Endocrine block 2017

Anterior Pituitary Disorders

Dr.Aishah AlEkhzaimy, MBBS,FRCPC,FACE

Pituitary Disorders

- **Anterior pituitary disorders:**
  - Non-functional pituitary tumor and mass-effect: **hypopituitrism**
  - Prolactin secreting cell disorder: prolactinoma
  - Growth hormone secreting cell disorder: acromegaly
  - ACTH secreting cell disorders: cushing's
  - TSH secreting cell tumor: TSH-secreting adenoma
  - Gonadotropin secreting adenoma
- **Posterior Pituitary disorders:**
  - Diabetes insipidus

Pituitary Development

- Anterior pituitary is recognizable by 4- 5th wk of gestation
- Full maturation by 20th wk
- 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
- Lies at the base of the skull as sella turcica
- Roof is formed by diaphragma sellae
- Floor by the roof of sphenoid sinus

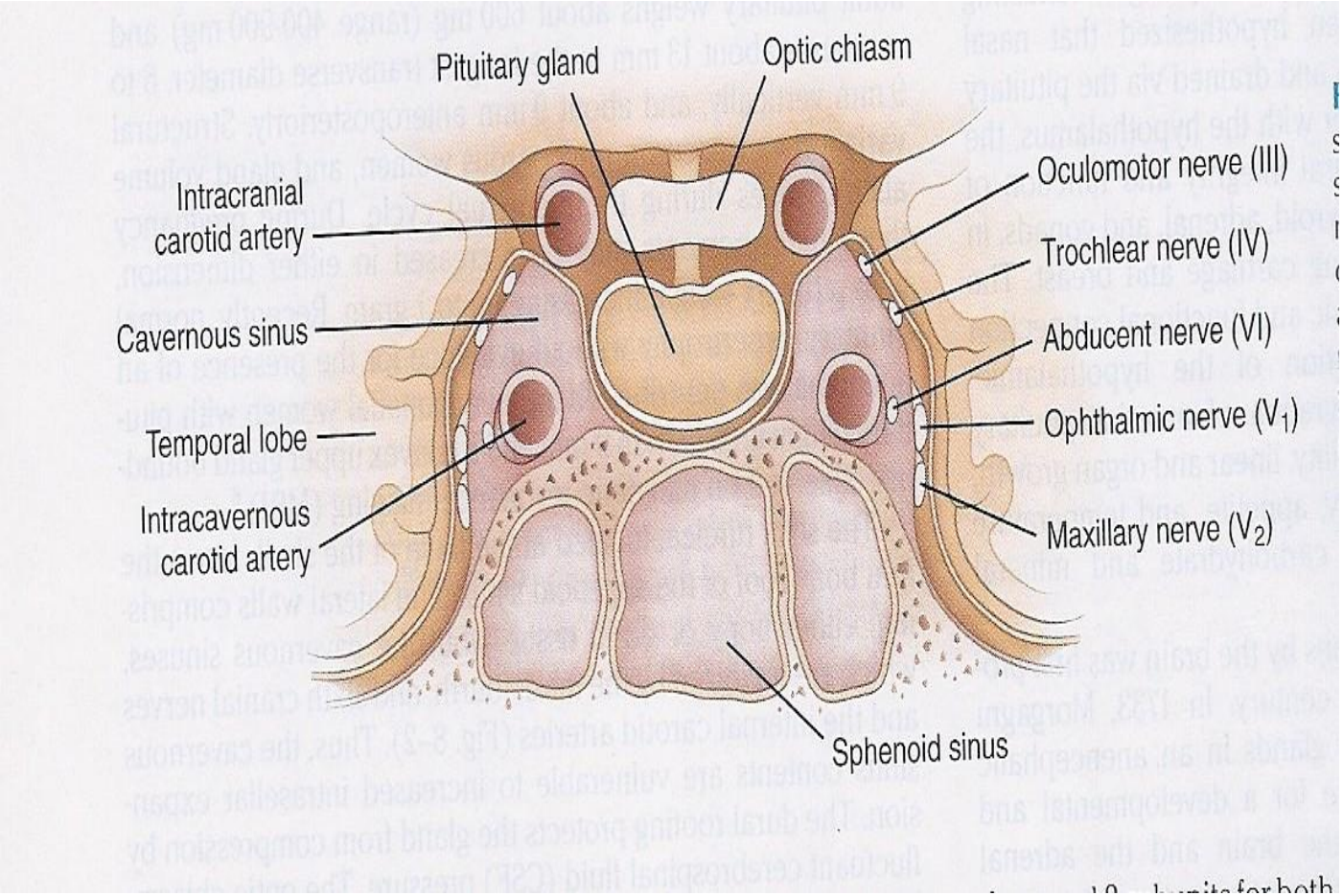
Pituitary Development

- 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

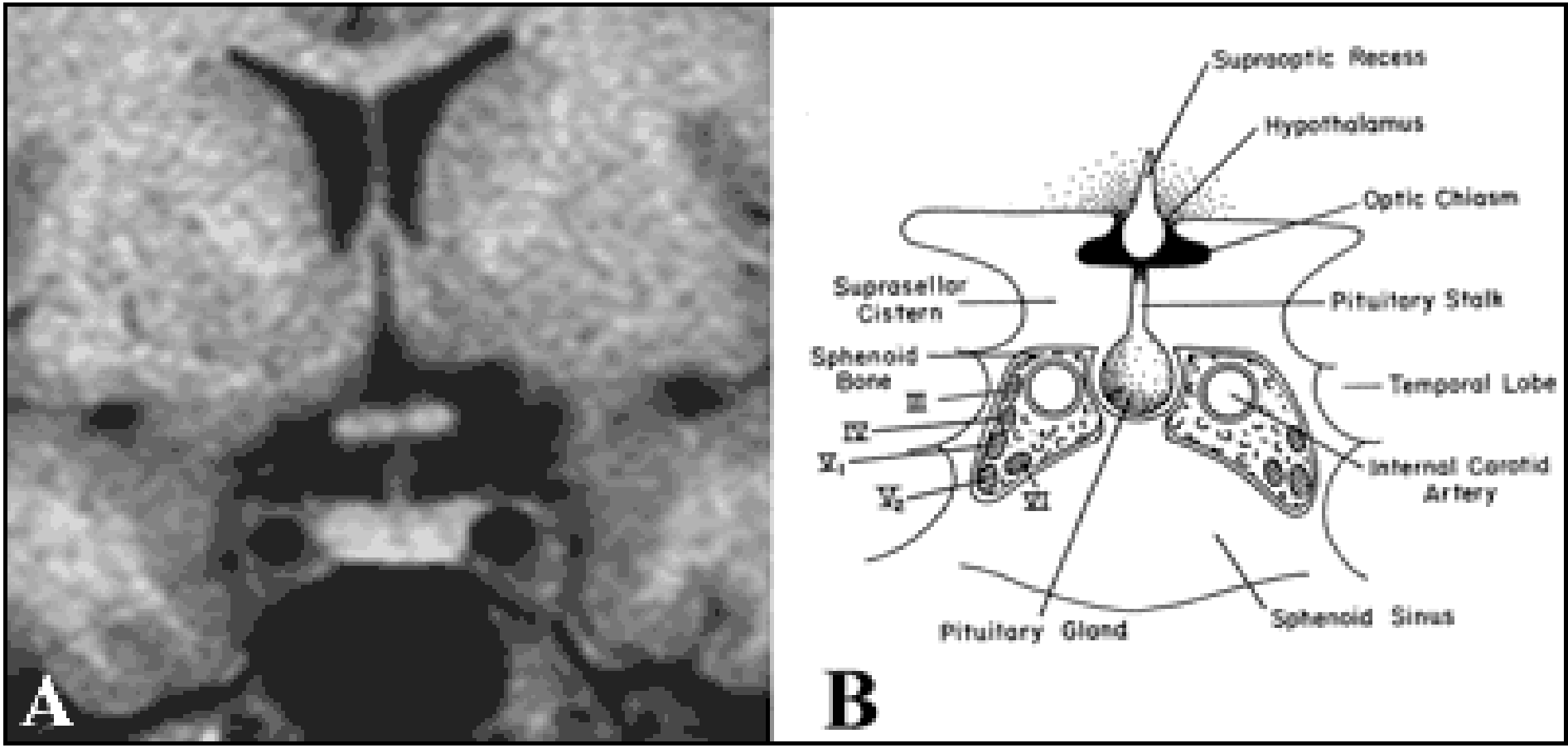
Pituitary Development

- Pituitary stalk and its blood vessels pass through the diaphragm
- Lateral wall by cavernous sinus containing III, IV, VI, V1, V2 cranial nerves and internal carotid artery with sympathetic fibers. Both adjacent to temporal lobes
- 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 sinsuses to jugular vein

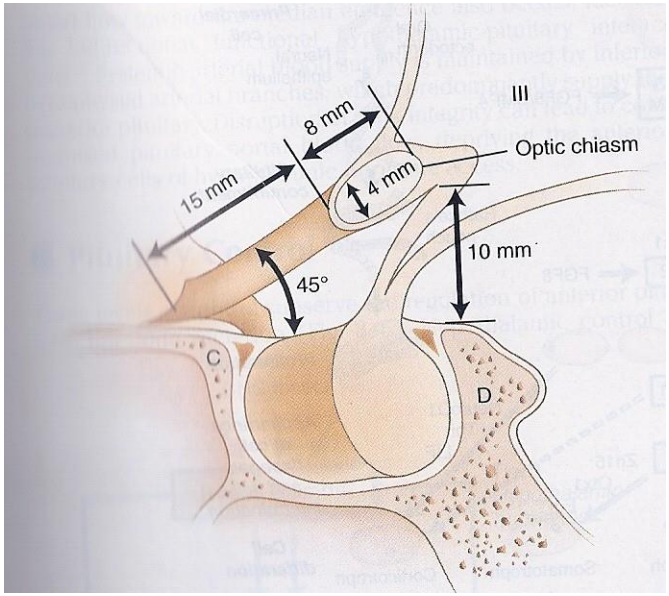
Pituitary Development



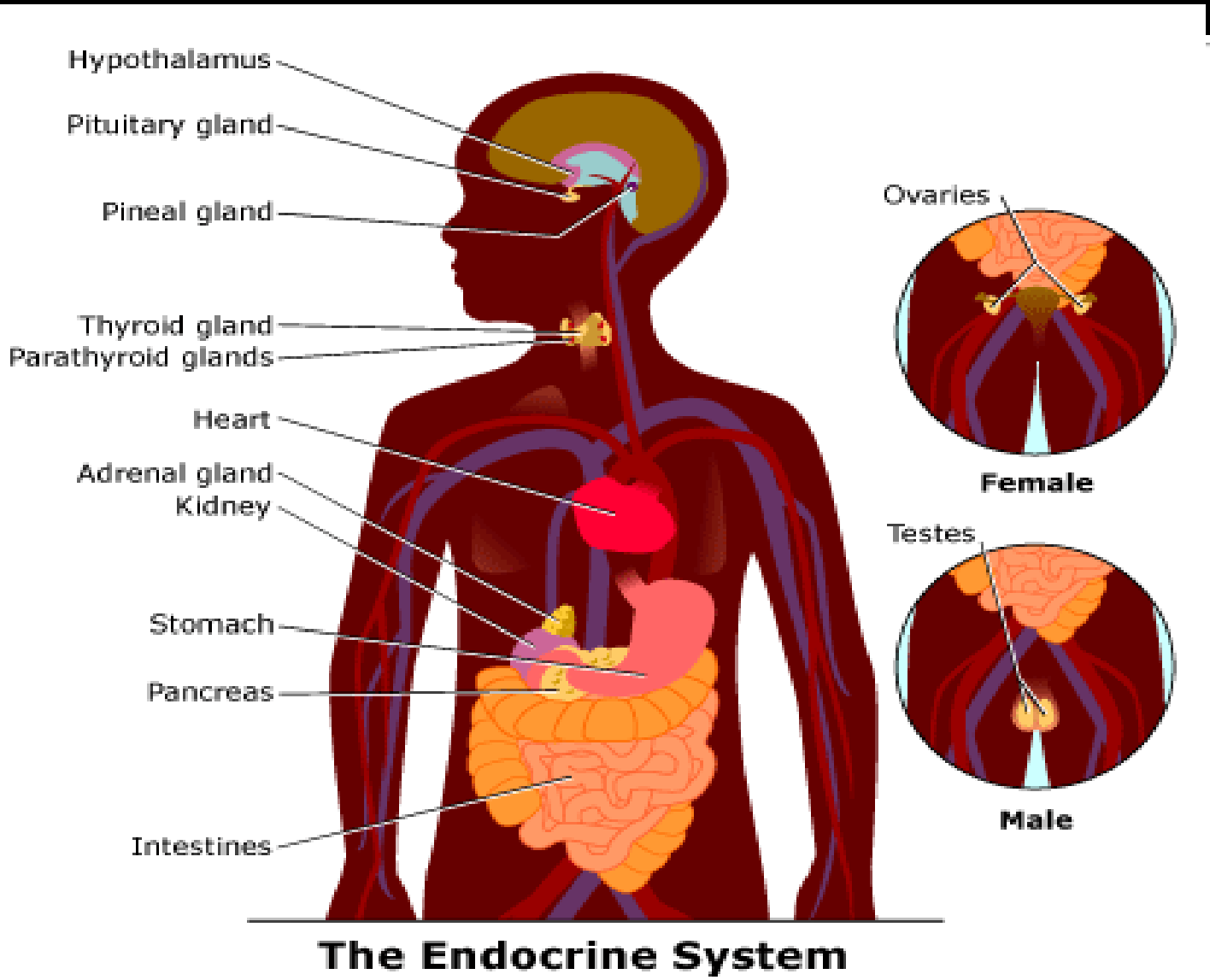
Normal Pituitary Anatomy



Pituitary Development



Endocrine system



Anterior Pituitary Function

	Corticotroph	Gonadotroph	Thyrotroph	Lactotroph	Somatotroph
Hormone	POMC, ACTH	FSH, LH	TSH	Prolactin	GH
Stimulators	CRH, AVP, gp-130 cytokines	GnRH, Estrogen	TRH	Estrogen, TRH	GHRH, GHS
Inhibitors	Glucocorticoids	Sex steroids, inhibin	T3, T4, Dopamine, Somatostatin, GH	Dopamine	Somatostatin, IGF-1, Activins
Target Gland	Adrenals	Ovary, Testes	Thyroid	Breast and other tissues	Liver, bone and other tissues
Trophic Effects	Steroid production	Sex Steroid, Follicular growth, Germ Cell maturation	T4 synthesis and secretion	Milk Production	IGF-1 production, Growth induction, Insulin antagonism

Anterior Lobe

- Growth hormone (GH)
- Gondadotrophs (LH/FSH)
- TSH
- Prolactin
- Corticotropin (ACTH)

Posterior Lobe

- Oxytocin
- Vasopressin

Etiology of Pituitary Masses

Etiology of Pituitary-Hypothalamic Lesions

- **Non-Functioning Pituitary Adenomas**
- **Endocrine active pituitary adenomas**
  - Prolactinoma
  - Somatotropinoma
  - Corticotropinoma
  - Thyrotropinoma
  - 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 aneursym**

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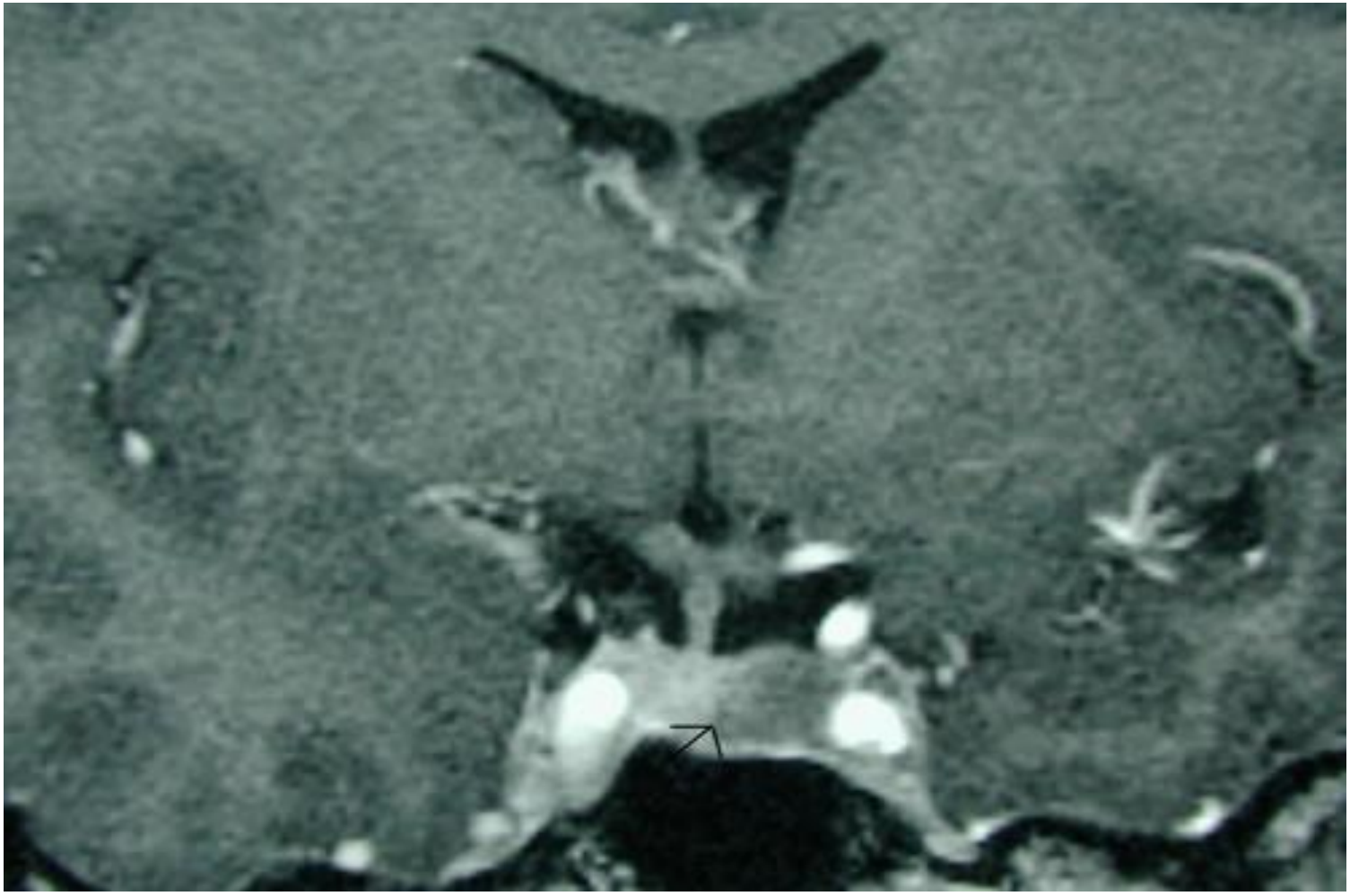
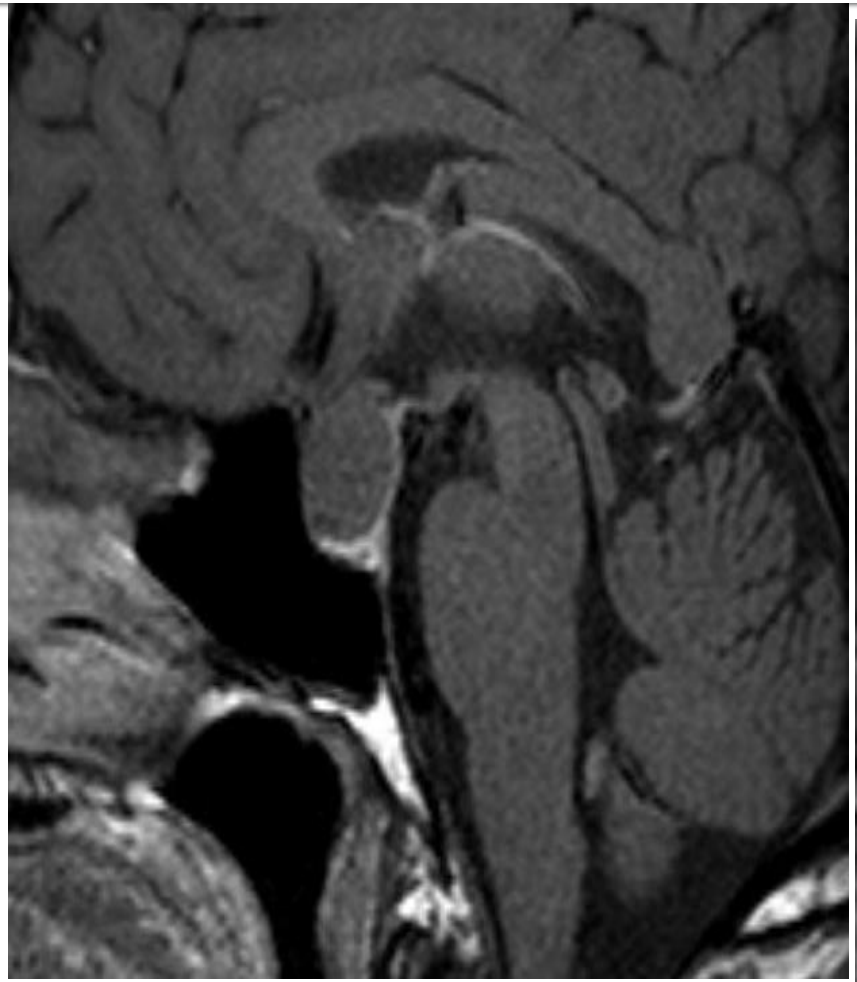
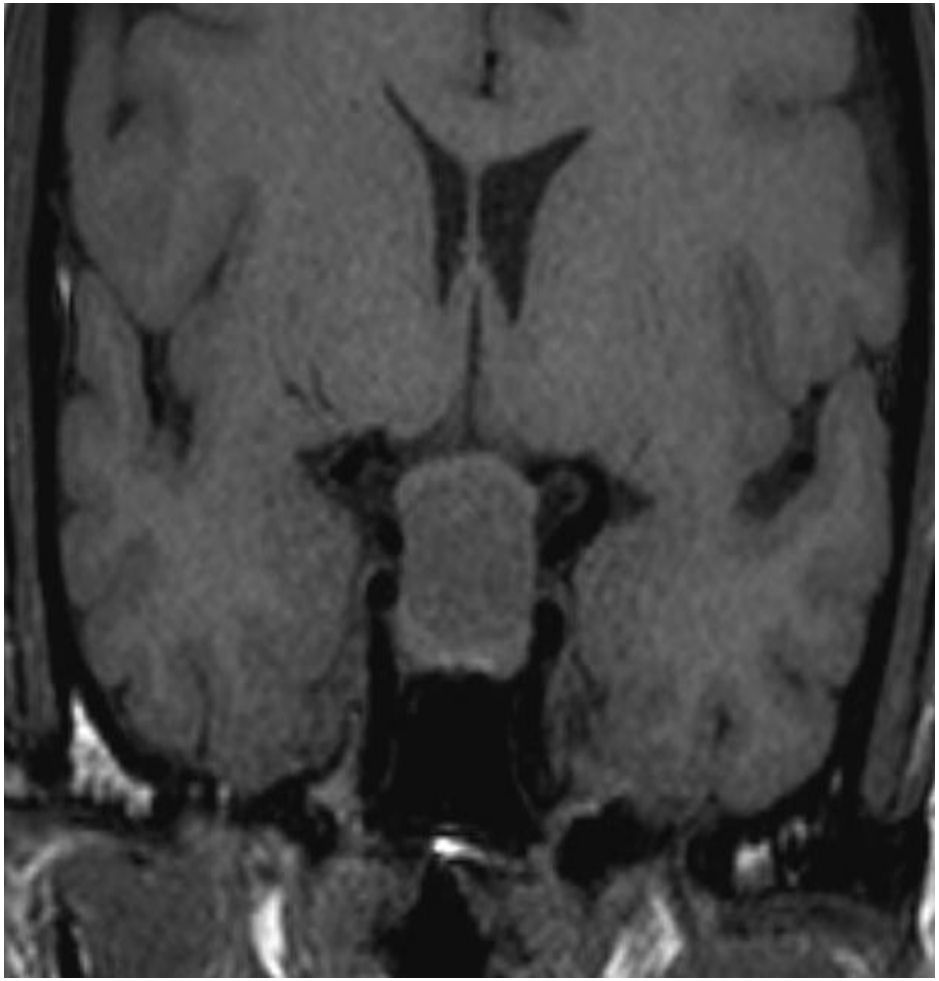






Disorders of Pituitary Function

- **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

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

- **Non-Functional pituitary lesion:**

- Absence of signs and symptoms of hormonal hypersecretion
- 25 % of pituitary tumor
- Needs evaluation either micro or macroadenoma
- Average age 50 – 55 yrs old, more in male

Non- functional pituitary adenoma

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

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%)

Non- functional pituitary adenoma

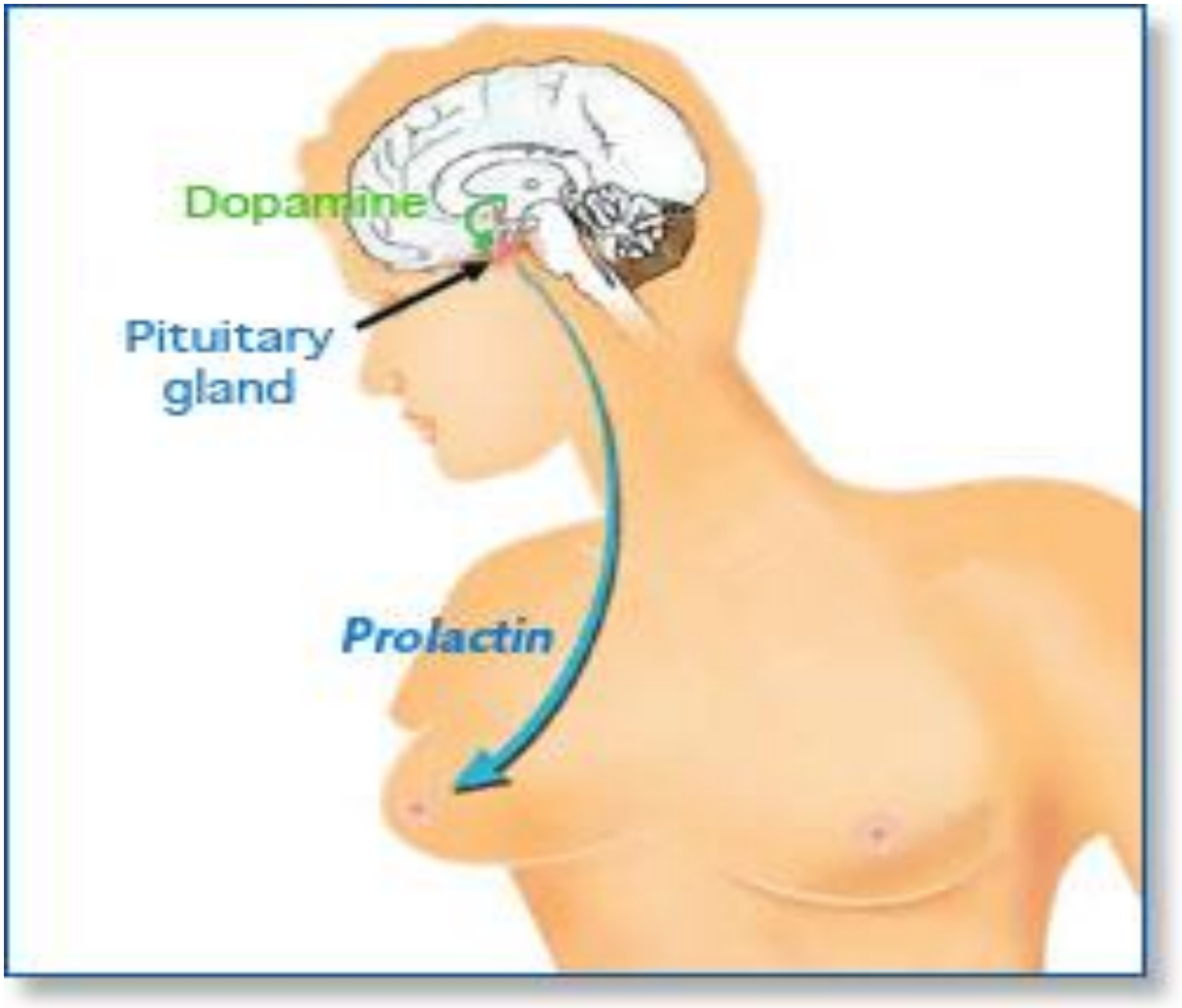
- **Treatment:**
- **Surgery if indicated**
  - recurrence rate 17 % if gross removal, 40 % with residual tumor
  - predictors of recurrence: young male, cavernous sinus invasion, extent of suprasellar extention of residual tumor, duration of follow up, marker; Ki-67

- **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
  - Somatostatin analogue

Functional pituitary mass

Prolactinoma



Prolactin

- Human prolactin is a 198 amino acid polypeptide
- Primary function is to enhance breast development during pregnancy and to induce lactation
- Prolactin also binds to specific receptors in the gonads, lymphoid cells, and liver
- Secretion is pulsatile; it increases with sleep, stress, pregnancy, and chest wall stimulation or trauma

Prolactin

- Secretion of prolactin is under tonic inhibitory control by dopamine, which acts via D2-type receptors located on lactotrophs
- Prolactin production can be stimulated by the hypothalamic peptides, thyrotropin-releasing hormone (TRH) and vasoactive intestinal peptide (VIP)

Clinical Features of Hyperprolactinemia/Prolactinoma

- Women may present with oligomenorrhea, amenorrhea, galactorrhea or infertility
- Men often have less symptoms than women (sexual dysfunction, visual problems, or headache) and are diagnosed later
- In both sexes, tumor mass effects may cause visual-field defects or headache

Prolactin

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Causes of Hyperprolactinemia

- **Hypothalamic Dopamine Deficiency**
  - Diseases of the hypothalamus(including tumors, arterio-venous malformations, and inflammatory processes
  - Drugs (e.g. alpha-methyldopa and reserpine)
- **Defective Transport Mechanisms**
  - Section of the pituitary stalk
  - Pituitary or stalk tumors

Causes of Hyperprolactinemia (continued)

- **Lactotroph Insensitivity to Dopamine**
  - Dopamine-receptor-blocking agents: phenothiazines (e.g. chlorpromazine), butyrophenones (haloperidol), and benzamides (metoclopramide, sulpiride, and domperidone)
- **Stimulation of Lactotrophs**
  - Hypothyroidism- increased TRH production (acts as a PRF)
  - Estrogens: stimulate lactotrophs
  - Injury to the chest wall: abnormal stimulation of the reflex associated with the rise in prolactin that is seen normally in lactating women during suckling

REMEMBER: Not all hyperprolactinemia is due to a prolactinoma

Work up of Patient with Hyperprolactinemia

- In females, pregnancy must always be ruled out
- Get a TSH- hypothyroidism is another common cause of elevated prolactin:
- Obtain detailed drug history- rule out medication effects
- Rule out other common causes including:
  - Nonfasting sample
  - Nipple stimulation or sex
  - Excessive exercise
  - History of chest wall surgery or trauma
  - Renal failure
  - Cirrhosis
- If no cause determined or tumor suspected, consider MRI, especially if high prolactin levels (> 100 ng/mL)

Prolactinomas

- Most common of functional pituitary adenomas
- 25-30% of all pituitary adenomas
- Some growth hormone (GH)–producing tumors also co-secrete PRL
- Of women with prolactinomas- 90% present with microprolactinomas
- Of men with prolactinomas- up to 60% present with macroprolactinomas

Management

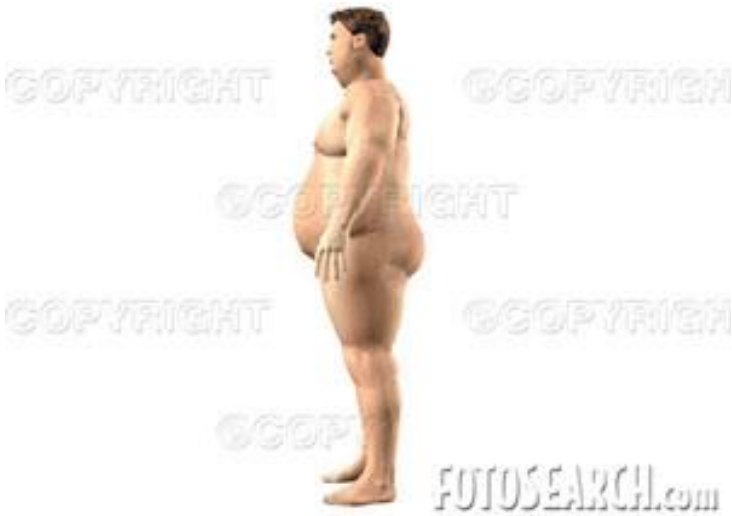
- Medical therapy: Dopamine agonist
- Surgical resection
- Radiation therapy

Growth hormone

- Pituitary tumor as mass effect →→ Growth hormone deficiency

- Hyperfunctioning mass →→ Acromegaly

Growth hormone deficiency

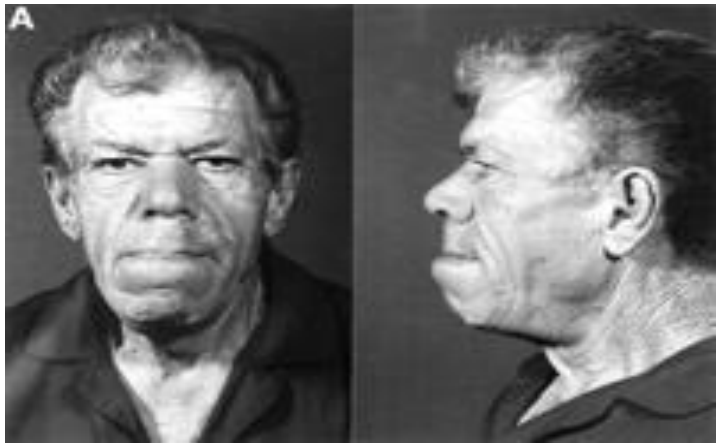


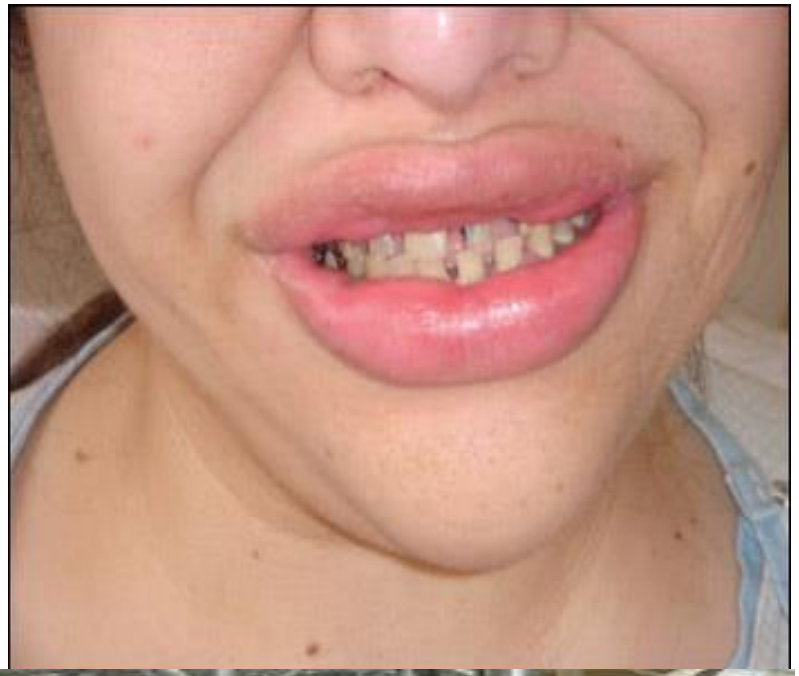
- Diagnosis in children and adult

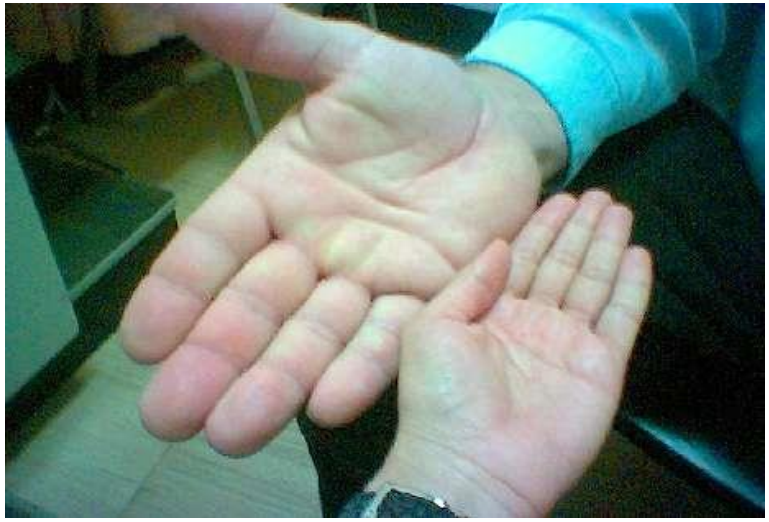
Diagnosis of GH-deficiency and management

- GH, IGF-I level
- Dynamic testing: clonidine stimulation test, glucagon stimulation, exercise testing, arginine-GHRH, insulin tolerance testing
- X-ray of hands: delayed bone age
- In Adult: Insulin tolerance testing, MRI pituitary to rule out pituitary adenoma
- Management: GH replacement

Acromegaly







Growth hormone disorder

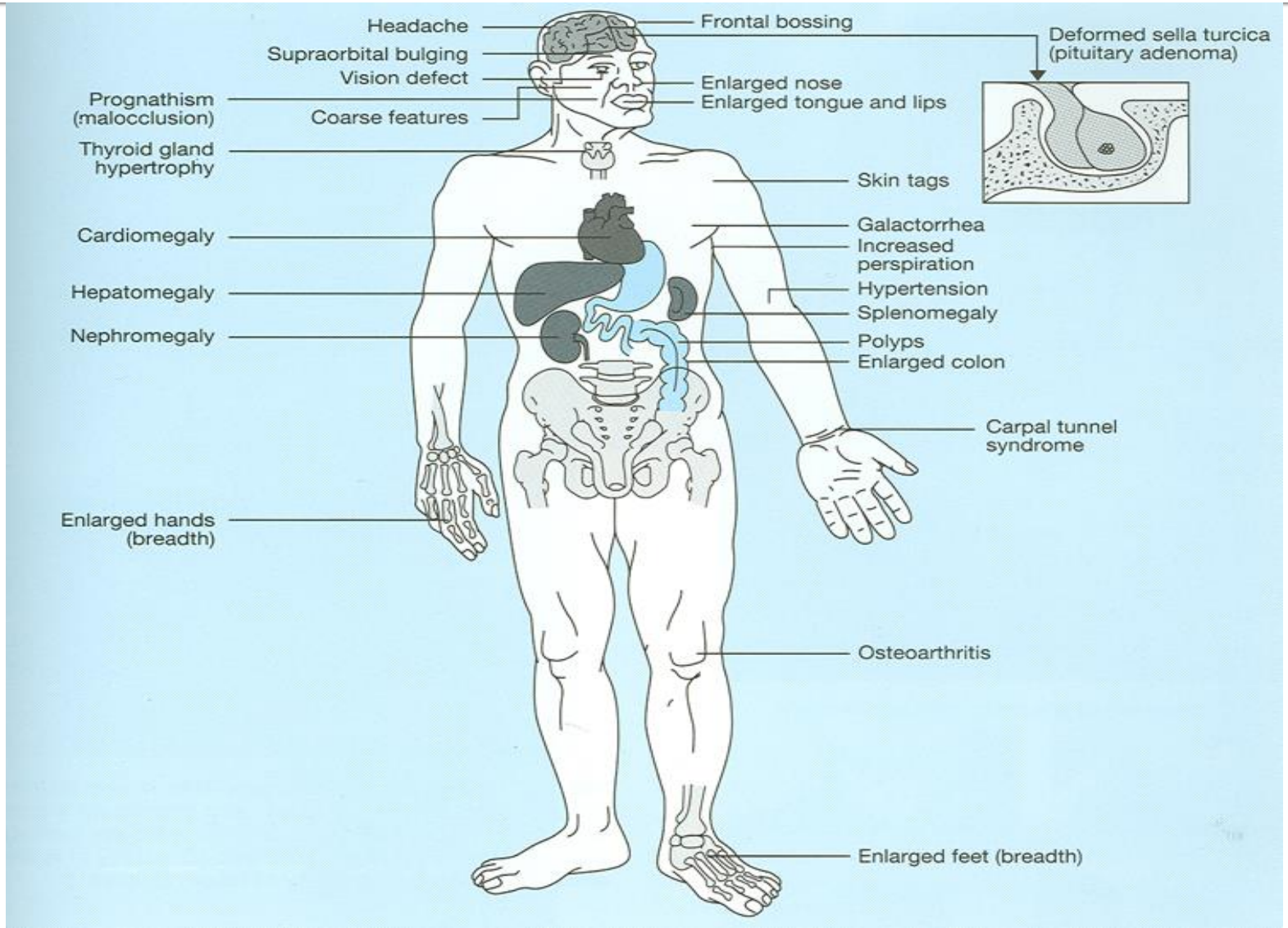
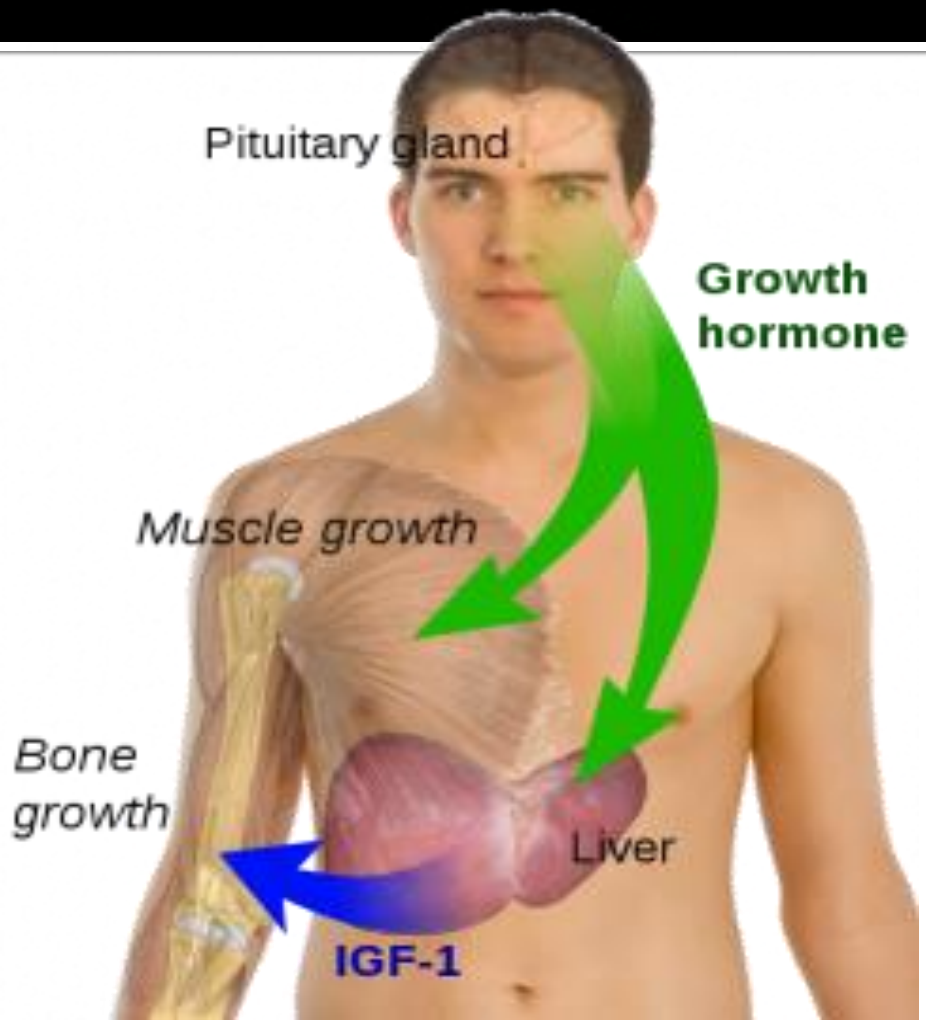


Table 1. Clinical Features of Acromegaly.

Local tumor effects	**Visceromegaly**
Pituitary enlargement	Tongue
Visual-field defects	Thyroid gland
Cranial-nerve palsy	Salivary glands
Headache	Liver
Somatic systems	Spleen
Acral enlargement, including thickness of soft tissue of hands and feet	Kidney
	Prostate
Musculoskeletal system	**Endocrine and metabolic systems**
Gigantism	Reproduction
Prognathism	Menstrual abnormalities
Jaw malocclusion	Galactorrhea
Arthralgias and arthritis	Decreased libido, impotence, low levels of sex hormone–binding globulin
Carpal tunnel syndrome	
Acroparesthesia	Multiple endocrine neoplasia type 1
Proximal myopathy	Hyperparathyroidism
Hypertrophy of frontal bones	Pancreatic islet-cell tumors
Skin and gastrointestinal system	Carbohydrate
Hyperhidrosis	Impaired glucose tolerance
Oily texture	Insulin resistance and hyperinsulinemia
Skin tags	Diabetes mellitus
Colon polyps	Lipid
Cardiovascular system	Hypertriglyceridemia
Left ventricular hypertrophy	Mineral
Asymmetric septal hypertrophy	Hypercalciuria, increased levels of 25-hydroxyvitamin D_3
Cardiomyopathy	Urinary hydroxyproline
Hypertension	Electrolyte
Congestive heart failure	Low renin levels
Pulmonary system	Increased aldosterone levels
Sleep disturbances	Thyroid
Sleep apnea (central and obstructive)	Low thyroxine-binding–globulin levels
Narcolepsy	Goiter

Growth hormone disorder



Acromegaly

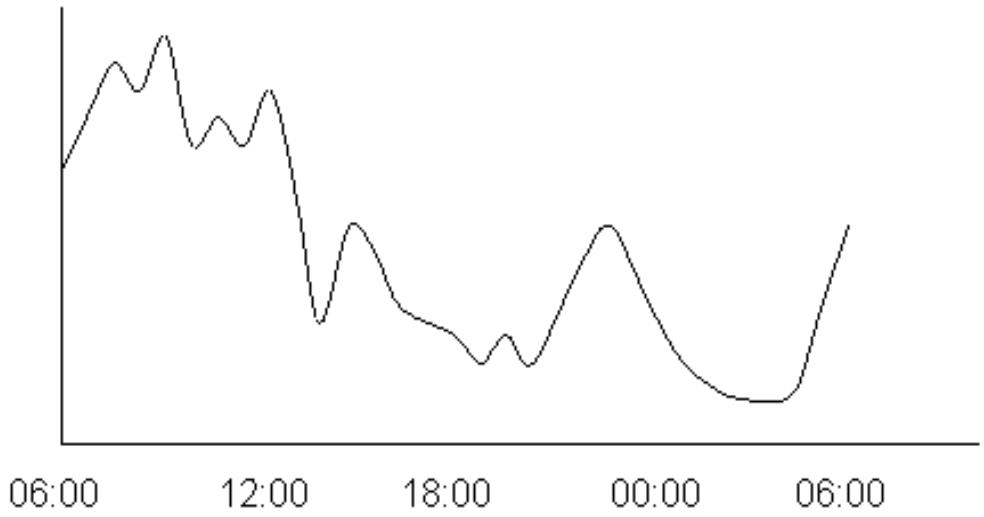
- Clinical picture and presentation
- GH level (not-reliable, pulsatile)
- IGF-I
- 75 g OGTT tolerance test for GH suppression
- Fasting and random blood sugar, HbA1c
- Lipid profile
- Cardiac disease is a major cause of morbidity and mortality
- 50 % died before age of 50
- HTN in 40%
- LVH in 50%
- Diastolic dysfunction as an early sign of cardiomyopathy

Growth hormone disorder- Acromegaly

- **Medical treatment:**
  - Somatostatin analogue
- **Surgical resection of the tumor**

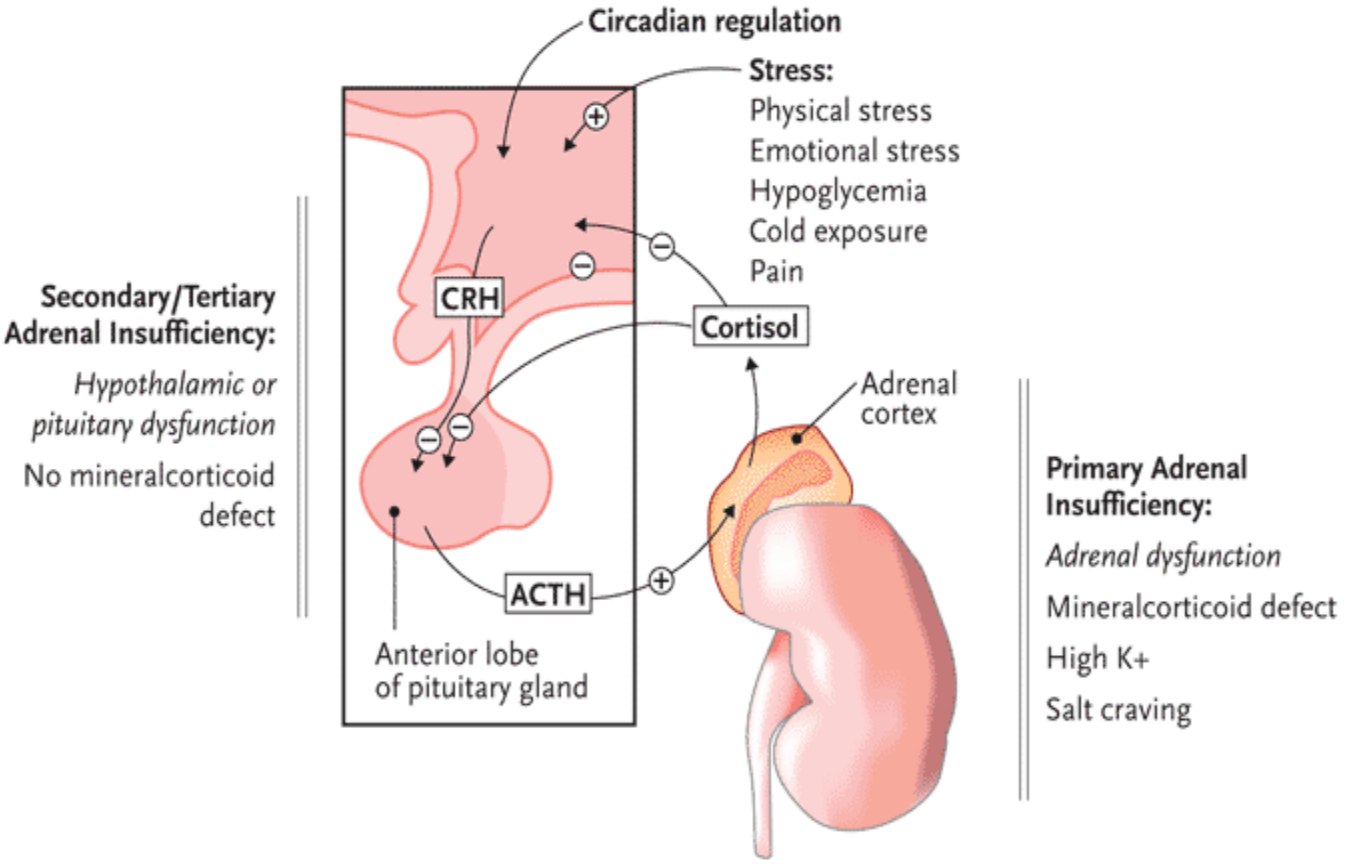
HPA-axis

- 2nd adrenal insufficiency
- glucgocorticoid replacement
- Circadian rhythm of cortisol secretion
- Early morning cortisol between 8-9 am



ACTH-disorders

ACTH-disorders



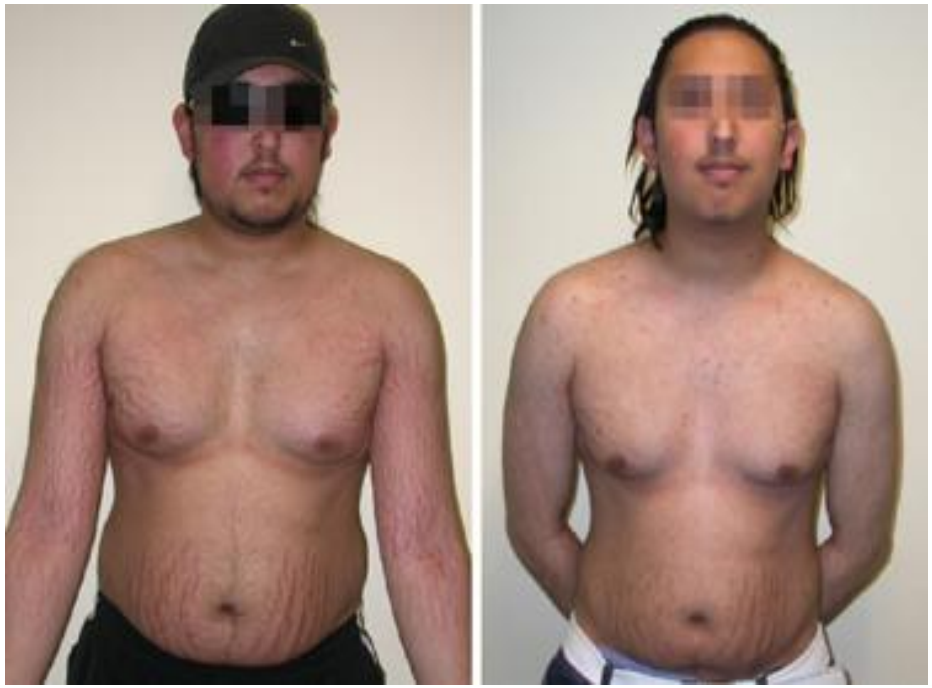
Hypoadrenalism

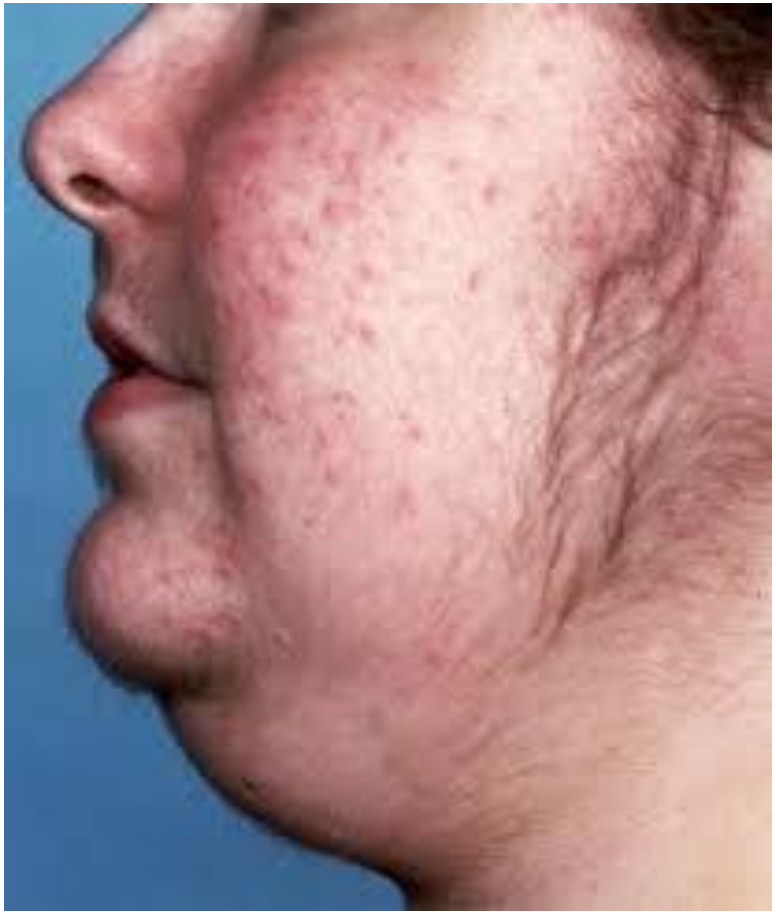
- Nausea
- Vomiting
- Abdominal pain
- Diarrhoea
- Muscle ache
- Dizziness and weakness
- Tiredness
- Weight loss
- Hypotension

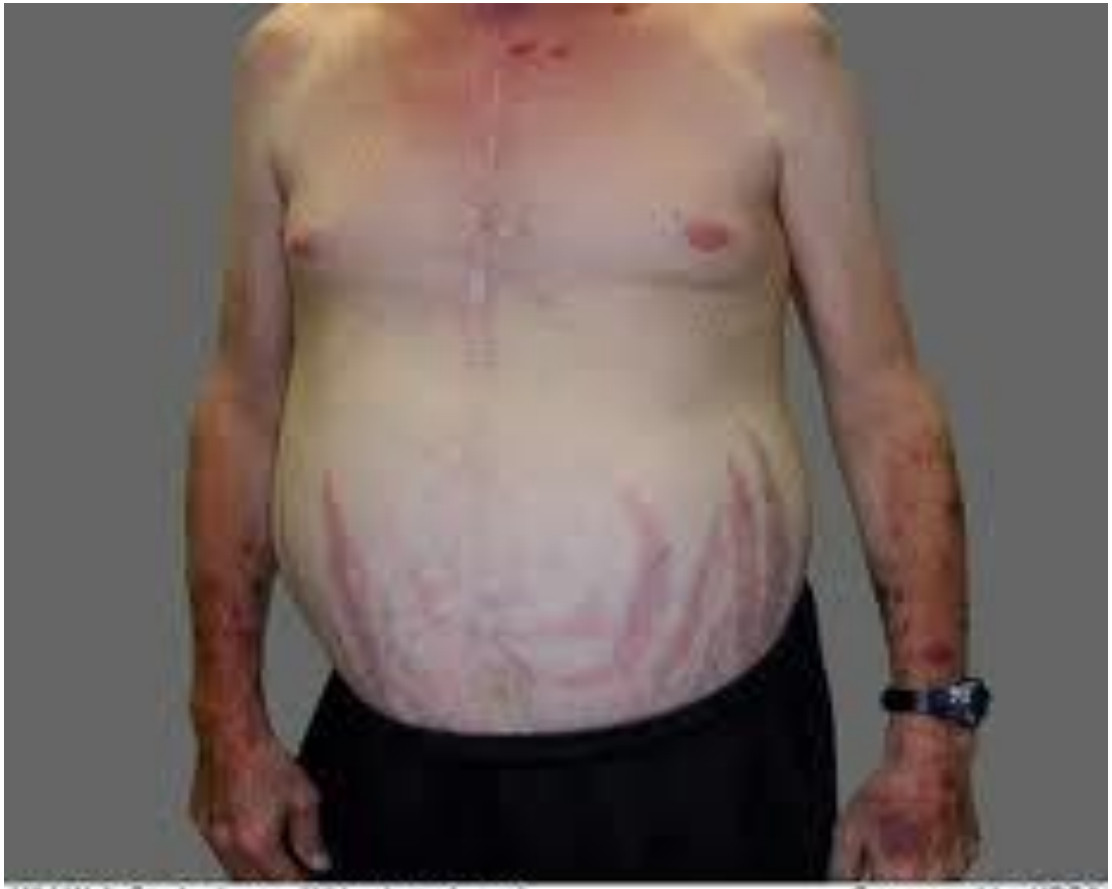
Management of hypoadrenalism

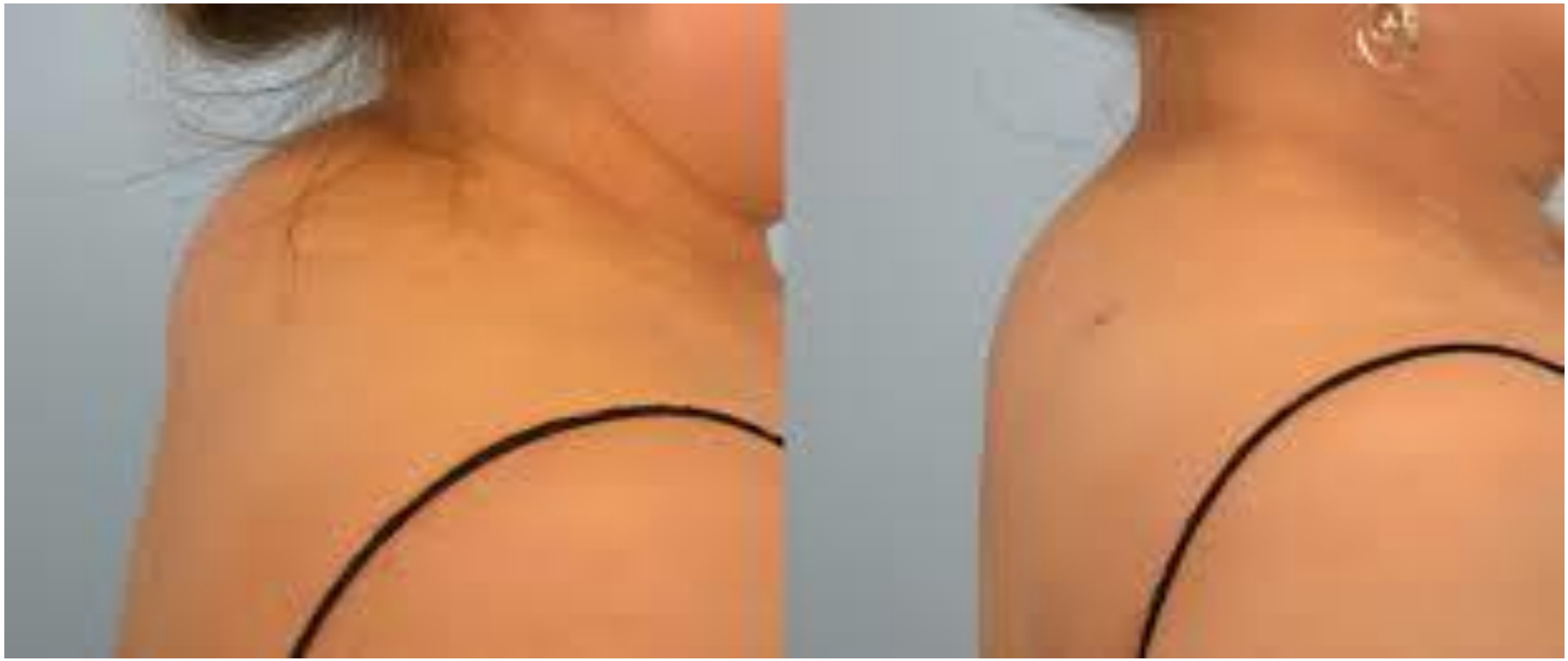
- Cortisol replacement

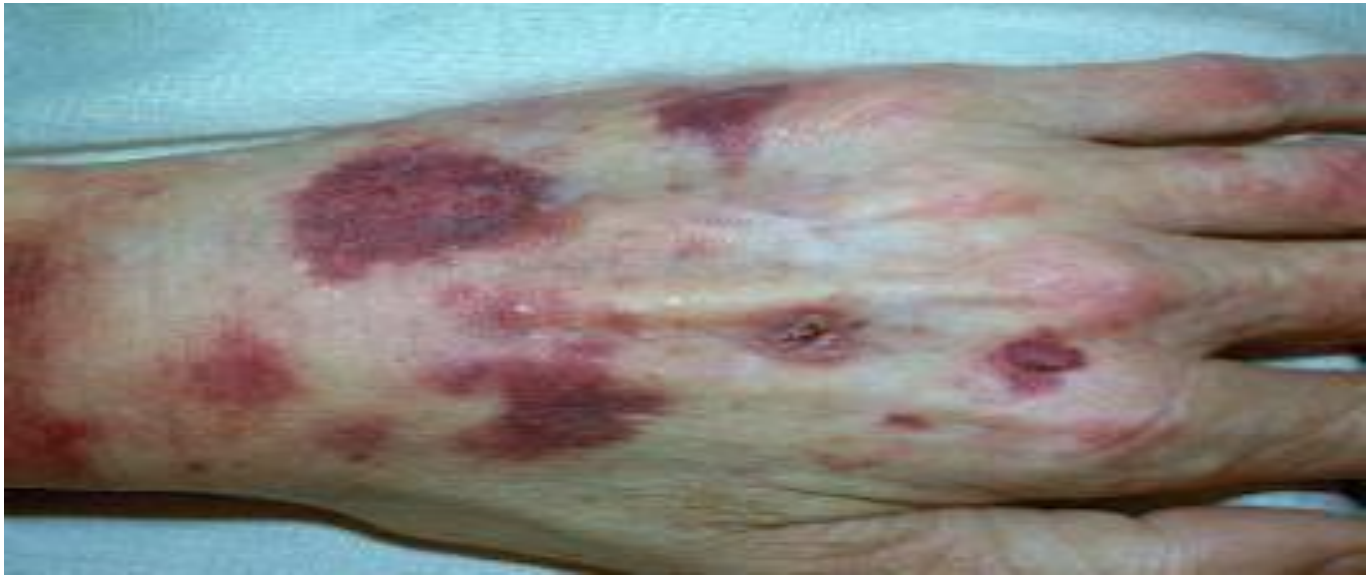
ACTH-Adenoma



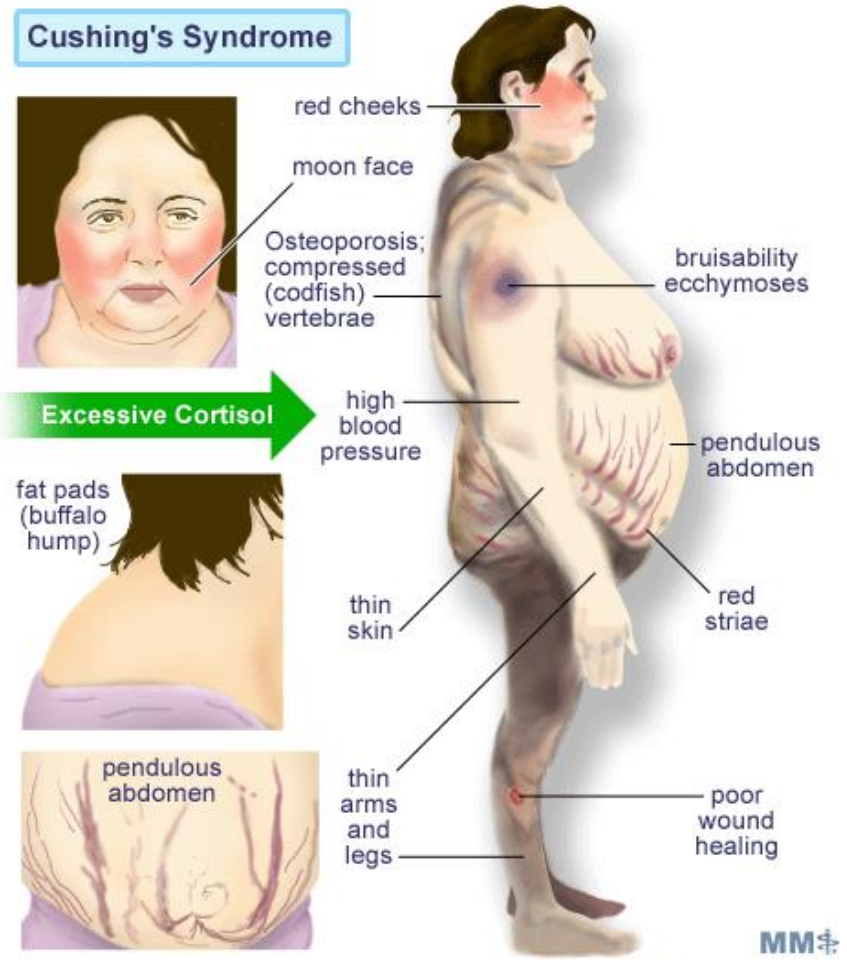



HIV Web Study (www.HIVwebstudy.org)
Supported by MRSA





HPA-axis (excessive cortisol)



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-Management

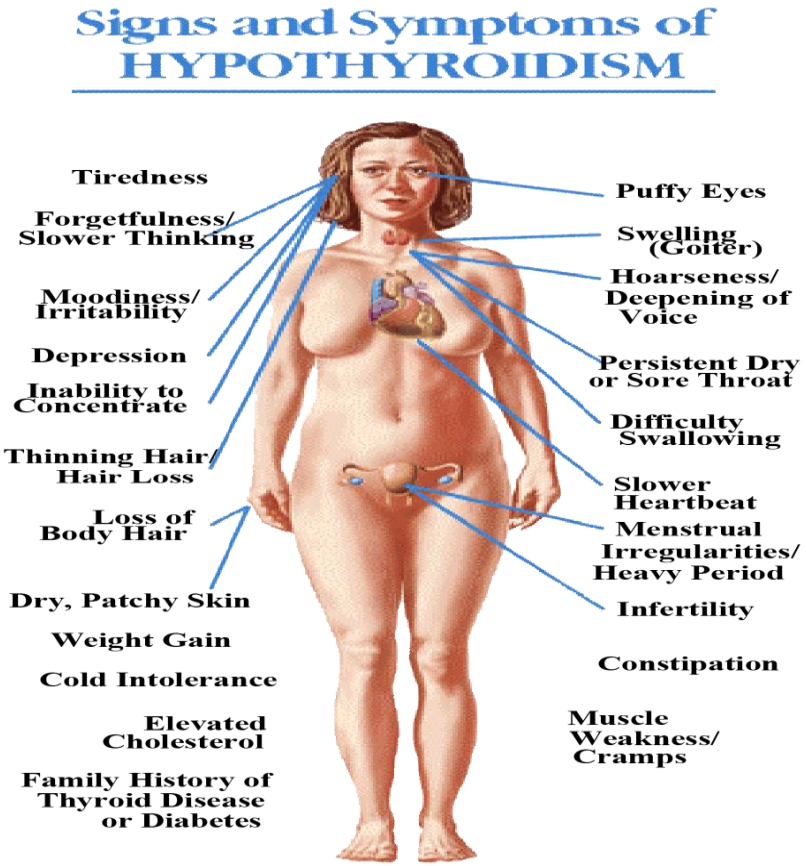
- Surgical resection of pituitary
- Medical Treatment

TSH-Hypothyroid

Fig. 2 A patient before and after successful treatment of primary hypothyroidism.

Central Hypothyroidism

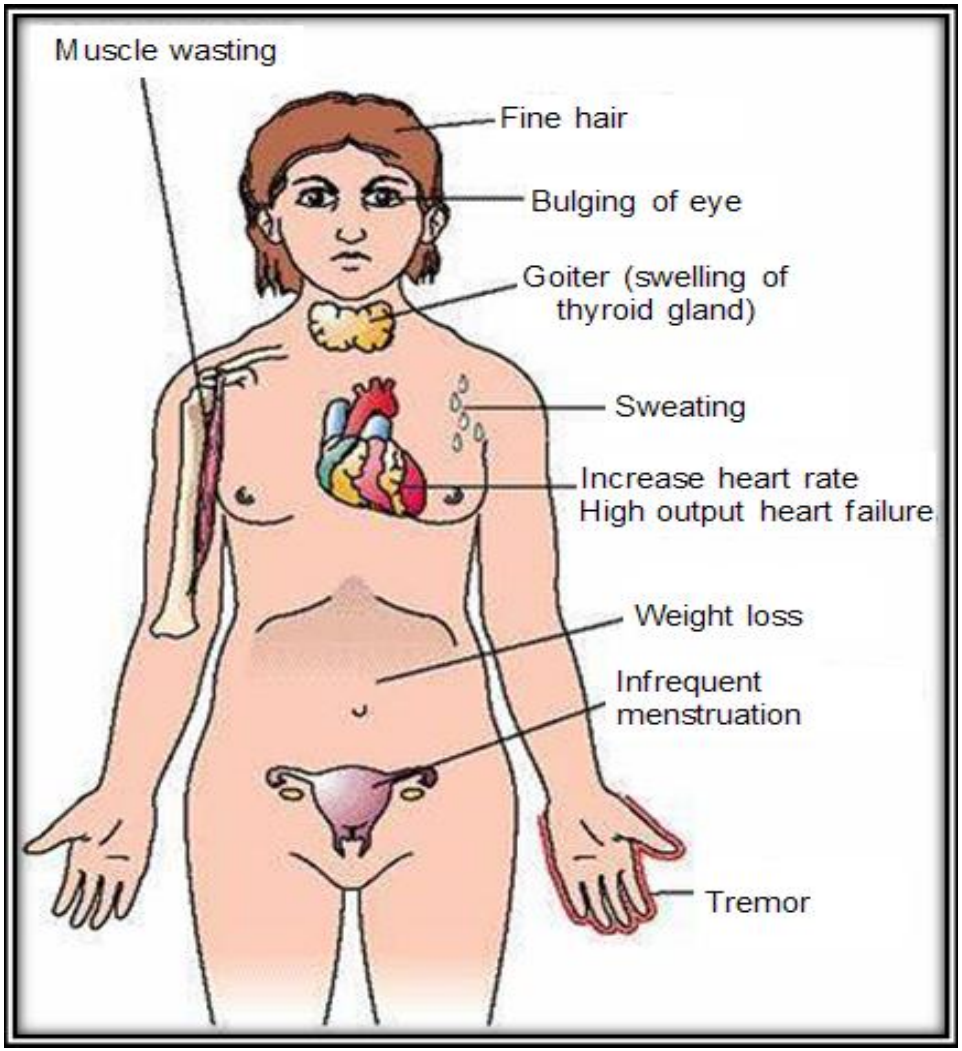
- Low TSH
- Low free T4 and T3



Central Hypothyroidism

- Thyroxine replacement
- Surgical removal of pituitary adenoma if large

TSH-hyperthyroid


Muscle wasting
Fine hair
Bulging of eye
Goiter (swelling of thyroid gland)
Sweating
Increase heart rate
High output heart failure
Weight loss
Infrequent menstruation
Tremor

TSH-Producing adenoma

- Very rare < 2.8 %
- Signs of hyperthyroidism
- High TSH, FT_4, FT_3
- 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 estridiol, FSH, thickened endometrium and polycystic ovaries

Gonadotroph Adenoma

- Surgical resection if large
- Radiation therapy

assessment of pituitary function

- Baseline: TSH, FT_4, FT_3, LH, FSH, Prolactin, GH, IGF-I,Testosterone, Estradiol
- MRI brain
- Neuropthalmic 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: all pituitary adenoma should be covered with stress dose of HC