Anterior Pituitary Disorders

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.

Color index:

1. Extra explanation
2. **Important**
3. **Doctors notes**

Please check the editing file before studying

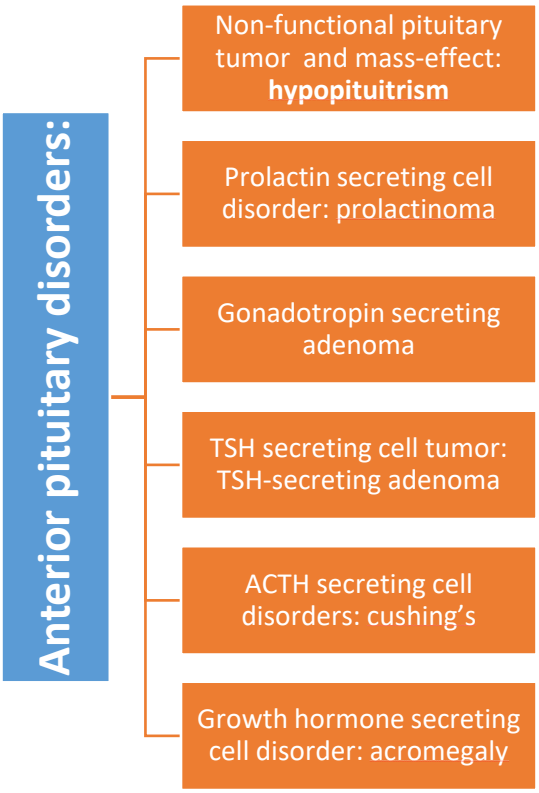
" أن أُجاهد في طلب العلم، أسخره لنفع الإنسان "

What will happen if T4 was low?

TRH and TSH increase and stimulate gland to produce hormone.

it is inappropriate response when T4 low and TSH normal

Most hormones from hypothalamus are releasing hormones. Most hormone from pituitary are stimulating hormones



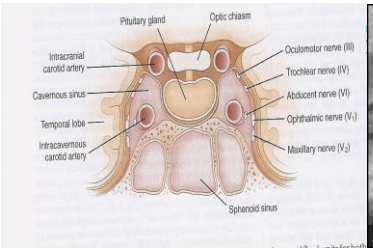
The table is very important

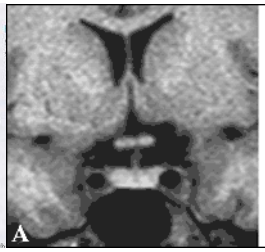
	Corticotroph	Gonadotroph	Thyrotroph	Lactotroph	Somatotroph
Hormone	**POMC, ACTH**	**FSH, LH**	**TSH**	**Prolactin**	**GH**
Stimulators	**CRH, AVP, gp-130 cytokines**	**GnRH, Estrogen**	**TRH**	**Estrogen, TRH**	**GHRH, GHS**
Inhibitors	**Glucocorticoids**	**Sex steroids, inhibin**	**T3, T4, Dopamine,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

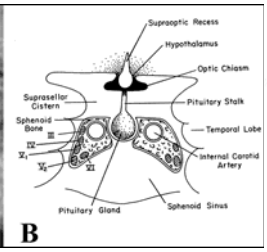
Pituitary Development:

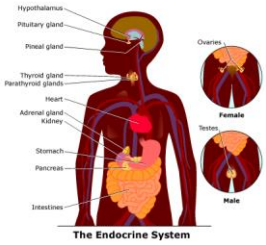
Anterior pituitary gland	Anterior pituitary is recognizable by 4- 5th wk of gestation
	Full maturation by 20th wk
	From Rathke's pouch, Ectodermal evagination of oropharynx
	Migrate to join neurohypophysis
	Portion of Rathke's pouch →→ Intermediate lobe
	Remnant of Rathke's pouch cell in oral cavity →→ 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

Posterior pituitary gland:	Posterior pituitary from neural cells as an outpouching from the floor of 3rd ventricle
Posterior pituitary gland cant produce any hormone just for storage	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
	Only storage: Oxyctocin, ADH (hypothalamic hormones) .
	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









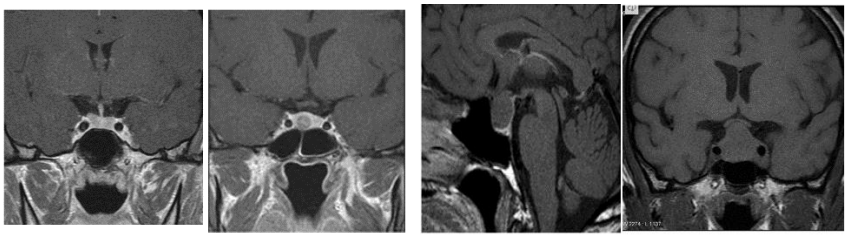
(A) Picture shows: Tumor extended upward. Moreover, the affect optic chiasm that will affect visual field(bitemporal hemianopia)

(B) يسألون المريض اذا يقدر يشوف السيارات اللي جمبه وهو يسوق او المرايا الجانبيه ؟عادة يجاوب لا بكذا يعرفون انه مأثر على optic chiasm

(C) . If the mass extend down edit will cause CSF drain from the nose If it affect temporal lobe it will cause seizure

othalamic Lesions:

- Non-Functioning Pituitary Adenomas
- adenomas:Prolactinoma,Somatotropinoma, Corticotropinoma, Thyrotropinoma, Other
- 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



Disorders of Pituitary Function:

Hypopituitarism

- Central hypoadrenalism(isolated, multiple, pan)
- hypogonadism, hypothyroidism or GH deficiency
- Panhypopituitarism

Hypersecretion of Pituitary Hormones(GH,LH,FSH,PRL,TSH,ACTH)

- Hyperprolactinemia
- Acromegaly (↑GH)
- Cushing's Disease (↑ coresterol)

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

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.

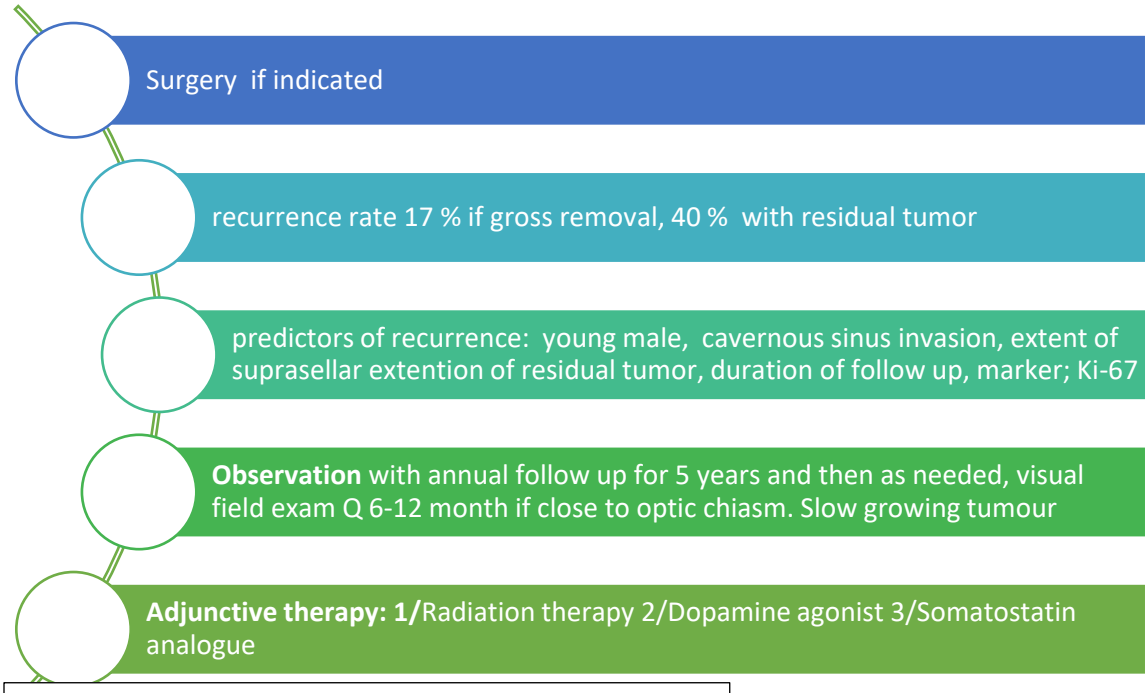
Non-Functional pituitary lesion:

(Nonfunctioning means hormone either normal or low)

- Absence of signs and symptoms of hormonal hypersecretion
- 25 % of pituitary tumor
- Needs evaluation either micro or macroadenoma
- Clinical (History and Examination) function (oversection or hyposecretion) Mass (headache, visual symptoms) .
- Biochemical : Screen Test
  Confirmatory Test
- Anatomical : MRI of sella turcica

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

Treatment:



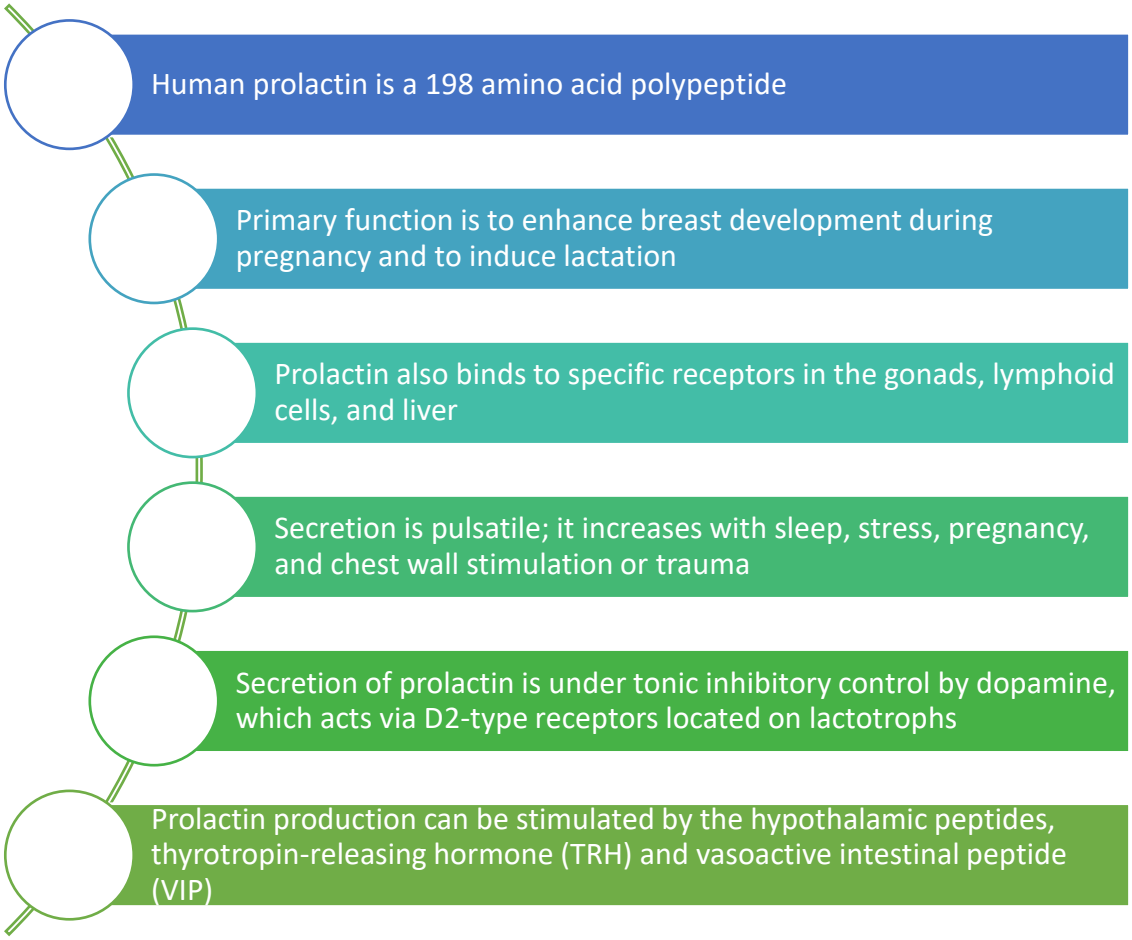
Non-functional pituitary adenoma	
C: Clinical	Asymptomtic , incidentaloma by imaging Mass-effect (mechanical pressure, hypopituitarism, visual (bitemproal hemianopia) Gonadal hypersecretion
B: Biochemical	GH,LH,FSH,TSH,ACTH: not high PRL : low ,high, normal
A: Anatomical	MRI
Treatment	Surgery if indicated Observation Adjunctive therapy: - Radiation therapy - Dopamine agonist - Somatostatin analogue

Functional pituitary mass:

Prolactin is the only hormone has no direct Releasing hormone

Prolactin

(REMEMBER: **Not all hyperprolactinemia is due to a prolactinoma**):



Low prolactin:

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

Causes of Hyperprolactinemia:

Hypothalamic Dopamine Deficiency	Defective Transport Mechanisms	Lactotroph Insensitivity to Dopamine	Stimulation of Lactotrophs
Diseases of the hypothalamus(including tumors, arterio-venous malformations, and inflammatory processes Drugs (e.g. alpha-methyldopa and reserpine)	Section of the pituitary stalk Pituitary or stalk tumors	Dopamine-receptor-blocking agents: phenothiazines (e.g. chlorpromazine), butyrophenones (haloperidol), and benzamides (metoclopramide, sulpiride, and domperidone)	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

when adenoma produce prolactin in high level, what will happen? In female, galactorrhea, infertility and amenorrhea (irregular cycle). in male, hypogonadism and gynecomastia, lebedo.

Clinical Features of Hyperprolactinemia/Prolactinoma:

In both sexes, tumor mass effects may cause visual-field defects or headache

Men often have less symptoms than women (sexual dysfunction, visual problems, or headache) and are diagnosed later

Women may present with oligomenorrhea, amenorrhea, galactorrhea or infertility

Normally prolactin increased during pregnancy, so the first thing should be done for lady with high prolactin level is pregnancy test.

45 years old with headache and amenorrhea prolactin is high. what is the treatment? Medical treatment (dopamine) in the same case, if the mass affects visual field we do not do surgery because the medical treatment causes the mass to shrink. Surgical treatment if there was no response to medical

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. 1<cm
- Of men with prolactinomas- up to 60% present with macroprolactinomas. 1>cm

Growth hormone:

Pituitary tumor as mass effect →→ Growth hormone deficiency

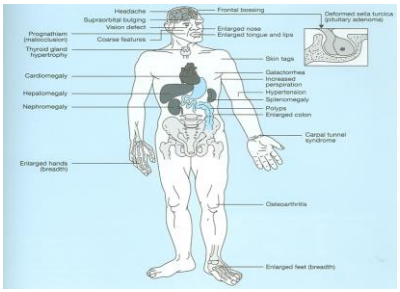
Hyperfunctioning mass →→ Acromegaly

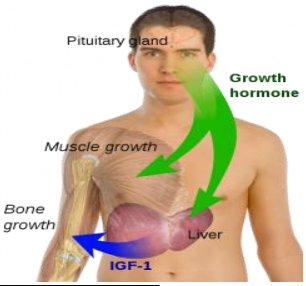
Isolated, pan hypopituitarism

when the Mass cause compression, the first hormone will be released is GH
what is the most important hormone for life?
Cortisol.

Disease:

- ➢ Children: Short stature
- ➢ Adult: ??





نعطي انسولين لشخص قصير وشاكين GH فبيصير عندنا بهذي الحالة ان عنده نقص ب hypoglycemia والطبيعي ان هذي نظرا لقلة السكر بالدم فلو ما افرز GHدلالة على نقص هرمون النمو

↑GH:
↑hand size, مايقدر يلبس gloves>called acral enlargement
↑feet size, يتغير مقاس الرجل >called acral enlargement
Knee pain
↑mandible size(jaw malocclusion), peace between teeth
Hypertrophy of frontal bones
↑risk of colon cancer
Headache
Seizures
hyperglycemia (DM in children)

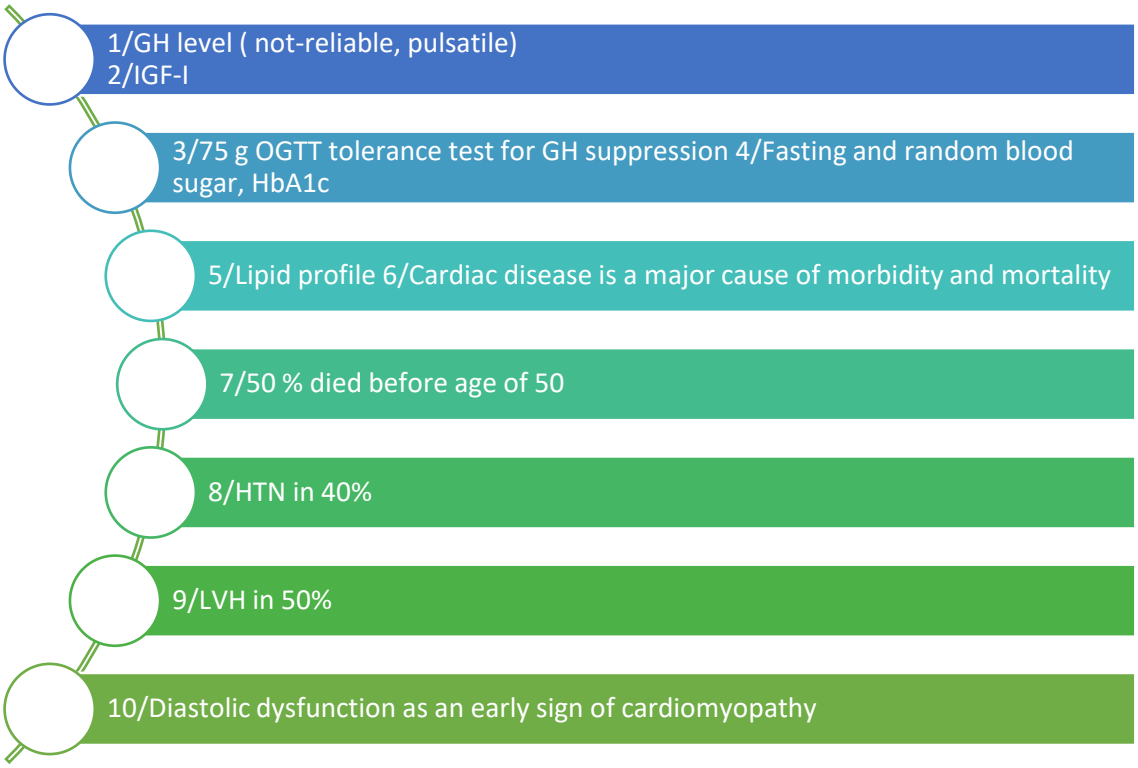
catecholamine, cortisol, GH and glucagon normally increase the glucose.

IGF1 is active form in muscle and skeleton.

↓GH:
Truncal obesity (in adult)>>because there is NO lipolysis

Acromegaly:

Clinical picture and presentation:



Medical treatment:

- Somatostatin analogue
- Surgical resection of the tumor

Important table

Growth hormone deficiency

C: Clinical	**Function : Short stature** **Mass-effect (mechanical pressure, hypopituitarism)**
B: Biochemical	Pituitary Function (LH,FSH.PRL, TSH, ACTH, cortisol,testesterone, T4) 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

Very important table

Prolactinomas

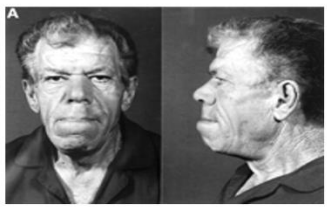
C: Clinical	**oligomenorrhea, amenorrhea or infertility** **Galactorrhea** **Mass-effect (mechanical pressure, hypopituitarism)** **Sexual dysfunction (in male)** ***asleep, stress, pregnancy, lactation and chest wall stimulation or trauma, Renal failure, Liver failure*** ***medication*** **O/E: Visual 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-secrtion
A: Anatomical	MRI
Treatment	**Medical – Medical – Medical (Dopamine agonist)** **Surgical- Radiation**

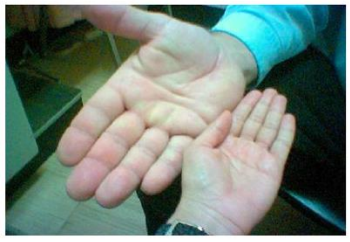
Acromegaly

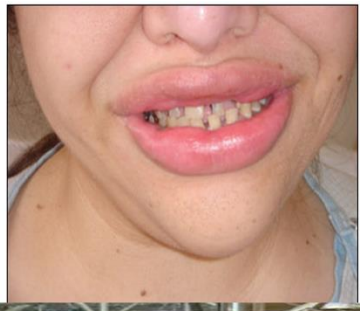
C: Clinical	**Function : Sweating, Enlargement (acral, face gross features, heart, tongue Jaw, gigantism in children , Galactorrhea** **Mass-effect (mechanical pressure, hypopituitarism)** ***HTN,CHF, OSA,constipation*** **O/E: Visual field defect (Bitemporal hemianopia)** **Gross features of Acromegaly**
B: Biochemical	Pituitary Function (LH,FSH.PRL, TSH, ACTH, cortisol,testesterone, T_4) Screen: IGF-1 Confirmatory Test : 75 g OGTT tolerance test for GH suppression Fasting and random blood sugar, HbA1c Lipid profile
A: Anatomical	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
Treatment	**Surgical – Medical (**Somatostatin analogue)- **Radiation**

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
Musculoskeletal system	Prostate
Gigantism	**Endocrine and metabolic systems**
Prognathism	Reproduction
Jaw malocclusion	Menstrual abnormalities
Arthralgias and arthritis	Galactorrhea
Carpal tunnel syndrome	Decreased libido, impotence, low levels of sex hormone–binding globulin
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

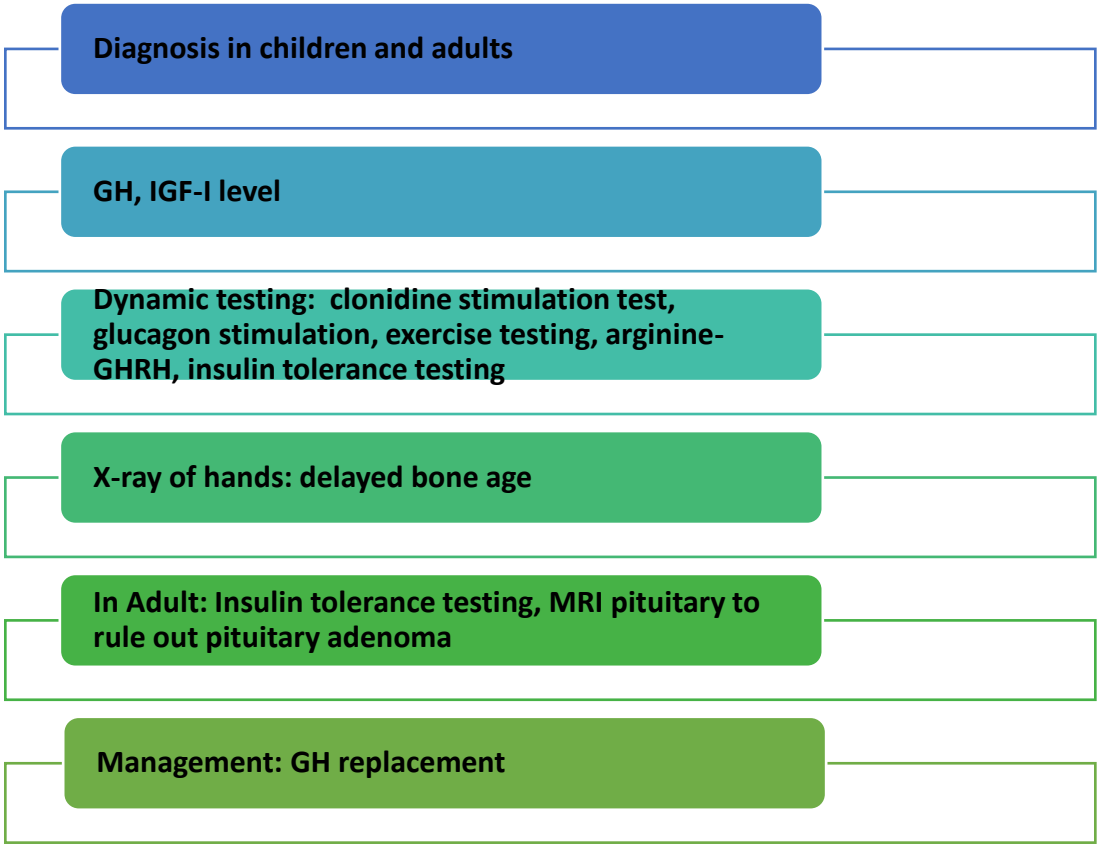






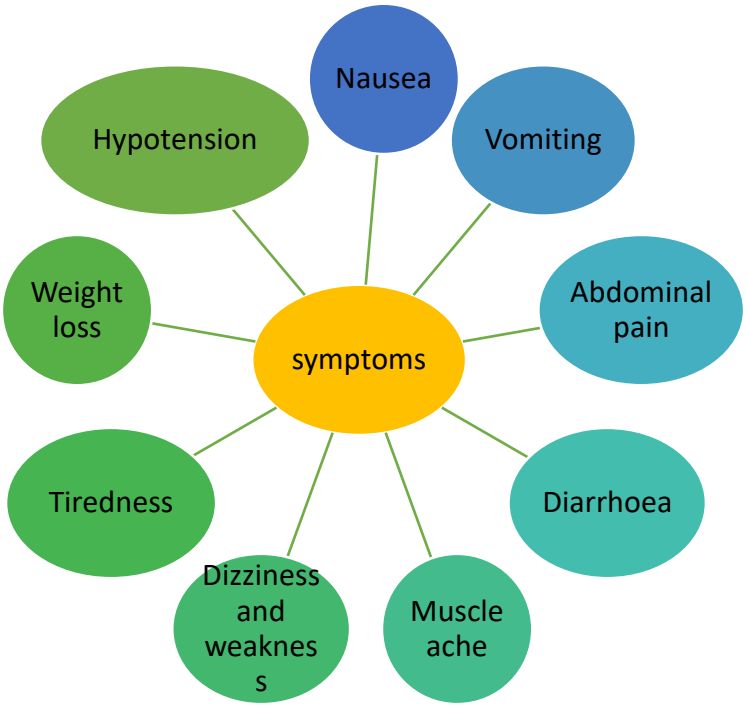
Diagnosis: first step>IGF-1
Why not diagnosed by GH test? BC IGF-1 value is constant during all the day not like GH which fluctuating during all the day

Growth hormone deficiency:



Treatment: GH replacement in children
In adult: عادة ما نعطيهم GH الا اذا كان عندهم truncal obesity or psychological problems

Hypoadrenalism



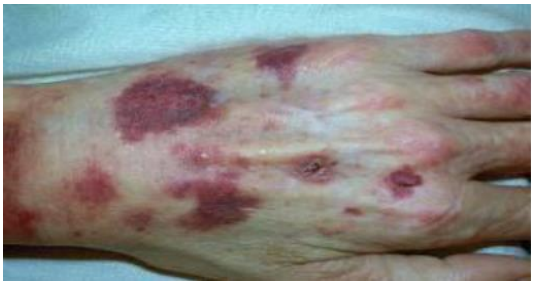
Other symptoms:
Moon like face ,Thin skin ,Fat pads (accumulation of fat in the dorsal neck),Truncal obesity,Red cheeks ,Thin arms and legs ,Hypertension ,Acne ,Hair over growth

Remember cortisol is the most important hormone for life.
What is the difference between staria in obesity and cushion syndrome.
the color. ACTH will stimulate the melatonin and cause the color.
ACTH has the same origin of melatonin.

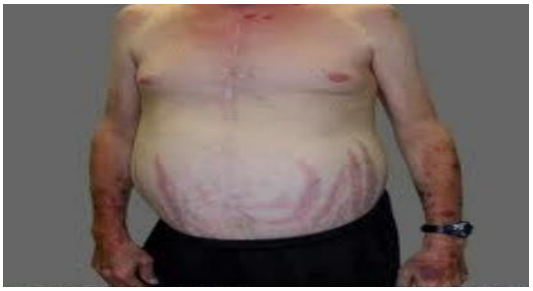
Management of hypoadrenalism

- **Cortisol replacement**

HPA-axis excessive cortisol:



excissive cortisol (cushings) ecchymosis



excissive cortisol (cushings) stria purple wide >1 cm

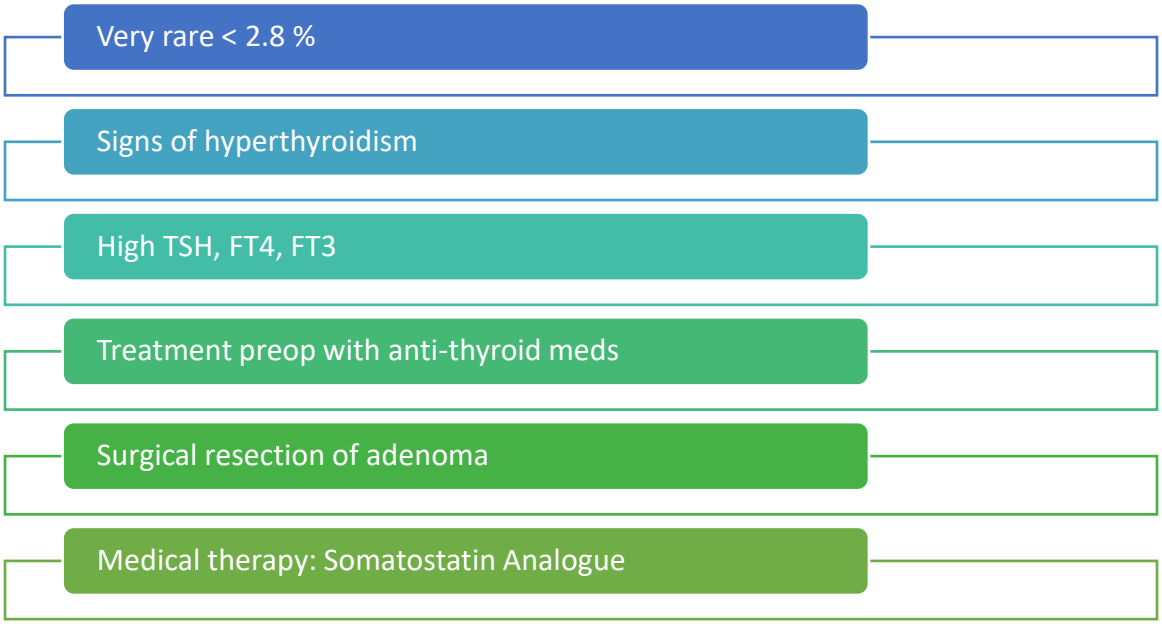
- ¡ 80 % HTN
- LVH
- Diastolic dysfunction, intraventricular septal hypertrophy
- ECG needed: high QRS voltage, inverted T-wave
  Echocardiogram preop
- OSA: 33% mild, 18% severe. Needs respiratory assessment and careful use of sedative during surgery
- Glucose intolerance in 60%, control of hyperglycemia
- 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

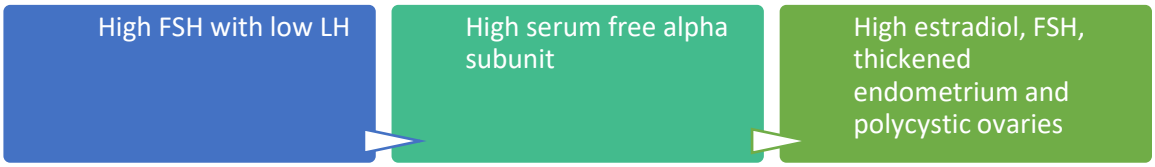
Central Hypothyroidism	
C: Clinical	Function : fatigue, weight gain, irregular menses, dry skin, depression, cold intolerance, increase sleep, slow thinking O/E: obesity, ? Depressed face, eye brow
B: Biochemical	Low T_4 , Low TSH
A: Anatomical	MRI
Treatment	Thyroxine replacement Surgical removal of pituitary adenoma if large

Central hypothyroidism

TSH producing adenoma



Gonadotroph adenoma vs. menopause and ovarian failure



Gonadotroph adenoma

- Surgical resection if large
- Radiation therapy

Assessment of pituitary function

- Baseline: TSH, FT4, FT3, LH, FSH, Prolactin, GH, IGFI,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

Questions

Q1–a boy has a pituitary gland disorder, he is 16 years old and looks like he is 10 , what is the hormone that is effected:

A-TSH. B-GH. C-FSH. D-prolactin.

Q2–what is the most common functional pituitary adenomas:

A-prolactinoma. B-hypoadrenalism. C-Cushing. D-gonadotrophs adenoma.

Q3–a patient come to the ER with severe headache when taking the vital signs ha has a high blood pressure and the doctor noticed that the patient has a moon face with red cheeks, what is the most likely diagnosis:

A-high amount of cortisol. B-Cushing's. C-A and B. D-none.

Q4– a patient come to the ER with severe headache when taking the vital signs ha has a high blood pressure and the doctor noticed that the patient has a moon face with red cheeks, which of the following will be seen in ECG:

A- low QRS voltage and inverted T wave.

B- - low QRS voltage and erect T wave.

C-- high QRS voltage and erect T wave.

D- high QRS voltage and inverted T wave.

Q5–excess amount of GH will lead to:

A-dwarfism. B-diabetes. C-acromegaly. D-infertility in women.

Q6–How to manage a patient with hypoadrenalism:

A-insulin. B-cortisol replacement. C-dopamine agonist. D-non.

Answers:

1-B

2-A

3-C

4-D

5-C

6-B

Videos

- Over view of pituitary gland tumor
- prolactinoma
- hyperprolactinemia
- hyperprolactinemia (2)
- Cushing

اللهم إني استودعتك ما حفظت وما فهمت، فردّه لي عند حاجتي إليه، إنك على كل شيءٍ قدير

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