Team Medicine

13#

Pituitary Disorders

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■ Slides ■ Doctors notes ■ Additional

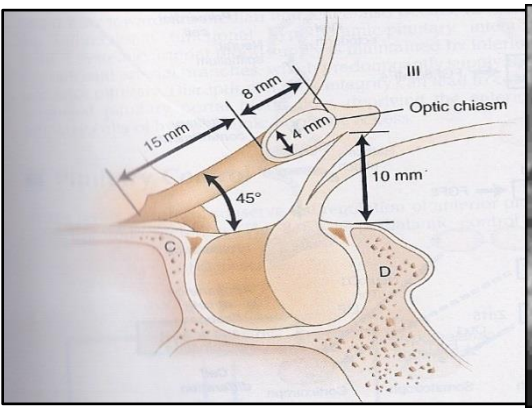
Pituitary Development & Anatomy

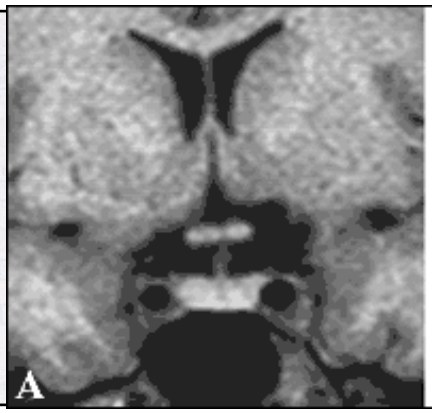
- **Anterior pituitary** is recognizable by 4- 5th week of gestation
- Full maturation by 20th week
- From Rathke's pouch, ectodermal envagination of oropharynx
- Migrate to join neurohypophysis
- Portion of Rathke's pouch →→ Intermediate lobe
- Remnant of Rathke's pouch cell in oral cavity →→ pharyngeal pituitary (abnormal)
- Lies at the base of the skull as sella turcica (literally, sella turcica = Turkish saddle)
- Roof is formed by diaphragma sellae
- Floor by the roof of sphenoid sinus

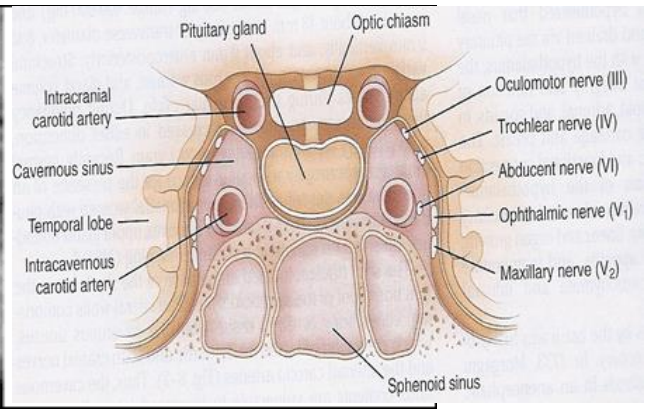
Diaphragma sella is formed by a reflection of dura matter preventing CSF from entering the sella turcica by this diaphragm

- **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 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

Height is 5-7 mm and 10 mm lateral dimension, height is 10. superior, middle supply ant. Pituitary. Inferior supply stalk and post pituitary artery. Normal pituitary stalk length 5- 7 mm , 2-3 mm in diameter







Pituitary Hormones

Anterior Lobe:

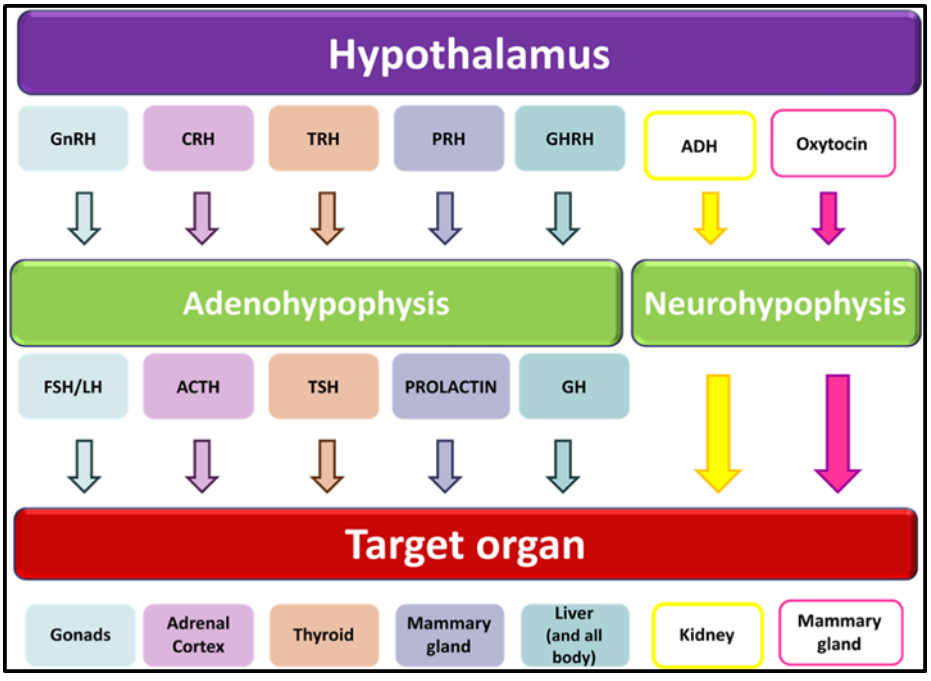
- Growth Hormone (GH)
- Gonadotrophs (LH, FSH)
- Thyroid Stimulating Hormone (TSH)
- Prolactin
- Corticotropin (ACTH)

Posterior Lobe:

- Oxytocin
- Vasopressin

Normal Physiology

	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



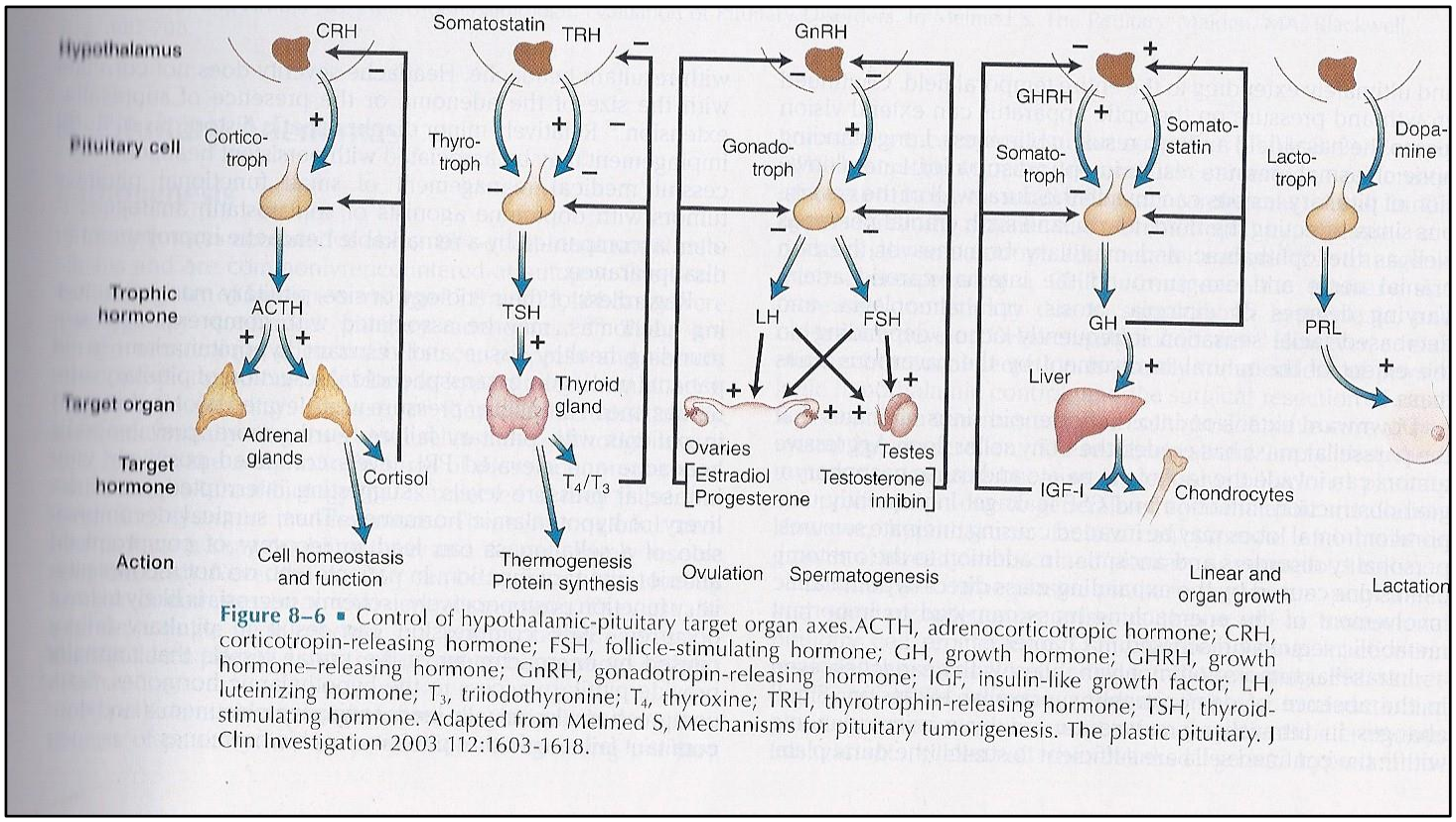


Figure 8–6 ▪ Control of hypothalamic-pituitary target organ axes.ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone–releasing hormone; GnRH, gonadotropin-releasing hormone; IGF, insulin-like growth factor;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

Ant. Pituitary: (under influence of hypothalamus → releasing hormones)

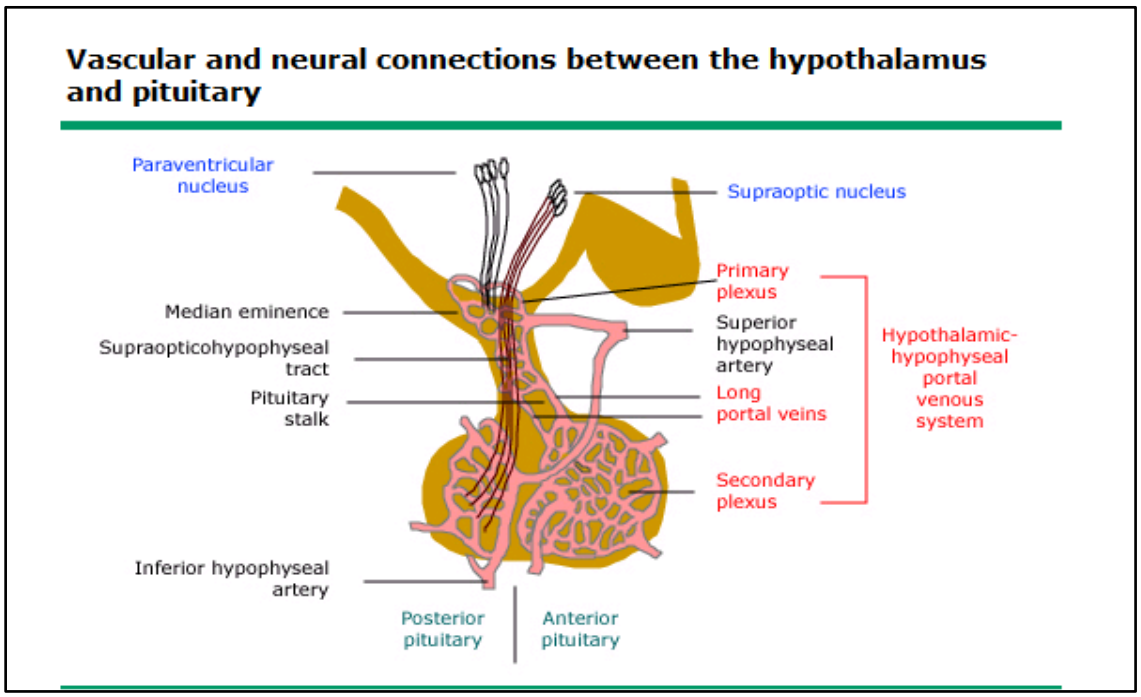
Every Hypothalamic-releasing hormone will control the corresponding Ant. Pituitary hormone

<u>All</u> releasing <u>hormones</u> are <u>stimulatory</u> except:

Dopamine → <u>inhibits</u> Prolactin

Somatostain → <u>inhibits</u> Growth hormone

These releasing hormones go through small capillary circulation to the Ant. pituitary



Anterior Pituitary Hormones

1. Growth Hormone (GH): increased by GRH , sleep , stress ,exercise , hypoglycemia , clonidine.

Clinical scenario:

If a young boy presents to the clinic complaining of short stature and his younger brother is taller than him. Maybe the boy has GH deficiency , but measuring the hormone alone is not enough. We have to stimulate the GH production and if it remains low than there is a problem.

We will admit the patient and take a blood sample during sleep; normally GH should increase during sleep Or after exercise or in the face of hypoglycemia.

We treat him by GH injections.

- Keep in mind :The commonest cause of short stature is genetic "he is short because his parents are short"

2. Prolactin: increased when there is interference with dopamine action or secretion, also during pregnancy & lactation.

Prolactin increase with any interference with Dopamine "you inhibit the inhibitor"

3. ACTH: ↑ BY CRH , stress

4. TSH: ↑ BY TRH stimulation

5. FSH & LH (increased by stimulation from GnRH):

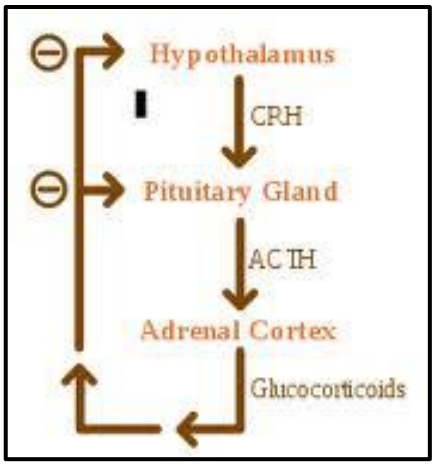
In men: stimulates testicular growth, spermatogenesis, production of testosterone.

In women: stimulates production of estrogen & progesterone, stimulates ovulation.

Negative Feedback Mechanism

- -ve Feedback mechanism works on two levels:

  pituitary and hypothalamus.
- It's very important when measuring the level of the target hormone (eg: T4) to also measure the level of the corresponding ant. pituitary hormone (eg: TSH) to determine at which level is the disturbance occurring.



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**

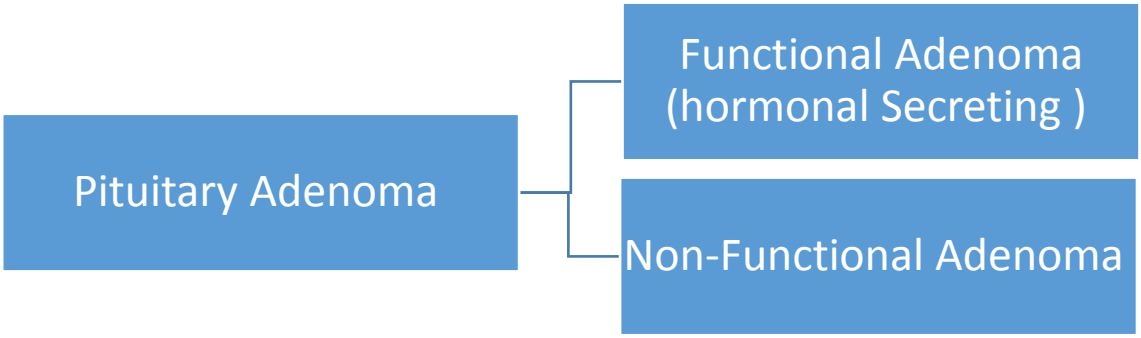


Table 1. Functioning Adenomas: Clinical Disease and Medical Therapy

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

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

❖ **Presentation:**

- As incidentaloma by imaging
- Symptoms of mass effects (mechanical pressure)
- Hypopituitarism (mechanism in box below)
- Gonadal hypersecretion

Mass effect: tumour expansion laterally → compression of cavernous sinus causing cranial nerve palsy like double vision, stretching meninges causing headache, or pushing temporal lobe causing seizure, pushing optic chiasm or headache from apoplexy. Hypopituitarism can occur from suprasellar mass because it might push the pituitary stalk and cut portal blood supply and the hypothalamus signal to the pituitary.

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

Guanine nucleatide stimulatory protein gene found in 40 % of somatotroph adenoma/ inactivation mutation in tumor supressing gene in MEN 1.

Clinical presentations of SELLAR MASS

TABLE 8–1 LOCAL EFFECTS OF AN EXPANDING PITUITARY OR HYPOTHALAMIC MASS

PITUITARY	CENTRAL
Adult hyposomatotrophism Growth failure Hypoadrenalism Hypogonadism Hypothyroidism	Dementia Headache Hydrocephalus Laughing seizures Psychosis
OPTIC TRACT	**NEURO-OPHTHALMOLOGIC TRACT**
Bitemporal hemianopia Blindness Loss of red perception Scotoma Superior or bitemporal field defect	**Field Defects** Bitemporal hemianopia (50%), amaurosis with hemianopia (12%), contralateral or monocular hemianopia (7%) Homonymous hemianopia Scotomas: Hemianopic; junctional; monocular central, arcuate, altitudinal **Acuity Loss** Color vision Contrast sensitivity Snellen Visual evoked potential **Pupillary Abnormality** Afferent defect Impaired light reactivity **Optic Atrophy** Cranial nerve palsy: Abducens, oculomotor, sensory trigeminal, trochlear Nystagmus Papilledema Postfixation blindness Visual hallucinations
HYPOTHALAMUS	
Appetite, behavioral, and autonomic nervous system dysfunctions Temperature dysregulation, obesity, diabetes insipidus Thirst, sleep	
CAVERNOUS SINUS	
Diplopia Facial numbness Ophthalmoplegia Ptosis	
TEMPORAL LOBE	
Uncinate seizures	
FRONTAL LOBE	
Anosmia Personality disorder	

Adapted from Melmed S. Acromegaly. In DeGroot LJ, Jameson JL, Burger H, et al (eds). Endocrinology, 4th Edition. Philadelphia: WB Saunders, 2001:300-312; and Arnold AC. Neuro-ophthalmologic Evaluation of Pituitary Disorders. In Melmed S. The Pituitary. Malden, MA: Blackwell, 2002:687-708.

Assessment of pituitary FUNCTION

- Baseline: TSH, FT4, FT3, 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
- Pre-op hormonal replacement: all pituitary adenoma should be covered with stress dose of HC

Treatment of Non- Functional pituitary masses

- **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 analog

Amennorrhea –Galactorrhea Syndrome

- CAUSED BY INCREASED PROLACTIN

Amenorrhea: is the absence of a menstrual period in a woman of reproductive age.

Galactorrhea: is the spontaneous flow of milk from the breast, unassociated with childbirth or nursing.

When a patient presents with amenorrhea the first thing you should do is role out is **pregnancy.**

Clinical note:

- **CAUSES:**

1. HYPOTHYROIDISM

Hypothyroidism meaning low T4 will cause an increase in TSH , TSH production is stimulated by TRH which is a stimulator for both TSH and prolactin.

2. DRUGS: which interfere with dopamine secretion or action

(Phenothiazines , Metoclopramide , Methyl-dopa, antidepressants)

3. PROLACTINOMA: prolactin secreting adenoma (most common functional pituitary adenoma)… Prolactinoma loses response to TRH.

Prolactin levels in prolactinoma are much more higher than those seen in hypothyroidism or drug induced Amenorrhea – galactorrhea

❖ **CLINICAL FEATURES :**

In women: galactorrhea, amenorrhea & infertility

In men: decreased libido, impotence & infertility

It can also cause mild gynecomastia, and very rarely Galactorrhea in men

-Why do patient manifest with these symptoms?

Because Prolactin interferes with gonadotropin hormones

TABLE 8–14 SIGNS AND SYMPTOMS OF PROLACTINOMAS

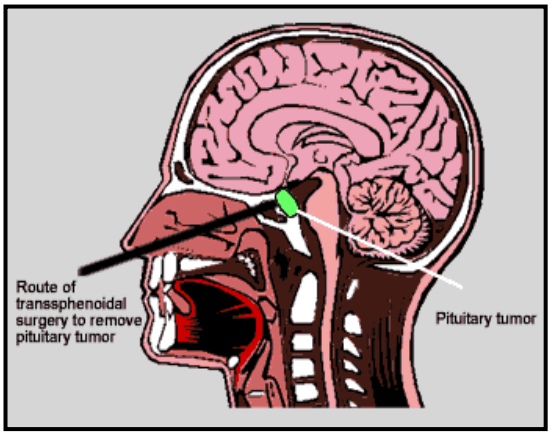
SIGNS AND SYMPTOMS ASSOCIATED WITH TUMOR MASS
Blurred vision or decreased visual acuity
Cranial nerve palsies
Headaches
Hydrocephalus (rare)
Pituitary apoplexy
Seizures (temporal lobe)
Symptoms of hypopituitarism
Unilateral exophthalmos (rare)
Visual field abnormalities
SIGNS AND SYMPTOMS ASSOCIATED WITH HYPERPROLACTINEM
Amenorrhea, oligomenorrhea, primary amenorrhea, infertility
Decreased libido, impotence, premature ejaculation, erectile dysfunction, oligospermia
Galactorrhea
Osteoporosis

❖ **DIAGNOSIS:**

1. **Hormonal : prolactin level (A very high level suggests a prolactinoma)**
2. **Radiological: in prolactinoma, CT or MRI of the pituitary**
   mass < 1 cm (microadenoma)
   mass > 1cm (macroadenoma)

❖ **TREATMENT :**

1. **Medical: bromocriptine, cabergoline (dopamine agonists)**
   Dopamine agonist can shrink tumor growth by interfering with the cells DNA syntheses
2. **Surgical: Transsphenoidal adenectomy (If tumor is causing pressure symptoms or if no response to medical treatment)**
3. **Radiation therapy**



(TRANS-SPHENOIDAL) ADENOMECTOMY

Growth hormone disorders

- **Pituitary tumor as mass effect →→ GROWTH HORMONE DEFICIENCY**
- **Hyperfunctioning mass →→ ACROMEGALY**

❖ **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

Produced by GH producing adenoma, in childhood it is called gigantism.

If the GH producing tumor has started its increase production of GH before the closer of the epiphysis, it will result in increase in linear bone growth. However, after the closure of the epiphysis the effects are mainly on the small bones (jaw, hands, and nose).

- Pituitary tumors are classified based on size to:

Less than 1 cm → **MICROADENOMA** ,

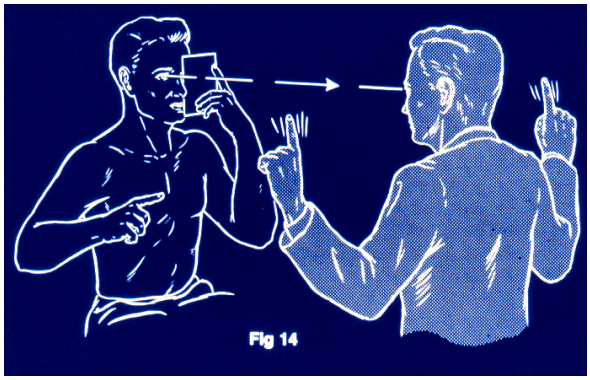
More than 1 cm → **MACROADENOMA**

GH producing adenomas are almost always Macro adenomas

❖ **CLINICAL FEATURES :**

1. **Due to the tumor (usually large macro adenoma): headache, dizziness. bitemporal hemianopia.**

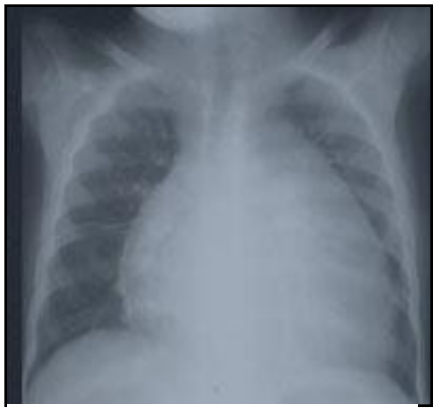
BITEMPORAL HEMIANOPIA is clinically tested for by **confrontation test**



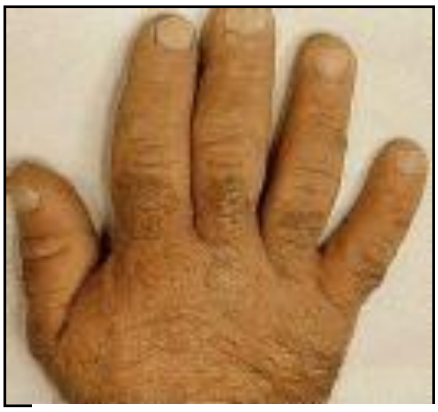
2. **<u>Due to invasion and destruction of the pituitary</u> → lack of secretion of other hormones**

3. **<u>Due to the increased GH production:</u>**

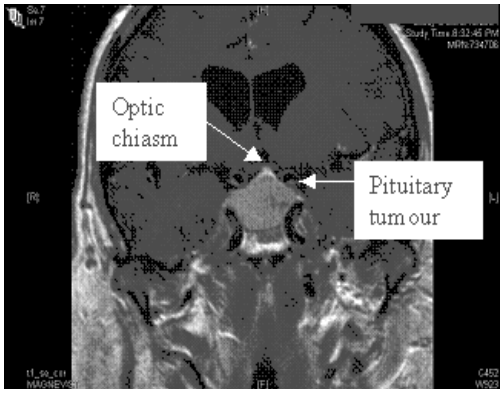
- **Acral and soft tissue enlargement → large thick hands & feet** (joint hypertrophy)
- **Thick skin , oily and sweaty**
- **Visceromegaly** (Hepatomegaly, thyroid enlargement)
- **Generalized symptoms → fatigue , lethargy & ↑ sleepiness .**
- **Arthralgia & degenerative arthrits**.
- **Carpal tunnel syndrome. (**Median nerve compression because of soft tissue enlargement**)**
- **Impaired glucose tolerance & diabetes**. (Anti insulin Effect)
- **Cardiovasc. effects (major cause of morbidity and mortality): HTN, cardiomegaly, LVF, CHF**… Diastolic dysfunction: early sign of cardiomyopathy



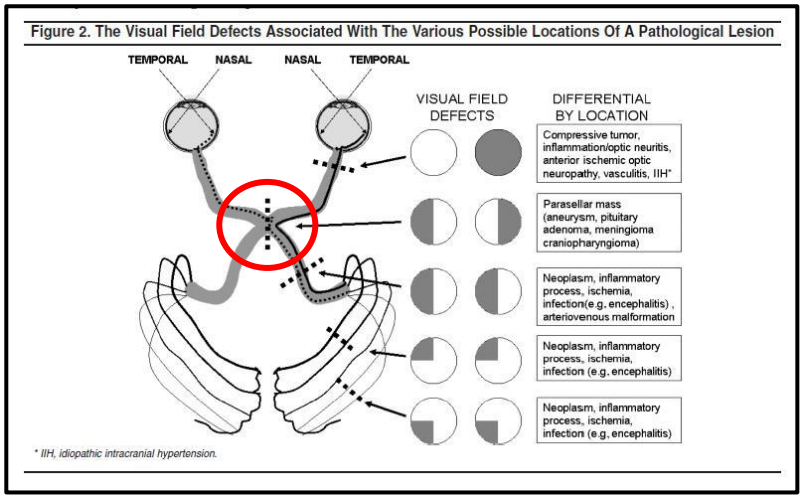
Cardiomegaly



Soft Tissue Enlargement



Pituitary tumor pressing on optic chiasm



Enlarged jaw and nose, also there is enlargement of the maxillary sinuses which causes deepening of the voice, prominent supraorbital ridge, and spacing between the teeth

Change are usually very subtle and gradual, the patient and his family might not notice them.

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

❖ DIAGNOSIS:

1. **CLINICAL PICTURE**
2. **Hormonal diagnosis: measure GH during Oral Glucose Tolerance Test (lack suppression of GH).** In normal people GH should be low after OGTT, but in acromegaly it remains elevated.
3. **Measure IGF-1: high in all patients with acromegaly.**
   (IGF-1 is under the influence of GH, it increase and decrease with GH)
   (We don't measure GH because it fluctuates throughout the day)
4. **Radiological diagnosis:**
   skull x-ray : thick heel pad≥22mm
   CT OR MRI of the sella turcica (increase in size of sella turcica)

 # In clinical practice we do both IGF-1 and OGTT

❖ TREATMENT :

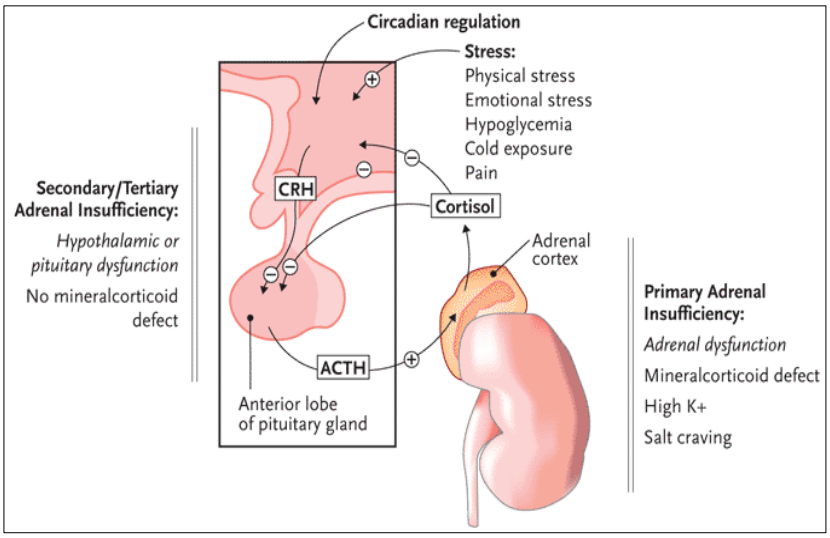
1. **Surgical (trans-sphenoidal) adenomectomy**
2. **Radiotherapy**
3. **Medical:**
   - **Somatostatin analogues (eg: octreotide)**
   - **Pegsivomant (Growth hormone receptor antagonist)**

 # Acromegaly patients are not treated only for cosmetic reasons but mainly because of the increase mortality and morbidity with the disease.

HPA- Axis and ACTH Disorders

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

Hypoadrenalism



❖ **Symptoms:**

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

❖ **Diagnosis:**

- Low ACTH and Low morning cortisol
- Stimulation test: Insulin tolerance test

❖ **Management**:

Steroid replacement

ACTH secreting cell disorders: Cushing's syndrome (excessive cortisol)

- 80 % HTN
- LVH
- Diastolic dysfunction, intraventricular septal hypertrophy
- ECG needed: high QRS voltage, inverted T-wave
- Echocardiogram pre op

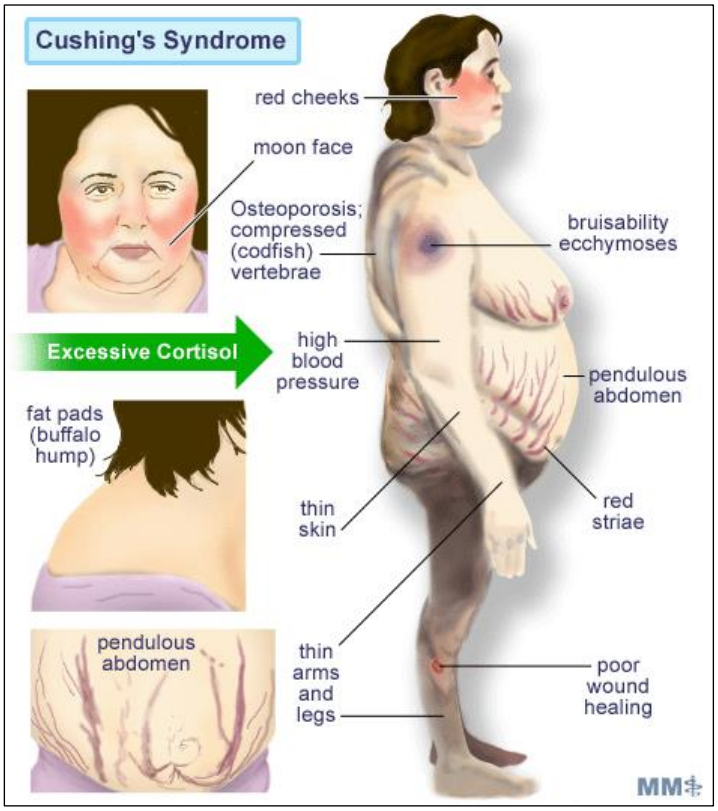
Remember:

Cushings **syndrome**: any condition that has increased cortisol, whether it was related to the adrenals, ectopic tumors, increased pituitary secretion or exogenous causes.

Cushings **disease**: when cortisol is increased because of the pituitary's increased secretion of ACTH.

I.e: When Cushing Syndrome is caused by pituitary secretion of excess ACTH → we call it Cushings Disease

- OSA (obstructive sleep apnea): 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



❖ **Diagnosis:**

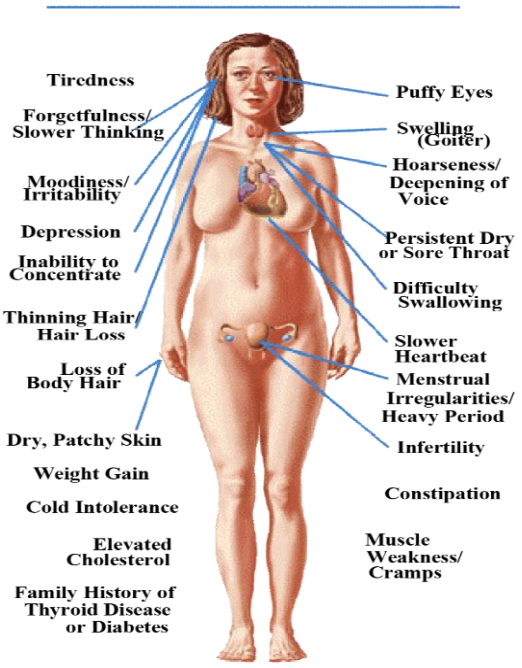
- 1 mg Dexamethasone suppression test
- 24 hr urine free cortisol
- Salivary cortisol
- ACTH level

❖ **Management:**

- Surgical resection of pituitary
- Medical Treatment

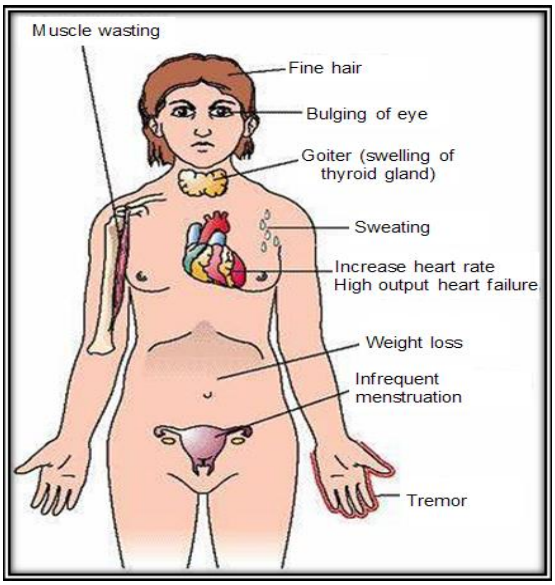
Central Hypothyroidism

- Low TSH
- Low free T4 and T3
- Thyroxine replacement
- Surgical removal of pituitary adenoma



TSH-Producing adenoma

- Very rare < 2.8 %
- Signs of hyperthyroidism
- High TSH, FT4, FT3
- Treatment pre-op with anti-thyroid meds
- Surgical resection of adenoma
- Medical therapy: Somatostatin Analogue



Gonadotropin secreting cell disorder

Gonadotroph adenoma vs. menopause & ovarian failure:

- High FSH, low LH
- High serum alpha subunit
- High estradiol
- Thickened endometrium and polycystic ovaries

Treatment:

- Trans-sphenoidal surgery (adenectomy)
- +/- radiation

Central Diabetes Insipidus:

- **Features**: Polydipsia and polyuria (2-15 L per day)
- Abrupt onset
- 30-50% of cases are idiopathic:
  - Decreased production by hypothalamus

- **Causes**:
  - Surgery or trauma
  - Rarely because of Sheehan's syndrome (mild, undetectable degree)

- **Diagnosis**:

  Water deprivation test (restrict fluid per os, or administer hypertonic saline to increase serum osmolality)

  - If urine osmolality still low and returns to normal after giving vasopressin → **Central** Diabetes Insipidus
  - If exogenous vasopressin does not change urine osmolality much → **Nephrogenic** Diabetes Insipidus

- **Treatment**:

- DDAVP (desmopressin acetate)
  - Synthetic analog
  - Not catabolized by vasopressinase
  - No vasopressor effect
  - Can be administered intranasally or orally
  - Safe in pregnancy and breast-feeding

Hypopituitarism

- **Causes** [7 i's]

1. **Infarction: Sheehan's syndrome**
   # It happens only in pregnancy, normally the pituitary increases in size during pregnancy and thus is vulnerable to ischemic necrosis due to blood loss and hypovolemic shock during and after childbirth.
   # The first manifestation of hypopituitarism in this case will be FAILURE OF POSTPARTUM LACTATION

2. **Iatrogenic: Radiation, surgery**
3. **Invasive: Large pituitary tumors (e.g. CRANIOPHARYNGIOMA)**
4. **Infiltration: Sarcoidosis, hemochromatosis**
5. **Injury: head trauma**
6. **Infections: TB**
7. **Idiopathic**

- **CLINICAL PICTURE:**

  Depends on hormones lost

  # Hypopituitarism can manifest as a deficiency in one, or more than one hormone. # Clinical picture will depend on the affected hormone.

  1. Lack of FSH LH: Hypogonadim, amenorrhea
  2. Lack of TSH: → hypothyroidism
  3. Lack of ACTH: → adrenocortical insufficiency
  4. Prolactin deficiency: failure of postpartum lactation
  5. If all of the above: Panhypopituitarism
  6. In children: GH: short stature

- **DIAGNOSIS:**

  1. Clinical: Hx and Px

  2. Biochemical studies:

  a) Baseline studies: TSH, ACTH, FSH, LH, prolactin GH
  b) Stimulation: 1) TRH
  2) LH-RH
  3) Insulin → hypoglycemia

  3. Radiological:

  - Lat. skull x=ray , CT , MRI

- **TREATMENT:**

  1. Remove cause

  2. Replacement therapy; depends on hormone lost

  3. THYROXINE in 2° hypothyroidism

  4. Hydrocortisone for 2° hypoadrenalism (20 mg at AM and 10 mg at PM)

  5. Growth hormone: for children

  6. Testosterone: monthly injections

  7. Estrogen + progesterone

  8. For induction of ovulation in women and for spermatogenesis in men we give FSH + LH

  (Only if fertility is of concern in this patient)

We don't give ant. Pituitary hormones (e.g. TSH or ACTH) because we care about the end target hormone

Summary

- Pituitary lesions can be divided into: Adenomas (functional and non-functional), malignancies, cysts, Empty sella syndrome, abscess, Lymphocytic hypophysitis, carotid aneurysm.
- Functional adenomas: secrete hormones, have different types according to the type of cells (prolactinomas, thyrotropinomas, somatotropinomas, corticotropinomas, other mixed endocrine active adenomas). Their symptoms are according to the hormone they produce.
- Non-functional adenomas: usually they produce mass effect (pressure on adjacent structures, sometimes might cut blood supply → hypopituitarism)
- Non-functional adenomas are treated by: surgery: transsphenoidal adenectomy (but might recur), observation, adjunctive therapy (radiation, somatostatin analogs, dopamine agonists)

- Prolactinoma: increased prolactin because of an adenoma secreting prolacting and not responding to TRH.
  Symptoms are: infertility in both genders… Galactorrhea, amenorrhea in women… Impotence, decreased libido in men.
  Other causes of increased prolactin other than prolactinomas: hypothyroidism, drugs (eg: dopamine antagonists)
  Treatment: Medical (dompamine agonists), surgery, radiation

- Acromegaly: caused by GH producing adenoma. Symptoms affect many organs in the body, the most dangerous symptoms are cardiovascular (associated with morbidity and mortality).
  Diagnosis: Measuring IGF-1, doing OGTT, MRI / CT.
  Treatment: surgery, radiation therapy, medical: somatostatin analog (eg:octreotide), GH receptor antagonist (pegsivomant).

- ACTH disorders:
  - **Hypo**adrenalism (if caused by pituitary): low ACTH, low cortisol
  Symptoms: nausea, vomiting, abdominal pain, diarrhea, muscle ache, dizziness and weakness, tiredness, weight loss, hypotension.

  Diagnosis: low ACTH, low cortisol… Insulin tolerance test (stimulation test)

  Treatment: hormone replacement therapy

- Cushings Syndrome (if caused by pituitary): high ACTH, high cortisol
Symptoms: truncal obesity, easy bruising, hirsutism… etc
Diagnosis: 1 mg Dexamethasone suppression test, 24 hr urine free cortisol, salivary cortisol, ACTH level

Treatment: Medical, Surgical

- Central hypothyroidism:
  Diagnosis: low TSH, low T3 and T4
  Treatment: thyroxine replacement, or surgery

- Central hyperthyroidism (TSH adenoma):
  High TSH, T4, T3
  Treatment pre-op with anti-thyroid meds, Surgical resection of adenoma, Medical therapy: Somatostatin Analogue

- Gonadotroph adenoma:
  High FSH, low LH, High estradiol, Thickened endometrium and polycystic ovaries.
  Treatment: Surgery (adenectomy) +/- radiation

- Central Diabetes Insipidus:
  Symptoms: Polydipsia and polyuria
  Diagnosis: water deprivation test
  Treatment: DDVAP (desmopressin acetate)

- Hypopituitarism:
  Causes (7 i's) : infarction, iatrogenic, invasive (eg: large pituitary tumors), infiltration (Sarcoidosis, hemochromatosis), injury, infections (TB), idiopathic
  Symptoms: correspond to the hormone that is deficient
  Diagnosis: Clinical, biochemical studies (Baseline studies: TSH, ACTH, FSH, LH, prolactin GH… Stimulation: TRH, LH-RH, Insulin → hypoglycemia), radiological
  Treatment: hormone replacement therapy

Questions

Question 1:

A worried mother brings her 12-year-old son to the pediatrician with concerns that he is "too tall". Both she and the patient's father are relatively short, as are other members of the family. The patient, a football player, complains only that his baseball cap, mitt and shoes do not fit anymore. On physical examination, the patient is above the growth curve for his age and has large hands and feet, frontal bossing of the cranium, prominent jaw and coarse features with oily skin.

The doctor suspects acromegaly, and the IGF-1 (insulin- like growth factor -1) levels are elevated. What test should be done to confirm the diagnosis?

A) Growth hormone levels
B) Oral glucose tolerance
C) GHRH levels
D) Somatostatin levels

Question 2:

A 32-year-old woman is postpartum (day 4 after delivery) for her 4th child. The delivery was complicated by massive hemorrhage. She desires to breast-feed, but her breast milk has not come in (normally, it begins 24-48 hours postpartum). She breast-fed all of her other children without delay. She also complains of fatigue, mental sluggishness, lightheadedness and racing heartbeat. On physical examination, she is pale, diaphoretic and weak.
Vital signs:
Temp = 36.2
Pulse = 100/min
BP = 90/70 mmHg

What is the diagnosis?

A) Sheehan syndrome
B) Prolactinoma
C) Hypothyroidism
D) Addison disease

Question 3:

A 32-year-old woman complains of recent visual problems and slight breast discharge (galactorrhea). She has not had her period for the last 6 months (secondary amenorrhea) and is upset that she couldn't get pregnant despite trying for the past year. She denies any history of schizophrenia, or being treated with neuroleptics (antipsychotics). Labs reveal -ve pregnancy test results, normal TSH, and high prolactin. Head MRI shows slight enlargement of the structure located in the sella turcica.

What drug can we use to treat this patient?
A) Somatostatin analog
B) Dopamine antagonist
C) Dopamine agonist
D) Lithium

Answers

Answer 1: B
After we measure IGF-1 levels (screening test for acromegaly), we confirm the test by OGTT (oral glucose tolerance test).
In normal people --> GH is suppressed
In acromegaly --> GH is elevated, or it remains the same

Answer 2: A
The patient's massive hemorrhage during delivery has led to ischemia and necrosis of the anterior pituitary gland, leading to low prolactin (inability to lactate), low FSH, ACTH, LH, TSH and GH..

Why is the posterior pituitary not harmed by the hemorrhage?
Because it has different blood supply since it has a different embryological origin than that of the anterior pituitary. And in pregnancy, ant. pituitary enlarges because of hypertrophy of prolactin secreting cells → increased blood supply demand (while posterior pituitary supply is still the same)… Thus when hemorrhage occurs → anterior pituitary is more susceptible to infarction

Answer 3: C
The patient's diagnosis is prolactinoma which is a pituitary adenoma. Treatment:
if the adenoma is large --> surgical resection
if small --> use dopamine agonists (bromocriptine)
Remember:
- Dopamine inhibits prolactin, that's why we give AGONIST of dopamine.
- In the medical history it is mentioned that there is no use of antipsychotics (eg: dopamine ANTAGONISTS). It's important to ask about it because dopamine antagonists --> suppress dopamine --> prolactin is not inhibited --> elevated prolactin

*** Sources of Questions and Answers:**

- First Aid Cases for the USMLE Step 1, 3rd ed., By: Tao Le and James S. Yeh

- USMLE Step 1 Secrets, 3rd ed., By: Thomas Brown and Sonali Shah

Explanations of answers were paraphrased a little bit.

Good luck!! :D