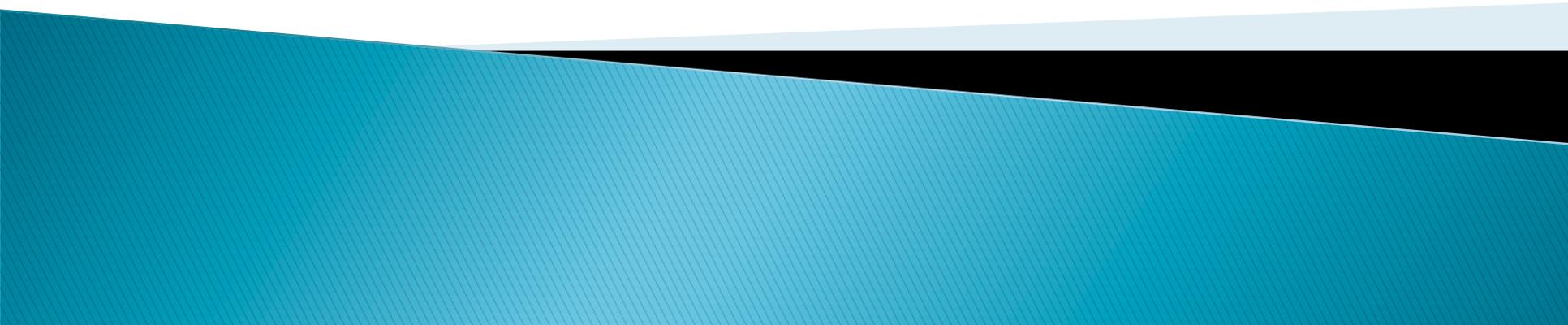


# INVESTIGATION PROTOCOLS IN PITUITARY ADENOMAS- FUNCTIONAL AND NON FUNCTIONAL



# Introduction

Pituitary gland

- Pituitary fossa

- Mass: 5 gms

- DIMENSIONS

- 7mm (Ht)

- 9mm (AP)

- 11m(transverse)

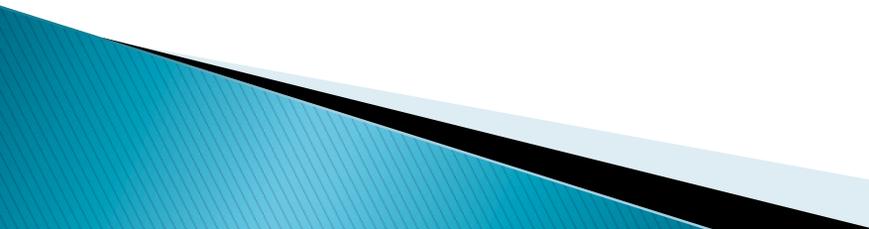
originates from Rathke's pouch and infundibulum

Cell type	hormone	Clinical syndrome	Tumor type
Somatotroph	Growth Hormone	Acromeg/gigan	Sparsely granulated GH cell
			Densely granulated GH cell
Lactotroph	Prolactin	Amen/galactor	Sparsely granulated prl
			Densely granulated prl
Somato/Lact	Gh+prl	Acro+hyperprl	Mixed GH-prl
		Acro+hyperprl	Mammo+somato
		Amen/Gal/Acro	Acido+stem cell
Corticotroph	Acth/Pomc/ B-lph/Msh	Cushings, nelson	Densely granulated acth
			Sparsely granulated acth
Gonadotroph	FSH,LH,A- Sub Unit	Hypopituitarism	Gonadotroph
Thyrotroph	TSH, A-sub Unit	Hyperthyroid/ Hypopituitarism	Thyrotroph
NULL Cell	None	Hypopituitarism	Null cell
			oncocytoma

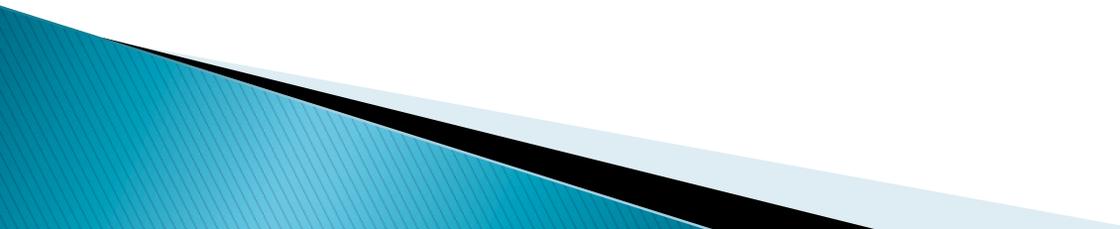
# Introduction

- ▶ 15% of intracranial tumors
- ▶ Present as incidental finding in 5–20%
- ▶ Broadly divided
  - (a) functional
  - (b) non functional

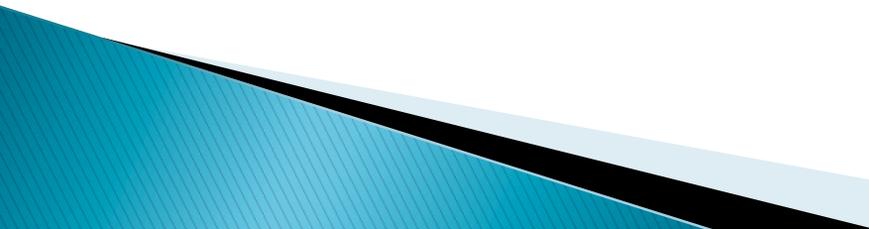
# INVESTIGATION PROTOCOL

- ▶ History and physical examination
  - ▶ Neuro- ophthalmology:  
    Acuity, field, fundus and movements
  - ▶ Hormone levels  
    Basal hormone and dynamic testing  
    Aim- hypersecretory state or insufficiency
  - ▶ Radiology      (a) X-Rays  
                    (b) MRI  
                    (c) NCCT/CECT
  - ▶ Routine blood investigation
- 

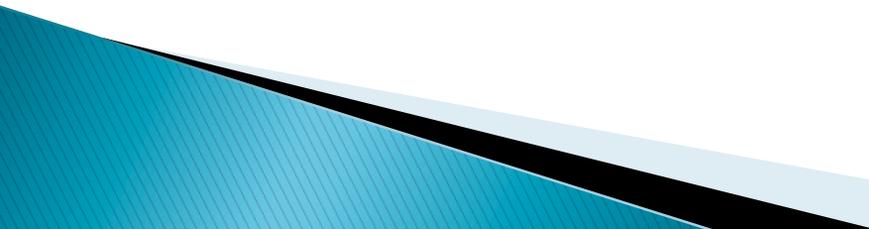
# Presentation

- ▶ Mass effect
  - ▶ Hyper secretion/ hypo secretion
  - ▶ Incidental finding
  - ▶ Apoplexy
- 

## Complete history and physical examination

- ▶ Eyes – visual acuity, visual field, fundoscopy
  - ▶ Neck– thyroid ,carotid bruit
  - ▶ Chest–gynaecomastia, galactorrhea
  - ▶ Abdomen–striae, obesity
  - ▶ Extremities–edema, enlargement
  - ▶ Skin–pigment, hair, bruises
- 

# MASS EFFECT

- ▶ Visual disturbances
    - Visual field defect usually very insidious and slowly progressive
    - Diplopia
    - Visual acuity
  - ▶ Hydrocephalus
  - ▶ Headache
  - ▶ Cranial nerve palsies
  - ▶ Raised intracranial pressure
- 

## ▶ Apoplexy

Acute presentation secondary to tumour  
haemorrhagic necrosis

- Headache
- Vomiting
- Blindness
- Ocular paresis
- Altered level of consciousness

- ▶ **Prolactin**

Galactorrhoea , amenorrhoea, osteoporosis

- ▶ **G.H**

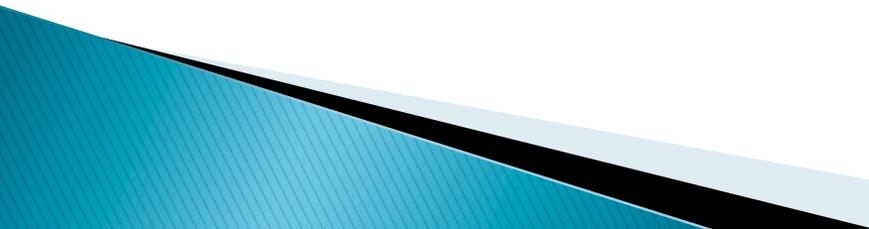
Acromegaly, organomegaly, D.M,

- ▶ **ACTH**

Cushing's disease, Diabetes mellitus, osteoporosis, obesity, hypertension

- ▶ **TSH**

Hyperthyroidism, cardiac dysrhythmia, heat intolerance



# Radiology

- ▶ X- Rays:

- Widening of sella

- Destruction of sellar floor

- Relation of median sphenoidal septum

- Aeration of sphenoid sinus– conchal  
sclerotic  
mixed

- ▶ NCCT+ CECT head/ sella with thin coronal cuts:
  - findings as seen in X-Rays
  - iso dense to adjacent brain parenchyma
  - intense contrast enhancement
  - calcifications uncommon (< 5%)
  - apoplexy– hyper density

## ▶ MRI brain:

Sagittal T1WI and coronal T1WI sellar and parasellar region with/without contrast 2.5mm thin contiguous slices and 5mm slices axial T2WI of whole brain.

Normal pituitary is iso intense to gray matter on T1WI with contrast enhancing

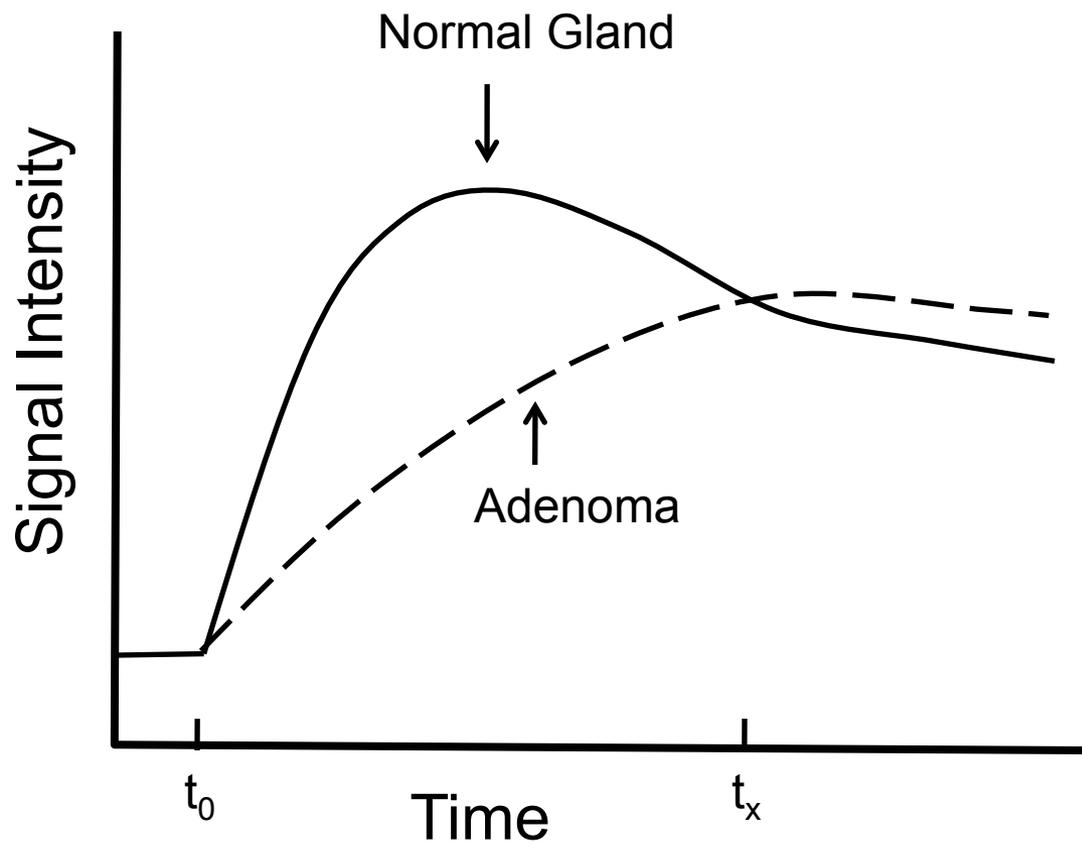
Pituitary adenoma classified based on size:

microadenoma <10mm

macroadenoma >10mm

giant pit adenoma >40mm

- ▶ **Macro adenoma** – they are hypo to isointense to gray matter on T1WI, contrast enhancing
- ▶ **Micro adenomas**– Dynamic contrast study done by 5 T1WI turbo spin 3mm thin slices repetitively at 20,40,60,80,100 sec after 10ml contrast injection at 2ml/sec.
  - Micro adenoma enhance and wash out quickly as compared to normal gland post contrast and hence appear hypointense
  - deviation of stalk
  - bulging of inferior and superior margin



# Hardy classification

- ▶ Pituitary adenoma:

- Grade 0– size < 10 mm, sella normal

- Grade 1– size < 10 mm, sella expanded

- Grade 2– size > 10 mm , sella expanded

- Grade 3– size > 10 mm, focal Destruction

- Grade 4– size > 10 mm, diffuse destruction

- Grade 5– distant spread

# Based on extension

- ▶ Suprasellar

  - 0– none

  - A– supra sellar cistern

  - B– ant recess of third ventricle obliterated

  - C– floor of third ventricle grossly displaced

- ▶ Parasellar

  - D– intracranial (intradural)

  - E– into or beneath the cavernous sinus

# Screening studies for pituitary lesion

- ▶ Hormone excess
  - serum prolactin
  - serum IGF-1
  - serum LH, FSH
  - serum  $\alpha$  sub unit
  - serum TSH
  - urinary 24 hr cortisol
- ▶ Hormone deficiency
  - serum cortisol
  - serum T4, free T3
  - serum testosterone (men)
  - serum estradiol (women)

# Dynamic test to identify pituitary hypersecretion

Dynamic stimulation/suppression testing may be useful in select cases to further evaluate pituitary reserve and/or for pituitary hyperfunction

- ▶ Acromegaly
  - Oral glucose test–
  
- ▶ Cushing's syndrome/disease–
  - (a) low dose dexamethasone
  - (b) low dose dexamethasone + CRH
  - (c) high dose dexamethasone
  - (d) Inferior petrous sampling + CRH

## Dynamic test to identify pituitary deficiency

- ▶ **ACTH** – low dose ACTH by giving 1 mcg iv and S. cortisol after 30 min less than 18 mcg/dl identifies central adrenal deficiency

# Prolactinoma

- ▶ 30 to 50% of endocrine active tumors
- ▶ Clinical features:
  - ▶ Amenorrhoea infertility, loss of libido, oligospermia
  - ▶ Galactorrhoea in 80% females and 30% men
  - ▶ Majority are microadenomas
  - ▶ 30% of them in women are self limiting

# Prolactinoma

- ▶ Prolactin

  - < 25 ng/ ml      normal

  - 25– 150ng/ml prolactinoma, stalk effect, drugs , Hypothyroid

  - > 150ng/ml– prolactinoma

- ▶ Hook effect– even large elevations will show normal PRL levels on testing due to large size of molecules. Do serial dilutions

- ▶ Not all hyperprolactinemia is due to a prolactinoma

# Causes of Hyperprolactinemia

## Medications

- Psychotropic (e.g.. haloperidol. resperidol)
- Antidepressants (e.g.. amoxapin)
- Estrogen
- Opiates
- Calcium channel blocker (veraparnil)
- Antihypertensives (a methyldopa. reserpine)
- Dopamine antagonists (domperidome. metoclopramide)

## Pituitary Pituitary adenoma

- Prolactin-secreting adenoma
- GH-secreting adenoma
- Secondary hyperprolactinemia. usually a macroadenoma

Other pituitary lesion. e.g.. inetastatic. sarcoid. aneurysm

Hypothalamic lesion

Head trauma

Pregnancy

Spinal cord lesions

Chest wall trauma

Nipple stimulation

# Cushings disease

- ▶ 15% of all pituitary adenomas in adults
- ▶ 90% microadenomas
- ▶ Common in women
- ▶ 55 % pit adenoma in children
- ▶ Clinical features:

Central obesity, purple striae, hypertension, diabetes, ecchymosis, poor wound healing, lipid abnormalities, neuropsychiatric problems

# Cushings disease

- ▶ **Best screening test**– 24 hr UFC level 95–100% sensitivity, 400 mcg/day of UFC is diagnostic.
- ▶ midnight plasma cortisol of 5.2mcg/dl is diagnostic of cushings
- ▶ **Low dose dexamethasone test**– 1 mg of dexa at 11.00 am and measurement of s. cortisol at 8.00 am
  - <5 mcg/dl– normal
  - 5–10 mcg/dl equivocal
  - >10mcg diagnostic
- ▶ **Plasma corticotropin level**–
  - >20pg/ml diagnostic
  - >10 pg/ml suggestive
  - <5pg/ml corticotroph independent

# Cushings disease

- ▶ **High dose dexamethasone suppression test**– if corticotropins  $>10$  pg/ml . 2mg of dexamethasone given every 6hrly for 2 days, if  $>69\%$  fall in 24 hr UFC (pre and post dexamethasone ) is 100% specific for CD
- ▶ **8 mg dexamethasone test** –8 mg dexamethasone is given at 11.00 pm and drop in  $>50\%$  s. cortisol indicates CD
- ▶ **Corticotropin releasing hormone stimulation test**– 1 mcg/kg CRH iv in morning, if increases  $>35\%$  corticotropin level at 15, 30 min above baseline yields 100% specificity and 93% sensitivity for CD

# Cushings disease

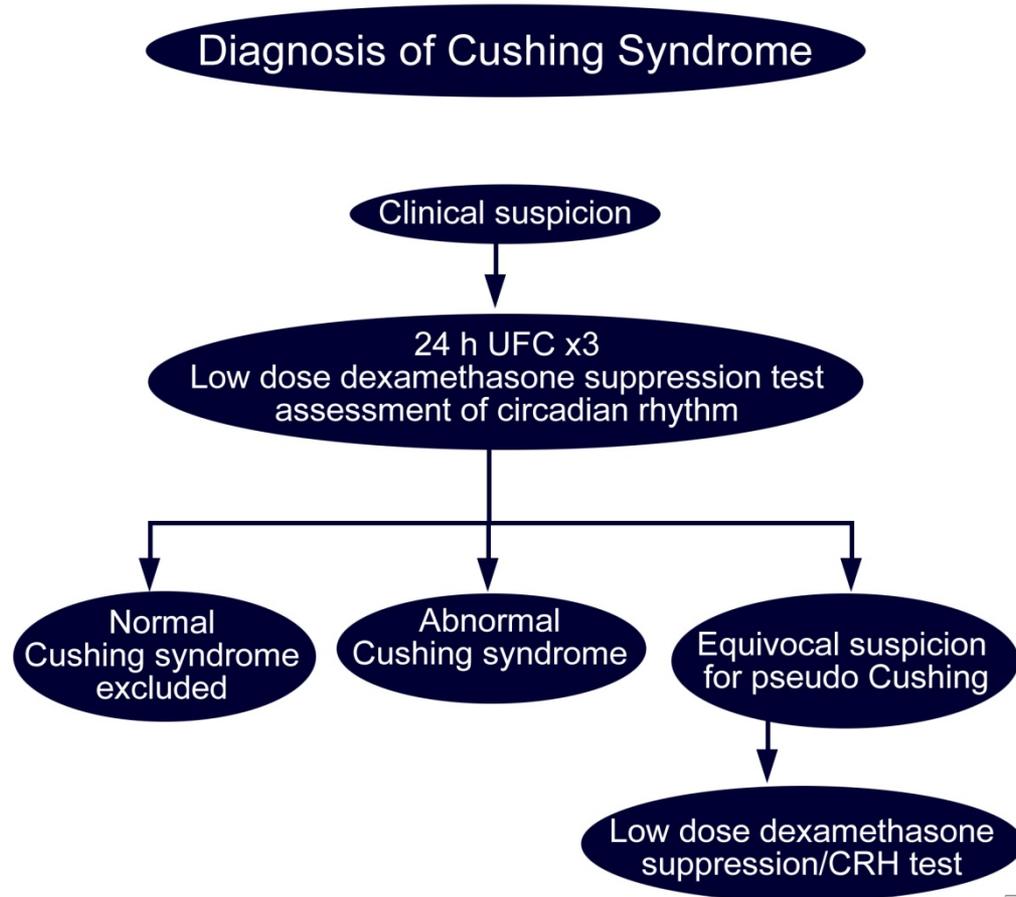
- ▶ Inferior petrosal sinus sampling
  - classical clinical and biochemical CD features with MRI negative patient
  - equivocal suppression and stimulation test

Diagnostic accuracy is 80–100% , blood samples are obtained at basal and 3,5,10 min after CRH administration and ips/ps ratio calculated

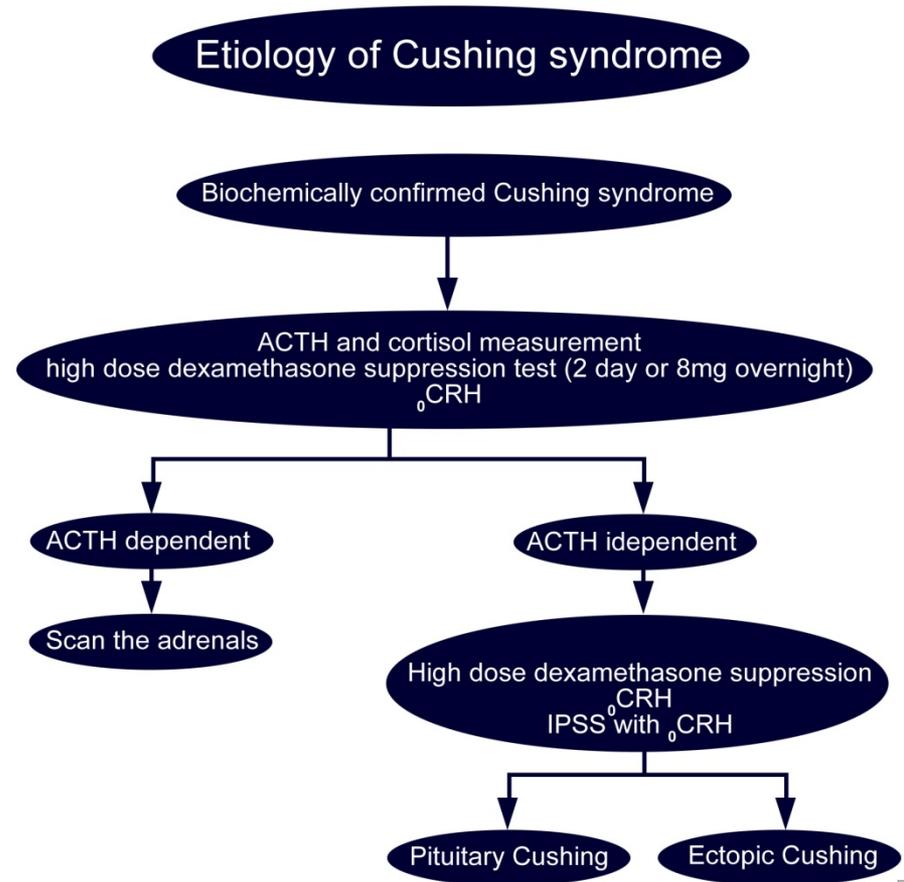
ips/ps >3      CD  
ips/ps <2      ectopic  
rarely 2–3      ectopic

IPS gradient helps in lateralization of adenoma

# Cushing's syndrome



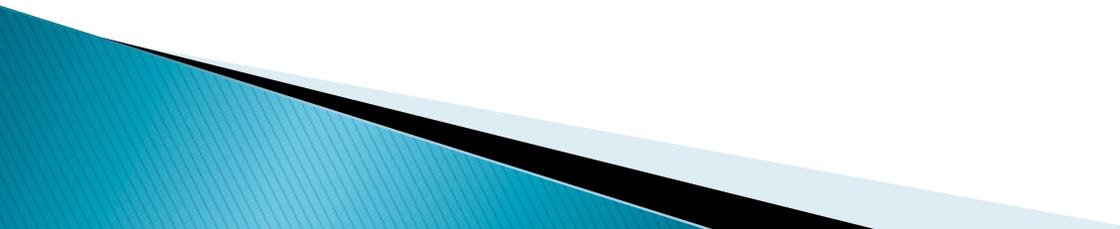
# Cushing's syndrome



# Acromegaly

- ▶ 4<sup>th</sup> decade of life
- ▶ 10.7 years
- ▶ Constitute 20% of all pituitary tumors
- ▶ Preop duration 10 years to diagnosis in adults and 3.1 years in children
- ▶ Pleuri hormonal

# ACROMEGALY

- ▶ Prepuberty–gigantism & precocious puberty
  - ▶ Pubescent–amenorrhea, hypogonadism
  - ▶ Adults–skeletal and soft tissue overgrowth and deformities, cardiac ,neuromuscular, respiratory, endocrine, metabolic complications and neoplastic transformation
- 

- ▶ **Random GH** – not useful gives false positive and false negative results
  - ▶ **Insulin like growth factor 1 (IGF-1)** – best for screening      represents average daily GH secretion
  - ▶ **Oral glucose GH suppression testing** – gold standard to confirm diagnosis :75 mg of glucose load normally suppresses GH > 2ng/ml RIA. GH nadir >2ng/ml RIA with adenoma confirms it
  - ▶ **GHRH stimulation test**
- 

# ACROMEGALY

- ▶ Chest and abdomen imaging for ectopic GHRH secreting tumors
- ▶ Empty sella shows pituitary infarction
- ▶ Scintigraphy
- ▶ Ancillary tests
  - Blood glucose, urine, cardiac and respiratory
  - Screening for colorectal neoplasia

Clinically Acromegaly, MRI pit adenoma, GH > 5ng/ml  
If GH < 5ng/ml

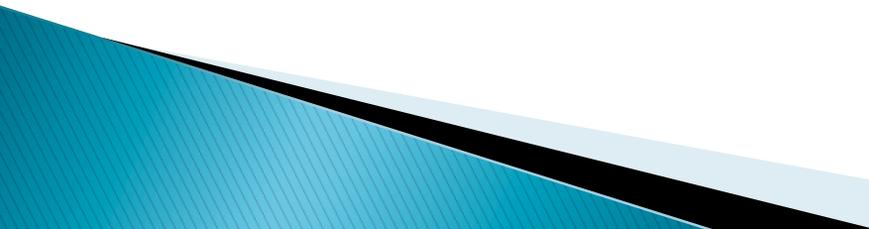


IGF-1, elevated  
If no



Oral glucose suppression test confirms it  
rarely MRI negative ,  
measure GHRH levels, CECT abd /chest

# Thyrotroph adenoma

- ▶ TSH secreting tumors
  - ▶ 1–2% of pit adenomas
  - ▶ Mixed hormonal secretion– 30%  
GH, PRL, Gonadotropins
  - ▶ 90% macroadenomas
  - ▶ Mean duration pt 9 yrs
  - ▶ Clinical features of goitre, warm skin, heat intolerance, cardiac arrhythmias and other hyperthyroid features,
- 

# Thyrotroph adenoma

- ▶ Lab investigations

TSH, Free t<sub>4</sub>, t<sub>3</sub> by direct method  
α-subunit, PRL, GH, SHB

Iodine scan/USG of thyroid

Dynamic testing with TRH

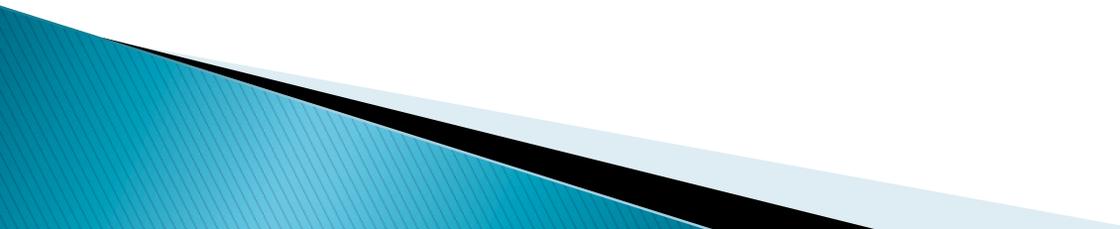
Clinical suspicion, MRI –pit adenoma, baseline  
TSH, free T4/T3, a-sub unit, PRL, GH

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graph TD; A[Clinical suspicion, MRI –pit adenoma, baseline TSH, free T4/T3, a-sub unit, PRL, GH] --> B[TSH normal, a-sub unit/TSH ratio <5.7 in normogonads, <29.1 in hypergonad, TSH elevated <0.7 in normogonads, <1.0 in hypergonads]; A --> C[MRI equivocal, TRH stimulation test];
```

TSH normal, a-sub unit/TSH ratio  
<5.7 in normogonads, <29.1 in hypergonad,  
TSH elevated <0.7 in normogonads,  
<1.0 in hypergonads

MRI equivocal, TRH stimulation test

# Gonadotropinomas

- ▶ 7–15% of pit adenomas
  - ▶ 40–50 % macroadenomas secrete gonadotropins
  - ▶ Clinical features of mass effect: visual symptoms, hypogonadism, amenorrhea, hypothyroid, hypocortisolism
- 

# Gonadotropinomas

- ▶ Lab investigations

basal hormonal levels

TRH stimulated gonadotropins, and sub units

normally causes absent FSH response and no more than 33% increase in LH and b- LH

primary hypogonadism LH,FSH elevated and don't respond to TRH

gonadotropinomas have greater than 60% increase in b-LH levels

# Multidisciplinary approach

Hormonal status–endocrinologist

Visual field –orthoptist

Monitor tumor recurrence –radiologist

Clinical observation–neurosurgeon

Blood test–biochemist

**THANK YOU**

