

Endocrine block (ENDO 225) 2019

Anterior Pituitary Disorders

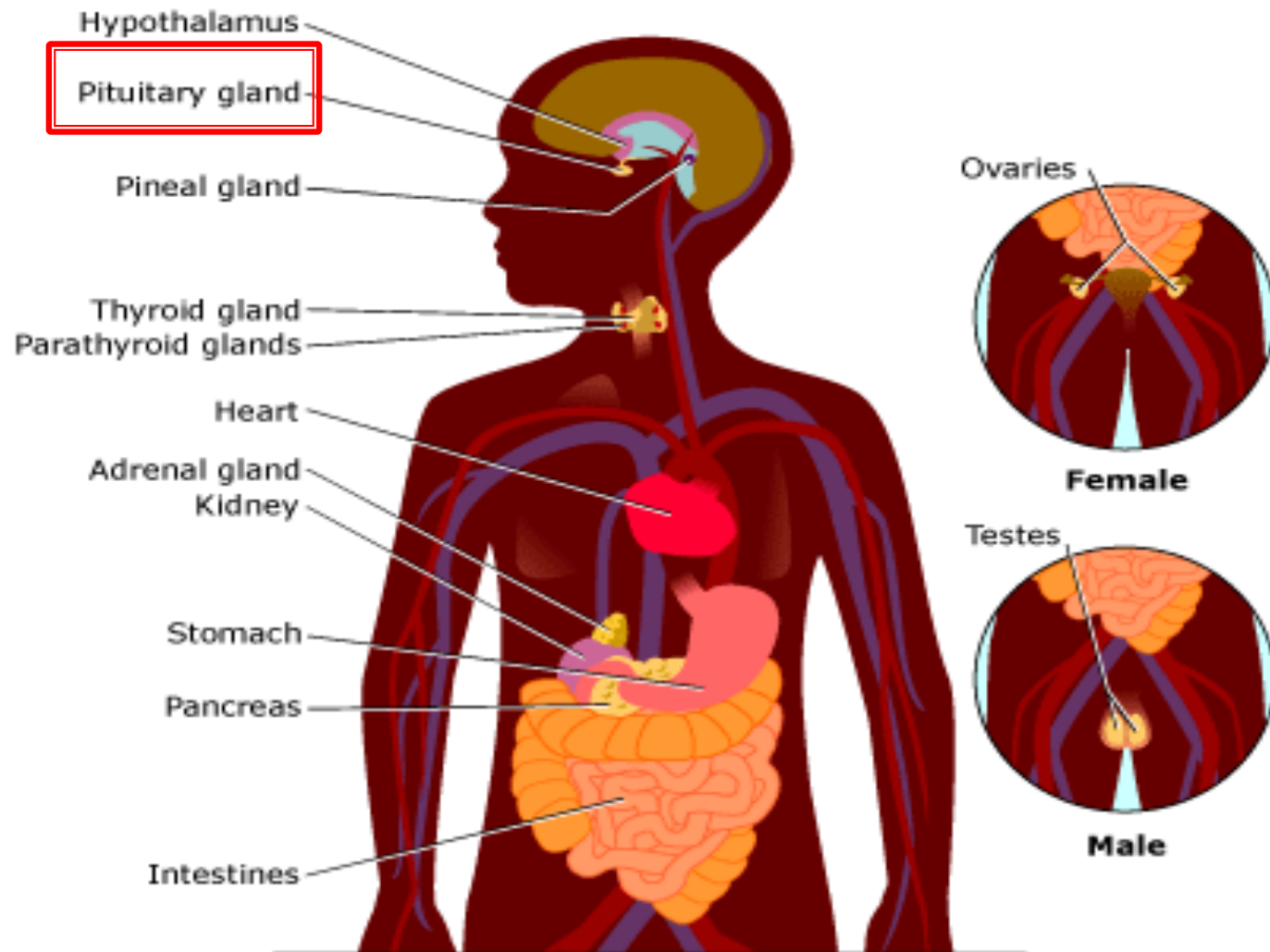
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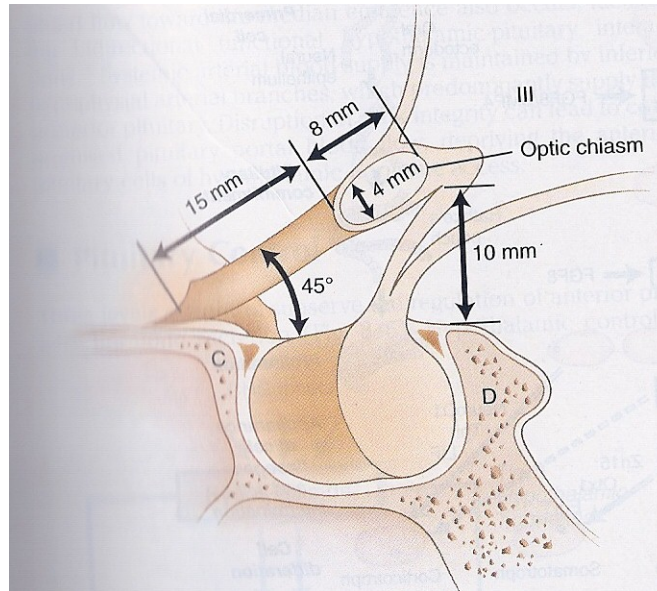
Objectives

- 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

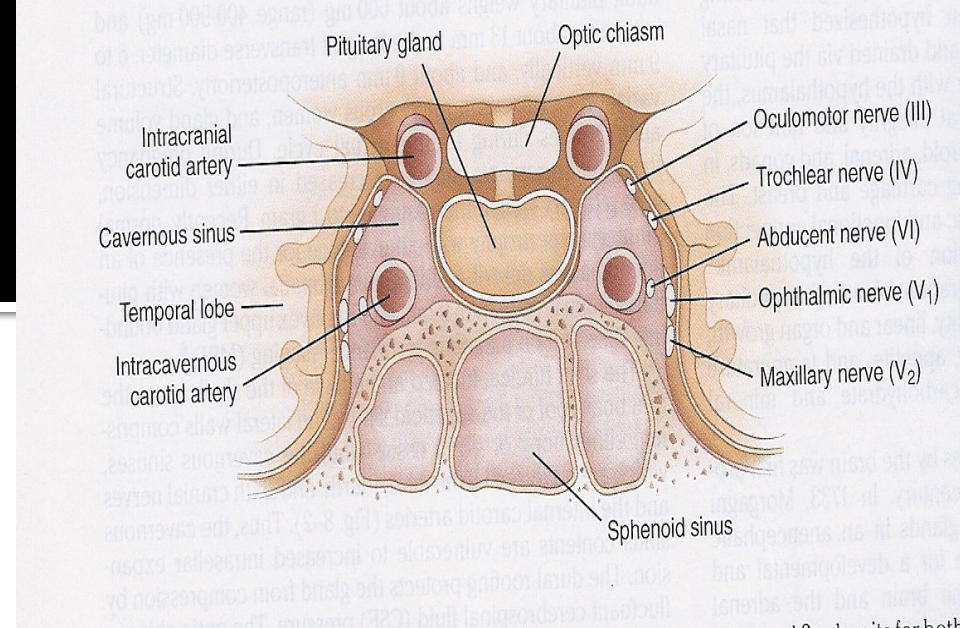
- Rathke's pouch,
Ectodermal evagination of oropharynx
- Synthesis and secrete
 - (GH,LH,FSH,PRL,TSH,ACTH)
- recognizable by 4- 5th wk of gestation and full maturation by 20th wk
- Portion of Rathke's pouch →→ Intermediate lobe
- Remnant of Rathke's pouch cell in oral cavity →→ pharyngeal pituitary

POSTERIOR PITUITARY (NEUROHYPOPHYSIS)

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

Sella turcica

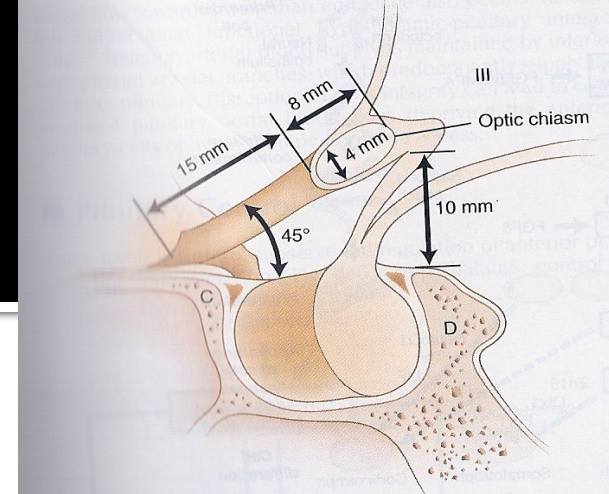
- Lies at the base of the skull
- **Roof** : diaphragma sellae
 - Pituitary stalk and its blood vessels pass through the diaphragm
- **Floor**: Sphenoid sinus
- **Lateral walls**: cavernous sinus
 - containing III, IV, VI, V₁, V₂ cranial nerves and internal carotid artery with sympathetic fibers.
 - Both adjacent to temporal lobes



Pituitary Development

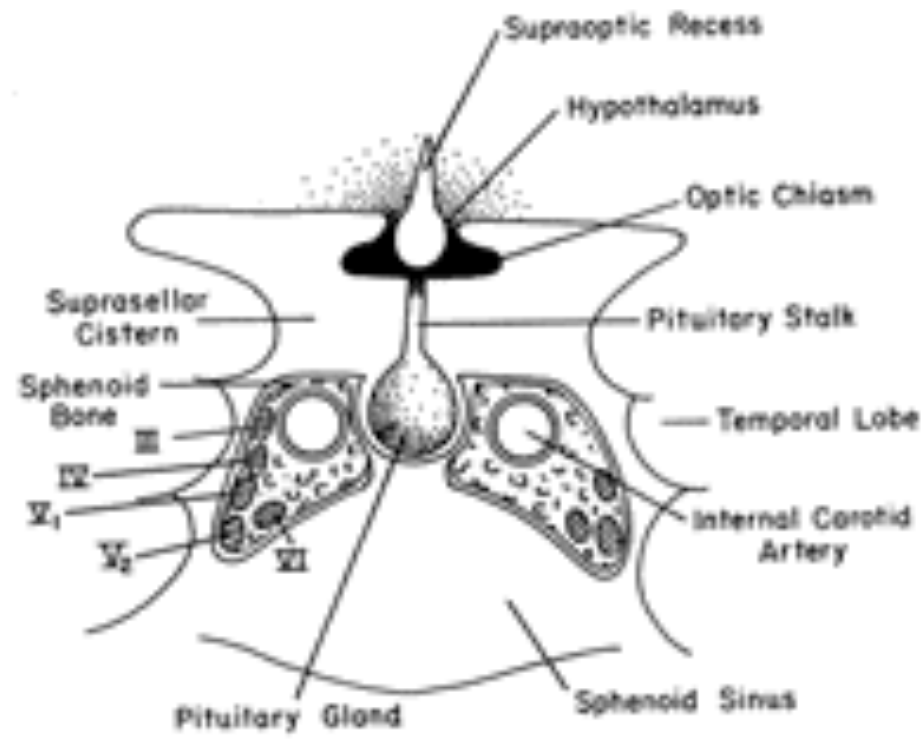
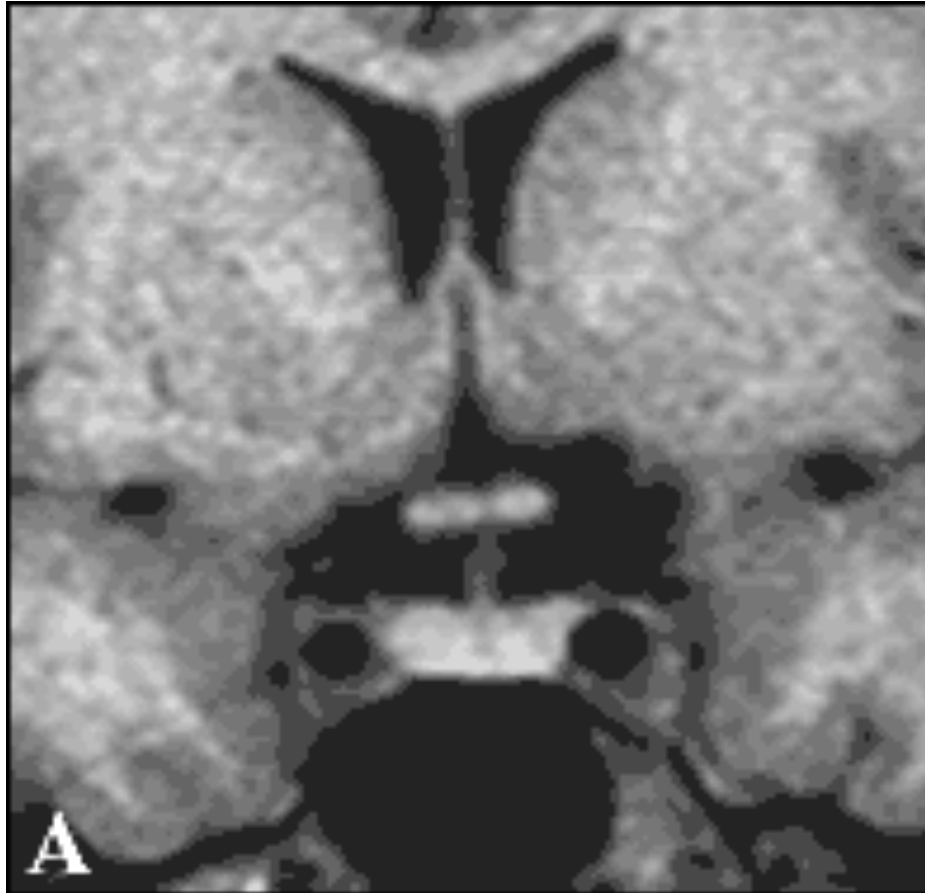
- Pituitary stalk in midline joins the pituitary gland with hypothalamus that is below 3rd ventricle
- Development of pituitary cells is controlled by a set of transcription growth factors like
 - Pit-1, Prop-1, Pitx2

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



B

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

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 = adrenocorticotrophic 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

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

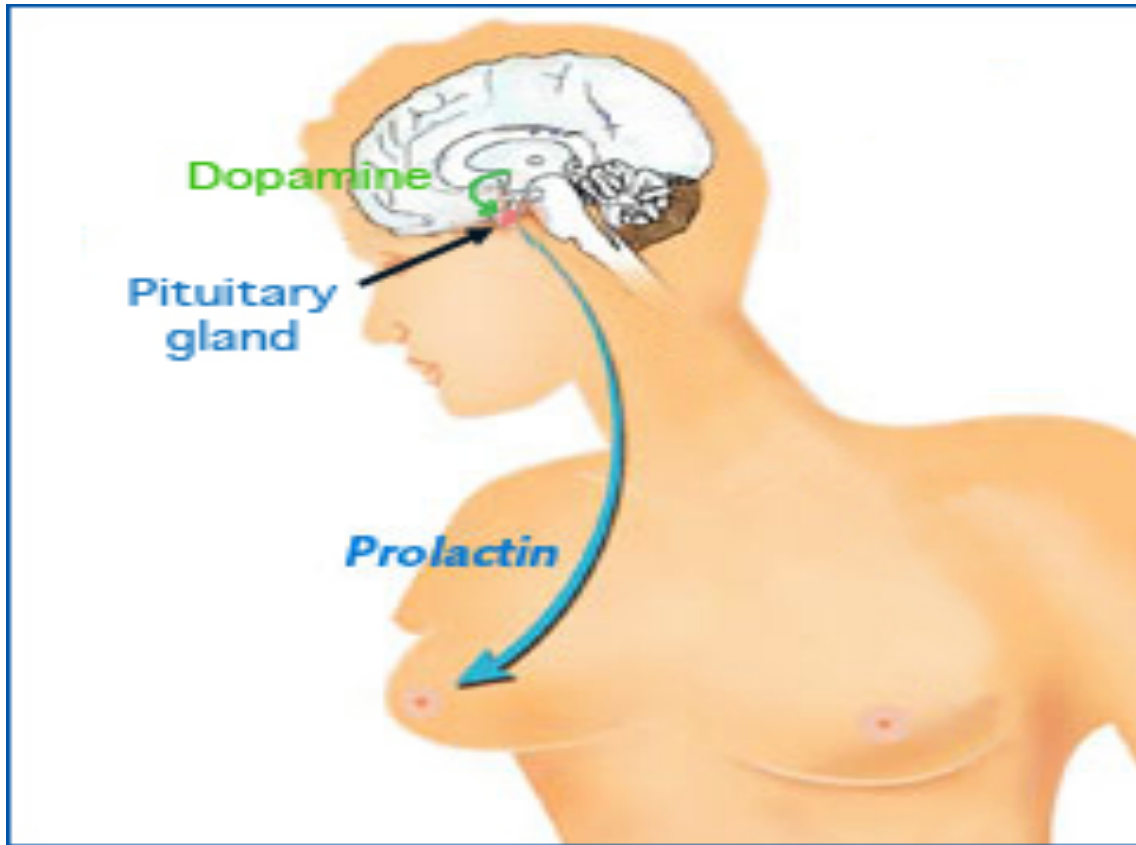
Non- functional pituitary adenoma

Table 2
Clinical characteristics of NFPA patients.

	Nomikos et al ¹⁵	Losa et al ¹⁶	Chang et al ¹⁷	Ferrante et al ⁵¹	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%)

Functional pituitary mass

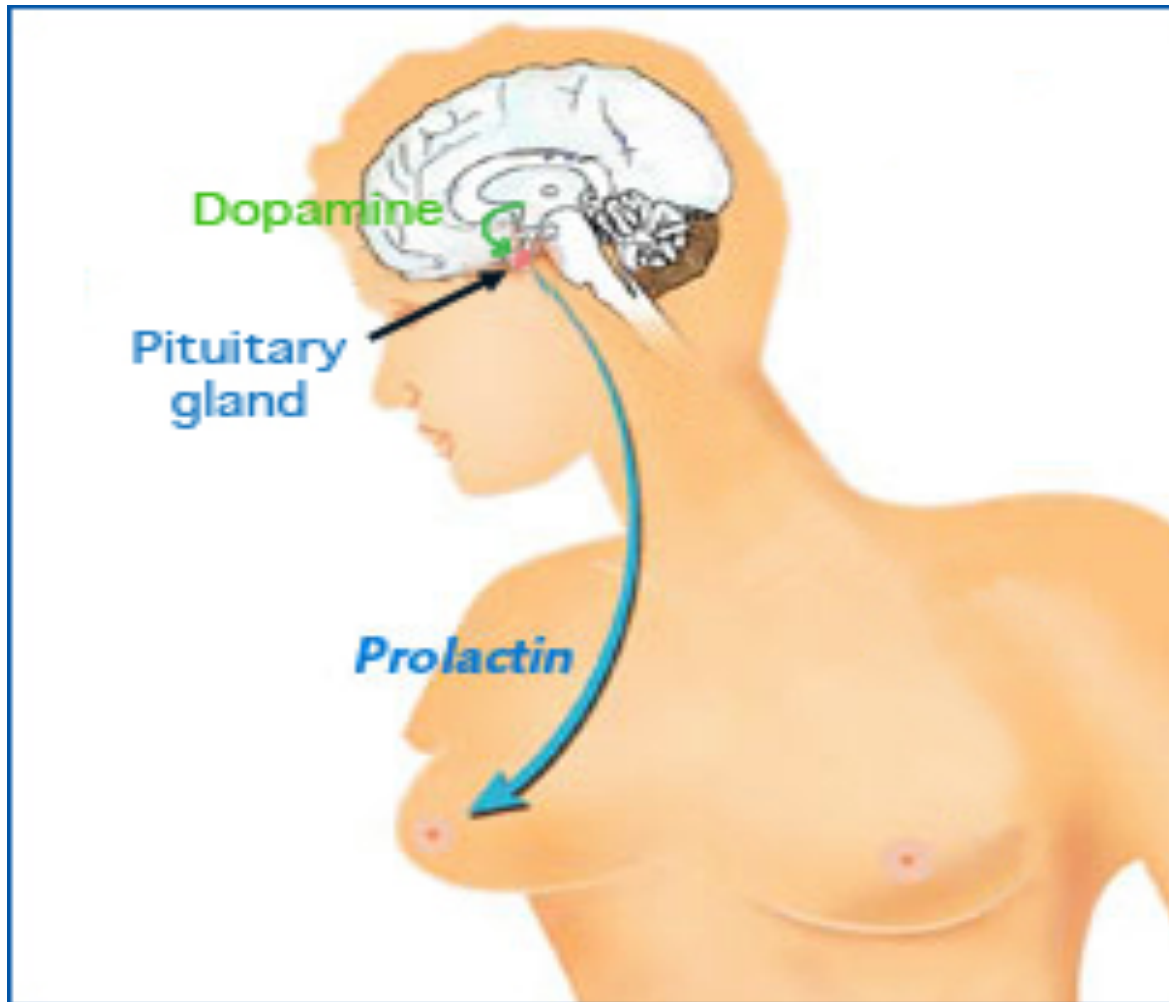
Prolactin



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

C: Clinical

oligomenorrhea, amenorrhea or infertility
Galactorrhea
Mass-effect (mechanical pressure, hypopituitarism)
Sexual dysfunction (in male)

*asleep, stress, pregnancy, lactation and chest wall stimulation or trauma, Renal failure, Liver failure
medication*

O/E: Visual field defect (Bitemporal hemianopia)
Nipple discharge

B: Biochemical

GH,LH,FSH,TSH,ACTH: normal or low
PRL : High
TSH: R/O Hypothyroidism(primary)
IGF-1: R/O acromegaly co-secrction

A: Anatomical

MRI

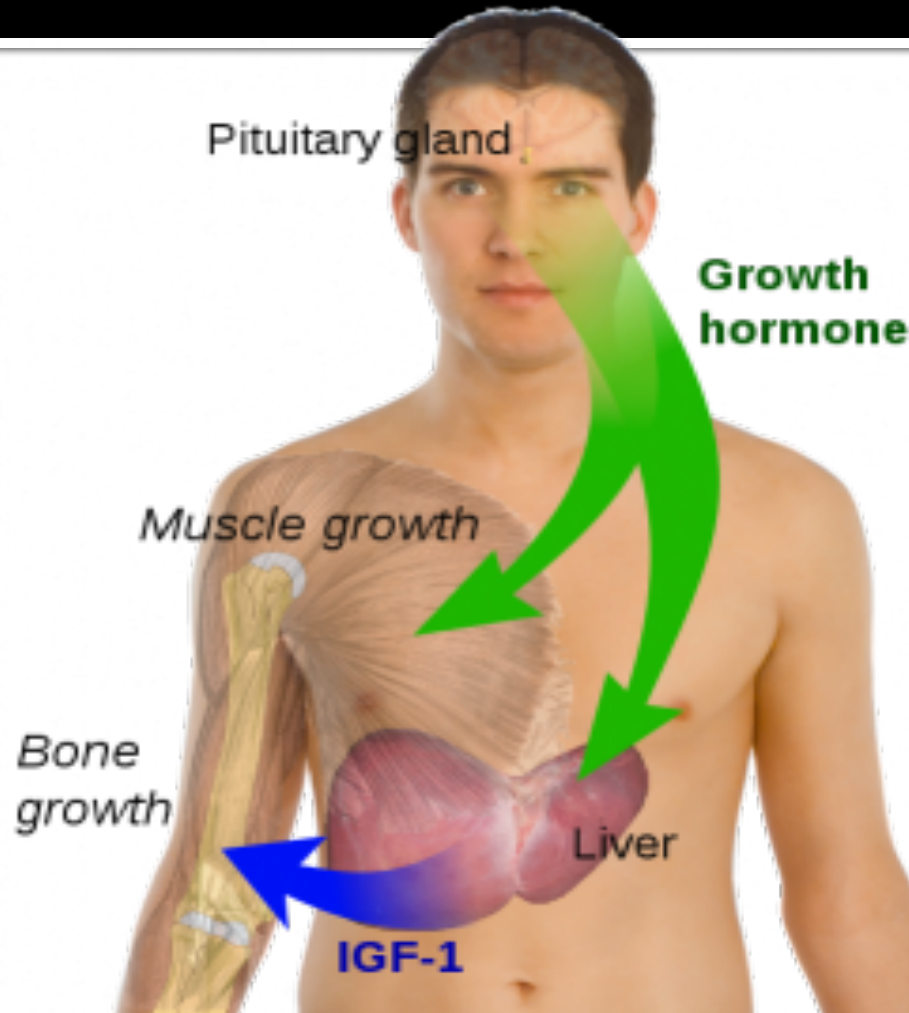
Treatment

Medical – Medical – Medical (Dopamine agonist)
Surgical- Radiation

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

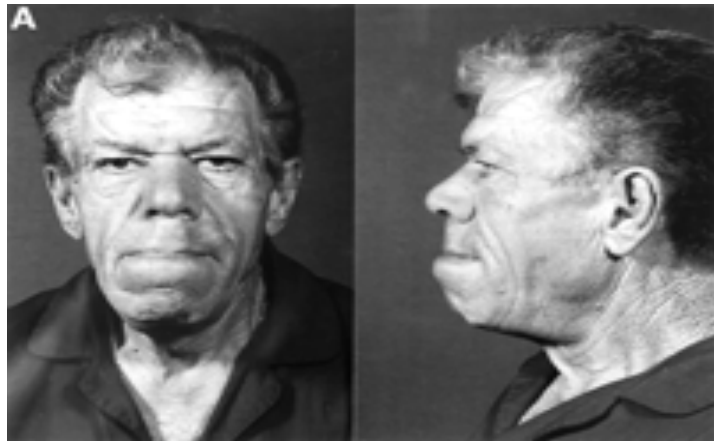


- Diagnosis in children and adult

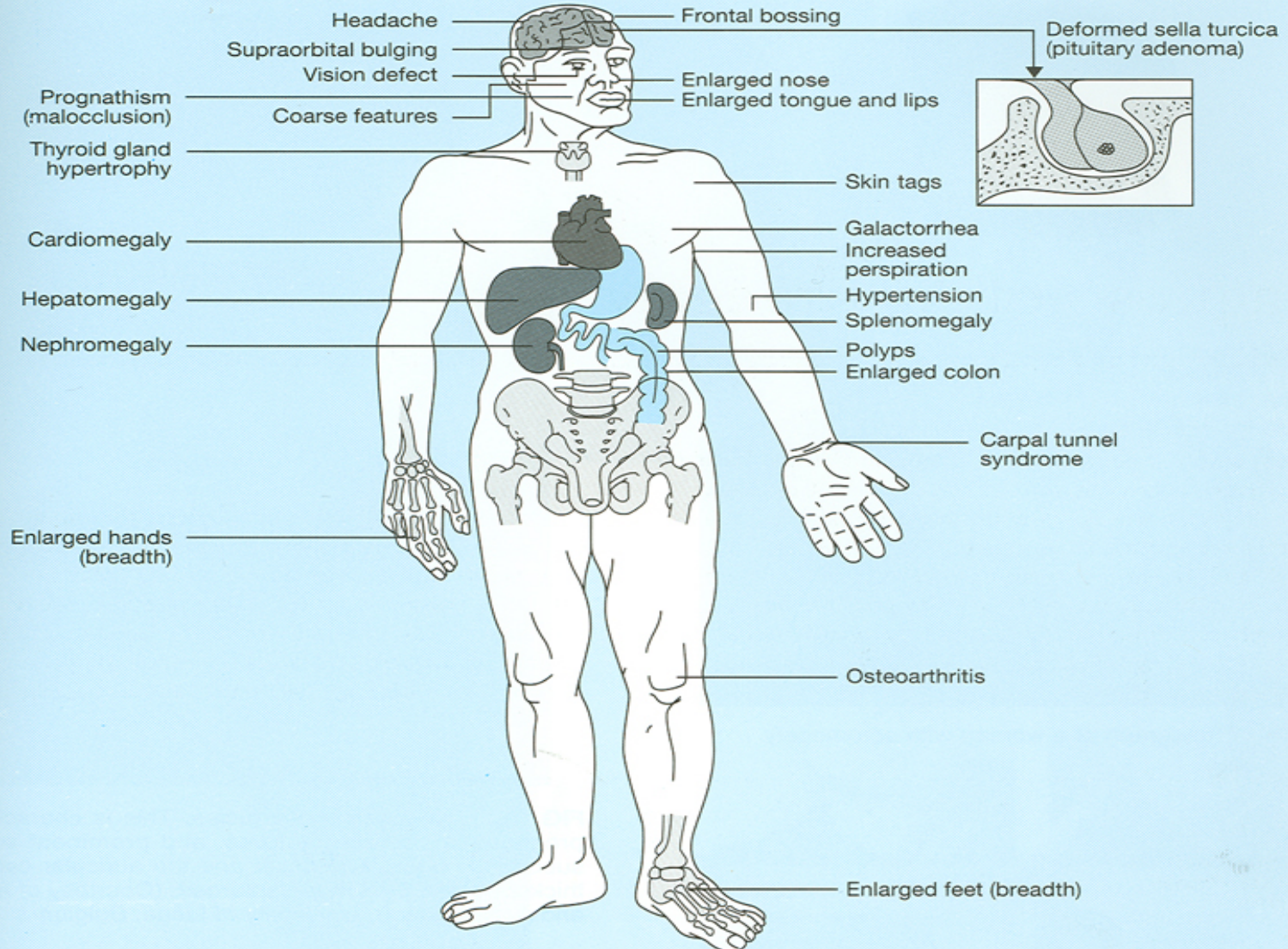
Growth hormone deficiency

C: Clinical	Function : Short stature Mass-effect (mechanical pressure, hypopituitarism)
B: Biochemical	Pituitary Function (LH,FSH.PRL, TSH, ACTH, cortisol,testosterone, T ₄) Screen: IGF-1 Dynamic testing: clonidine stimulation test glucagon stimulation exercise testing, arginine-GHRH insulin tolerance testing
A: Anatomical	X-ray of hands: delayed bone age MRI
Treatment	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 D₃
 Urinary hydroxyproline

Electrolyte

Low renin levels
 Increased aldosterone levels

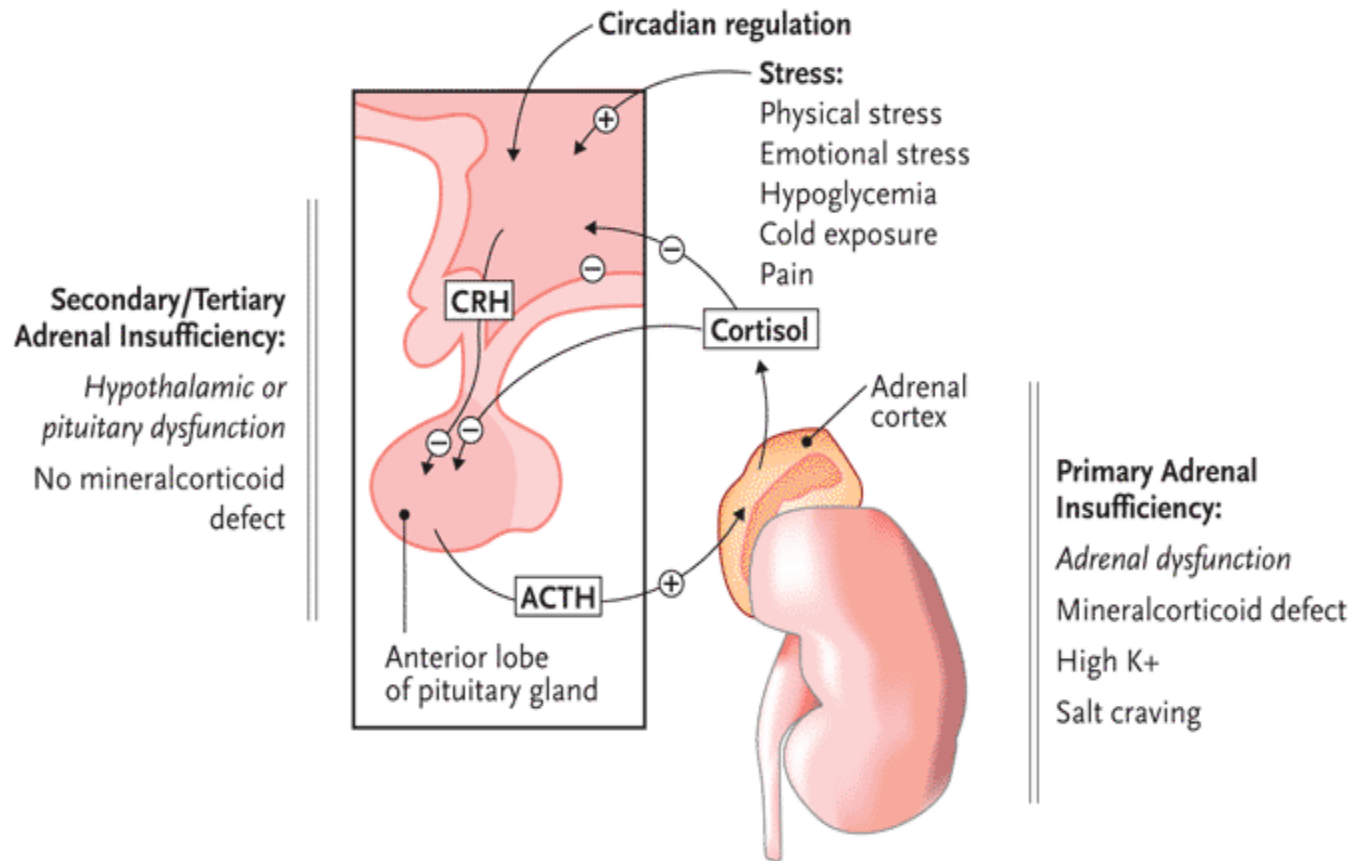
Thyroid

Low thyroxine-binding-globulin levels
 Goiter

Acromegaly

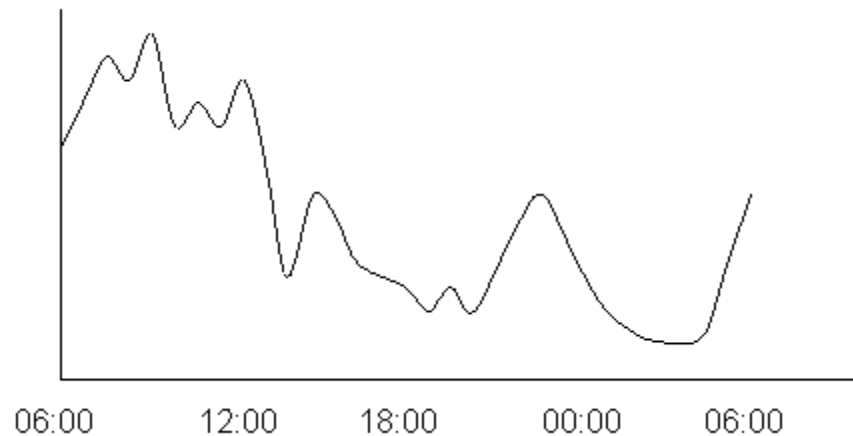
C: Clinical	<p>Function : Sweating, Enlargement (acral, face gross features, heart, tongue Jaw, gigantism in children , Galactorrhea</p> <p>Mass-effect (mechanical pressure, hypopituitarism)</p> <p><i>HTN,CHF, OSA,constipation</i></p> <p>O/E: Visual field defect (Bitemporal hemianopia) Gross features of Acromegaly</p>
B: Biochemical	<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>
A: Anatomical	<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>
Treatment	Surgical – Medical (Somatostatin analogue)- Radiation

ACTH-disorders



HPA-axis

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



ACTH-disorders



Back To
Main
Menu

HealAll.info/hypertension

Cortisol low (Hypoadrenalism)

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

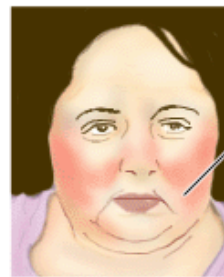


Management of hypoadrenalism

- **Cortisol replacement**

HPA-axis (excessive cortisol)

Cushing's Syndrome



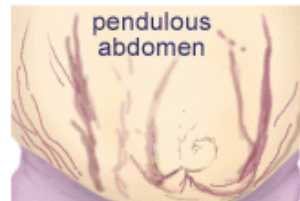
red cheeks

moon face

Osteoporosis;
compressed
(codfish)
vertebrae

Excessive Cortisol

fat pads
(buffalo
hump)



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)

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

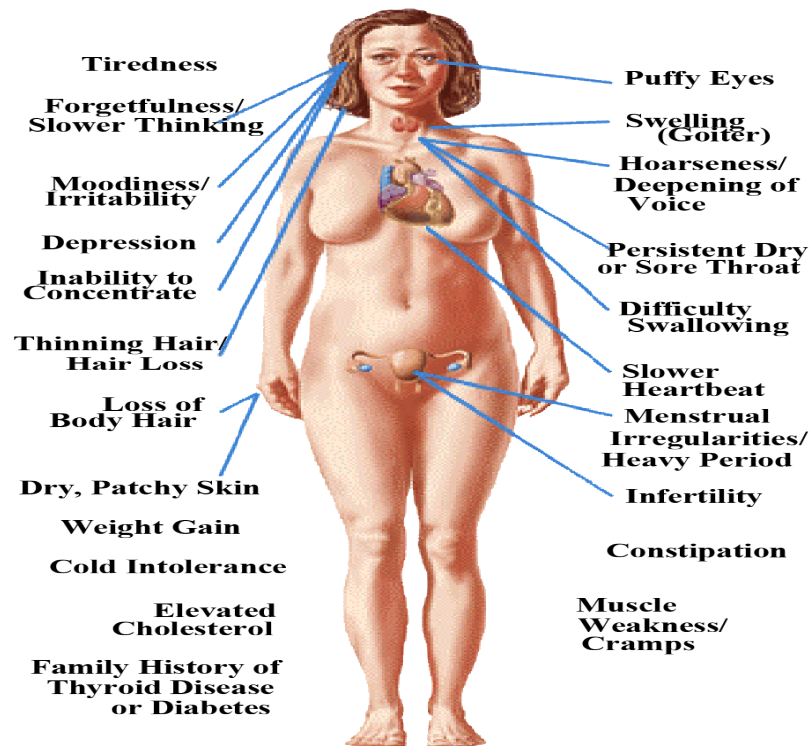
TSH-Hypothyroid



Central Hypothyroidism

- Low TSH
- Low free T₄ and T₃

Signs and Symptoms of HYPOTHYROIDISM

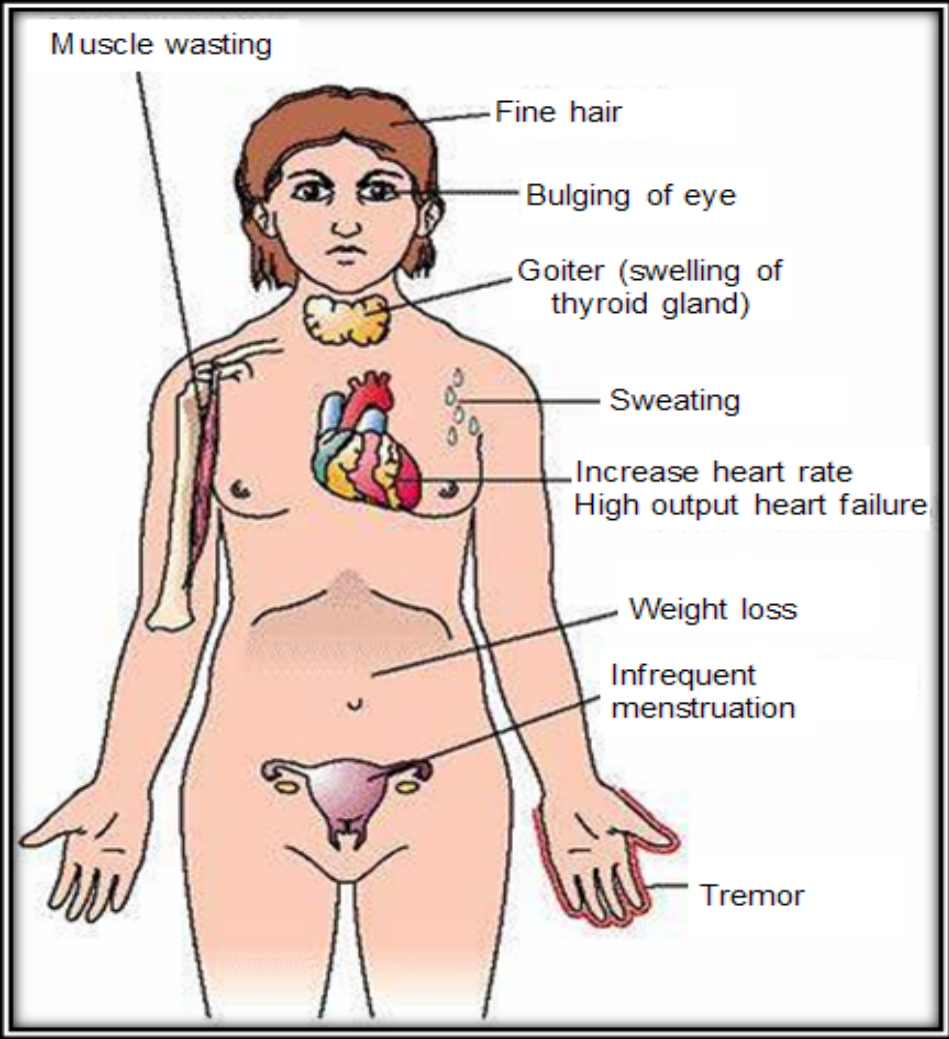


Central Hypothyroidism

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

TSH-hyperthyroid





TSH-Producing adenoma

- Very rare < 2.8 %
- Signs of hyperthyroidism
- High TSH, FT₄, FT₃
- 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, FT₄
 - 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