Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Pituitary disorders

Objectives :

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

Done by :

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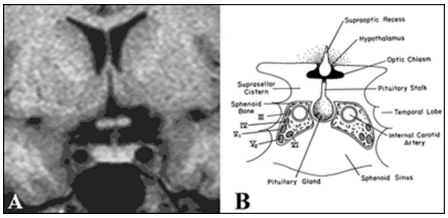
Resources :

Doctor's slides + Team 436
Lecturer: Prof. Riad Sulimani & Dr. Ayisha Ekhzaimy
Same as 436 slides: Yes

Pituitary Gland



Pituitary Anatomy

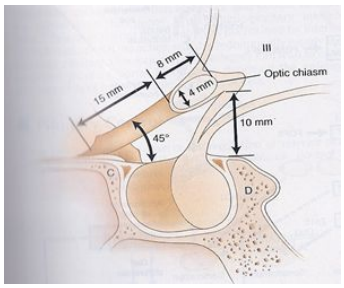
Sella turcica

- 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

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)

- 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 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 Gland

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**	Dopamine	**T3, T4, GH, Somatostatin, Dopamine.**	**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

Anterior Pituitary Hormones

- **G**o **L**ook **F**or **T**he **A**denoma **P**lease
- 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)

Pituitary Disorders

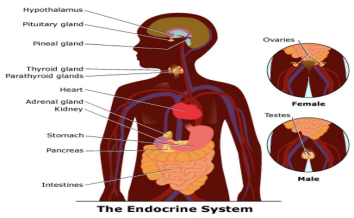
- **Anterior Pituitary Disorders**
  Function :
  -Hypersecretion: (GH,LH,FSH,PRL,TSH,ACTH)
  -Hyposecretion: hypopituitarism (isolated, multiple, pan)
  Masses:
  -Functioning = Hypersecretion
  -Non- Functioning
  -With /without mass-effect:
  -Space occupying lesion (compression symptoms, hypopituitarism)

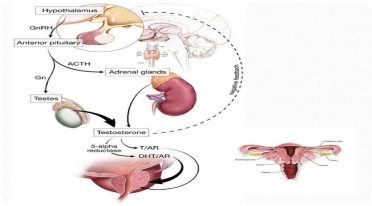
- **Posterior Pituitary disorders**
  Diabetes insipidus

Hypothalamic-Pituitary Axis

- The hypothalamus is the coordinator of Endocrine system
- Received signals from cortical brain, autonomic function, environment cues like light and temperature
- It affects function of thyroid gland, adrenal, gonads, growth, milk production and water balance
- nonendocrine functions such as temperature regulation, the activity of the autonomic nervous system, and control of appetite.

The hypothalamus is the master organ. It produces hormones that either stimulate or inhibit the corresponding anterior pituitary hormones. Eg. TRH only stimulates TSH release and nothing else

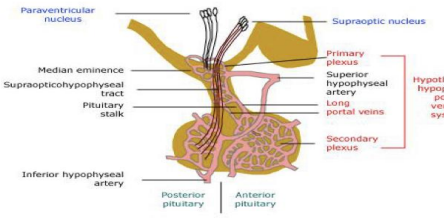


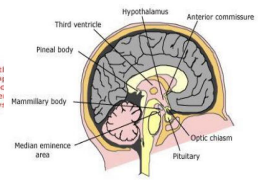


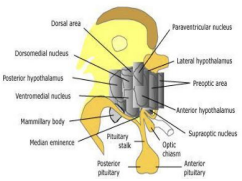
Remember:
-Anterior pituitary produces hormones
-Posterior pituitary stores hormones (oxytocin and ADH)

Hypothalamus

- At the base of the brain, below third ventricle, above pituitary gland and optic chiasm
- Hypothalamus is connected to the pituitary gland by pituitary stalk which connect median eminence to the pituitary gland
- Multiple nuclei in anterior part producing hormones to anterior pituitary
- Paraventricular and supraoptic nuclei produce ADH (very important for survival) to control poster pituitary function







Function:

- Terminals of hypothalamic neurons are in the median eminence carrying the hormones through capillary plexus to the pituitary gland
- Release all the hormones to control the pituitary function beside neuroendocrine function

"Puberty and pregnancy both cause physiological enlargement of the pituitary gland"

The hypothalamic-hypophyseal portal venous system is very important and any problem here would cause pituitary infarction.

Case: a pregnant woman gave birth at home and lost a lot of blood. She was later sent to the hospital and given 3 liters of blood. She is fine now but complains of inability to lactate. What could have caused this?
Hypovolemia in pregnant women is more likely to cause infarction of the pituitary gland as the gland is enlarged during pregnancy. This infarction will lead to a loss of prolactin producing cells and hence an inability to lactate.

The patient later started complaining of fatigue, dry skin and cold intolerance due to the development of secondary hypothyroidism.

All hypothalamic hormones are stimulatory except for two:
-Somatostatin - inhibits GH
-Dopamine - inhibits Prolactin

Hypothalamic Hormones

- The hypothalamus is the coordinator of Endocrine system
- Received signals from cortical brain, autonomic function, environment cues like light and temperature
- It affects function of thyroid gland, adrenal, gonads, growth, milk production and water balance
- nonendocrine functions such as temperature regulation, the activity of the autonomic nervous system, and control of appetite.

Hypothalamic stimulatory hormones	Pituitary hormones
Corticotropin-releasing hormone - 41 amino acids; released from paraventricular neurons as well as supraoptic and arcuate nuclei and limbic system	**Adrenocorticotropic hormone** - basophilic corticotrophs represent 20 percent of cells in anterior pituitary; ACTH is product of proopiomelanocortin (POMC) gene
Growth hormone-releasing hormone - two forms, 40 and 44 amino acids	**Growth hormone** - acidophilic somatotrophs represent 50 percent of cells in anterior pituitary
Gonadotropin-releasing hormone - 10 amino acids; mostly released from preoptic neurons	**Luteinizing and follicle-stimulating hormone** - gonadotrophs represent about 15 percent of anterior pituitary cells
Thyrotropin-releasing hormone - three amino acids; released from anterior hypothalamic area	Thyroid-stimulating hormone - thyrotropes represent about five percent of anterior pituitary cells
Prolactin-releasing factors - include serotonin, acetylcholine, opiates, and estrogens	**Prolactin** - lactotrophs represent 10 to 30 percent of anterior pituitary cells
Hypothalamic inhibitory hormones	
Somatostatin - 14 amino acids	Inhibits the release of growth hormone
Prolactin-inhibiting factors - includes dopamine	Major prolactin control is inhibitory

If a patient has acromegaly due to a pituitary adenoma and the surgeon wasn't able to remove the entire tumor, we give them somatostatins
If a patient presents with fatigue, dry skin and cold intolerance and we are suspecting hypothyroidism we have to measure T3, T4 and TSH levels.
If T3 and T4 are low while TSH is high this is due to primary hypothyroidism.
If all are low then its secondary hypothyroidism

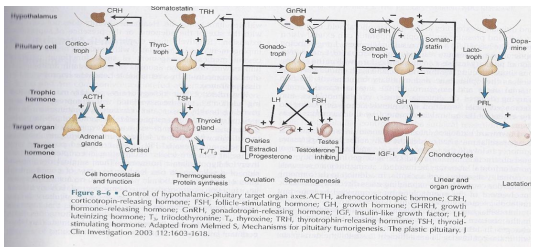
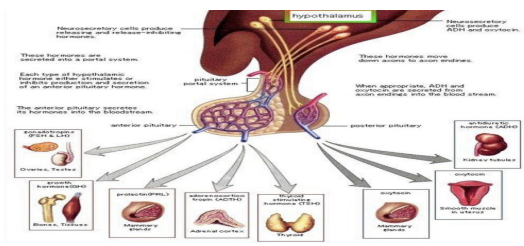
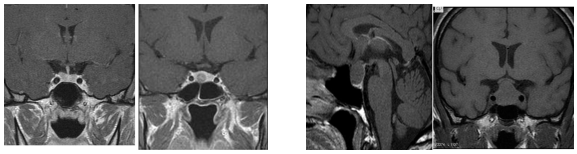


Figure 8–6 • Control of hypothalamic-pituitary target organ axes ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone–releasing hormone; GnRH, gonadotropin-releasing hormone; IGF, insulin-like growth factor; LH, luteinizing hormone; T_3, triiodothyronine; T_4, thyroxine; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone. Adapted from Melmed S. Mechanisms for pituitary tumorigenesis. The plastic pituitary. J Clin Investigation 2003 112:1603-1618.



Etiology of Pituitary Masses

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, Mucoceles, Others
- Empty sella syndrome
- Pituitary abscess
- Lymphocytic hypophysitis
- Carotid aneurysm
- TB
- sarcoidosis

Disorders of Pituitary Function

- **Hypopituitarism**
  Central hypoadrenalism, hypogonadism, hypothyroidism or GH deficiency
  Panhypopituitarism
  Sheehan syndrome
- **Hypersecretion of Pituitary Hormones**
  Hyperprolactinemia
  Acromegaly
  Cushing's Disease

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

Etiology of Pituitary Masses

Non- functional pituitary adenoma

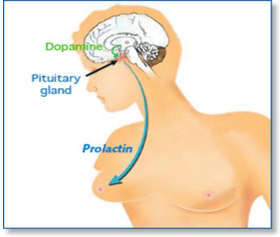
C: Clinical	Asymptomtic , incidentaloma by imaging Mass-effect (mechanical pressure, hypopituitarism, visual (bitemproal hemianopia) Gonadal hypersecretion
B: Biochemical	GH,LH,FSH,TSH,ACTH: not high PRL : low ,high, normal
A: Anatomical	MRI
Treatment	**Surgery if indicated** **Observation** **Adjunctive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

Important

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%)

Prolactin Disorder



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.

Prolactinomas

- Most common of functional pituitary adenomas
- 25-30% of all pituitary adenomas
- 10% are lactotroph and somatotroph such as GH producing
- Presents with amenorrhea and infertility
- Prolactinomas lose TRH response
- Microadenomas <10mm on MRI
- Macroadenomas >10mm
- Some growth hormone (GH)–producing tumors also co-secrete PRL
- Prolactinomas women: 90% present with microprolactinomas
- Prolactinomas in men : 60% present with macroprolactinomas

"Why? because females will have amenorrhea and they will seek medical care immediately but males won't show early signs unless the tumor is big enough causing mass effect"

Hyperprolactinemia

Causes:

1. Disruption of dopamine (tumor, trauma, infiltrative lesions)
2. Hypothyroid (increases TRH)
3. Estrogen increase (pregnancy)
4. Chest wall burns - nueronal effect like suckling
5. Chronic renal failure, returns to nml after transplant
6. Drugs (verapamil, H2 blockers, estrogens, opiates, dopamine receptor antagonists, reserpine, a-methyldopa)

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

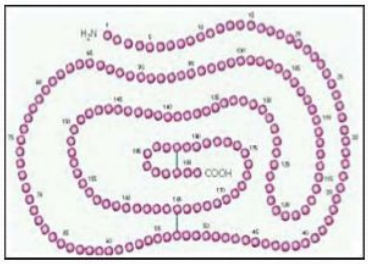
Treatment Pregnancy Not Desired

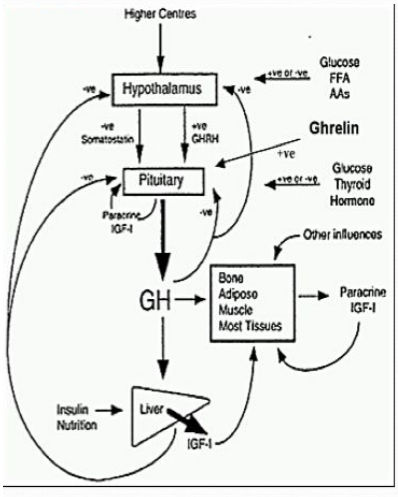
- Treat only if symptomatic
  (HA, vision changes)
- Dopamine agonist (Bromocriptine)
  1.25mg qhs 1 wk, then BID
  If intolerant with nausea, may give vaginally
  Not recommended for breastfeeding
- Transsphenoidal surgery if unsuccessful

GH is:
- Stimulates by GHRH
- Inhibited by somatostatin

Growth Hormone

- Polypeptide hormone
- Somatotrophs of anterior pituitary
- Action is mediated by IGF-I
- Half life is 20-50 mins
- Has a binding protein: GHBPs
- **Pulsatile secretion:** variable level in the blood
- Binds to its receptor on cell- surface: cytokine receptor
- Lack intrinsic enzyme activity
- Has similar receptor structure to others: leptin, IL-2, PRL
- Controlled by HP and peripheral factors
- GHRH stimulates it, somatostatin inhibits





Case: A young boy whose parents are worried that he is too short because his clothes are the same size for 3 years and his younger brother is taller than him. If you suspect GH deficiency measure levels while sleeping, after exercise or after insulin injection, they should be high. If GH levels are low consider Dx.

However the most common cause of short stature is FAMILIAL, so check the height in parents and siblings to compare.

Due to GH having a pulsatile secretion we cannot just measure it randomly. We stimulate GH then measure to see if levels increased or not

↑↑ GH: Important! there is always a question from here

- Physiologic: sleep, exercise, stress, fasting (hypoglycemia)
- Pathologic: Liver cirrhosis, AN, CRF, starvation
- Pharmacologic: Estrogen, ACTH, ADH, GHRH,Ghrelin, dopamine agonist, K infusion,serotonin arginine and **Insulin** (as it produces hypoglycemia which increases GH levels)

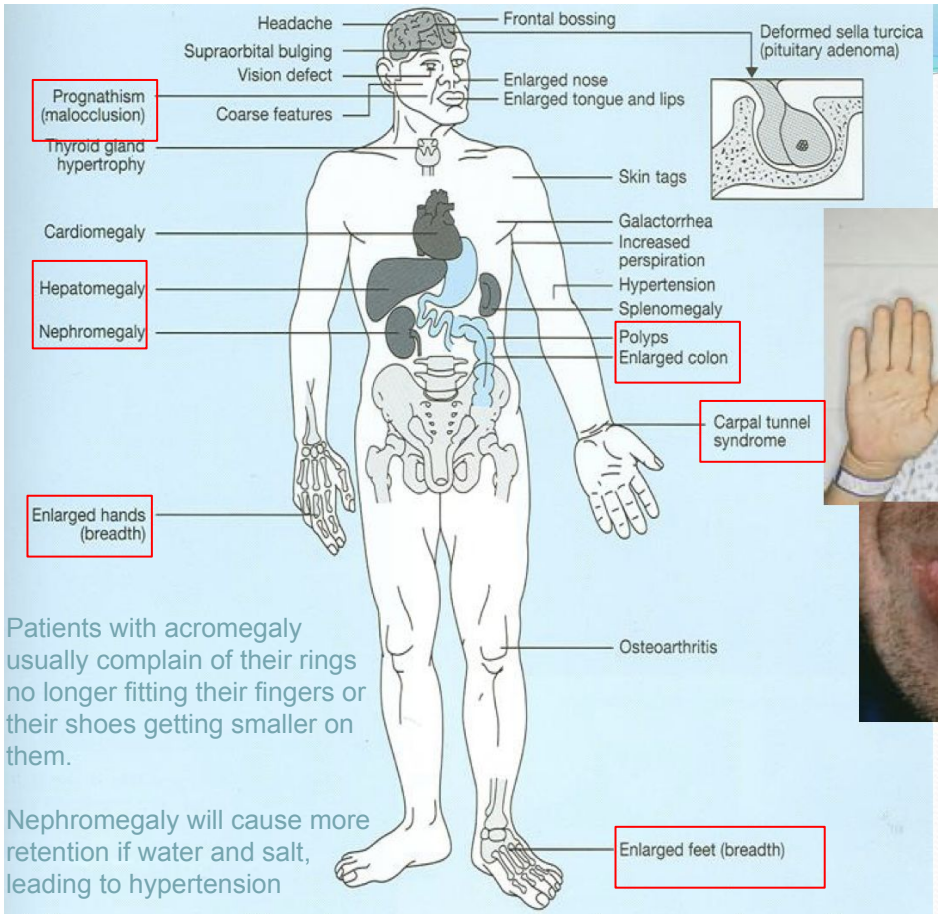
↓↓ GH:

- Physiologic: ↑glucose, ↑ FFAs,
- Pharmacologic: Somatostatin, GH,GC, PG
- Pathologic: ↑ or ↓ T4, Obesity

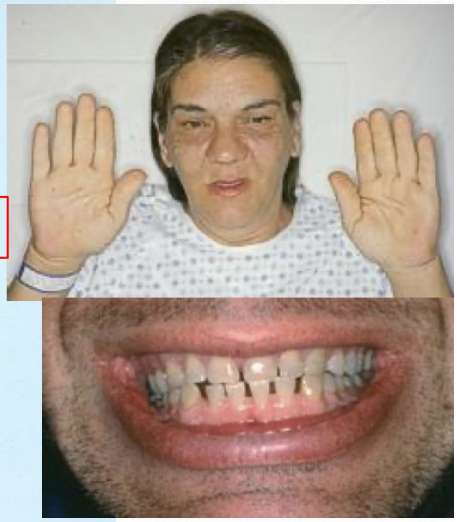
Acromegaly

If a GH pituitary adenoma develops before the closure of the epiphysis it will lead to gigantism (patient will be very tall). However, if it occurs after the closure it will lead to acromegaly

- 98% GH pituitary adenoma
- ⅓ of all functional pituitary adenomas
- Stimulates growth of skin, connective tissue, cartilage, bone, and viscera
- Nitrogen retention, insulin antagonism, and lipogenesis



VERY IMPORTANT.
Often asked about



Patients with acromegaly usually complain of their rings no longer fitting their fingers or their shoes getting smaller on them.

Nephromegaly will cause more retention if water and salt, leading to hypertension

Risks of Long Term Excess GH

- Arthropathy
- Neuropathy
- Cardiomyopathy
- Respiratory obstruction
- Diabetes Mellitus
- Hypertension: exaterbates cardiomyopathy
  - NOT Reversible
- increased risk of tumors:
  - leiomyomata
  - colon polyps

Reduced overall survival by an average of 10 year

Neck enlargement may lead to Obstructive Sleep Apnea.

Diabetes mellitus could occur because GH (like cortisol) has anti insulin effects.

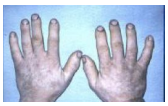
Q: Which of the following could cause colon cancer? ACROMEGALY, do colonoscopy every 3-5 years

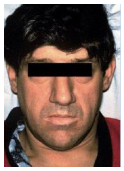
Cause of death is CVS events!

Growth Hormone Disorders

Acromegaly

Diagnosis:
-GH, IGF-I
-Oral glucose tolerance testing
-To assess excess GH secretion





Treatment:
-Goal: lower the serum insulin-like growth factor to normal for age/gender
-Surgically accessible micro- or Macroadenomas (Transsphenoidal surgery)
-2nd Line therapy: Somatostatin analogs or Dopamine agonists
-3rd Line therapy: Somatostatin receptor antagonist
Last resort: Radiation

GH deficiency

Diagnosis:
-In Children: 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 (until the bone has fused)

IGF1 is produced in the liver in response to GH. IGF1 levels mirror those of GH.

For oral glucose tolerance testing we give them 100g of glucose then we measure GH levels every hour. Normally GH levels will decrease. However, in case of acromegaly GH levels will remain high.

The treatment for acromegaly is always SURGERY!!! The entire tumor must be removed buy if remnant are still present after the surgery then give somatostatin agonists to completely cure acromegaly.

Note that after treatment of acromegaly the bones will not revert back to their normal structure. Only soft tissue will return to normal (eg. heart and colon).

If levels of GH do NOT increase after stimulatory test consider GH deficiency

Principle in endocrinology: After making a hormonal Dx we use imaging to confirm the Dx (eg. MRI)

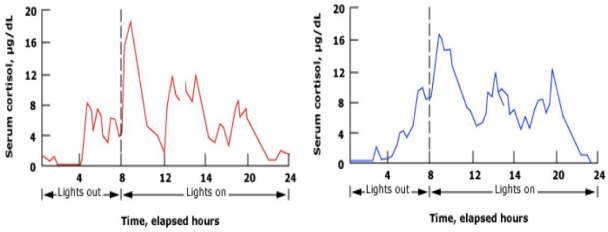
Table 1. Clinical Features of Acromegaly.

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

Cushing's Disease

Cortisol under ACTH

- Stable circadian rhythm
- Early morning rhythm cortisol between 8-9 am
- Altered by:
  Physical stress
  Psychological stress
  CNS and pituitary disorder
  liver and renal failure
- High ACTH leading
- More common in females 3-8 times than in men
- Generally not common : 5-25 per million



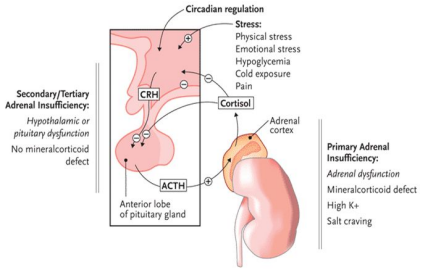
- Cortisol is produced by the zona fasciculata in the adrenal glands.
- The secretion of cortisol is highest in the morning (6-7 am) in people with a normal sleeping pattern.
- Cushing DISEASE means that there is hypercortisolism secondary to excess ACTH production from the anterior pituitary.
- The commonest cause of cushing syndrome is iatrogenic (eg. taking steroids for autoimmune diseases).

Symptoms of cushing:

Know all the list of symptoms of cushing and they are asked about frequently in exams.

Explanatory notes about the symptoms of cushing syndrome:

- Central obesity characterized by thin limbs
- Hirsutism due to an increase in androgen production.
- osteoporosis and proximal muscle weakness, may complain of difficulty when performing prayers and climbing stairs
- they develop glucose intolerance bc cortisol has anti insulin effect
- prone to fungal infection



Diagnosis	Treatment	
-24 hr urine free cortisol -Overnight 1 mg dexamethasone suppression testing Patient takes dexamethasone at night and cortisol is measured in the morning. If cortisol is not suppressed in the morning it indicates cushing -ACTH level and Pm cortisol -MRI pituitary: for pituitary adenoma	**-Transsphenoidal surgery** treatment of choice -Pituitary irradiation if entire adenoma couldn't be resected -Adrenalectomy (surgical, Mitotane) *Nelson's Syndrome: expanding intrasellar tumor and hyperpigmentation	**Pregnancy:** -1st Trimester: surgery -2nd Trimester: Adrenal Enzyme Inhibitors vs. surgery -3rd Trimester: Early delivery, enzyme inhibitors until lung maturity

ACTH-disorders

Cortisol low (Hypoadrenalism)	
Symptomes	**Management**
Nausea, Vomiting, Abdominal pain, Diarrhea, Dizziness and Weakness, Tiredness, Muscle ache, Hypotension, Weight loss	Cortisol replacement

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

Cushings (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

Notes on **Hyperprolatinemia** (imp. Topic will be asked about in exam):

-It can occur in both males and females
-The list of causes of high prolactin levels is important
-Some IMPORTANT drugs may cause dopamine inhibition leading to hyperprolactinemia, most importantly H2-Blockers (like Ranitidine and cimetidine) and antipsychotic drugs (eg. those used for schizophrenia)

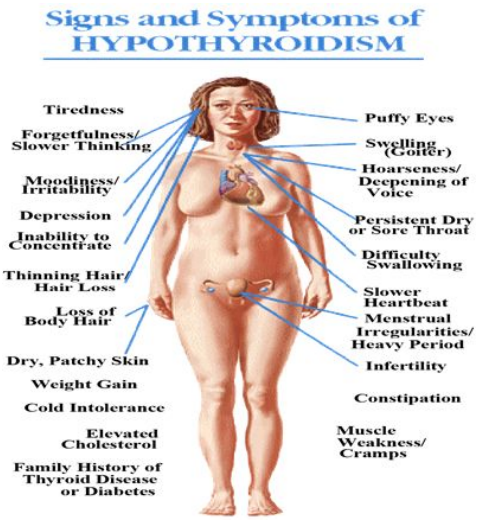
*Prolactinomas are the most common functional pituitary adenoma!!

**Always Treated medically by Dopamine agonist (Bromocriptine)

TSH-Hypothyroid

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 T4 , Low TSH

- **A: Anatomical**
  MRI

- **Treatment**
  Thyroxine replacement
  Surgical removal of pituitary adenoma if large

TSH-Hyperthyroid

TSH-Producing adenoma

- **Very rare < 2.8 %**

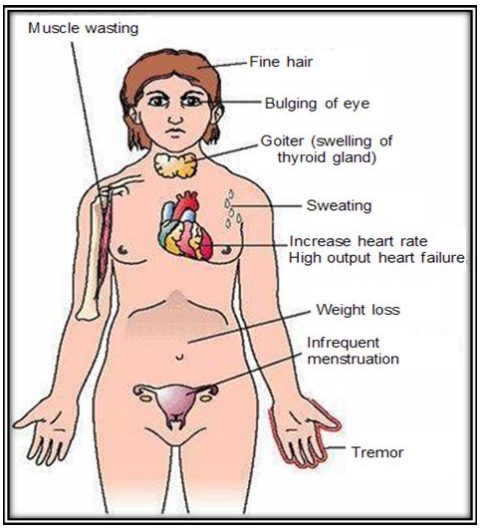
- **Signs of hyperthyroidism**

- **High TSH, FT4, FT3**

- **Treatment preop with anti-thyroid meds**

- **Surgical resection of adenoma**

- **Medical therapy: Somatostatin Analogue**



Gonadotroph

Gonadotroph adenoma

- Usually considered non-functioning
  Secrete inefficiently, variably
- Present with neurological symptoms
- Difficult to Diagnose
  Rule out other adenomas
  Prepubertal girls = breast devel, vag. Bleeding
  Premenopausal = amenorrhea, oligo

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

Treatment of non-functioning and gonadotrophin macroadenomas

- Transsphenoidal Surgery
- +/- Radiation therapy

Hypopituitarism

Hypopituitarism could be for a specific hormone or it could involve all hormones, also known as panhypopituitarism

- **76% tumor or treatment of tumor**
  Mass effect of adenoma on other hormones
  Surgical resection of non-adenomatous tissue
  Radiation of pituitary (check hormones 6 months after and then yearly)
- **13% extrapituitary tumor**
  Craniopharyngioma (a childhood tumor that causes hypopituitarism)
- **8% unknown**
- **1% sarcoidosis**
- **0.5% Sheehan's syndrome** (caused by excess blood loss (hemorrhage) or extremely low blood pressure during or after labor)

Infiltrative Lesions

- **Hereditary Hemochromatosis**
  Fe deposition in pituitary
  Gonadotropin deficiency most common
  Tx: repeat phlebotomy
- **Pituitary Apoplexy**
  Sudden hemorrhage into pituitary urgent condition
  Sever, sudden HA; diplopia; hypopituitarism
  Sudden ACTH def. Is life-threatening hypotension
  Tx: surgical decompression

Diabetes Insipidus (D.I)

Central D.I

- Polydipsia and polyuria (2-15 Liters/day)
- Abrupt onset
- 30-50% are idiopathic
  Dec. production by hypothalamus
- Surgery or Trauma (most cases are idiopathic)
- Rare with Sheehan's
  Mild, undetectable degree

Due to loss of ADH

Patient usually cannot fast during ramadan due to excess fluid loss

Differential Dx for DI:
Psychogenic polydipsia

Diagnosis of Central D.I

- Water Deprivation test:
  -Restrict p.o. Fluids or administer hypertonic saline to increase serum osmolality to 295-300 mosmol/kg (nml: 275-290)
  -Central D.I: urine osmolality still low and returns to normal after administer vasopressin
  -Nephrogenic D.I: exogenous vasopressin does not alter urine osmolality much (kidneys are not responding to ADH)
  -When we confirm Dx, we do an MRI to exclude any tumors

Treatment of Central D.I

- DDAVP (Desmopressin Acetate) Nasal spray
  - Synthetic analog
  - Not catabolized by vasopressinase
  - No vasopressor action
  - Administered intranasally (rec.) or p.o.
  - Titrate 10-20ug qd or bid
  - Safe in pregnancy and breastfeeding

Assessment of Pituitary Function

- Baseline:
  - TSH, FT4
  - LH, FSH, and (Testosterone or Estradiol)
  - Prolactin
  - GH, IGF-I
  - ACTH, cortisol and electrolyte
- MRI brain we also can do CT if the patient can't do MRI for any reason
- 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:
  - maybe need to be covered with stress dose of HC

Summary

	Anterior Pituitary Disorders	Hypothalamus & Posterior Pituitary Disorders
Hypersecretion	**1- Prolactinoma:** - High prolactinemia. - Presents with **galactorrhea**, decrease lipido and amenorrhea. - Tx: **Medically** (*Bromocriptine*). **2- GH Secreting Adenoma:** - High IGF-1. - Causes **acromegaly** (in adults), **gigantism** (in children). - Presents with DM, facial changes, CVD and Acral enlargement. - Tx: **Surgery** (1st line) **3- ACTH secreting adenoma:** - Result in **Cushing DISEASE**. - High cortisol, high ACH. - Presents with typical cushing features. - Tx: **Surgery** followed by radiation. **4- TSH secreting adenomas:** - Rare. - Present as usual hyperthyroidism - High T3,T4 and TSH. **5- Gonadotropin secreting adenomas:** - very rare.	**Syndrome Of Inappropriate Antidiuretic Hormone (SIADH):** - Caused by disordered hypothalamic–pituitary secretion or ectopic production of ADH. - Causes low serum Na and osmolality, also high urine Na and osmolality. - Tx: **Treating the underlying cause** and **fluid restriction**.
Hyposecretion	**Deficiency of hypothalamic-releasing hormones or pituitary hormones Causes: (Seven I's)** - Invasive: pituitary tumors. - Infarction: Sheehan's syndrome. - Iatrogenic: surgery. - Infiltration: Sarcoidosis, hemochromatosis. - Injury: trauma. - Infections: TB. - Idiopathic. - Tx: **remove the cause** and **start HRT**.	**Diabetes insipidus:** - Decreased the amount of ADH. - Manifest **polydipsia** and **polyuria**. - Serum Na is high, ↑ urine volume, and ↓ urine osmolality. - Tx: **medically** (*Desmopressin Acetate*) Synthetic analog of ADH if the cause centrally due to pituitary source.

Questions

1. A 15-year-old girl complains of headaches which started 6 weeks ago. The headaches initially occurred 1–2 times a week but now occur up to five times a week, they are not associated with any neurological problems, visual disturbances, nausea or vomiting. The girl also reports a white discharge from both of her nipples. She has not started menstruating. The most appropriate investigation is:

A. CT scan
B. Thyroid function tests
C. MRI scan
D. Serum prolactin measurement

2. 49-year-old man presents with a history of difficulty sleeping. He reports feeling increasingly tired and general weakness which he attributes to his poor sleep pattern. Additionally, the patient has noticed he has gained weight and sweats very easily. On examination, the patient has coarse facial features. The most likely diagnosis is:

A. Hyperthyroidism
B. Cushing's disease
C. Acromegaly
D. Hypothyroidism

3. A 47-year-old woman is referred to the endocrine clinic complaining of a two month history of tiredness. Despite wearing several items of clothing, the patient appears intolerant to the room temperature. She has noticed an increase in weight, particularly around her waist. The most appropriate investigation is:

A. Thyroid stimulating hormone (TSH)
B. Total tetraiodothyronine level (T4)
C. Tri-iodothyronine level (T3)
D. Ultrasound scan of the neck

Answers:

1. D / 2. C / 3. A