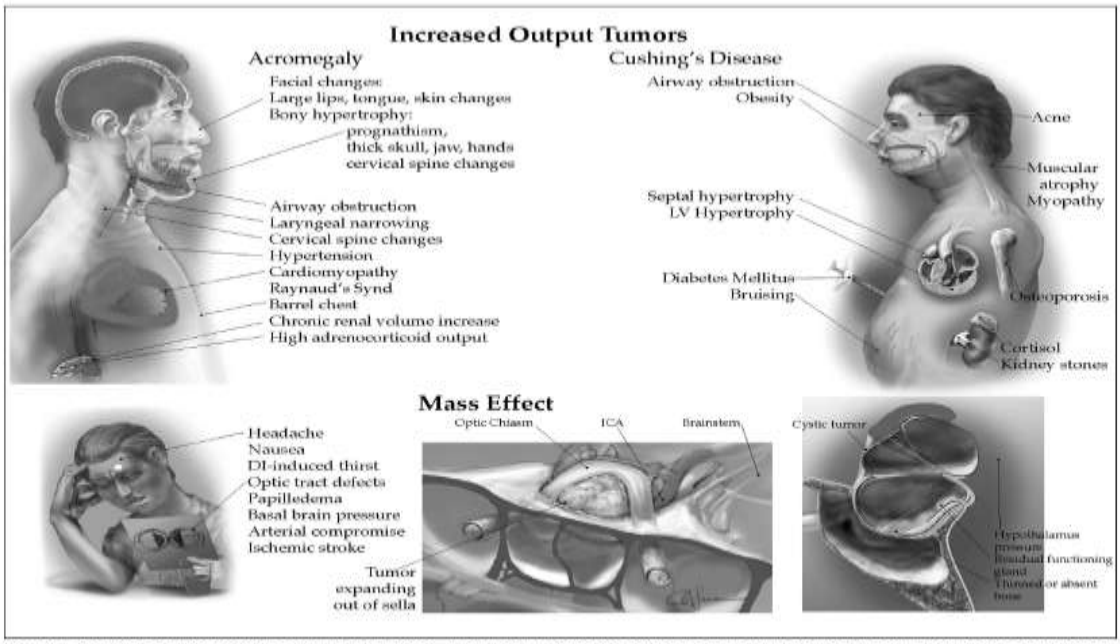
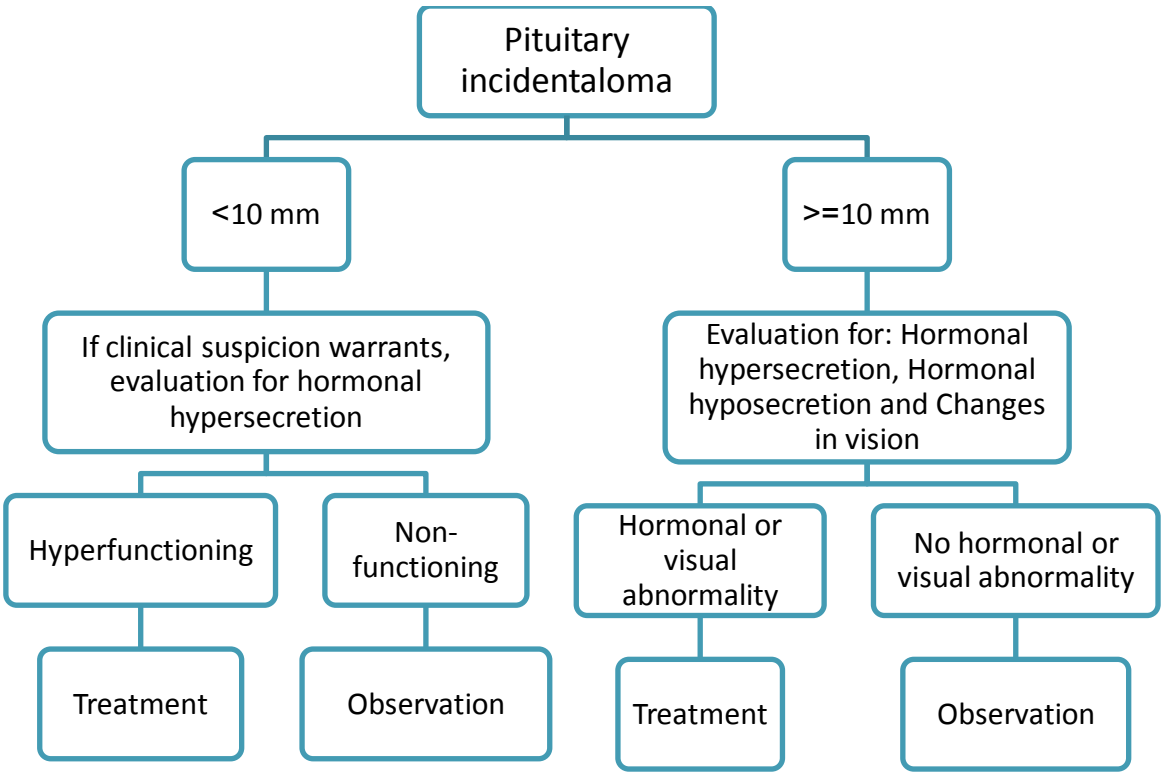


Figure 1. Systemic and mass effects of pituitary tumors. A pituitary tumor may present with wide-ranging systemic manifestations secondary to the central role of the pituitary gland in the endocrine system. Also, any expanding intrasellar mass may produce local effects secondary to pressure on adjacent structures within the brain. DI = diabetes insipidus, ICA = internal carotid artery.

❖ Approach to the patient with an incidental abnormality on MRI of the pituitary gland :



Prolactinoma

Exercises affect prolactin levels in women

- **Premenopausal women**
  - Menstrual dysfunction (oligomenorrhea or amenorrhea10 to 20 %)
  - Infertility (luteal phase abnormalities or anovulation).
  - Galactorrhea.
- **Postmenopausal women** (already hypogonadal)
  - It must be large enough to cause headaches or impair vision,
  - Incidental sellar mass by MRI.
- **Men**
  - Decreased libido and infertility.
  - Erectile dysfunction

This table was not mentioned in females' slides

Partial list of drugs known to cause hyperprolactinemia and/or galactorrhea :

Typical antipsychotics	Gastrointestinal drugs
Chlorpromazine, Clomipramine fluphenazine], prochlorperazine, thioridazine	Cimetidine (Tagamet)
Haloperidol (Haldol)	Metoclopramide (Reglan)
Pimozide (Orap)	Antihypertensive agents
Atypical antipsychotics	Methyldopa (Aldomet)
Risperidone (Risperdal)	Reserpine (Hydromox, Serpasil, others)
Molindone (Moban)	Verapamil (Calan, Isoptin)
Olanzapine (Zyprexa)	Opiates
Antidepressant agents*	Codeine
Clomipramine (Anafranil)	Morphine
Desipramine (Norpramin)	

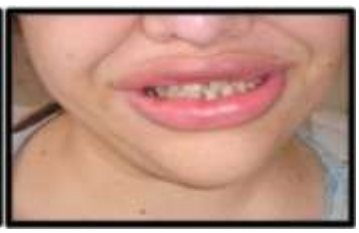
Growth Hormone

- ❖ Hyperfunctioning mass → Acromegaly
- ❖ Pituitary tumor as mass effect → Growth hormone deficiency (Short stature)

➢ **Signs of Acromegaly**

- ✓ Nose is widened and thickened
- ✓ Cheekbones are obvious
- ✓ Forehead bulges
- ✓ Lips are thick
- ✓ Facial lines are marked
- ✓ Overlying skin is thickened
- ✓ Mandibular overgrowth
- ✓ Prognathism
- ✓ Maxillary widening
- ✓ Teeth separation
- ✓ Swelling of the hands in a patient with acromegaly, which resulted in an increase in glove size and the need to remove rings.

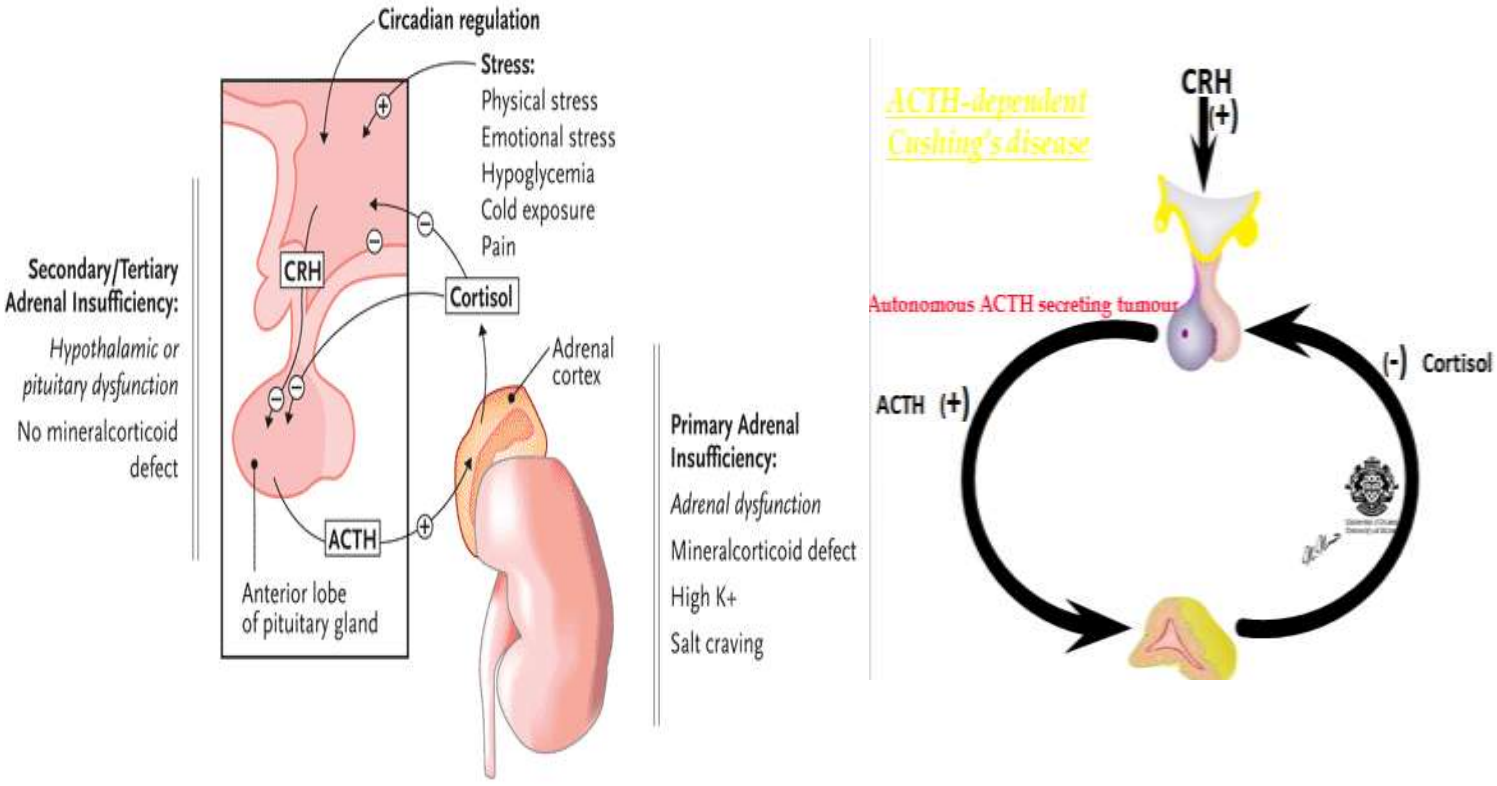




ACROMEGALY:

Diagnosis	➢ **GH level (not-reliable, pulsatile)** ➢ **IGF-I is the best screening test** ➢ **75 g OGTT tolerance test for GH suppression is the gold standered** **Other :** ✓ **Fasting and random blood sugar, HbA1c** ✓ **Lipid profile**
Complications	**1- Cardiac disease is a major cause of morbidity and mortality.** 2- 50 % died before age of 50. 3- HTN in 40%. 4- LVH in 50%. 5- Diastolic dysfunction as an early sign of cardiomyopathy.
Treatment	1-Medical: ✓ Somatostatin analogue ✓ Pegvisomant 2-Surgical resection of the tumour

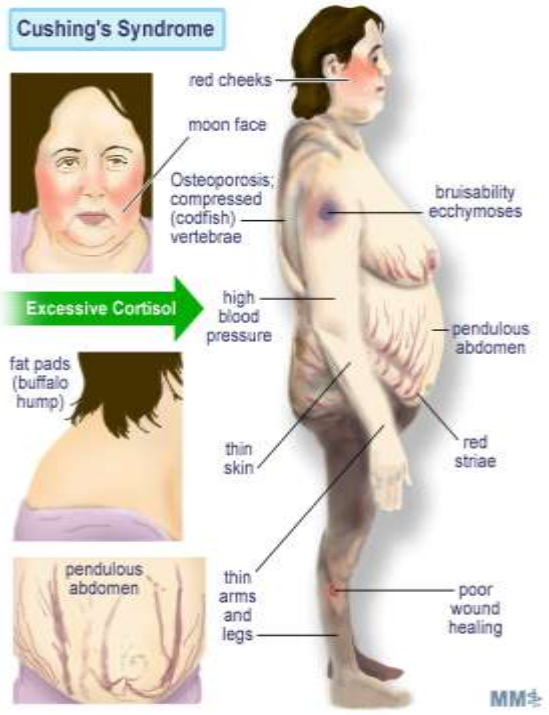
ACTH disorders



Physiology and Pathophysiology:

Normally, CRH is released by the hypothalamus to stimulate ACTH secretion by the anterior pituitary gland, then ACTH stimulate the cortisol secretion in the adrenals. A feedback mechanism from adrenal gland to both hypothalamus and pituitary gland to stop the stimulation. But in case of ***ACTH-dependent Cushing's disease*** the secretion of ACTH will be increased.

Cushing's syndrome



Diagnosis	Percent of patients
ACTH-dependent Cushing's syndrome	
Cushing's disease	68
Ectopic ACTH syndrome	12
Ectopic CRH syndrome	<<1
ACTH-independent Cushing's syndrome	
Adrenal adenoma	10
Adrenal carcinoma	8
Micronodular hyperplasia	1
Macronodular hyperplasia	<<1
Pseudo-Cushing's syndrome	
Major depressive disorder	1
Alcoholism	<<1

HPA-axis (Excessive cortisol):

HPA-axis= Hypothalamic Pituitary Adrenal Axis.

- 80 % HTN
- LVH
- Diastolic dysfunction, intraventricular septal hypertrophy
- ECG needed: high QRS voltage, inverted T-wave
- Echocardiogram preop
- OSA: 33% mild, 18% severe. Needs respiratory assessment and careful use of sedative during surgery
- Glucose intolerance in 60%, control of hyperglycemia
- Osteoporosis with vertebral fracture→→ positioning of patient in OR (50 %), 20 % with fracture
- thin skin→→ difficult IV cannulation, poor wound healing

Obstructive sleep apnea is the most common type of sleep apnea and is caused by obstruction of the upper airway. It is characterized by repetitive pauses in breathing during sleep

TSH-producing adenoma

- Very rare < 2.8 %
- Signs of hyperthyroidism
- High TSH, FT4, FT3
- Treatment: preoperative with anti-thyroid medications.

Questions:

1. **Cushing's syndrome is referred to :**
   a) Adrenal hyperfunction
   b) Adrenal hypofunction
   c) Pituitary hyperfunction
   d) Pituitary hypofunction

2. **Best screening test for acromegaly :**
   a) GH level
   b) IGF-I
   c) 75 g OGTT tolerance test for GH suppression

Answers:

1. A & C

2. B