Essentials of Diagnosis, Treatment and Prevention of Major Endocrine Diseases:

Diseases of the hypothalamic-pituitary system. Its part in correction of the functional activity of the endocrine glands.

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

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US MLE TEST

A 42-year-old man presents to a new family physician to establish care. According to the patient, he has been healthy his entire life and rarely visits doctors, although he recently got married and his wife insisted that he see a doctor at least once. He reports no past medical or surgical history. His physical exam is notable for an elevated blood pressure (150/90), and the findings seen in Figure. What will be the most likely cause of death for this patient?

1. Respiratory disease, 2. Cardiovascular disease,
3. Malignancy , 4. Chronic kidney disease, 5. Liver failure

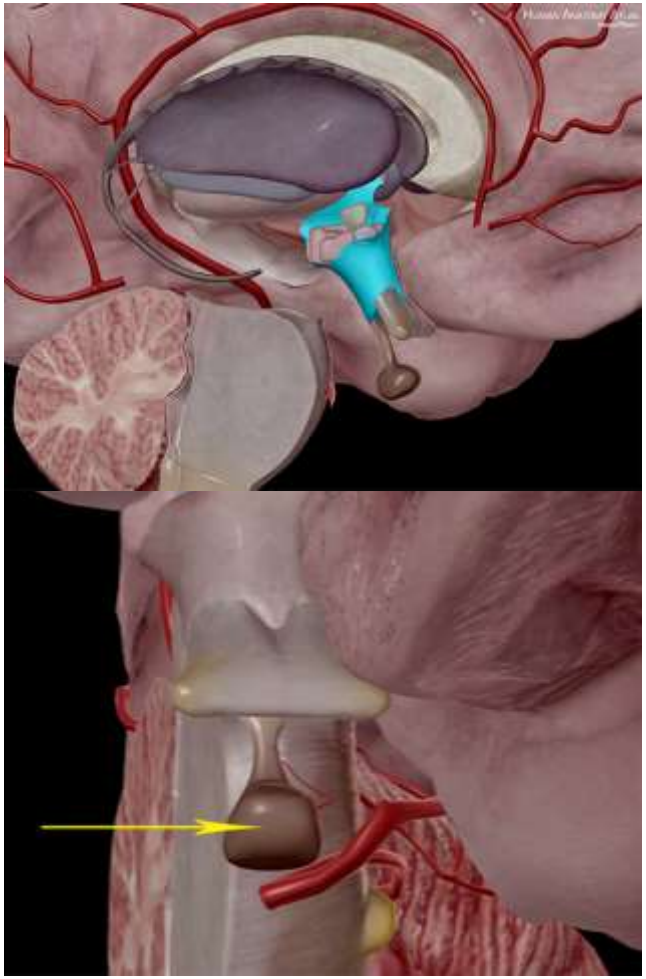
https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

US MLE TEST

Correct Answer 2: This patient has acromegaly, the most common cause of death from which is cardiovascular disease.
Incorrect Answers:
1: Despite the soft tissue enlargement seen in acromegaly, there is no evidence of an increased incidence of respiratory disorders.
3: While acromegaly is associated with increased incidence of malignancy, cardiovascular disease is a far more common cause of death.
4: Acromegaly is associated with kidney enlargement and increased risk of kidney cancer, but there is no demonstrated increased risk of chronic kidney disease.
5: Although acromegaly is associated with hepatomegaly, it is not known to cause liver toxicity or liver failure.

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

Plan of the Lecture



- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

s-media-cache-ak0.pinimg.com/236x/5a/a6/18/5aa618c9a609f5128337b826716c812c.jpg info.visiblebody.com/endocrine-system-hypothalamus-and-pituitary

Definition

Diseases of the Hypothalamic-Pituitary System 1

- The hypothalamus and pituitary form a functionally integrated complex

https://en.wikipedia.org/wiki/Hypothalamic_disease

Definition

Diseases of the Hypothalamic-Pituitary System 2

- Damage to the hypothalamic-pituitary system can impact the responsiveness and normal functioning of the pituitary and may cause inhibited signalling to the pituitary and/or decreased functioning of the pituitary leading to deficiencies of one or more of the following hormones: thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), beta-endorphin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL) and melanocyte–stimulating hormones (MSH)

https://en.wikipedia.org/wiki/Hypothalamic_disease

Definition

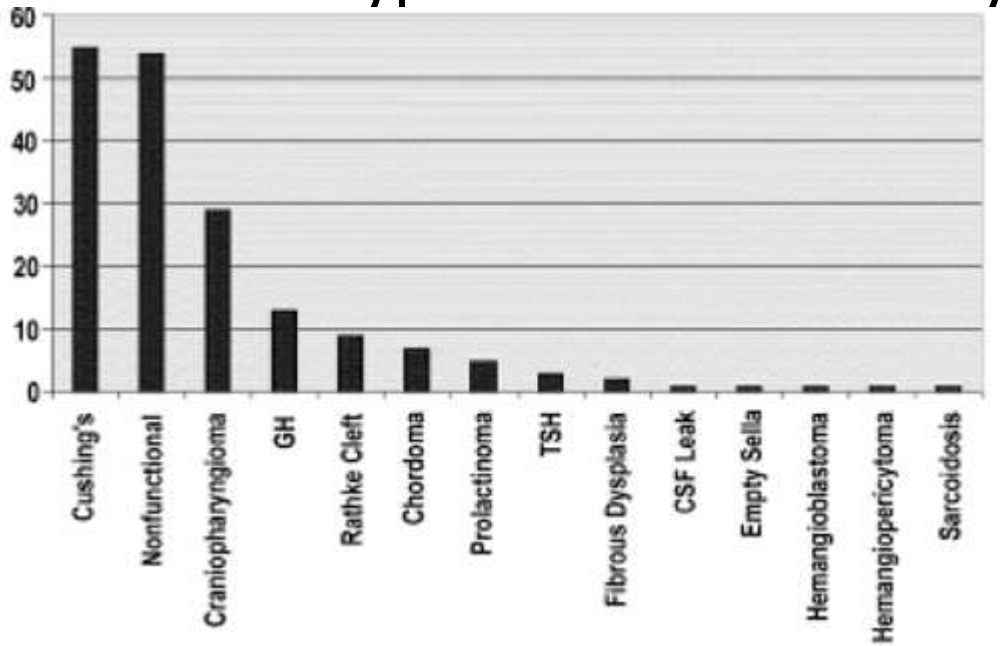
Diseases of the Hypothalamic-Pituitary System 3

- Damage to the hypothalamic-pituitary system may too cause excess pituitary hormone secretion.

https://en.wikipedia.org/wiki/Hypothalamic_disease

Epidemiology

Diseases of the Hypothalamic-Pituitary System

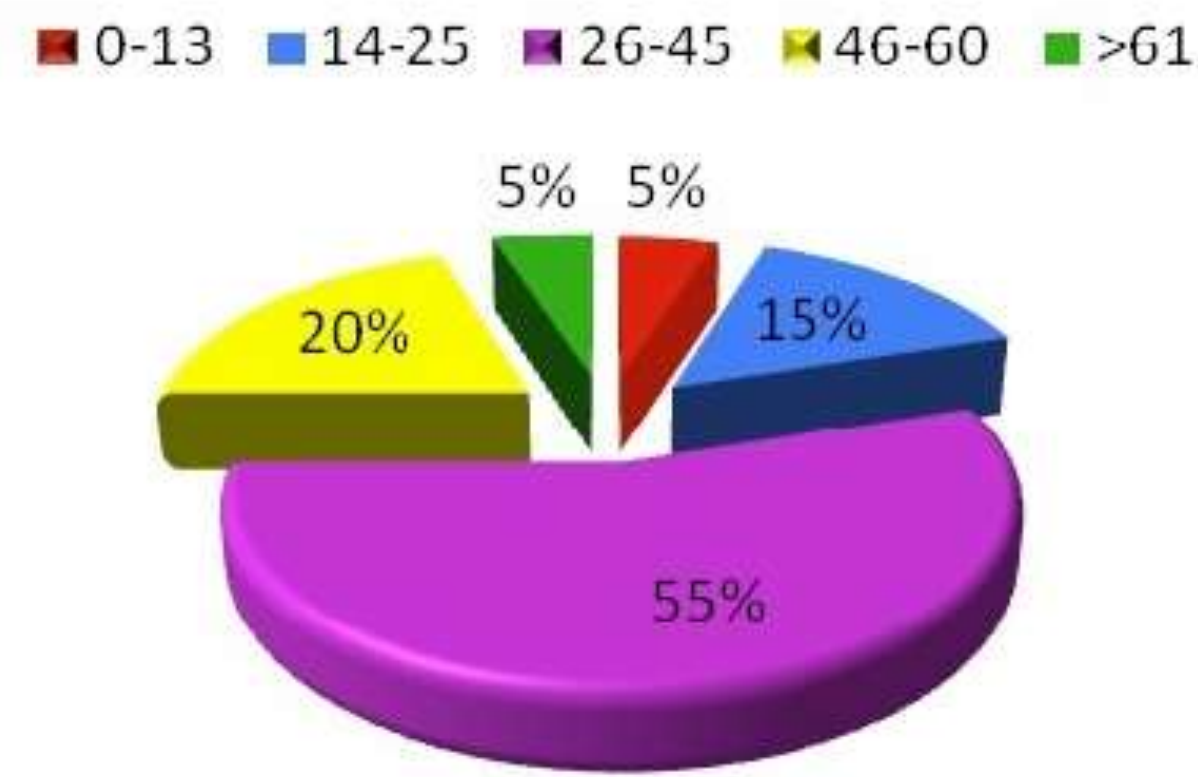


The breakdown of diseases distribution. Pituitary adenomas and craniopharyngiomas are the most common lesions encountered.GH = growth hormone; TSH = thyroid-stimulating hormone.

http://www.medscape.com/viewarticle/527723_3

Epidemiology

Diseases of the Hypothalamic-Pituitary System



A pie chart demonstrating the distribution by age of patients with pituitary tumors.

http://www.ajns.paans.org/IMG/jpg/FIG_2-3.jpg

Epidemiology

Diseases of the Hypothalamic-Pituitary System

Diagnosis code	Diagnosis	No of cases sampled	No of cases examined	No of missing records
ICD-8				
25300	Acromegaly	59	53	6
25301	Pituitary gigantism	5	4	1
25302	Pituitary adenoma, eosinophilic	4	4	0
25308	Hyperpituitarism, other specified	3	3	0
25309	Hyperpituitarism, not specified	1	0	1
25329	Pituitary adenoma, chromophobe	36	29	7
25801	Pituitary adenoma, basophilic	5	4	1
19439	Malignant neoplasm of pituitary gland and craniopharyngeal duct	0	0	0
22620	Benign neoplasm of pituitary gland	26	21	5
22629	Benign neoplasm of pituitary gland and craniopharyngeal duct	0	0	0
ICD-10				
E22.0	Acromegaly and pituitary gigantism	223	218	5
E22.1	Hyperprolactinaemia	578	116	4
E22.8	Other hyperfunction of pituitary gland	23	23	0
E22.9	Hyperfunction of pituitary gland, unspecified	28	27	1
C75.1	Malignant neoplasms, pituitary gland	4	4	0
D35.2	Benign neoplasm of other and unspecified endocrine glands, pituitary gland	460	93	5
D44.3	Neoplasm of uncertain or unknown behaviour of endocrine glands, pituitary gland	49	48	1
Total		1504	647	37

Distribution of all diagnosis codes for pituitary disorders. ICD, International Classification of Diseases.

https://www.dovepress.com/acromegaly-according-to-the-danish-national-registry-of-patients-how-v-peer-reviewed-fulltext-article-CLEP

Risk Factors and Etiology

Diseases of the Hypothalamic-Pituitary System 1

- Anorexia
- Bleeding
- Bulimia
- Genetic disorders
- Growths (tumors)
- Head trauma

He Pingping from China and Sultan Kosen from Turkey.

http://phabulousphive.weebly.com/uploads/4/0/5/9/40590611/2202450.jpg?250

Risk Factors and Etiology

Diseases of the Hypothalamic-Pituitary System 2

- Infections and swelling (inflammation)
- Malnutrition
- Radiation
- Surgery
- Hyperironemia

He Pingping from China and Sultan Kosen from Turkey.

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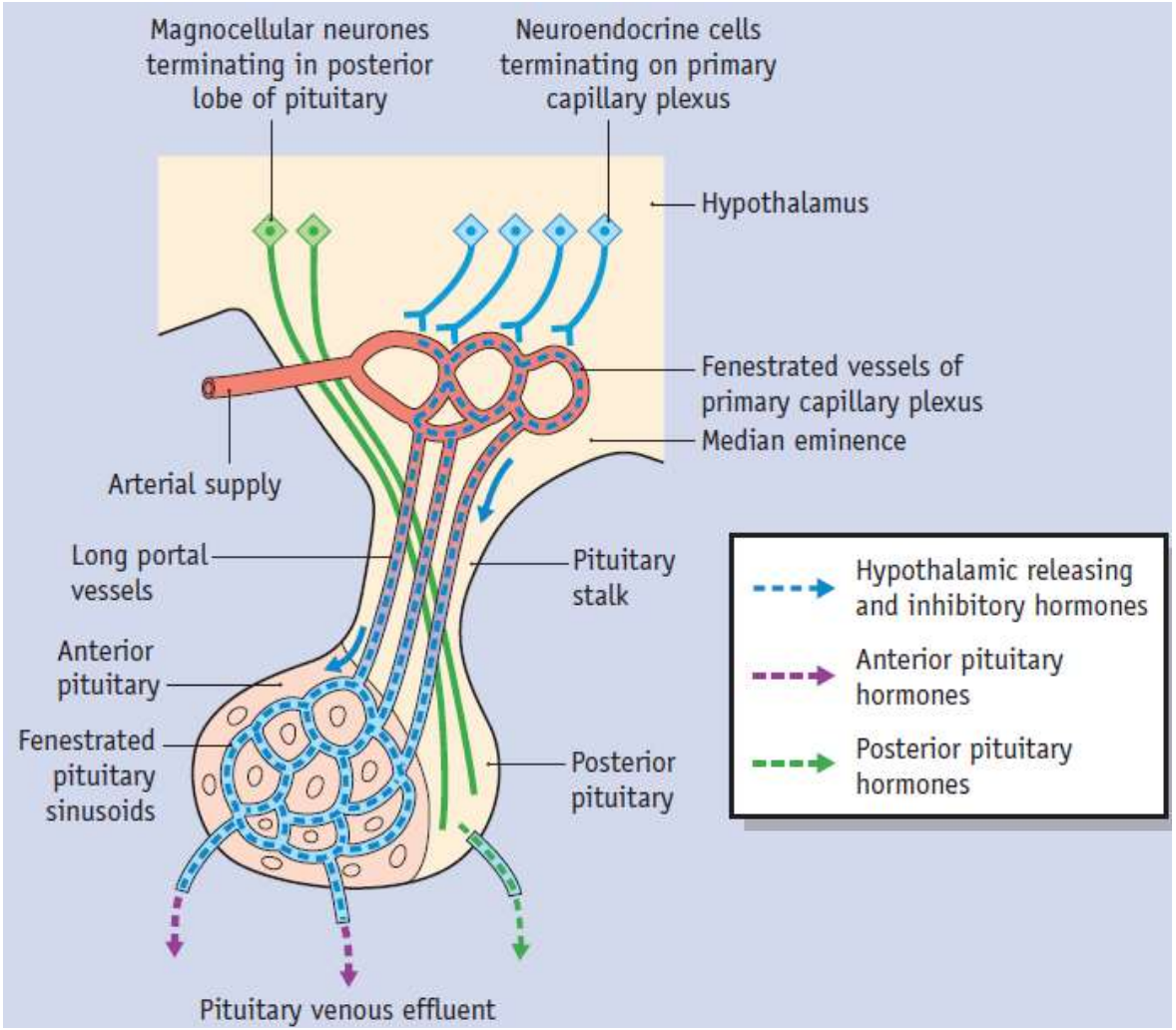
Mechanisms

Hypothalamo-Anterior Pituitary Link



http://medical-dictionary.thefreedictionary.com/Hypopituitarism

Mechanisms

Diseases of the Hypothalamic-Pituitary System

Commonly hormone deficiencies may include:

- Gonadotropin deficiency involves LH and FSH affecting the reproductive system in men and women and menstruation in women
- TSH deficiency leads to hypothyroidism
- ACTH deficiency leads to a reduction in the secretion of adrenal hormones, resulting in hypoadrenalism
- GH deficiency has a variety of different negative effects at different ages (e.g., in newborn infants may be hypoglycemia or micropenis, while in later infancy and childhood growth failure is more likely)

http://medical-dictionary.thefreedictionary.com/Hypopituitarism

Mechanisms

Diseases of the Hypothalamic-Pituitary System

Other hormone deficiencies:

- PRL deficiency leads to diabetes insipidus

Multiple hormone deficiencies:

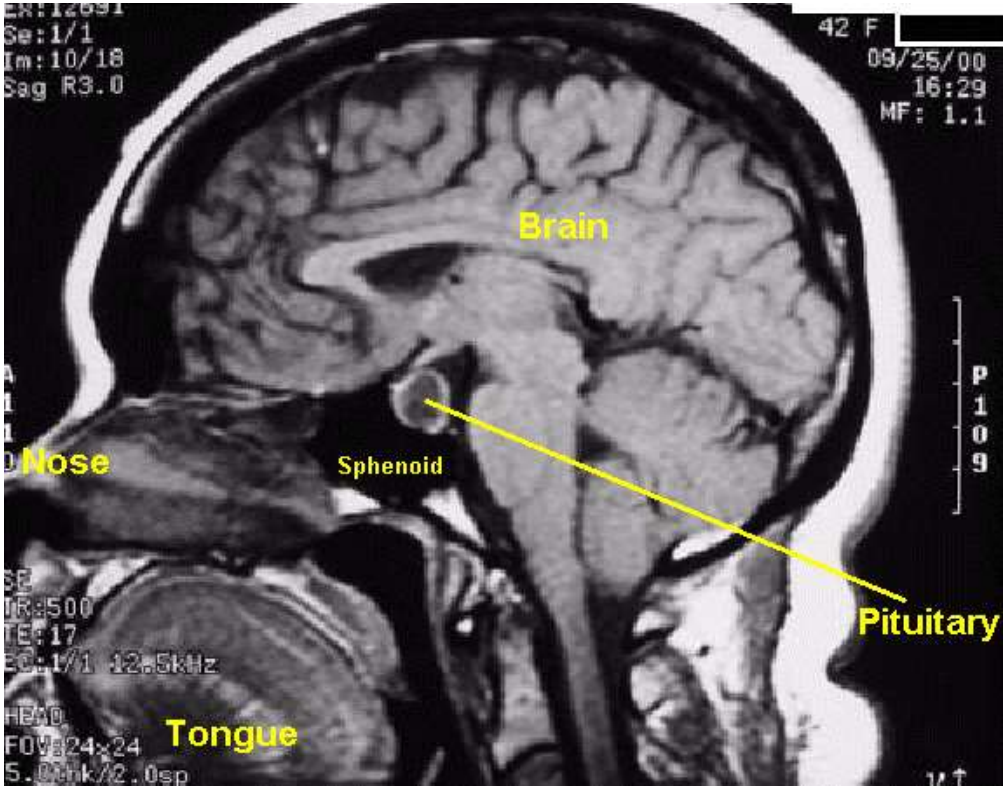
- Deficiency of a single pituitary hormone
- Generally, GH is lost first, then LH deficiency follows
- The loss of FSH, TSH and ACTH follow much later
- The progressive loss of pituitary hormone secretion is a slow process, which can occur over a period of months or years

Panhypopituitarism (pituitary failure) represents the loss of all hormones released by the anterior pituitary gland.

http://medical-dictionary.thefreedictionary.com/Hypopituitarism

Mechanisms

Diseases of the Hypothalamic-Pituitary System



Pituitary tumours may produce excess hormone, or they can block hormone production, or it can be 'non-functioning'.

http://www.northernendocrine.com.au/pituitary_20.html

International Classification of Diseases

Chapter IV

(E00-E90) Endocrine, nutritional and metabolic diseases

E22 Hyperfunction of pituitary gland

E23 Hypofunction and other disorders of pituitary gland

E23.0 Hypopituitarism

E23.1 Drug-induced hypopituitarism

E23.2 Diabetes insipidus

E23.3 Hypothalamic dysfunction, not elsewhere classified

E23.6 Other disorders of pituitary gland

E23.7 Disorder of pituitary gland, unspecified

http://apps.who.int/classifications/icd10/browse/2016/en#/E00-E07

Clinical Classification 1

- Pituitary tumors (adenomas)
- Hypopituitarism
  - Somatotropin (GH) Deficiency
  - Gonadotropin Deficiency
  - Corticotropin Deficiency
  - Thyrotropin Deficiency
- Excess Pituitary Hormone Secretion
  - Prolactinomas
  - Acromegaly
  - Cushing's Disease
  - Thyrotropin-Secreting Adenoma

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Clinical Classification 2

- Nonfunctional and Glycoprotein-secreting Pituitary Adenomas
- Lymphocytic Hypophysitis
- Empty Sella
- Pituitary Apoplexy
- Diabetes Insipidus

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Partial List of Tumor Symptoms

- Headaches
- Loss of vision

http://www.nytimes.com/health/guides/disease/hypothalamic-dysfunction/overview.html

Partial List of Hypothyroidism Symptoms

- Cold intolerance
- Constipation
- Depressed mood
- Fatigue
- Hair or skin changes
- Hoarseness
- Impotence
- Loss of body hair and muscle (in men)
- Mental slowing
- Menstrual cycle changes
- Weight gain

http://www.nytimes.com/health/guides/disease/hypothalamic-dysfunction/overview.html

Partial List of Low Adrenal Function Symptoms

- Dizziness
- Weakness

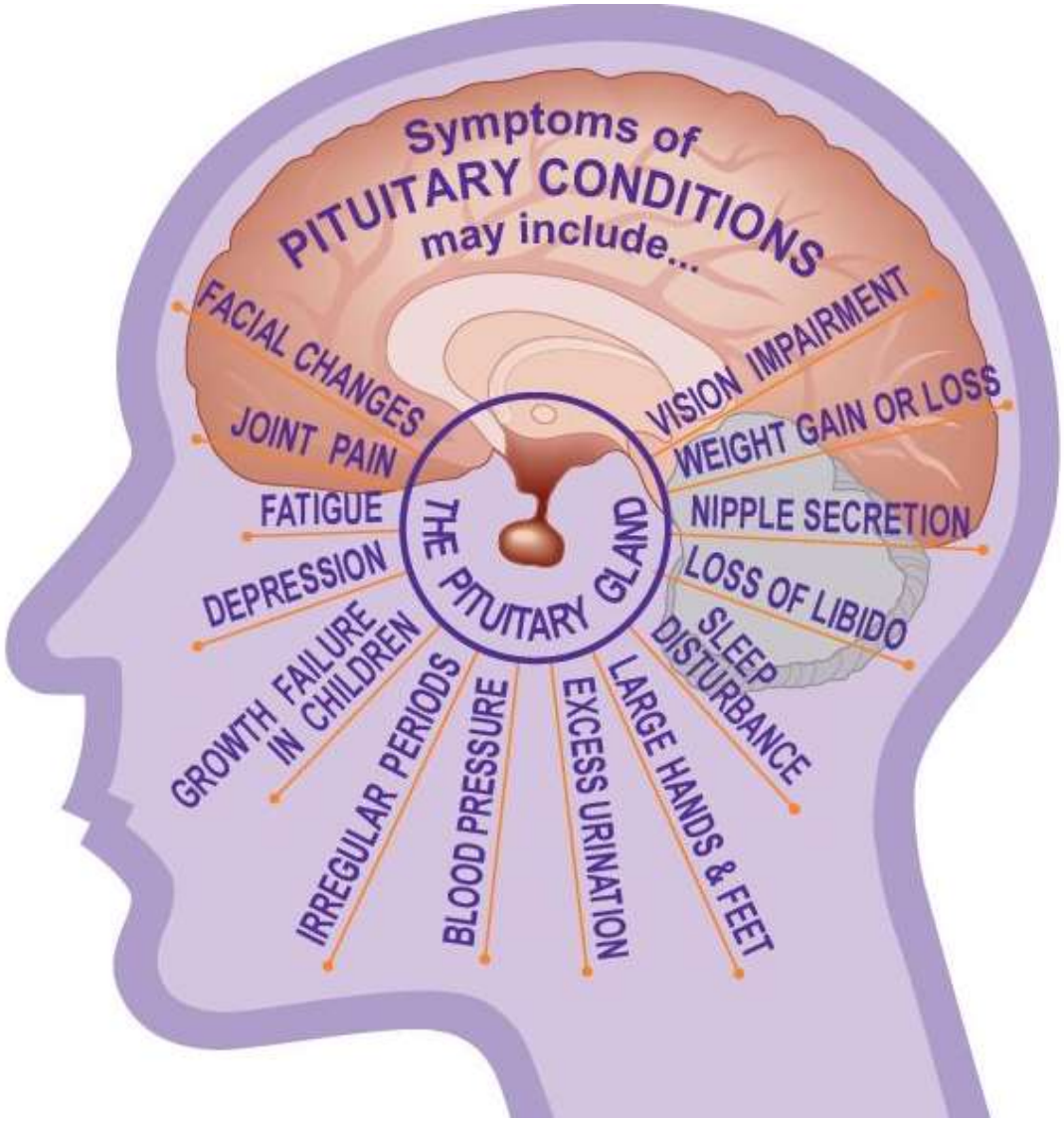
http://www.nytimes.com/health/guides/disease/hypothalamic-dysfunction/overview.html

Partial List of Other Symptoms

- Body temperature problems
- Emotional problems
- Excess thirst
- Obesity
- Uncontrolled urination
- Kallmann's syndrome (a type of hypothalamic dysfunction that occurs in men) symptoms:
- Lowered function of sexual hormones (hypogonadism)
- Inability to smell

http://www.nytimes.com/health/guides/disease/hypothalamic-dysfunction/overview.html

Partial List of Signs and Symptoms



http://cephalicvein.com/2016/07/pituitary-tumor-symptoms/

Partial List of Signs and Symptoms

http://cephalicvein.com/wp-content/uploads/2016/08/pituitary-tumor-symptoms-brain-tumor-symptoms-causes-risk-factors-and-treatment.jpg

US MLE TEST

A 67-year-old female presents with complaints of fatigue, nausea, and headache that have developed over the past several weeks. Her past medical history is significant for hypertension, diabetes mellitus, CHF, and small cell lung cancer diagnosed and treated 3 years previously. Vital signs are as follows: T 37.3 C, HR 82, BP 142/86, RR 16, O2Sat 97% on RA. On physical exam, peripheral edema is absent, and she is alert and oriented to person, place, and time. Abnormalities noted on initial labwork include glucose 138 mg/dL and sodium 122 mEq/L. Follow-up testing reveals a urine osmolality of 310 mmol/kg and a serum osmolality of 268 mmol/kg; BUN and creatinine levels are within normal limits. Which of the following is the best next step in the management of this patient?

1. Demeclocycline administration, 2. Initiate demospressin nasal spray, 3. Fluid restriction, 4. Hypertonic saline infusion, 5. Lithium carbonate administration

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

US MLE TEST

Correct Answer 3: This patient's presentation of hyponatremia, history of small cell lung cancer, and urine/serum osmolality values is consistent with a diagnosis of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Initial treatment of SIADH is with water restriction.

Incorrect Answers:

1: Demeclocycline inhibits the effect of ADH at the kidney; however, this measure is only indicated if hyponatremia becomes severe or profoundly symptomatic (typically below 120 mEq/L).

2: Desmopressin is indicated in the treatment of diabetes insipidus; it would likely worsen this patient's situation and further decrease serum Na levels.

4: Hypertonic saline is indicated in severe or significantly symptomatic cases of hyponatremia.

5: Lithium carbonate, much like demeclocycline, inhibits the effect of ADH at the kidney; however, this measure is rarely used and would only indicated if hyponatremia becomes severe or symptomatic.

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

Pituitary Tumors

Etiology 1

- Pituitary adenomas (microadenomas <10 mm, macroadenomas ≥10 mm) arise from adenohypophyseal cells and are almost always benign
- Pituitary adenomas discovered by computed tomography (CT) or magnetic resonance imaging (MRI) examination, in the absence of any symptoms or clinical findings, are referred to as pituitary incidentalomas

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Pituitary Tumors

Etiology 2

- Pituitary adenomas are rarely associated with parathyroid and neuroendocrine hyperplasia or neoplasia as part of the multiple endocrine neoplasia type I (MEN I) syndrome
- Pituitary carcinomas are extremely rare, but metastases from other solid malignancies (mainly breast and lung) can occur.

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Pituitary Tumors

Signs and Symptoms 1

- Pituitary tumors can manifest with signs and symptoms of pituitary hypofunction, hormone hypersecretion, or mass effect
- Impingement on the chiasma by a pituitary tumor results in visual field defects, most commonly bitemporal hemianopia

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Pituitary Tumors

Signs and Symptoms 2

- Patients with sellar mass pressing on the optic chiasma should have a Humphrey visual field test
- Lateral extension of the pituitary mass to the cavernous sinuses can result in diplopia, ptosis, or altered facial sensation
- There is no specific headache pattern associated with pituitary tumors and, in some patients, the headache is unrelated to pituitary adenoma.

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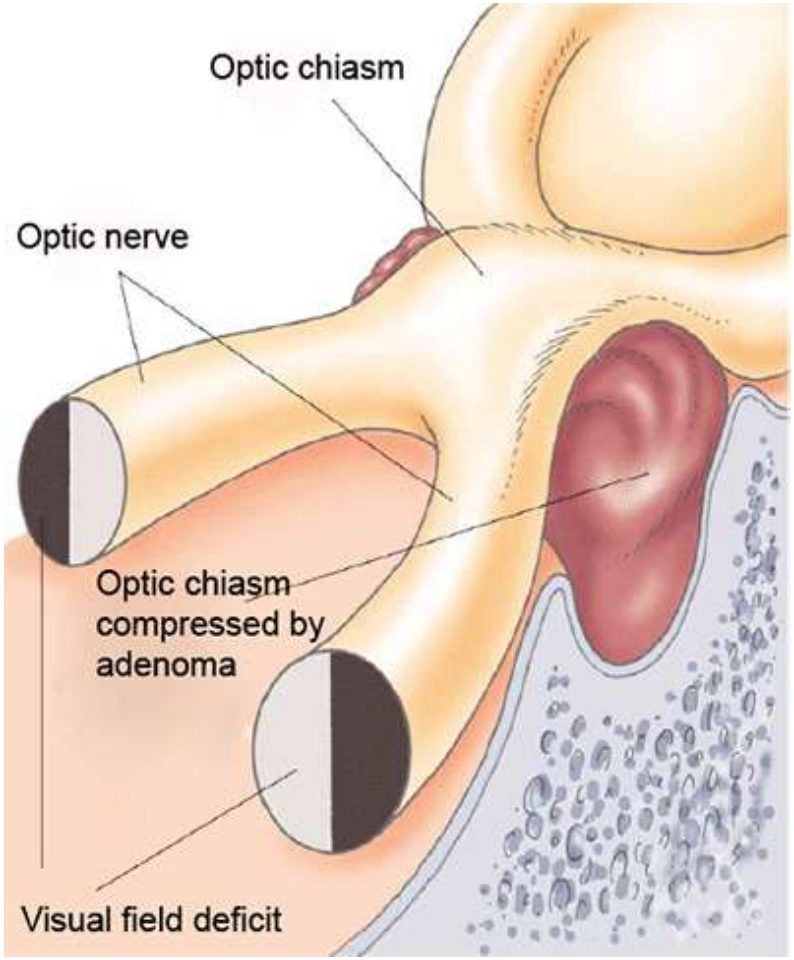
Pituitary Tumors

Signs and Symptoms



Impingement on the chiasma by a pituitary tumor results in visual field defects, most commonly bitemporal hemianopia.

http://cephalicvein.com/wp-content/uploads/2016/08/pituitary-tumor-symptoms-department-of-neurosurgery-tokai-university-hospital.gif

Pituitary Tumors

Diagnosis and Treatment 1

- Magnetic resonance imaging (MRI) is the best method for the visualizing hypothalamic-pituitary anatomy
- Once a pituitary adenoma is found, it is necessary to determine its type (secretory vs. nonsecretory), pituitary function, and whether there is any visual field defect

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Pituitary Tumors

Diagnosis and Treatment 2

- The treatment include reduction or complete removal of the tumor, elimination of mass effect, normalization of hormone hypersecretion, and restoration of normal pituitary function
- Some patients with large tumors require additional medical, and radiation therapies
- The most important factor in pituitary surgery is the availability of an experienced neurosurgeon.

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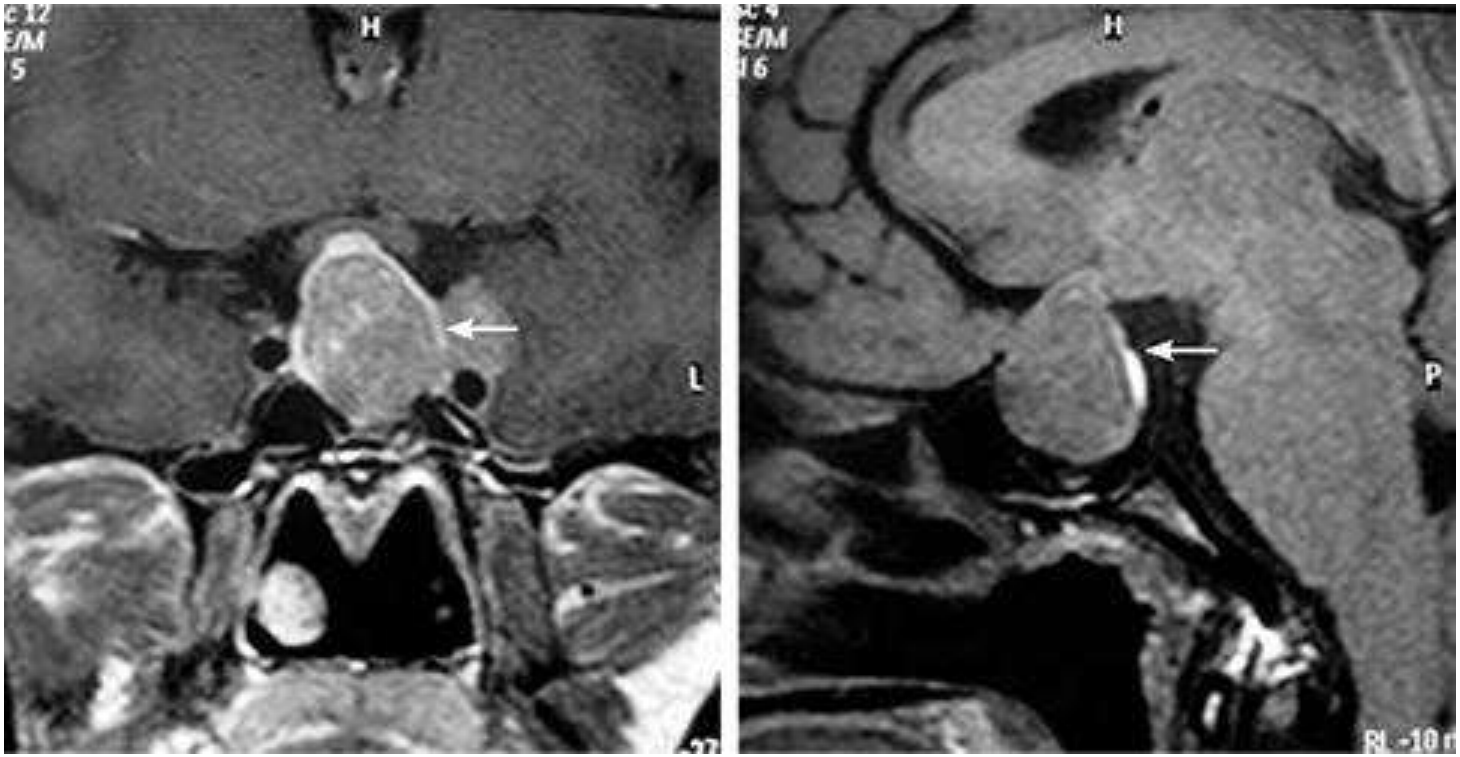
Pituitary Tumors

Diagnosis and Treatment



Large non-functioning pituitary adenoma disclosed in a patient with macroprolactinemia (arrows).

http://www.scielo.br/img/revistas/abem/v58n1//0004-2730-abem-58-1-0009-gf06.jpg

US MLE TEST

A 34-year-old man with a history of major depressive disorder presents to the emergency room with altered mental status. Vital signs are stable, and he appears euvolemic on exam. Serum sodium is 120. The patient's hyponatremia is attributed to newly prescribed fluoxetine. Which of the following is another cause of euvolemic hyponatremia?

1. Congestive heart failure, 2. Nephrosis, 3. Prerenal acute kidney injury, 4. Mineralocorticoid deficiency, 5. Lung malignancy

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US MLE TEST

Correct Answer 5: A cause of euvolemic hyponatremia is SIADH as a result of a paraneoplastic production of ADH from a small cell lung cancer. Plasma osmolality will be low, and urine osmolality will be inappropriately high.
Incorrect Answers:
1 and 2: Congestive heart failure and nephrosis cause hypervolemic hyponatremia, which would result in Urine Na < 10, Fractional Excretion Na < 1%.
3: Prerenal acute kidney injury is a cause of hypovolemic hyponatremia. One would expect Urine Na < 20, Fractional Excretion Na < 1%.
4: Mineralocorticoid deficiency causes hypovolemic hyponatremia. One would expect Urine Na > 20 and Fractional Excretion Na > 1%.

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

Hypopituitarism

Etiology 1

- Pituitary adenomas are the most common cause of hypopituitarism, but other causes include parasellar diseases, pituitary surgery, radiation therapy, inflammatory and granulomatous diseases, and head injury
- The sequential loss of pituitary hormones secondary to a mass effect is in the following order: GH, LH, FSH, TSH, ACTH, and prolactin

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Hypopituitarism

Etiology 2

- Isolated deficiencies of various anterior pituitary hormones can occur
- In general, pituitary microadenomas are rarely associated with hypopituitarism
- Diabetes insipidus is almost never seen in patients with pituitary adenomas at presentation.

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Hypopituitarism

Somatotropin (GH) Deficiency 1

- GP deficiency in premenopausal women is recognized early on account of amenorrhea, infertility or loss of libido
- Men often delay presentation on developing impotence or loss of libido, though with wider recognition of effective management of erectile dysfunction this pattern is reversing, provided other practitioners check for hormonal causes

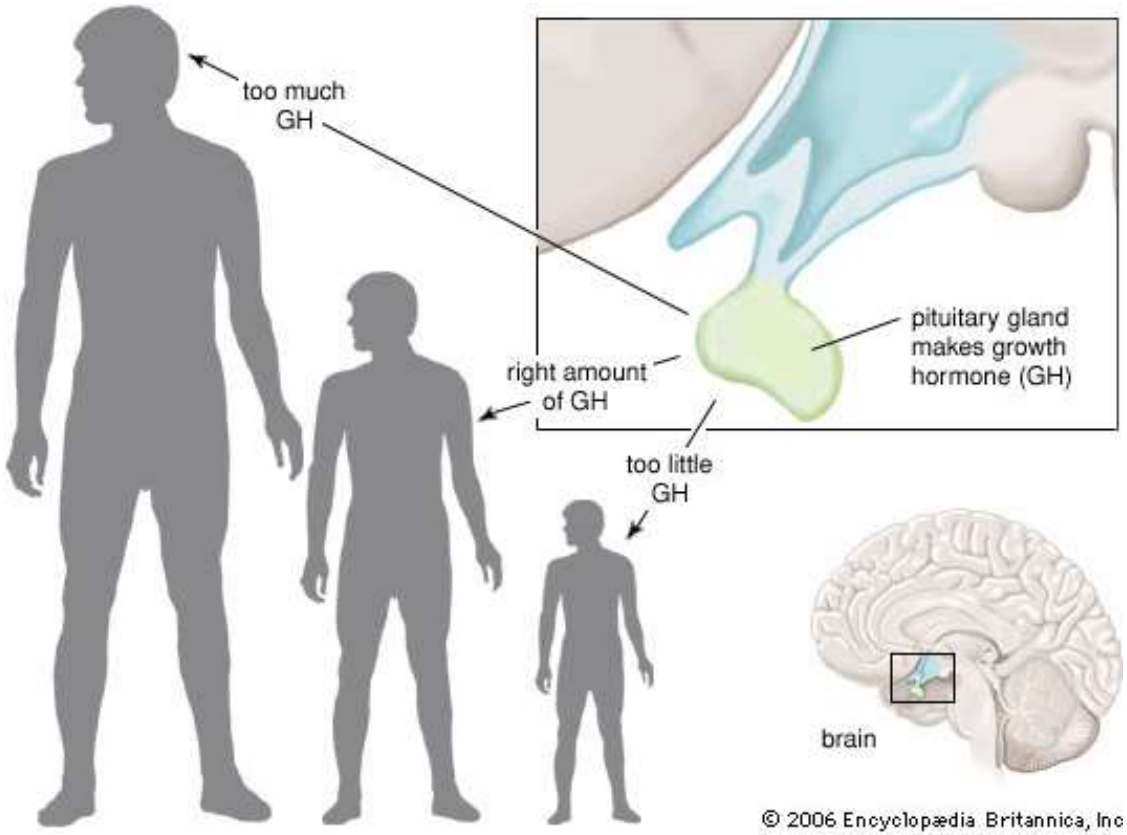
Hypopituitarism

Somatotropin (GH) Deficiency 2

- Patients with GH deficiency have increased body fat and decreased lean body mass, and they might have decreased bone mineral density
- GH deficiency is evaluated by dynamic testing, including the insulin tolerance test or GH-releasing hormone (RH)/arginine test
- Adult GH deficiency is diagnostically valuable and clinically important, since recombinant GH therapy is available.

Hypopituitarism

Somatotropin (GH) Deficiency



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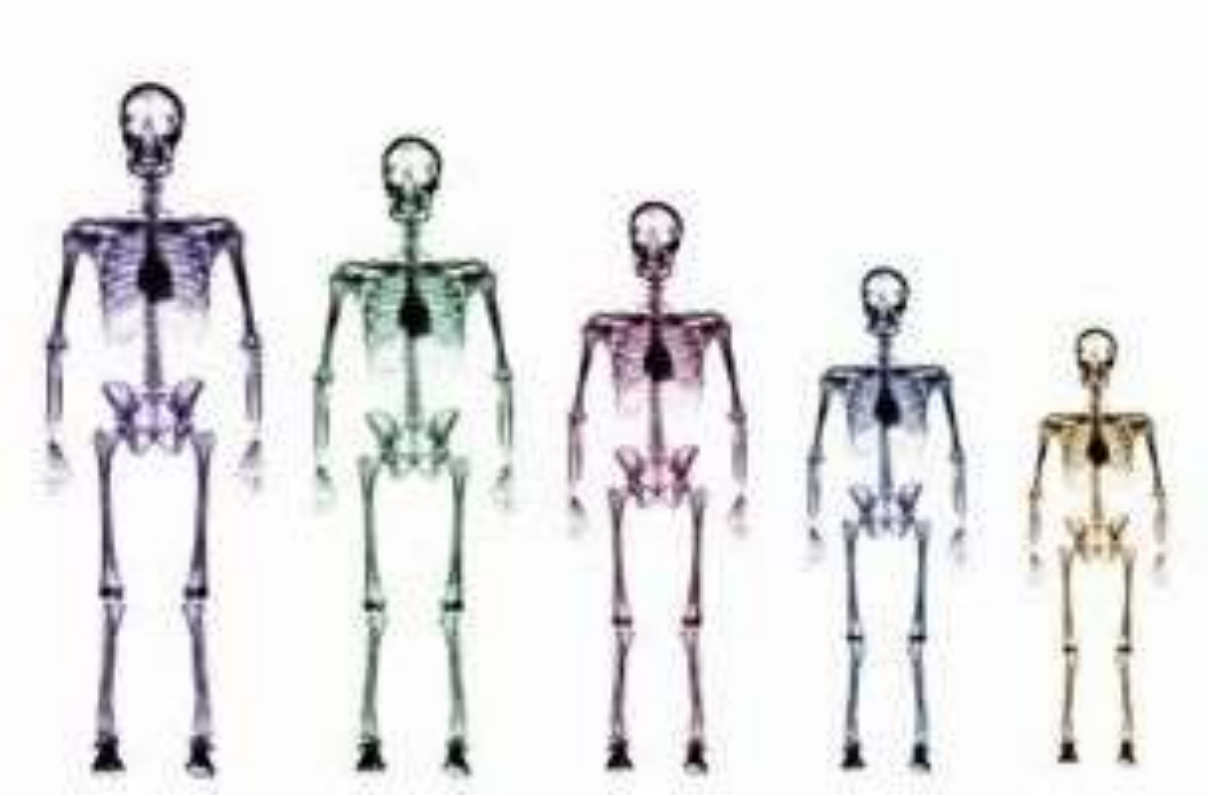
Hypopituitarism

Somatotropin (GH) Deficiency



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Hypopituitarism

Gonadotropin Deficiency or Hypogonadism 1

- In women, hypogonadism causes infertility and oligomenorrhea or amenorrhea often associated with lack of libido, hot flushes, and dyspareunia
- In men, hypogonadism is diagnosed less often, because decreased libido and impotence may be considered functions of aging
- Osteopenia is a consequence of long-standing hypogonadism and responds to hormone replacement therapy

medical-dictionary.thefreedictionary.com/Hypopituitarism levelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/pituitary-disorders/

Hypopituitarism

Gonadotropin Deficiency or Hypogonadism 1

- Hypogonadism is diagnosed in the presence of low or normal LH and FSH levels in women, or in men with testosterone levels <200 ng/dL
- Estrogen replacement is necessary in women to prevent osteoporosis and to treat hot flushes, decreased libido, and vaginal dryness
- Testosterone in man may be replaced by intramuscular injection, transdermal patch, or a gel (oral testosterone is not recommended).

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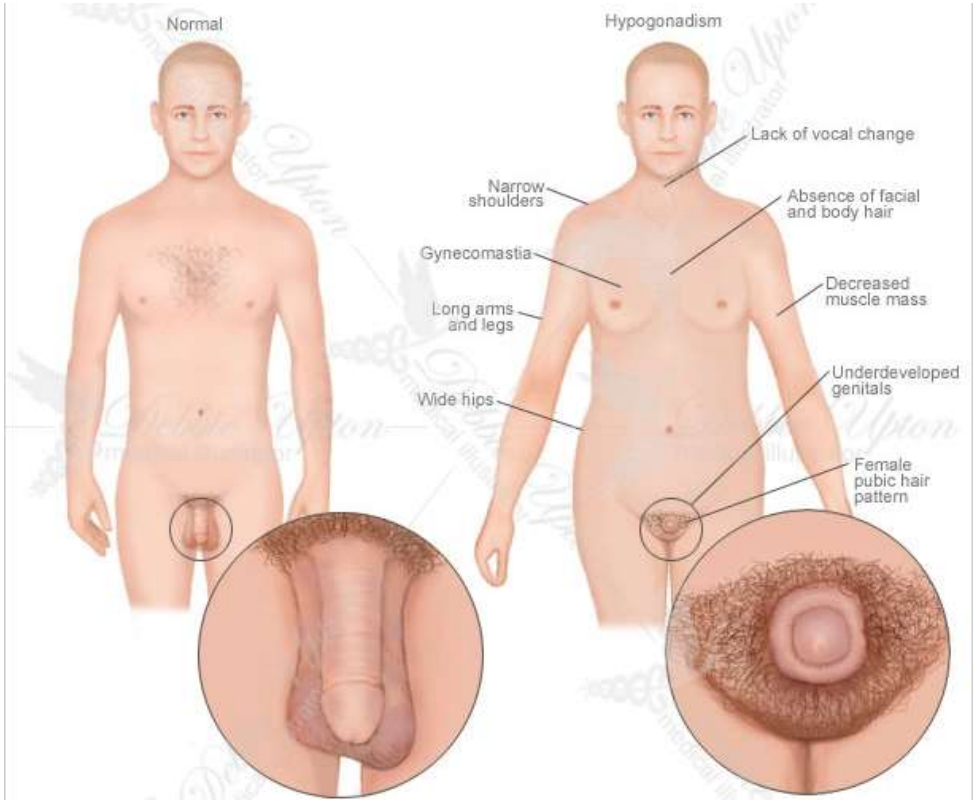
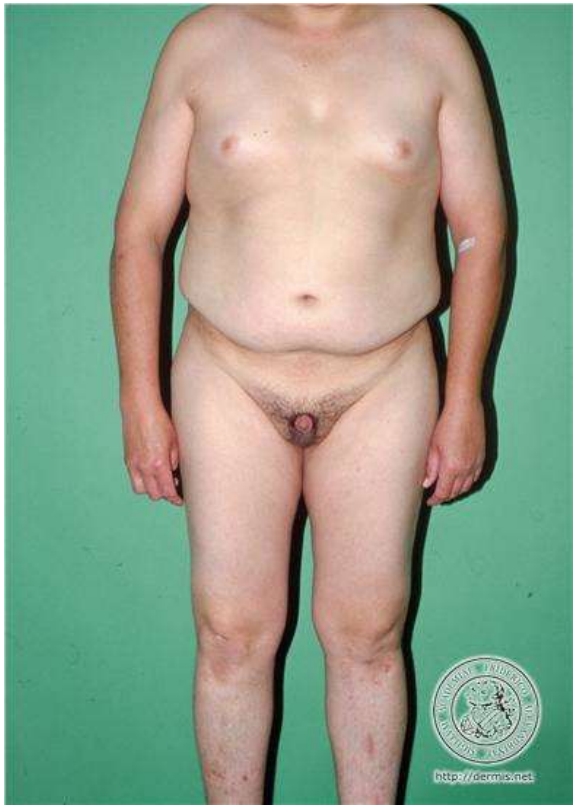
Hypopituitarism

Gonadotropin Deficiency or Hypogonadism





dxline.info/img/new_ail/hypogonadism.jpg dxline.info/img/new_ail/hypogonadism_4.jpg

Hypopituitarism

Corticotropin (ACTH) Deficiency 1

- Patients with ACTH deficiency maintain mineralocorticoid secretion because aldosterone is regulated primarily by the renin-angiotensin system and serum potassium concentration
- Symptoms include chronic malaise, fatigue, anorexia, low-grade fever, hypoglycemia, and less often hyponatremia

Hypopituitarism

Corticotropin (ACTH) Deficiency 2

- An ACTH stimulation test and early morning (8 am) plasma cortisol level measurement are initial tests: cortisol level <3 µg/dL confirms adrenal insufficiency, a level >15 µg/dL makes the diagnosis unlikely, and a levels in the intermediate range demands additional cosyntropin stimulation test (CST).

Hypopituitarism

Corticotropin (ACTH) Deficiency 3

- Hydrocortisone replacement is necessary in doses (15 – 20) mg/day, with the highest one given in the morning
- In case of an acute distress patients should be instructed to carry a medical alert, and double replacement dosage for 2 to 3 days.

Hypopituitarism

Thyrotropin (TSH) Deficiency 1

- TSH deficiency are similar to those in patients with primary hypothyroidism, including malaise, fatigue, leg cramps, dry skin, and cold intolerance
- The diagnosis cannot be established only through measurement of TSH because these patients might have a normal TSH level
- If secondary hypothyroidism is clinically suspected, TSH and free thyroxine (T_4) should be measured together: usually, patients have a low or normal TSH level along with a low free T_4 level

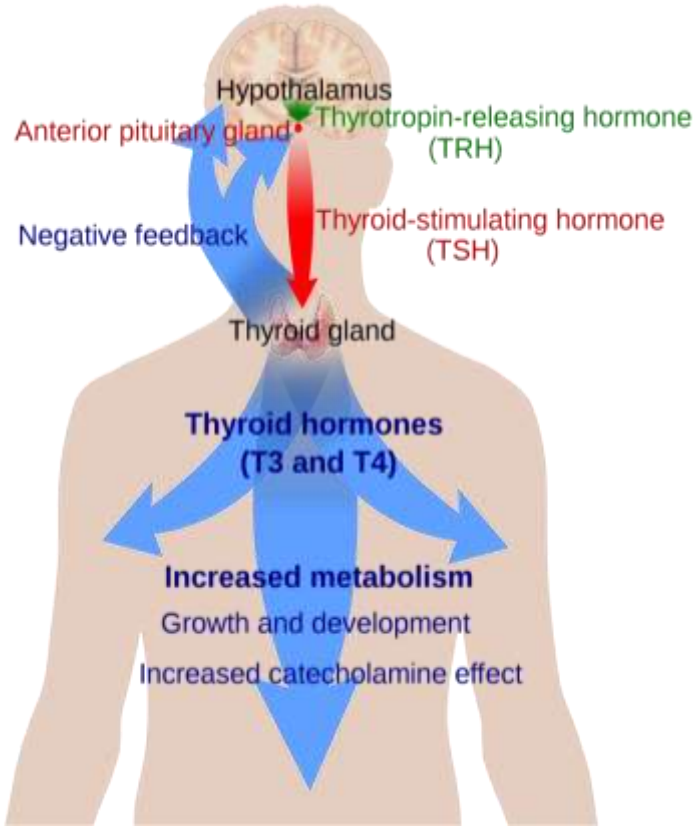
Hypopituitarism

Thyrotropin (TSH) Deficiency 2

- Therapy for TSH deficiency is similar to that for primary hypothyroidism
- The levothyroxine replacement dose should be adjusted according to the patient's clinical status and free T_4 and free triiodothyronine (T_3) levels, but not TSH.

Hypopituitarism

Thyrotropin (TSH) Deficiency



If TSH deficiency (secondary hypothyroidism) is clinically suspected, TSH and free thyroxine (T_4) should be measured together: usually, patients have a low or normal TSH level along with a low free T_4 level

https://upload.wikimedia.org/wikipedia/commons/thumb/d/d1/Thyroid_system.svg/2000px-Thyroid_system.svg.png

Excess Pituitary Hormone Secretion

Prolactinomas: Clinical Features 1

- Prolactinomas are pituitary adenomas that secret PRL in varying degrees and account for about 30% of all pituitary adenomas
- Prolactinomas are more common in women, with a peak incidence during the childbearing years
- Clinical features related to excess prolactin
- Women of reproductive age mainly present with oligomenorrhea, amenorrhea, galactorrhea, or infertility

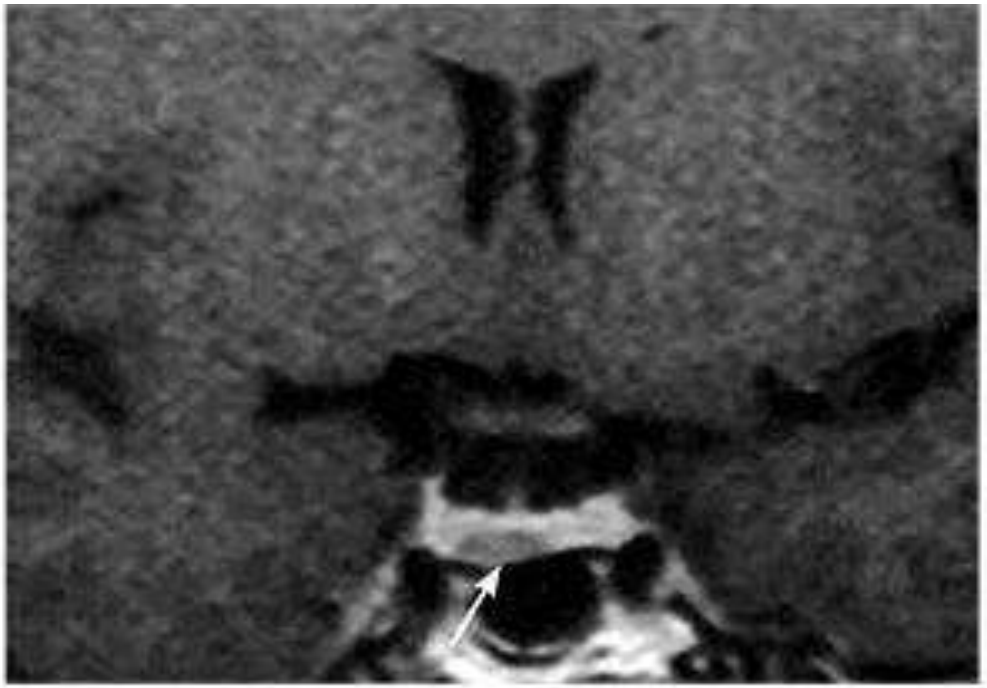
Excess Pituitary Hormone Secretion

Prolactinomas: Clinical Features 1

- Men and postmenopausal women usually come to medical attention because of mass effect, such as headaches and visual field defects
- The majority of patients with a serum PRL level >100 µg/L have prolactinoma
- A serum PRL level <100 µg/L in the presence of a large pituitary adenoma suggests stalk compression.

Excess Pituitary Hormone Secretion

Prolactinomas: Diagnosis

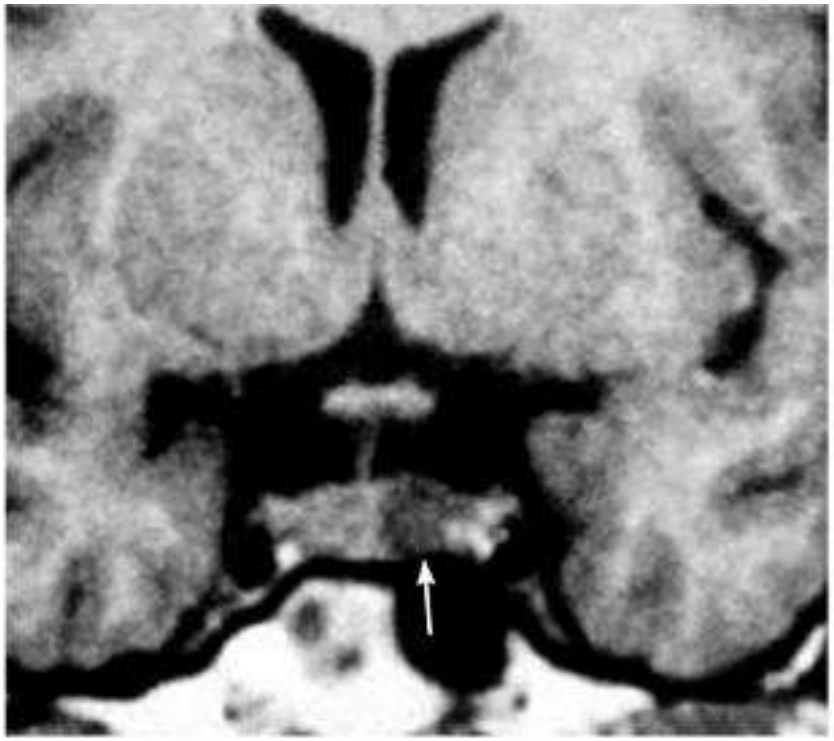


Microprolactinoma in a patient with primary hypothyroidism (arrow). This condition should be considered whenever PRL levels remain elevated following normalization of TSH and free T_4.

http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302014000100009

Excess Pituitary Hormone Secretion

Prolactinomas: Diagnosis



Microprolactinoma in a patient with macroprolactinemia (arrow). After PEG precipitation, PRL recovery was low (25%) but PRL levels remained elevated (93 ng/mL).

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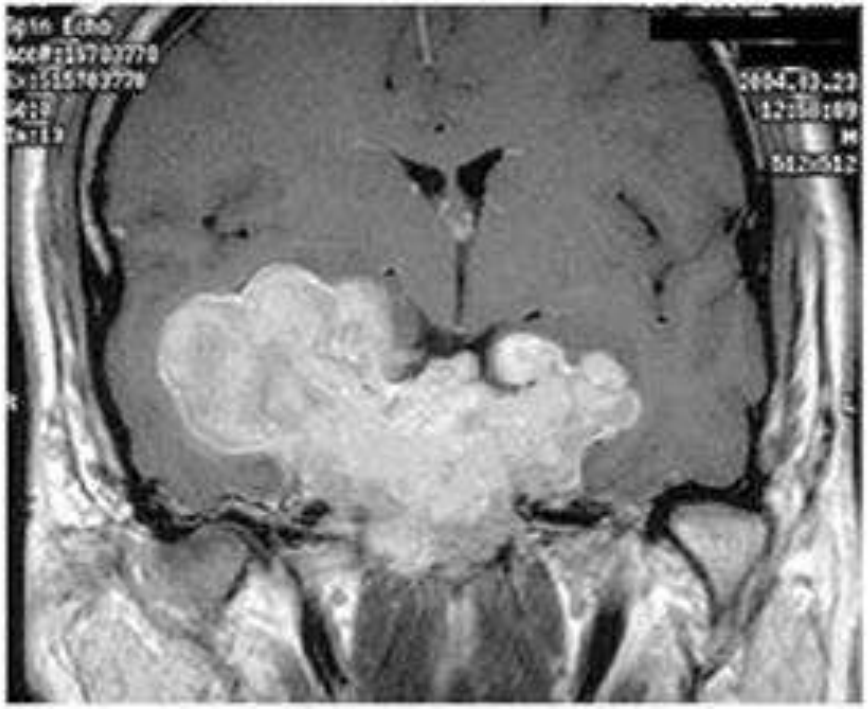
Excess Pituitary Hormone Secretion

Prolactinomas: Diagnosis



Giant invasive pituitary prolactinoma with falsely low serum PRL (103 ng/mL.) due to the hook effect. PRL levels rose to 13,144 ng/mL after a 1:100 serum sample dilution (Adapted from Ref. 89).

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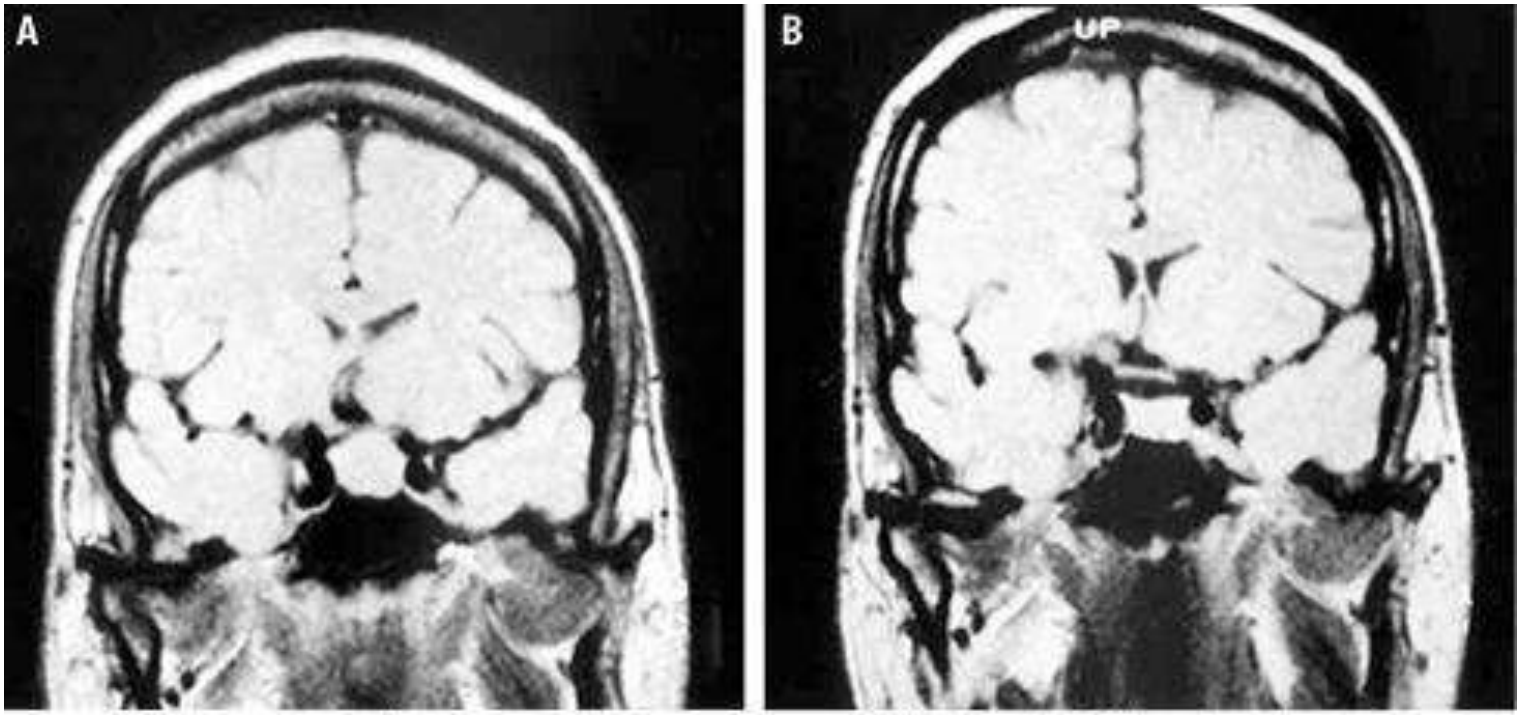
Excess Pituitary Hormone Secretion

Prolactinomas: Diagnosis



Diffuse pituitary enlargement in a patient with primary hypothyroidism-induced hyperprolactinemia, before (A) and after (B) L-thyroxine replacement.

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Excess Pituitary Hormone Secretion

Prolactinomas: Treatment 1

- Dopamine agonists are the therapy of choice for most patients, and they are effective in decreasing adenoma size and restoring normal PRL level; the most common side effects include nausea, headache, dizziness, nasal congestion, and constipation
- Cabergoline and bromocriptine are potent inhibitors of PRL secretion and often cause tumor shrinkage; cabergoline is more potent, and may be taken only twice a week.

Excess Pituitary Hormone Secretion

Prolactinomas: Treatment 2

- Surgery is reserved for patients who are intolerant of or refractory to medical therapy
- Radiation therapy may be considered for patients who poorly tolerate dopamine agonists and cannot be cured by surgery.

Excess Pituitary Hormone Secretion

Acromegaly: Clinical Features 1

- Acromegaly is a rare disease caused by a GH-secreting pituitary adenoma in more than 99% of patients
- Excess GH before the fusion of the epiphyseal growth plates results in gigantism

Excess Pituitary Hormone Secretion

Acromegaly: Clinical Features 2

- Clinical features include arthralgias, neuropathic, carpal tunnel syndrome, coarsening of facial features, excessive sweating, goiter, hypertension, heart failure, arrhythmias, impaired glucose tolerance, macroglossia, tooth gaps, pituitary mass effect and insufficiency, sensory and motor peripheral neuropathies, sleep apnea, etc.

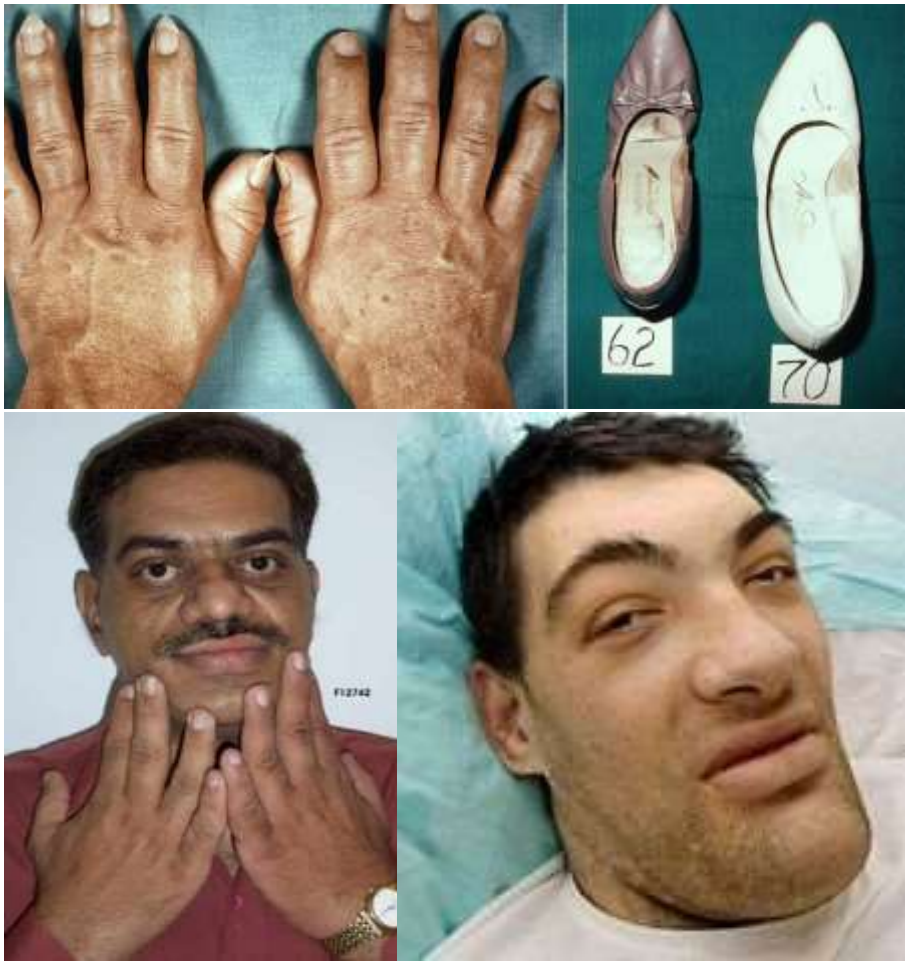
Excess Pituitary Hormone Secretion

Acromegaly: Clinical Features 3

- Acromegalic patients carry an increased risk of malignancy such as premalignant adenomatous colon polyps and colon cancer
- Random GH levels are associated with increased morbidity and mortality if untreated.

Excess Pituitary Hormone Secretion

Acromegaly: Clinical Features 4



- The most commonly notice symptom is abnormal enlargement of the hands and feet. Enlargement of the feet may require increasingly larger shoe size.

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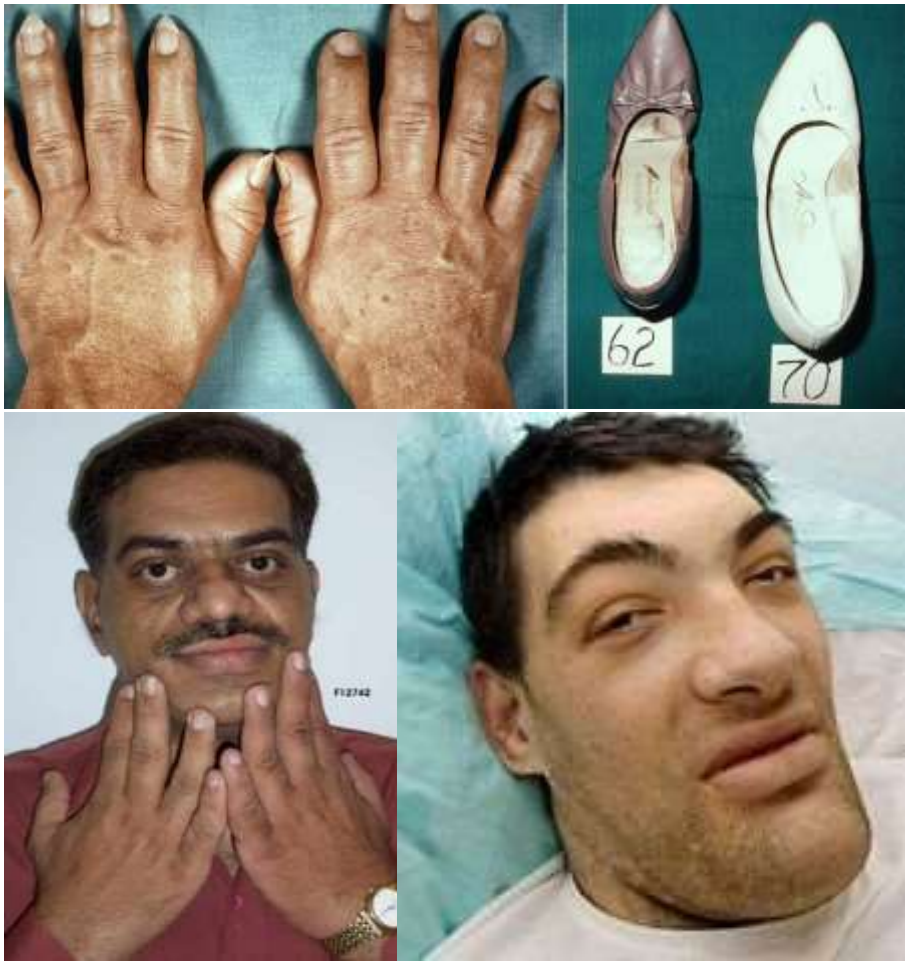
Excess Pituitary Hormone Secretion

Acromegaly: Clinical Features 5



- Changes in facial features can include enlargement of forehead and jaw with pronounced under bite, spreading teeth and enlarging tongue. The nose and lips may enlarge as well.

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Excess Pituitary Hormone Secretion

Acromegaly: Treatment 1

- The goal of therapy for most patients is to achieve a normal sex- and age-adjusted IGF-1 and GH less than 2 ng/mL
- Surgery is the treatment of choice even if a cure cannot be achieved
- Even a subtotal resection of the tumor will improve the efficacy of subsequent adjuvant therapy

Excess Pituitary Hormone Secretion

Acromegaly: Treatment 2

- Somatostatin analogues inhibit GH secretion mainly by binding to somatostatin receptors and result in normalization of IGF-1 in up to 65% of patients
- Pegvisomant has higher affinity to GH receptors than native GH but inhibits its dimerization, which is necessary for the action of GH
- Dopamine agonists have variable efficacy but may be an attractive first-line therapy, especially in those with cosecretion of prolactin and GH.

Excess Pituitary Hormone Secretion

Cushing's Disease: Symptoms 1

- Cushing's disease (CD) comprises symptoms and signs associated with prolonged exposure to inappropriately high levels of plasma ACTH-dependent free glucocorticoids
- The striae in CS are usually red-purple, more than 1 cm wide, and located on the abdomen, upper thighs, breasts, and arms
- Increased skin pigmentation is rare and only occurs in the ectopic ACTH syndrome

Excess Pituitary Hormone Secretion

Cushing's Disease: Symptoms 2

- Supraclavicular and dorsocervical fat pads (buffalo hump) and moon face are nonspecific and are seen in many patients of obesity clinics
- Women complain of menstrual irregularity (84%) and hirsutism (especially vellous hypertrichosis of the face), and men and women exhibit loss of libido (≤100%)
- Psychiatric abnormalities occur in 50% of patients.

Excess Pituitary Hormone Secretion

Cushing's Disease: Clinical Features

Central obesity
Unexplained osteoporosis
Proximal myopathy
Wide purplish striae (>1 cm)
Facial plethora
Spontaneous bruising
Hypokalemia
Serial photographs

http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/pituitary-disorders/#cetextbox3

Excess Pituitary Hormone Secretion

Cushing's Disease: Endogenous Causes

ACTH-Dependent Cushing's Syndrome
Cushing's disease (67%)
Ectopic ACTH secretion (12%)
Ectopic CRH secretion (<1%)
ACTH-Independent Cushing's Syndrome
Adrenal adenoma (10%)
Adrenal carcinoma (8%)
Micro- and macronodular adrenal hyperplasia (1%)

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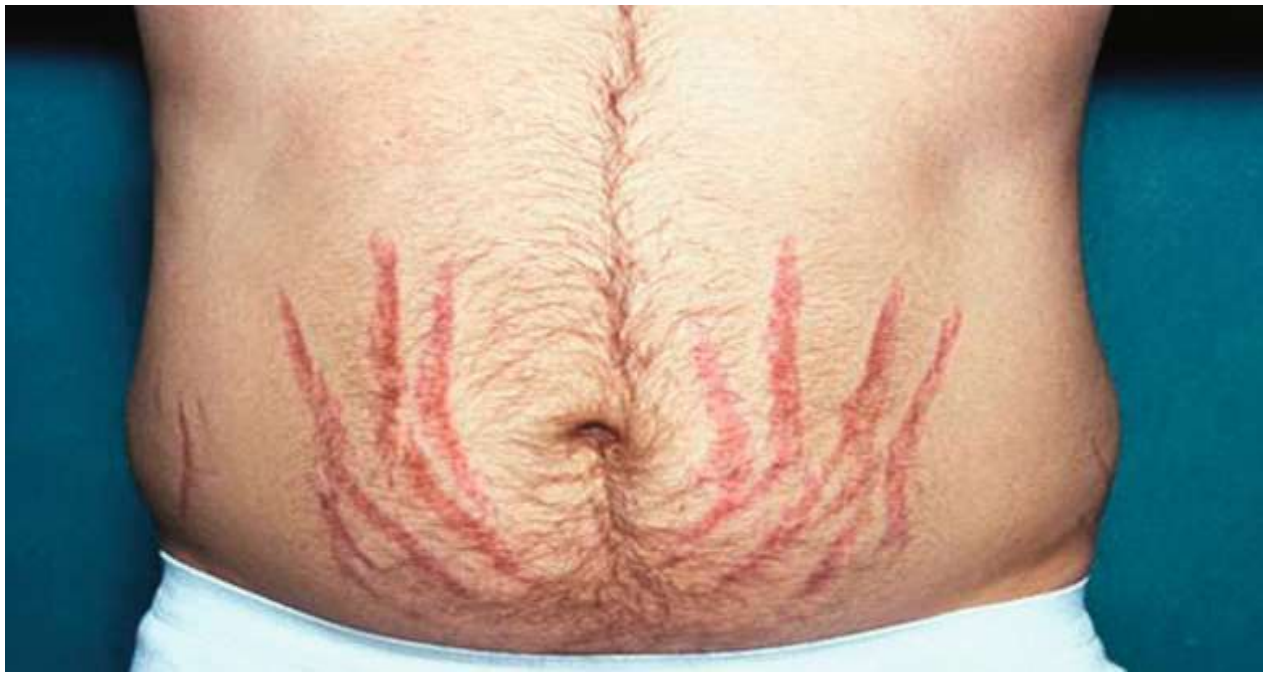
Excess Pituitary Hormone Secretion

Cushing's Disease: Endogenous Causes



Red purplish abdominal striae 1 cm in width in a patient with CD

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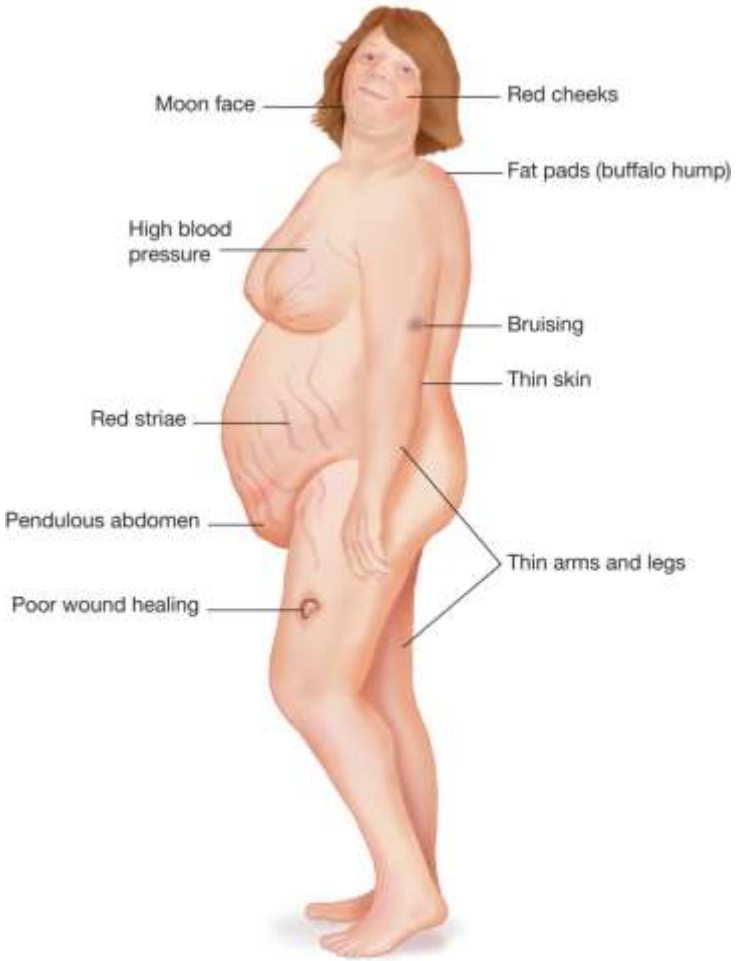
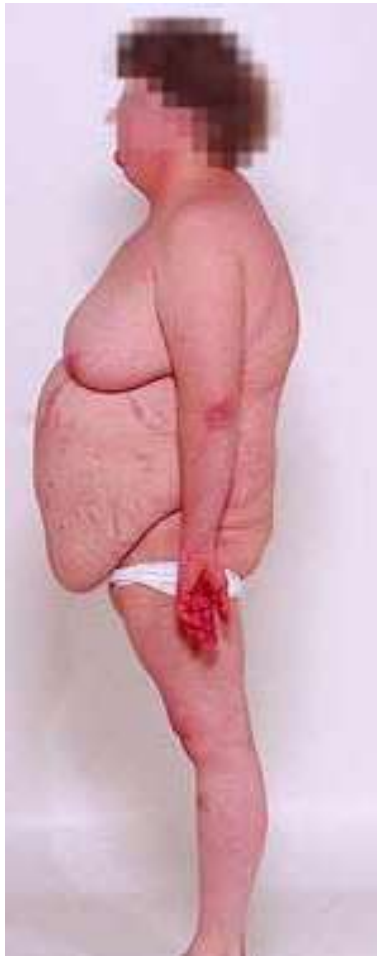
Excess Pituitary Hormone Secretion

Cushing's Disease: Endogenous Causes





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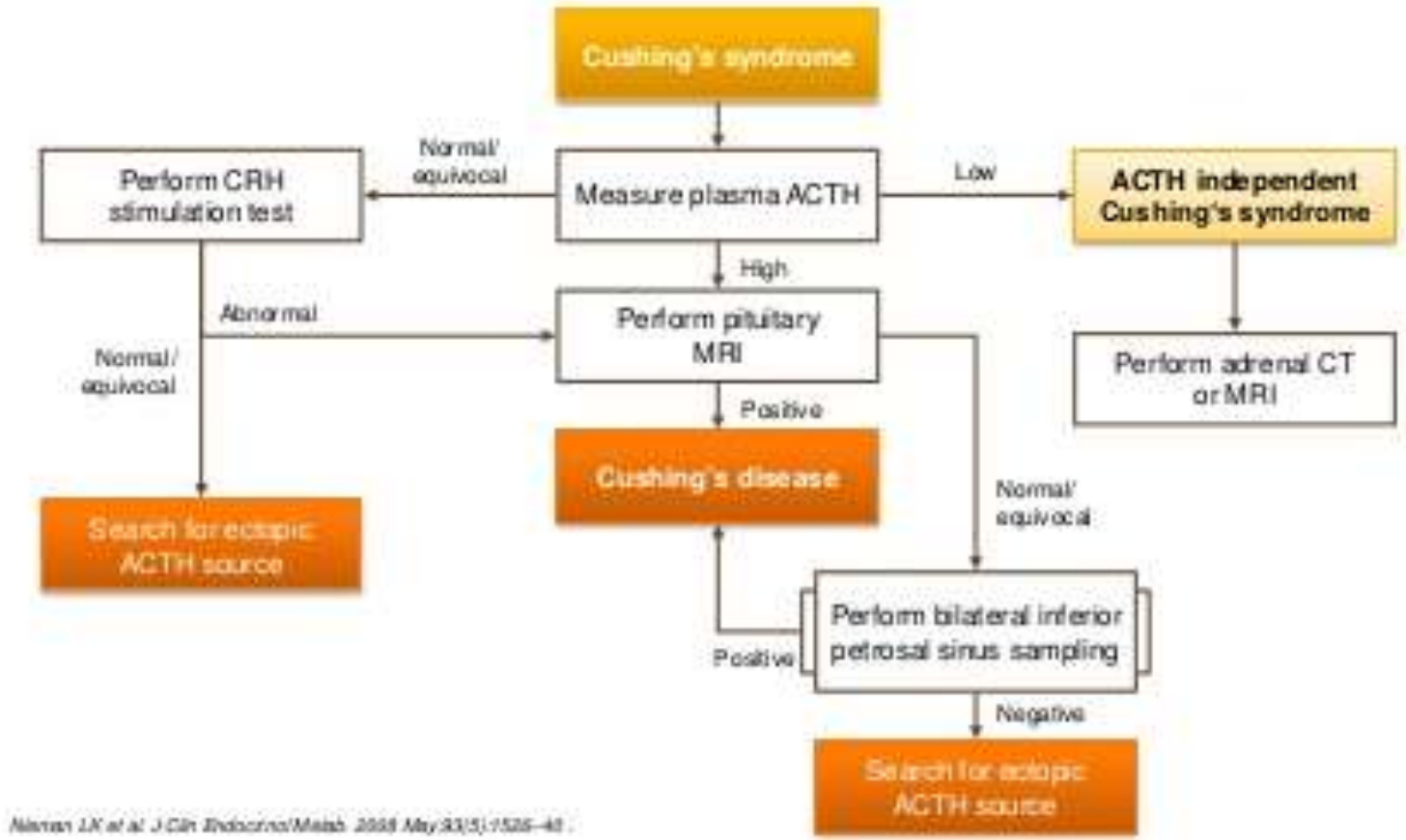
Excess Pituitary Hormone Secretion

Cushing's Disease: Differential Diagnosis



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Excess Pituitary Hormone Secretion

Cushing's Disease: Treatment 1

- Surgical removal of the ACTH-secreting pituitary tumor is the treatment of choice
- Availability of an experienced neurosurgeon is crucial, and the long-term remission rate is about 60 to 80% following surgery
- A low (<3 µg/dL) or undetectable postoperative cortisol level off glucocorticoids is considered to be a good marker for long-term cure

Excess Pituitary Hormone Secretion

Cushing's Disease: Treatment 2

- Other options include reoperation and radiotherapy
- Bilateral adrenalectomy is reserved for those who continue to be hypercortisolemic
- Medical therapy (ketoconazole) has limited value because of the associated toxicity and gradual decrease in efficacy
- During therapy, liver function tests need to be closely monitored.

Excess Pituitary Hormone Secretion

Thyrotropin-Secreting Adenoma 1

- TSH-secreting pituitary adenomas account for <1% of all pituitary tumors at mean age 40 years, with a slight female predominance
- Symptoms secondary to hyperthyroidism and goiter are the initial complaints, if the disease remains undiagnosed
- The most important feature is elevation of serum T_4 and T_3 levels, with an inappropriately normal or elevated TSH level only shortly before surgery.

Excess Pituitary Hormone Secretion

Thyrotropin-Secreting Adenoma 2

- In patients with TSH-secreting adenomas, surgery is the primary therapeutic approach
- Radiation is generally used for those with residual tumor
- Somatostatin analogues are effective for control of excess TSH production leading possibly to a decrease in tumor size
- Beta blockers should be initiated in uncontrolled hyperthyroidism
- Antithyroid medications may be used only shortly before surgery.

Nonfunctional and Glycoprotein-Secreting Pituitary Adenomas 1

- Nonfunctional and glycoprotein-secreting pituitary tumors account for about 25% to 30% of all pituitary adenomas
- Many clinically nonfunctional pituitary adenomas are glycoprotein-producing tumors and usually manifest with clinical features related to mass effect, including visual field defect, hypopituitarism, and headache

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Nonfunctional and Glycoprotein-Secreting Pituitary Adenomas 2

- The standard treatment for patients with mass effect is surgery, mainly through the trans-sphenoidal approach
- Radiotherapy is indicated in patients with residual pituitary tumor following surgical debulking or in those who are not surgical candidates
- The use of high-dose dopamine agonists has been associated with a decrease in tumor size in only about 10% of patients.

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Lymphocytic Hypophysitis 1

- Lymphocytic hypophysitis is a rare autoimmune inflammatory lesion of the pituitary gland, commonly affecting young women during late pregnancy or in the postpartum period
- Lymphocytic hypophysitis is associated with other autoimmune disorders, mainly Hashimoto's thyroiditis and Addison's disease
- The clinical manifestations relate to mass effect or hypopituitarism

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Lymphocytic Hypophysitis 2

- The corticotropin axis is the most commonly affected axis.
- The chronologic association with pregnancy or the postpartum period and isolated ACTH deficiency is a diagnostic clue.
- Trans-sphenoidal surgery is the therapy of choice for patients with pituitary mass effect
- It is important to monitor patients with varying degrees of hypopituitarism, because some have recovery of their pituitary axes.

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Empty Sella 1

- The empty sella is defined as a sella that, regardless of its size, is completely or partly filled with cerebrospinal fluid
- An empty sella of normal size is a common incidental autopsy finding
- An empty sella is called secondary when it is seen after surgery, irradiation, or medical treatment for a pituitary pathology

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Empty Sella 2

- Most patients have no pituitary dysfunction, but partial or complete pituitary insufficiency has been reported
- The discovery of an empty sella needs to be followed by an endocrine evaluation to determine whether there is any associated pituitary dysfunction
- Management usually involves reassurance and hormone replacement, if necessary.

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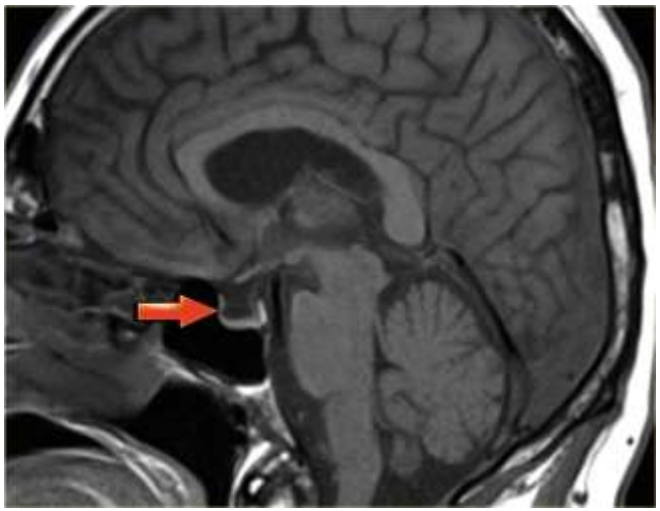
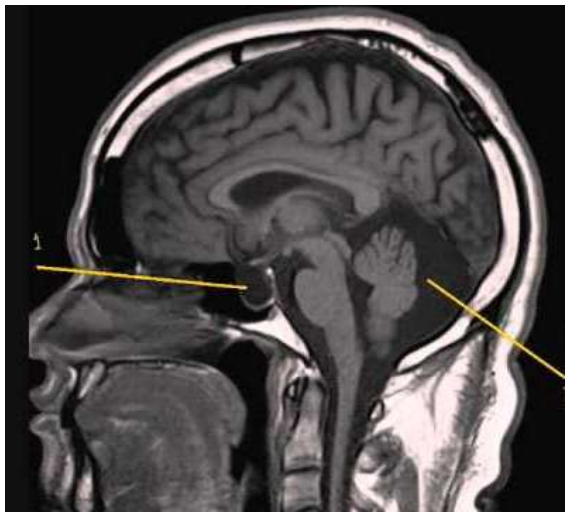
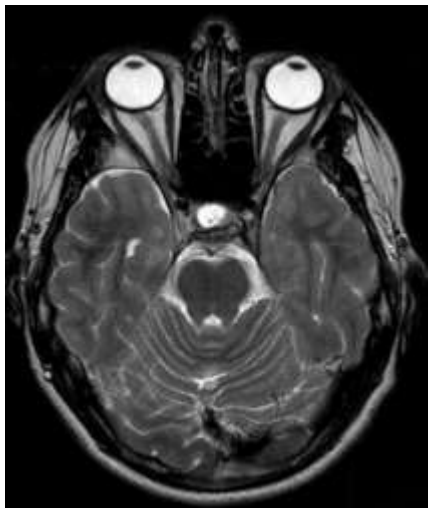
Empty Sella

The empty sella is defined as a sella that, regardless of its size, is completely or partly filled with cerebrospinal fluid

wikimedia.org/wikipedia/commons/2/2e/Empty_Sella_MRT_T2_ax_002.jpg i.ytimg.com/vi/PIHNN3yvzWo/hqdefault.jpg radiologyassistant.nl/data/bin/a509797a621c41_hypertension2.jpg

Pituitary Apoplexy 1

- Pituitary apoplexy is a rare endocrine emergency resulting from hemorrhagic infarction of a preexisting pituitary tumor
- The clinical manifestations are related to rapid expansion of the tumor secondary to hemorrhage, with compression of the pituitary gland and the perisellar structures leading to headache, hypopituitarism, visual field defect, and cranial nerve palsies

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Pituitary Apoplexy 2

- Headache is the most prominent symptom in most patients with clinically evident pituitary apoplexy
- Once pituitary apoplexy is suspected, stress-dose glucocorticoids (e.g., dexamethasone 4 mg every 8 hours IV) should be initiated and pituitary MRI should be performed
- Patients with mass effect benefit from tumor and blood clot debulking, which leads to resolution of visual field defects and improvement of cranial nerve palsies in most patients.

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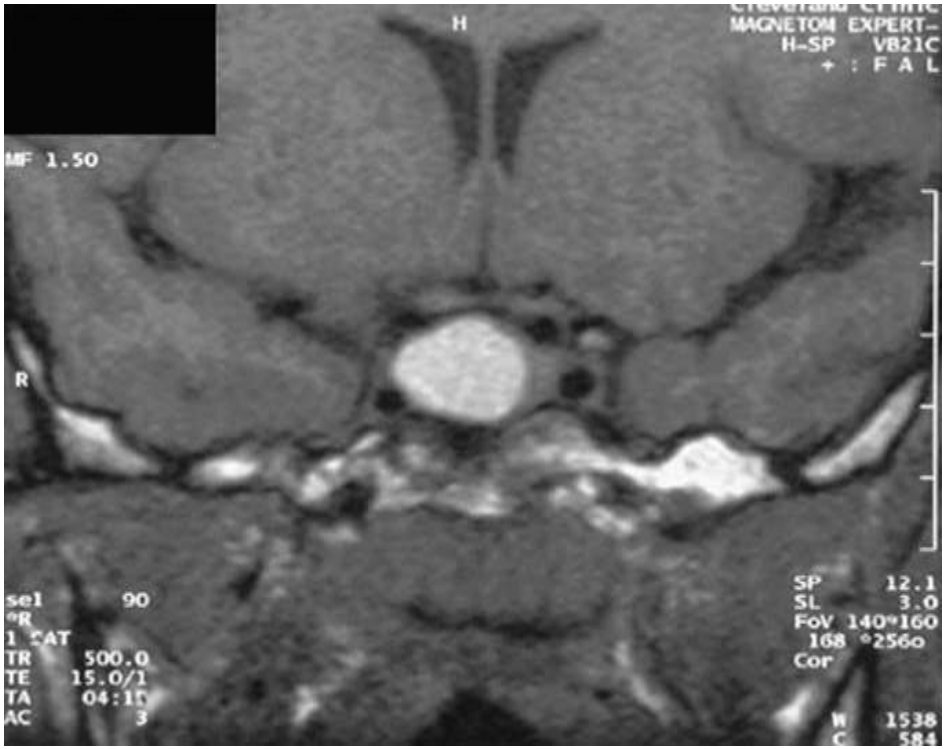
Pituitary Apoplexy



Pituitary apoplexy is a rare endocrine emergency resulting from hemorrhagic infarction of a preexisting pituitary tumor

http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/pituitary-disorders/images/PituitaryDisordersfig8_large.jpg

Diabetes Insipidus

Types and Clinics 1

- Diabetes insipidus (DI) is characterized by the chronic excretion of abnormally large volumes (>50 mL/kg) of dilute urine
- DI is usually underdiagnosed because the symptoms and signs are benign and many patients ignore them or are unaware of them
- There are four major types of DI: central (neurogenic) DI, nephrogenic DI, primary polydipsia, and gestational DI

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Diabetes Insipidus

Types and Clinics 2

- Central DI is secondary to inadequate ADH secretion
- DI results in few symptoms, including polydipsia and polyuria
- Nocturia of a large urine volume is often the primary reason for which patients seek medical attention
- DI is not associated with any abnormality on the physical examination or routine laboratory evaluation, except a low urine osmolality.

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Diabetes Insipidus

Diagnosis 1

- Once DM and hypercalcemia have been excluded, patients should have 24-hour urinary volume measured during ad libitum fluid intake
- DI is diagnosed in those with urinary output >50 mL/kg/day, urinary osmolality <300 mOsm/kg, and creatinine excretion 14-18 mg/kg body weight as an indicator of an accurate 24-hour urine collection

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Diabetes Insipidus

Diagnosis 2

- Measurement of spot urine osmolality is unreliable to exclude or diagnose DI, because it may be decreased significantly in an otherwise healthy person who drinks large amounts of water
- Patients with DI who are conscious usually have sufficient thirst to maintain a normal serum sodium level in spite of polyuria

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Diabetes Insipidus

Diagnosis 3

- Once the diagnosis has been established, the next step is to differentiate the type of DI
- A water deprivation test may need to be performed by an experienced endocrinologist to differentiate among types of partial DI.

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Diabetes Insipidus

Involved Systems and Mechanisms

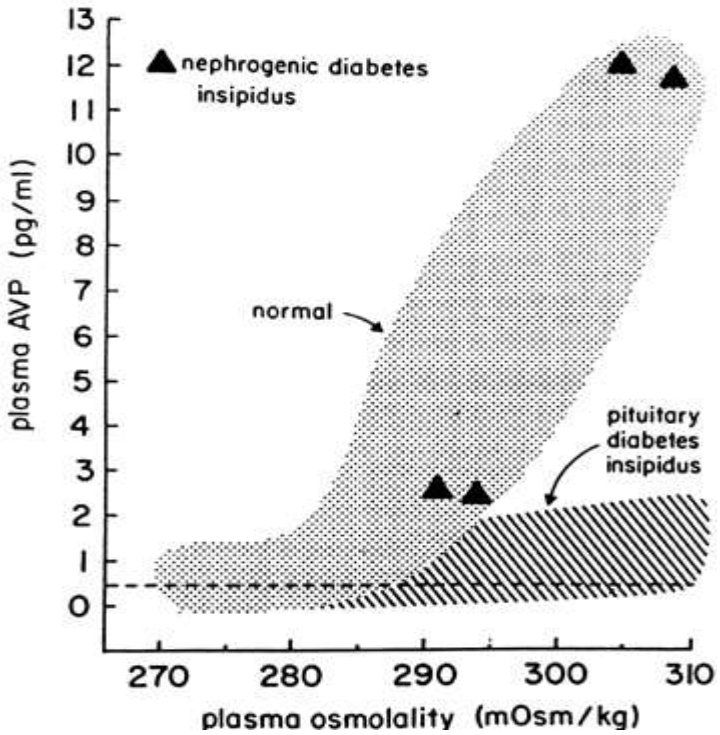
	Urine Osmolality (mOsm/kg)	
Diagnosis	**After fluid deprivation**	**After desmopressin**
Neurogenic DI	<300	>800
Nephrogenic DI	<300	<300
Primary Polydipsia	>800	>800
Partial DI or Polydipsia	300-800	<800

There are four major types of DI: central (neurogenic) DI, nephrogenic DI, primary polydipsia, and gestational DI.

http://www.geekymedics.com/wp-content/uploads/2011/07/Fluid-Deprivation-Test.png

Diabetes Insipidus

Involved Systems and Mechanisms



Correlation of plasma arginine vasopressin (AVP) with plasma osmolality in normal subjects, in patients who have central (pituitary) diabetes insipidus, and in those who have nephrogenic diabetes insipidus.

http://www.geekymedics.com/wp-content/uploads/2011/07/Fluid-Deprivation-Test.png

Diabetes Insipidus

Therapy 1

- The treatment of choice for central diabetes insipidus is intranasal synthetic replacement for vasopressin (desmopressin acetate) at doses of 5 to 20 mcg daily
- Central diabetes insipidus has responded to chlorpropamide with a 25% to 75% reduction in polyuria

http://pedsinreview.aappublications.org/content/21/4/122

Diabetes Insipidus

Therapy 2

- Oral repletion of water often is sufficient to reverse acute dehydration in diabetes insipidus
- There are no effective pharmacologic agents to treat a compulsive water drinker
- A low-osmolar, low-sodium diet should be initiated to manage congenital nephrogenic diabetes insipidus.

http://pedsinreview.aappublications.org/content/21/4/122

Diabetes Insipidus

Therapy 3

- The therapy of choice for central DI is the administration of the ADH analogue desmopressin (DDAVP)
- It is available in a subcutaneous form or as an oral or nasal spray
- The spray or oral form of desmopressin is usually started at bedtime and is gradually titrated for the desired antidiuretic effect.

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US MLE TEST

Correct Answer 5: A cause of euvolemic hyponatremia is SIADH as a result of a paraneoplastic production of ADH from a small cell lung cancer. Plasma osmolality will be low, and urine osmolality will be inappropriately high.
Incorrect Answers:
1 and 2: Congestive heart failure and nephrosis cause hypervolemic hyponatremia, which would result in Urine Na < 10, Fractional Excretion Na < 1%.
3: Prerenal acute kidney injury is a cause of hypovolemic hyponatremia. One would expect Urine Na < 20, Fractional Excretion Na < 1%.
4: Mineralocorticoid deficiency causes hypovolemic hyponatremia. One would expect Urine Na > 20 and Fractional Excretion Na > 1%.

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

US MLE TEST

A 45-year-old female undergoes a transphenoidal approach for a pituitary prolactinoma. Surgery proceeded without complications and the entire mass was removed. The patient's urine output is 4 L on post-operative day 1, and labs are significant for serum Na of 145 mEq/L (normal: 135-145). Urine osmolality is 185 mOsm/kg, and urine specific gravity is 1.004 (normal: 1.012 to 1.030). Which of the following choices is the next best step?

1. Water restriction, 2. Loop diuretic, 3. CT scan of the brain, 4. 0.45% NaCl administered intravenously, 5. Desmopressin

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

US MLE TEST

Correct Answer 5: The patient's history and lab results are consistent with post-surgical central diabetes insipidus. The most reasonable next step is administration of desmopressin or chlorpropamide.
Incorrect Answers:
1: Water restriction can be used to distinguish central DI from primary polydipsia - however, in this situation, the clinical picture points toward central DI.
2: Loop diuretics are not used in the treatment of DI.
3: CT scan of the brain would likely reveal post-operative changes, but not help diagnose DI.
4: Administration of fluids would not be sufficient for treatment of DI.

https://www.medbullets.com/step1-endocrine/9019/pheochromocytoma

Hypopituitarism

Etiology 1

- Pituitary adenomas are the most common cause of hypopituitarism, but other causes include parasellar diseases, pituitary surgery, radiation therapy, inflammatory and granulomatous diseases, and head injury
- The sequential loss of pituitary hormones secondary to a mass effect is in the following order: GH, LH, FSH, TSH, ACTH, and prolactin

clevelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/pituitary-disorders/

Prognosis and Prophylaxis

- Many causes of hypothalamic dysfunction are treatable
- Most of the time missing hormones can be replaced.

http://www.nytimes.com/health/guides/disease/hypothalamic-dysfunction/overview.html

Abbreviations

ACTH - adrenocorticotropic hormone

CD - Cushing's disease

CST - cosyntropin stimulation test

FSH - follicle-stimulating hormone

GH - growth hormone

LH - luteinizing hormone

MRI - magnetic resonance imaging

MSH - melanocyte–stimulating hormones

AVP - plasma arginine vasopressin

RH - releasing hormone

TSH – thyroid stimulating hormone (TSH)

PEG - polyethylene glycol

PRL - prolactin

Diagnostic and Treatment Guidelines

- Hypothalamic and anterior pituitary disorders
- Hypothalamic-pituitary dysfunction
- Hypothyroidism
- Hyperthyroidism
- AANS - The pituitary gland and pituitary tumors
- Endocrine testing protocols: hypothalamic pituitary adrenal axis
- And management
- Medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients
- Glucocorticoid Replacement in Pituitary Surgery: Guidelines for Perioperative Assessment