

Endocrine block (ENDO 225) 2019

# Anterior Pituitary Disorders

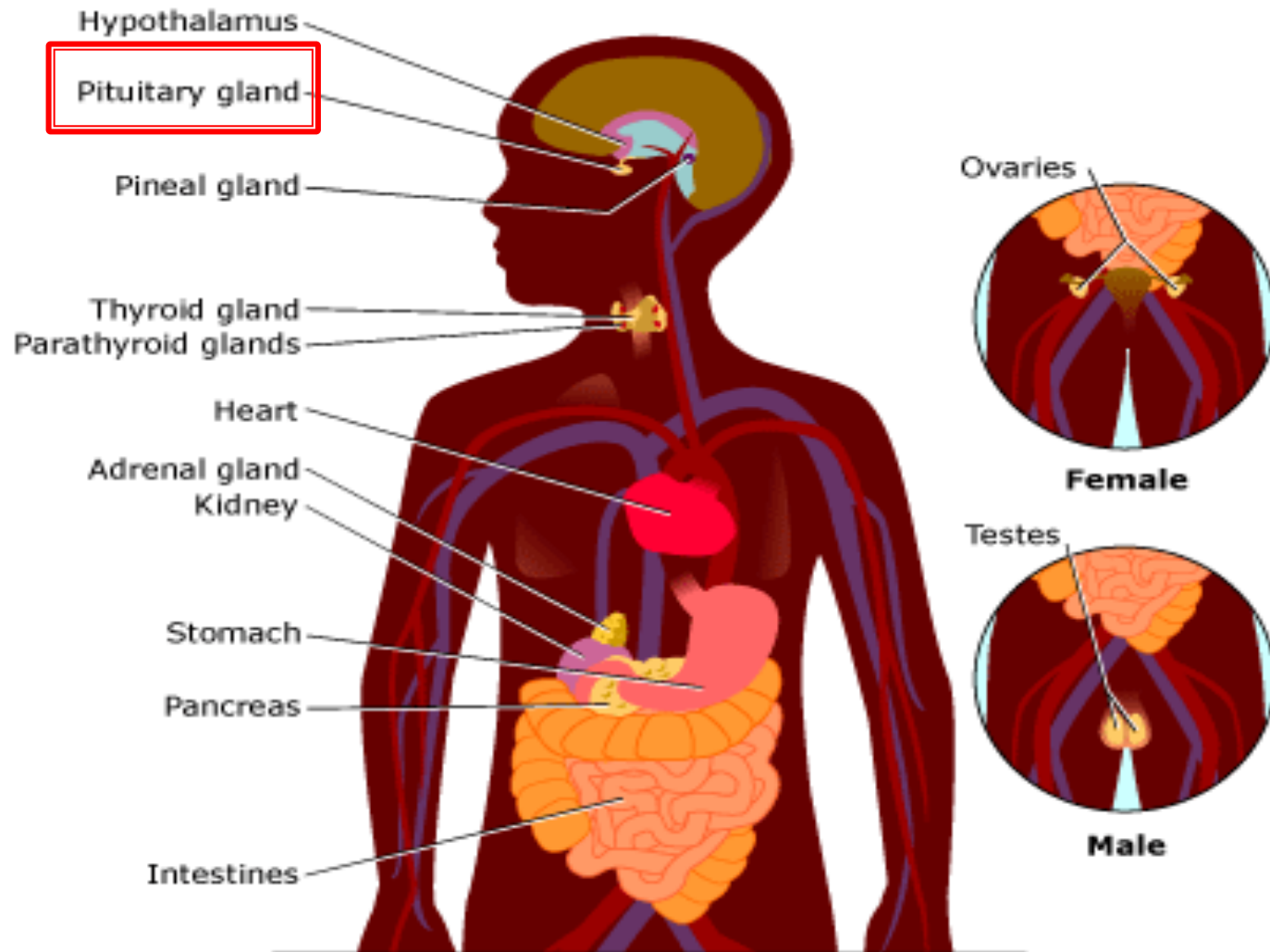
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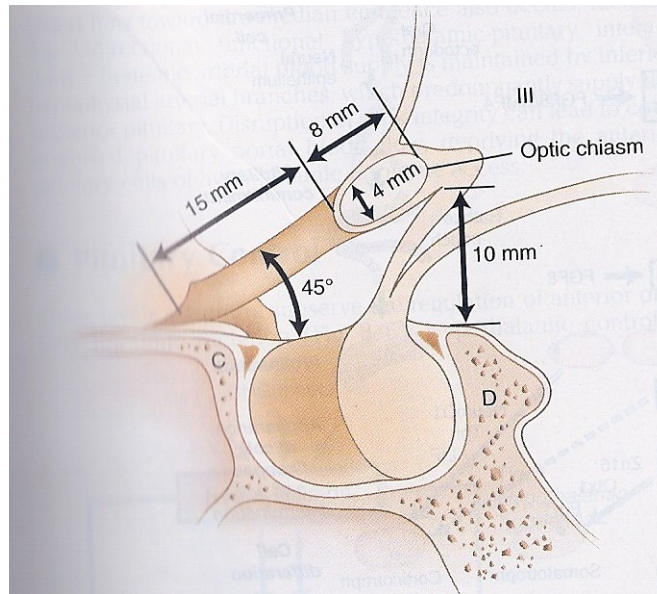
# Objectives

- To understand basic pathophysiology and feedback for anterior pituitary hormones.
- Know about clinical approach for common anterior pituitary gland disorders:
  - Common clinical presentations.
  - Main laboratory investigations.
  - Radiological investigations
  - Describe lines of management for each of these conditions.

# Endocrine system



# Pituitary Gland



# Pituitary Development

## ANTERIOR PITUITARY

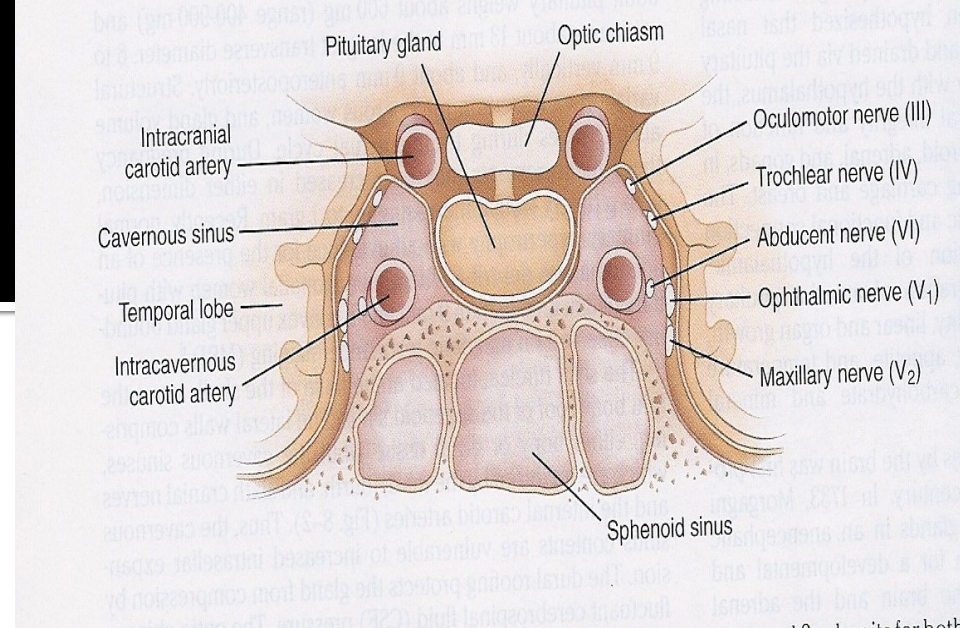
- Rathke's pouch,  
Ectodermal evagination of oropharynx
- Synthesis and secrete
  - (GH,LH,FSH,PRL,TSH,ACTH)
- recognizable by 4- 5<sup>th</sup> wk of gestation and full maturation by 20<sup>th</sup> wk
- Portion of Rathke's pouch →→ Intermediate lobe
- Remnant of Rathke's pouch cell in oral cavity →→ pharyngeal pituitary

## POSTERIOR PITUITARY (NEUROHYPOPHYSIS)

- neural cells as an outpouching from the floor of 3<sup>rd</sup> ventricle
- Only storage:
  - Oxytocin,ADH (hypothalamic hormones)

# Sella turcica

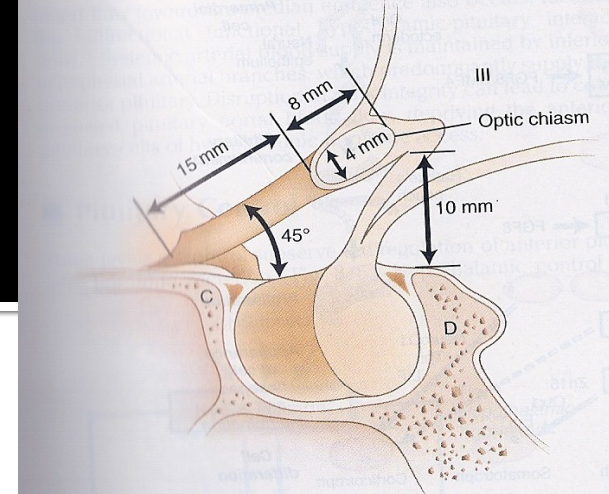
- Lies at the base of the skull
- **Roof** : diaphragma sellae
  - Pituitary stalk and its blood vessels pass through the diaphragm
- **Floor**: Sphenoid sinus
- **Lateral walls**: cavernous sinus
  - containing III, IV, VI, V<sub>1</sub>, V<sub>2</sub> cranial nerves and internal carotid artery with sympathetic fibers.
  - Both adjacent to temporal lobes



# Pituitary Development

- Pituitary stalk in midline joins the pituitary gland with hypothalamus that is below 3<sup>rd</sup> ventricle
- Development of pituitary cells is controlled by a set of transcription growth factors like
  - Pit-1, Prop-1, Pitx2

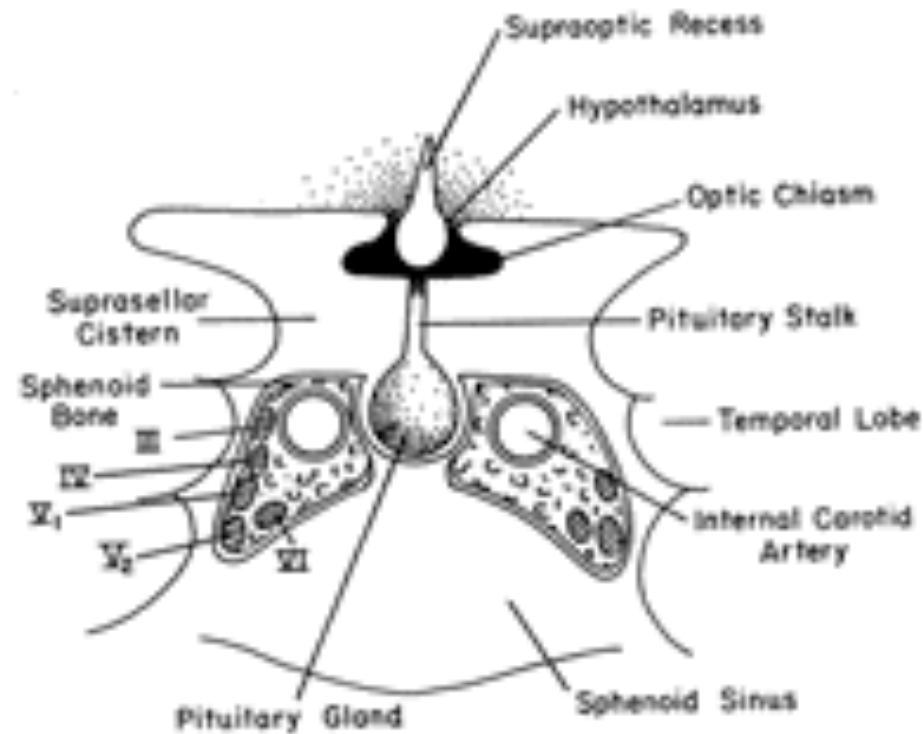
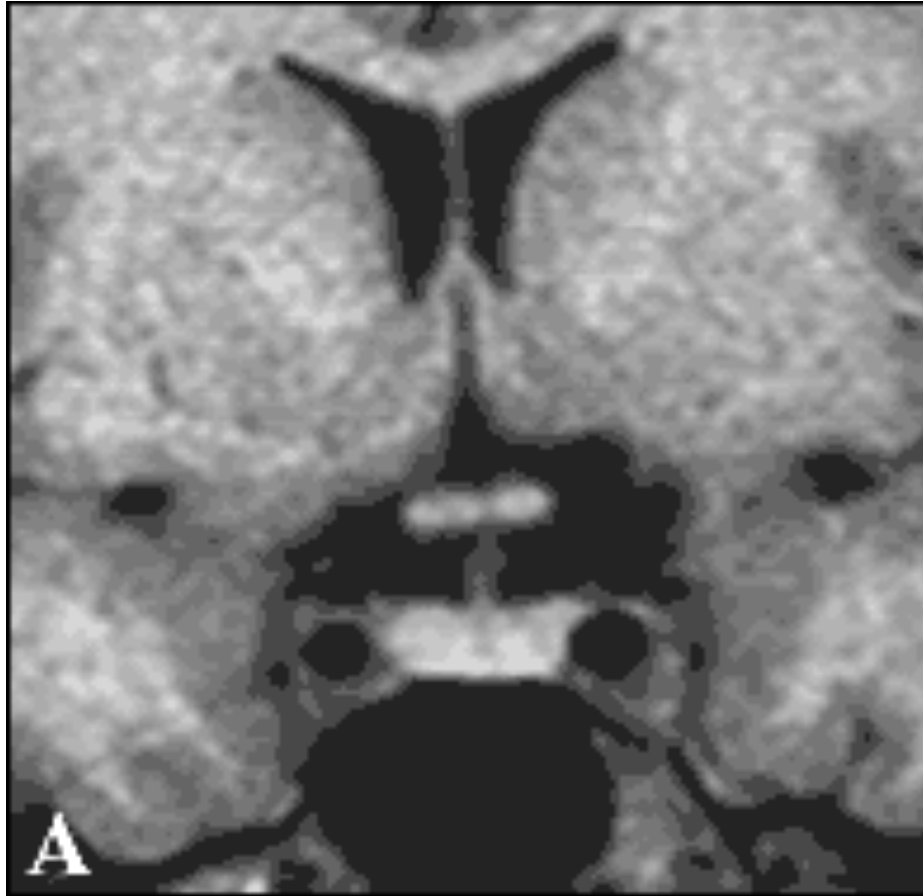
# Pituitary Development



- Pituitary gland measures
  - 15 X 10 X 6 mm, weighs 500 mg but about 1 g in women
- Optic chiasm
  - lies 10 mm above the gland and anterior to the stalk
- Blood supply :
  - superior, middle, inferior hypophysial arteries ( internal carotid artery) running in median eminence from hypothalamus
- Venous drainage:
  - to superior and inferior petrosal sinuses to jugular vein



# Normal Pituitary Anatomy



# Pituitary Disorders

- **Anterior pituitary disorders**
- **Posterior Pituitary disorders**

# Anterior Pituitary Disorders

- **Function :**
  - **Hypersecretion:** (GH,LH,FSH,PRL,TSH,ACTH)
  - **Hyposecretion:** hypopituitarism ( isolated, multiple, pan)
- **Masses**
  - **Functioning = Hypersecretion**
  - **Non- Functioning**
  - **With /without mass-effect:**
    - **Space occupying lesion ( compression symptoms, hypopituitarism )**

# Posterior Pituitary disorders

- **Diabetes insipidus**

# Anterior Pituitary Function

	Somatotroph	Gonadotroph	Lactotroph	Thyrotroph	Corticotroph
<b>Stimulators</b>	<b>GHRH</b> <b>GHS</b>	<b>GnRH</b> <b>E2</b>	----- <b>TRH, E2</b>	<b>TRH</b>	<b>CRH</b> <b>AVP</b> <b>gp-130</b> <b>cytokines</b>
<b>Inhibitors</b>	<b>IGF-1</b> <b>Somatostatin</b> <b>Activins</b>	Testosterone, E2 <b>inhibin</b>		<b>T3, T4</b> <b>Dopamine</b> <b>Somatostatin</b> <b>GH</b>	<b>Steroid</b>
<b>Hormone</b>	GH	LH,FSH	PRL	TSH	ACTH,POMC
<b>Target Gland</b>	Liver & other tissues	<b>Ovary, Testes</b>	<b>Breast &amp; other tissues</b>	Thyroid	<b>Adrenals</b>
Target Hormone	IGF-1	Testosterone, E2		T <sub>4</sub>	cortisol
<b>Trophic Effects</b>	<b>IGF-1</b> <b>production,</b> <b>Growth</b> <b>induction,</b> <b>Insulin</b> <b>antagonism</b>	<b>Sex Steroid</b> <b>Follicular</b> <b>growth</b> <b>Germ Cell</b> <b>maturation</b>	<b>Milk Production</b>	<b>T4 synthesis</b> <b>and secretion</b>	<b>Steroid</b> <b>production</b> Androgen

# Pituitary Function

- **Anterior Pituitary Hormones**
  - **Go Look For The Adenoma Please**
  - GH , LH, FSH, TSH, ACTH, Prolactin
  - A compressive adenoma in pituitary will impair hormone production in this order
- **Posterior Pituitary Hormones**
  - Oxytocin
  - ADH( vasopressin)
  - Remember (storage not synthesis)

# **Etiology of Pituitary Masses**

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# Anterior Pituitary Disorders

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# Etiology of Pituitary-Hypothalamic Lesions

- **Non-Functioning Pituitary Adenomas**
- **Endocrine active pituitary adenomas**
  - Prolactinoma ( PRL-oma)
  - Somatotropinoma ( GH secreting adenoma, Acromegaly)
  - Corticotropinoma ( ACTH secreting adenoma, Cushing's disease )
  - Thyrotropinoma (TSH-oma, rare )
  - Other mixed endocrine active adenomas
- **Malignant pituitary tumors:** Functional and non-functional pituitary carcinoma
- **Metastases in the pituitary (breast, lung, stomach, kidney)**
- **Pituitary cysts:** Rathke's cleft cyst, Mucocoeles, Others
- **Empty sella syndrome**
- **Pituitary abscess**
- **Lymphocytic hypophysitis**
- **Carotid aneurysm**





# Anterior Pituitary Disorders

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# Disorders of Pituitary Function

- **Hypopituitarism**

- Central hypoadrenalism, hypogonadism, hypothyroidism or GH deficiency
- Panhypopituitarism

- **Hypersecretion of Pituitary Hormones**

- Hyperprolactinemia
- Acromegaly
- Cushing's Disease

# 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

# Evaluation of Pituitary lesion

ANESTH ANALG  
2005;101:1170-81

REVIEW ARTICLE NEMERGUT ET AL. 1171  
TRANSSPHENOIDAL PITUITARY SURGERY

**Table 1.** Functioning Adenomas: 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 adenomas)	None	20	None

ACTH = adrenocorticotropic hormone, FHS = follicle-stimulating hormone, LH = luteinizing hormone, TSH = thyroid-stimulating hormone.

# Evaluation of Pituitary lesion

- **C: Clinical** ( History and Examination)
  - function ( oversecretion or hyposecretion )
  - Mass ( headache, visual symptoms )
- **B: Biochemical**
  - Screen Test
  - Confirmatory Test
- **A: Anatomical**
  - MRI of sella turcica
- Then treatment:
  - Surgical – Medical – Radiation
  - Medical – Surgical – Radiation



# Non- functional pituitary adenoma

<b>C: Clinical</b>	Asymptomatic , incidentaloma by imaging Mass-effect ( mechanical pressure, hypopituitarism, visual ( bitemporal hemianopia) Gonadal hypersecretion
<b>B: Biochemical</b>	GH,LH,FSH,TSH,ACTH: not high PRL : low ,high, normal
<b>A: Anatomical</b>	MRI
<b>Treatment</b>	<b>Surgery if indicated</b> <b>Observation</b> <b>Adjunctive therapy:</b> <ul style="list-style-type: none"><li>- Radiation therapy</li><li>- Dopamine agonist</li><li>- Somatostatin analogue</li></ul>

# Non- functional pituitary adenoma

**Table 2**

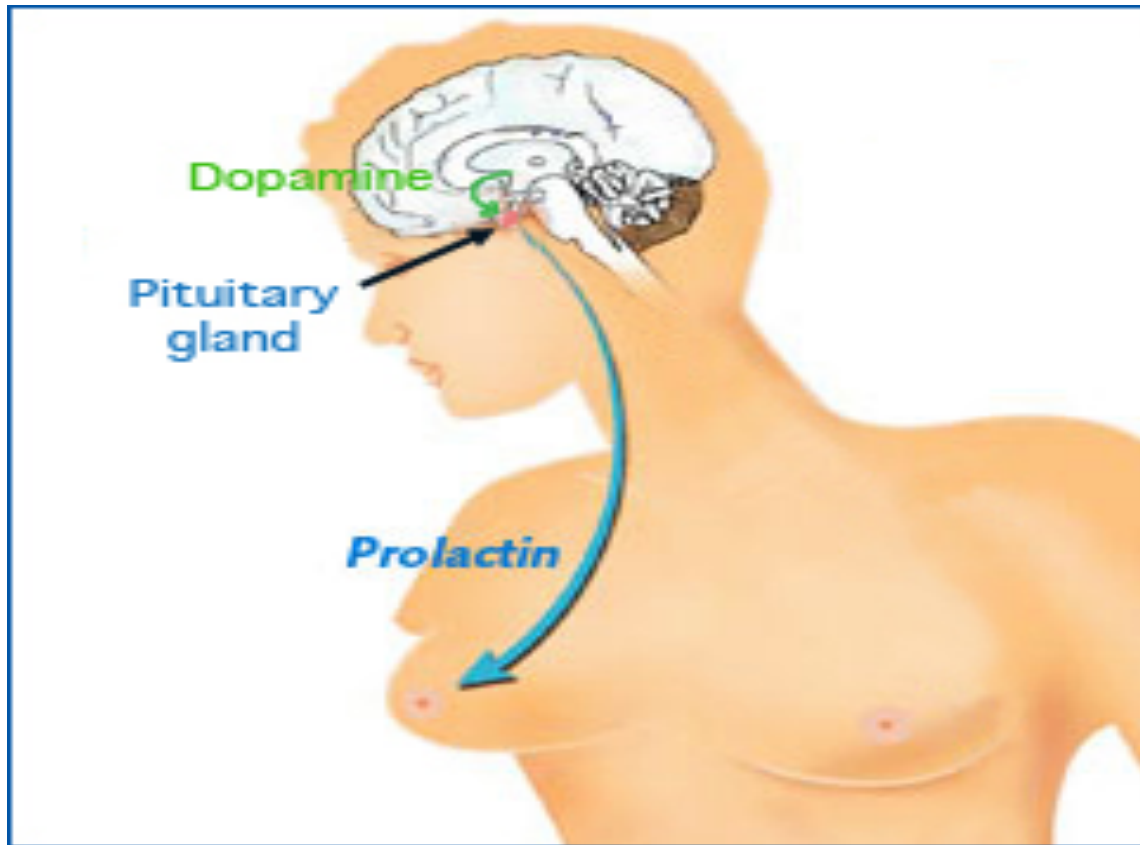
Clinical characteristics of NFPA patients.

	Nomikos et al <sup>15</sup>	Losa et al <sup>16</sup>	Chang et al <sup>17</sup>	Ferrante et al <sup>51</sup>	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 Documented	345 (47.8%)	–	342 (51.6%)	118 (40%)	805/1679 (48%)
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%)

# Functional pituitary mass

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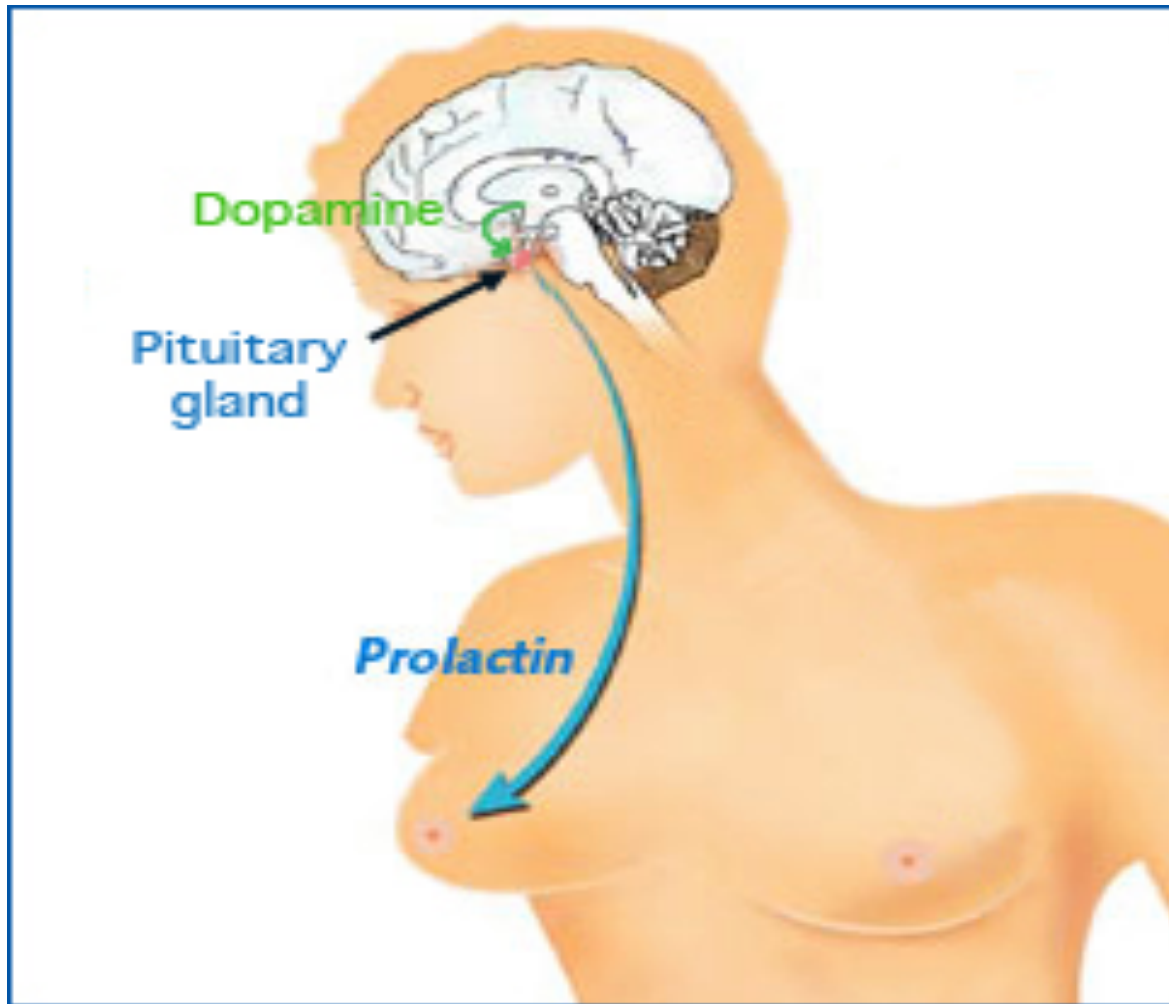
# Prolactin



# Prolactin - Low

- No clinical significant if there is no mass invading the hypothalamus.
- N.B. :
  - PRL is the only pituitary hormone that is inhibited by hypothalamus.

# Prolactinoma ( Mass + high level)



# Prolactinomas

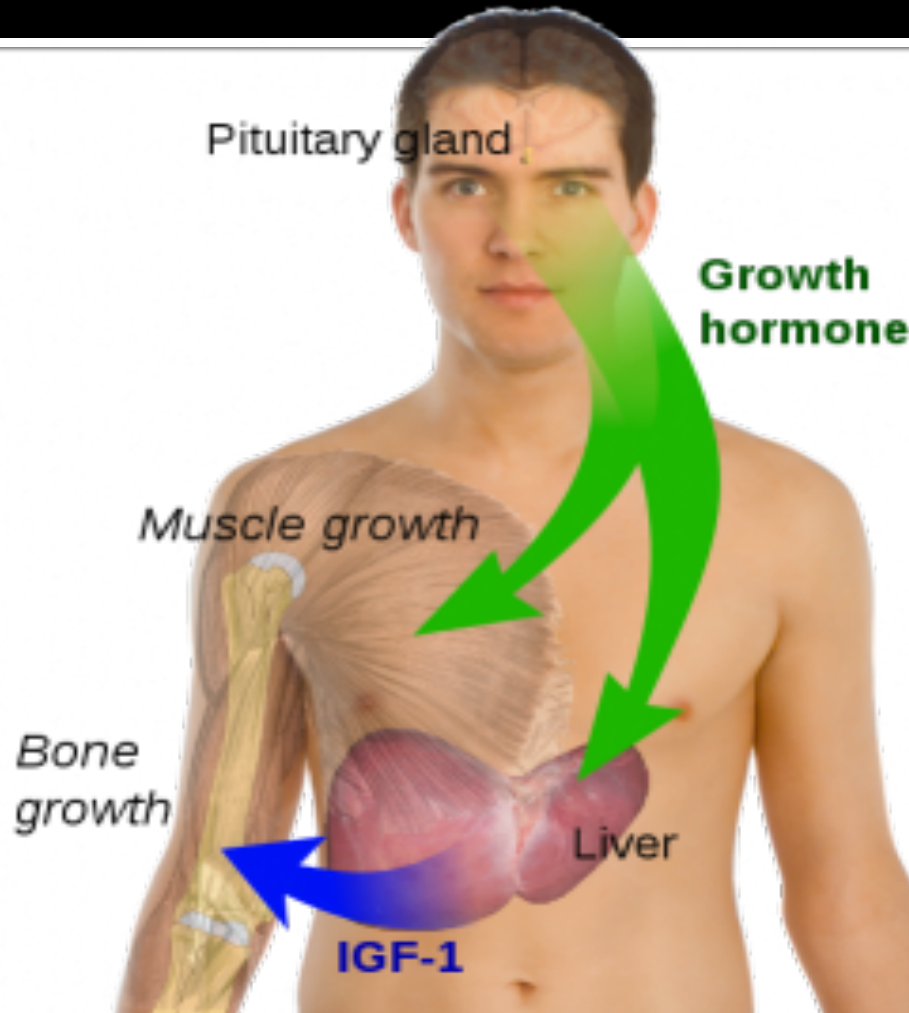
<b>C: Clinical</b>	<p>oligomenorrhea, amenorrhea or infertility Galactorrhea Mass-effect ( mechanical pressure, hypopituitarism) Sexual dysfunction (in male)</p> <p><i>asleep, stress, pregnancy, lactation and chest wall stimulation or trauma, Renal failure, Liver failure medication</i></p> <p>O/E: Visual field defect ( Bitemporal hemianopia) Nipple discharge</p>
<b>B: Biochemical</b>	<p>GH,LH,FSH,TSH,ACTH: normal or low PRL : High TSH: R/O Hypothyroidism( primary) IGF-1: R/O acromegaly co-secretion</p>
<b>A: Anatomical</b>	<p>MRI</p>
<b>Treatment</b>	<p><b>Medical – Medical – Medical ( Dopamine agonist)</b> <b>Surgical- Radiation</b></p>

# Prolactinomas

- **Most common** of functional pituitary adenomas
- 25-30% of all pituitary adenomas
- Some growth hormone (GH)–producing tumors also co-secrete PRL
- Prolactinomas **women:**
  - 90% present with microprolactinomas
- Prolactinomas in **men :**
  - 60% present with **macro**prolactinomas



# Growth hormone disorder



# Growth hormone deficiency

- Isolated, pan hypopituitarism
- Pituitary tumor as mass effect →→ Growth hormone deficiency
- Disease :
  - Children: Short stature
  - Adult: ??

# Growth hormone deficiency

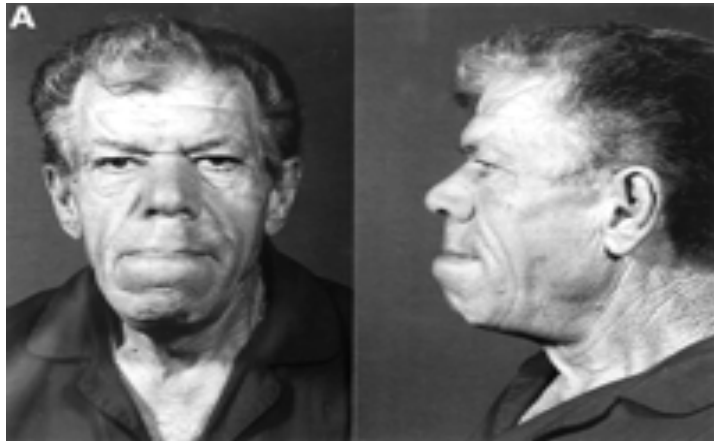


- Diagnosis in children and adult

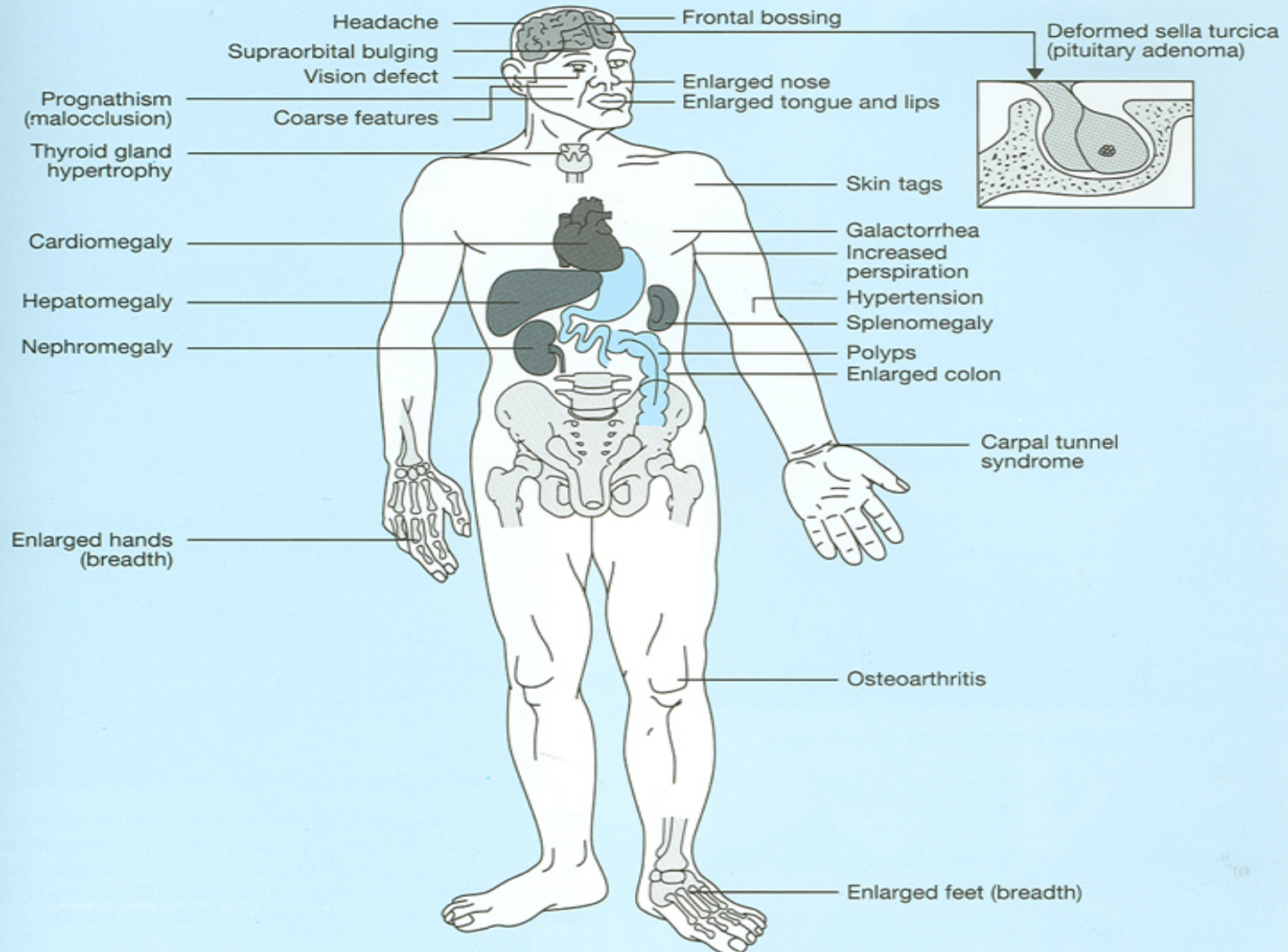
# Growth hormone deficiency

<b>C: Clinical</b>	<b>Function : Short stature</b>  <b>Mass-effect ( mechanical pressure, hypopituitarism)</b>
<b>B: Biochemical</b>	Pituitary Function (LH,FSH.PRL, TSH, ACTH, cortisol,testosterone, T <sub>4</sub> ) Screen: IGF-1 Dynamic testing: clonidine stimulation test glucagon stimulation exercise testing, arginine-GHRH <b>insulin tolerance testing</b>
<b>A: Anatomical</b>	X-ray of hands: delayed bone age MRI
<b>Treatment</b>	GH replacement

# Acromegaly



# Growth hormone - Acromegaly



# Growth hormone - Acromegaly

**Table 1. Clinical Features of Acromegaly.**

**Local tumor effects**

Pituitary enlargement  
 Visual-field defects  
 Cranial-nerve palsy  
 Headache

**Somatic systems**

Acral enlargement, including thickness of soft tissue of hands and feet

**Musculoskeletal system**

Gigantism  
 Prognathism  
 Jaw malocclusion  
 Arthralgias and arthritis  
 Carpal tunnel syndrome  
 Acroparesthesia  
 Proximal myopathy  
 Hypertrophy of frontal bones

**Skin and gastrointestinal system**

Hyperhidrosis  
 Oily texture  
 Skin tags  
 Colon polyps

**Cardiovascular system**

Left ventricular hypertrophy  
 Asymmetric septal hypertrophy  
 Cardiomyopathy  
 Hypertension  
 Congestive heart failure

**Pulmonary system**

Sleep disturbances  
 Sleep apnea (central and obstructive)  
 Narcolepsy

**Visceromegaly**

Tongue  
 Thyroid gland  
 Salivary glands  
 Liver  
 Spleen  
 Kidney  
 Prostate

**Endocrine and metabolic systems**

**Reproduction**

Menstrual abnormalities  
 Galactorrhea  
 Decreased libido, impotence, low levels of sex hormone-binding globulin

**Multiple endocrine neoplasia type 1**

Hyperparathyroidism  
 Pancreatic islet-cell tumors

**Carbohydrate**

Impaired glucose tolerance  
 Insulin resistance and hyperinsulinemia  
 Diabetes mellitus

**Lipid**

Hypertriglyceridemia

**Mineral**

Hypercalciuria, increased levels of 25-hydroxyvitamin D<sub>3</sub>  
 Urinary hydroxyproline

**Electrolyte**

Low renin levels  
 Increased aldosterone levels

**Thyroid**

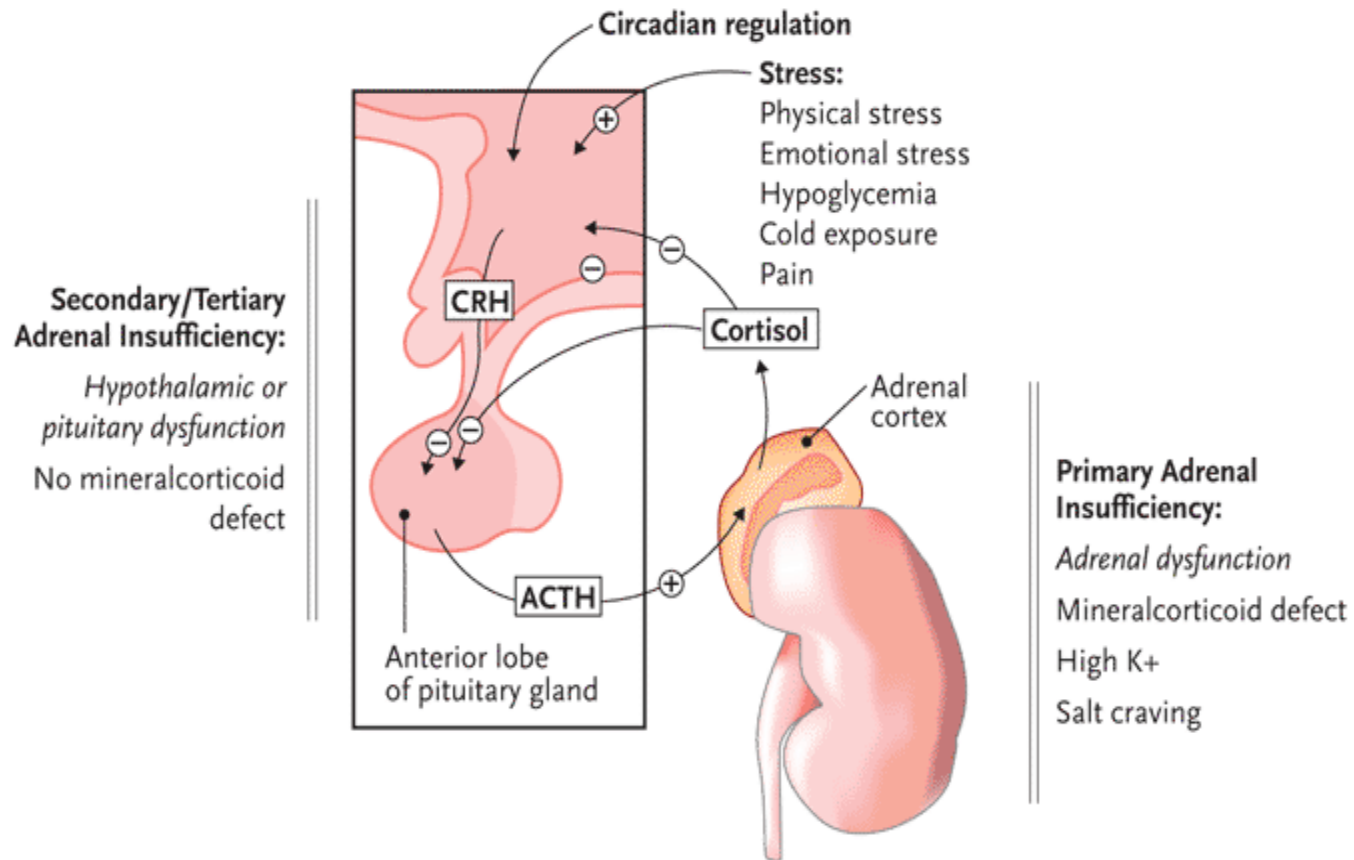
Low thyroxine-binding-globulin levels  
 Goiter

# Acromegaly

<b>C: Clinical</b>	<p>Function : Sweating, Enlargement (acral, face gross features, heart, tongue Jaw, gigantism in children , Galactorrhea</p> <p>Mass-effect ( mechanical pressure, hypopituitarism)</p> <p><i>HTN,CHF, OSA,constipation</i></p> <p>O/E: Visual field defect ( Bitemporal hemianopia) Gross features of Acromegaly</p>
<b>B: Biochemical</b>	<p>Pituitary Function (LH,FSH.PRL, TSH, ACTH, cortisol,testosterone, T4) Screen: IGF-1 Confirmatory Test : 75 g OGTT tolerance test for GH suppression</p> <p>Fasting and random blood sugar, HbA1c Lipid profile</p>
<b>A: Anatomical</b>	<p>MRI Echo: Cardiac disease is a major cause of morbidity and mortality 50 % died before age of 50 HTN in 40%, LVH in 50% , Diastolic dysfunction as an early sign of cardiomyopathy</p>
<b>Treatment</b>	<b>Surgical – Medical (Somatostatin analogue)- Radiation</b>

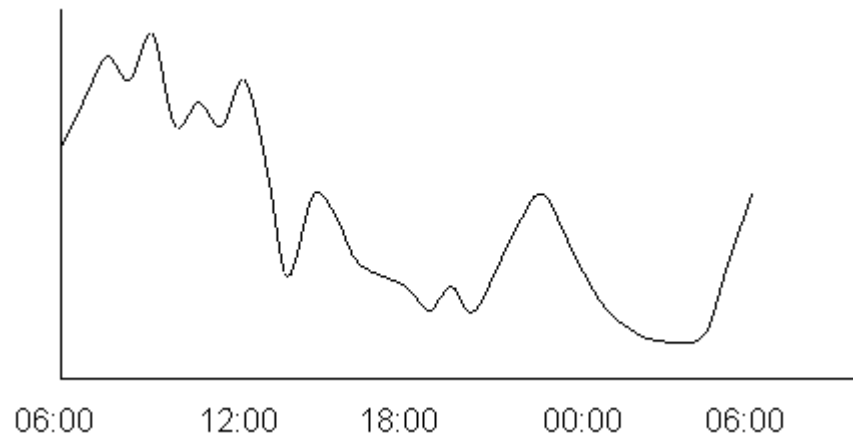


# ACTH-disorders



# HPA-axis

- Circadian rhythm of cortisol secretion
- Early morning cortisol between 8-9 am



# ACTH-disorders



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[HealAll.info/hypertension](https://HealAll.info/hypertension)

# Cortisol low (Hypoadrenalism)

- Nausea, Vomiting, abdominal pain, Diarrhea
- Dizziness and weakness, Tiredness, Muscle ache
- Hypotension
- Weight loss

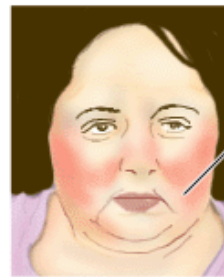


# Management of hypoadrenalism

- **Cortisol replacement**

# HPA-axis ( excessive cortisol)

## Cushing's Syndrome



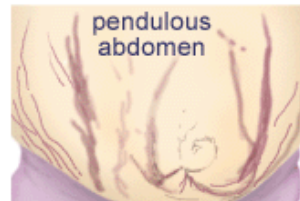
red cheeks

moon face

Osteoporosis;  
compressed  
(codfish)  
vertebrae

Excessive Cortisol

fat pads  
(buffalo  
hump)



pendulous  
abdomen

high  
blood  
pressure

thin  
skin

thin  
arms  
and  
legs

bruising  
ecchymoses

pendulous  
abdomen

red  
striae

poor  
wound  
healing

# ACTH-Adenoma



# excessive cortisol (Cushing's) Hirsutism in women





# excessive cortisol (Cushing's)

## Stria (purple, wide >1cm)



# excessive cortisol (Cushing's)



# excessive cortisol (Cushing's) ecchymosis



# HPA-axis ( excessive cortisol)

- 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

# Cushing's ( excessive cortisol)

<b>C: Clinical</b>	<b>Function : Hirsutism, acne, easily bur DM,HTN, irregular period, proximal weakness, recurrent infections, depression</b> <b>O/E: hirsutism, acne, moon face, central obesity, stria, proximal weakness, supraclavicular fat pad,</b>
<b>B: Biochemical</b>	High cortisol , high ACH  24hrs for UFC 1MG DST Midnight salivary cortisol
<b>A: Anatomical</b>	MRI
<b>Treatment</b>	Surgical – Medical - Radiation

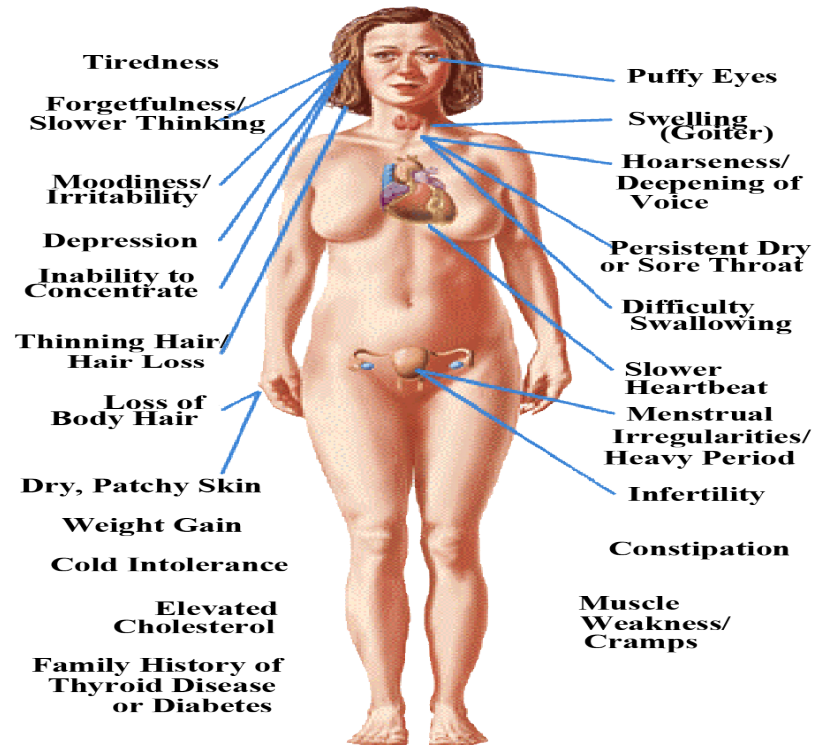
# TSH-Hypothyroid



# Central Hypothyroidism

- Low TSH
- Low free T<sub>4</sub> and T<sub>3</sub>

## Signs and Symptoms of HYPOTHYROIDISM



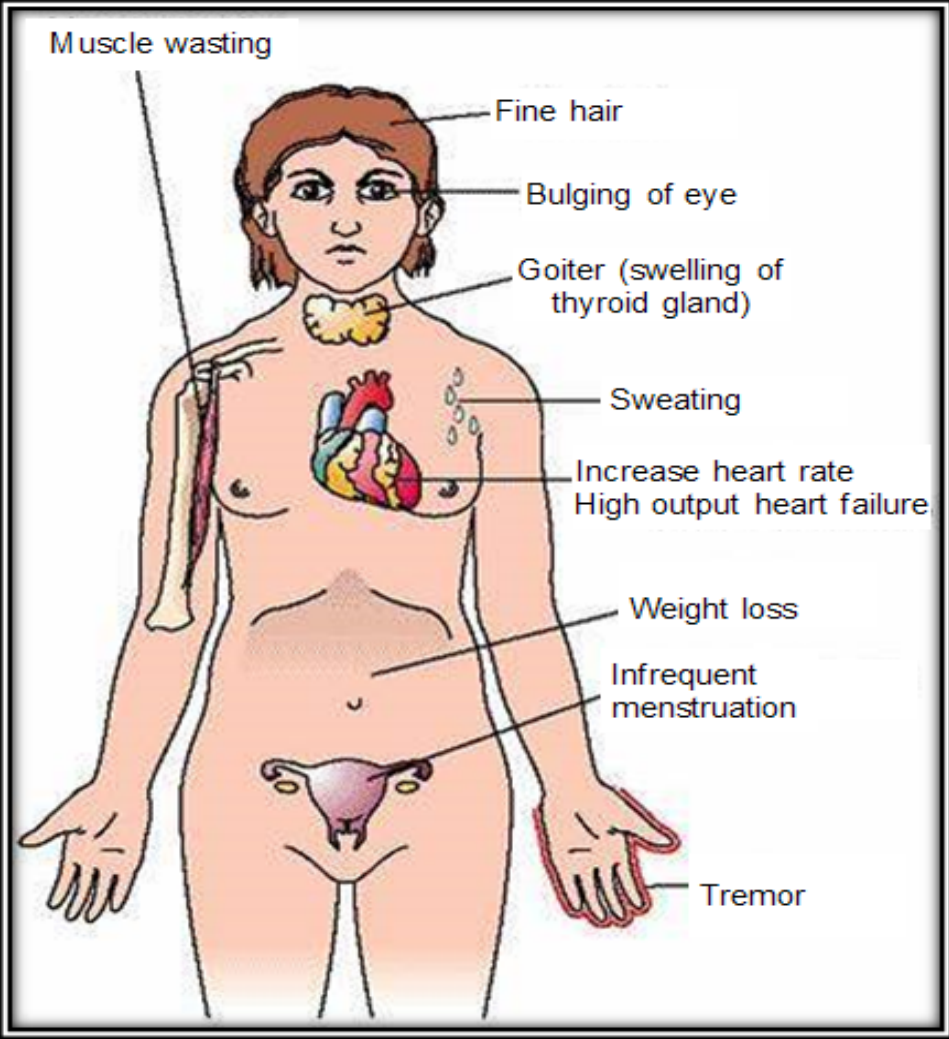
# Central Hypothyroidism

<b>C: Clinical</b>	Function : fatigue, weight gain, irregular menses, dry skin, depression, cold intolerance, increase sleep, slow thinking O/E: obesity, ? Depressed face, eye brow
<b>B: Biochemical</b>	Low T <sub>4</sub> , Low TSH
<b>A: Anatomical</b>	MRI
<b>Treatment</b>	Thyroxine replacement Surgical removal of pituitary adenoma if large



# TSH-hyperthyroid





# TSH-Producing adenoma

- Very rare < 2.8 %
- Signs of hyperthyroidism
- High TSH, FT<sub>4</sub>, FT<sub>3</sub>
- Treatment preop with anti-thyroid meds
- Surgical resection of adenoma
- Medical therapy: Somatostatin Analogue

# Gonadotroph adenoma vs. menopause and ovarian failure

- High FSH with low LH
- High serum free alpha subunit
- High estradiol, FSH, thickened endometrium and polycystic ovaries

# Gonadotroph Adenoma

- Surgical resection if large
- Radiation therapy

# assessment of pituitary function

- Baseline:
  - TSH, FT<sub>4</sub>
  - LH, FSH, and (Testosterone or Estradiol)
  - Prolactin
  - GH, IGF-I
  - ACTH, cortisol and electrolyte
- MRI brain
- Neurophthalmic evaluation of visual field
- Cardiac and respiratory assessment
- Anesthesiologist for airway and perioperative monitoring
- Neurosurgeon
- ENT for Endonasal evaluation for surgical approach
- Preop hormonal replacement:
  - maybe need to be covered with stress dose of HC