433 Teams

MEDICINE

9| Pituitary Disorders

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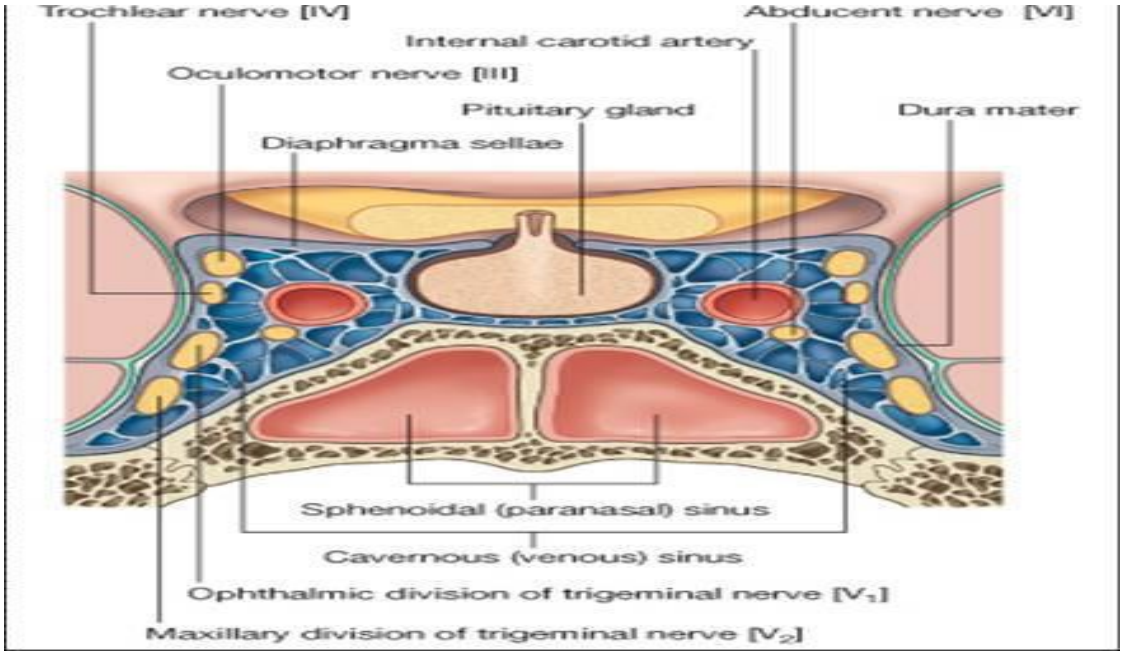
Slides - Step-Up medicine - Kaplan Notes - Extra explanation - Doctor Notes

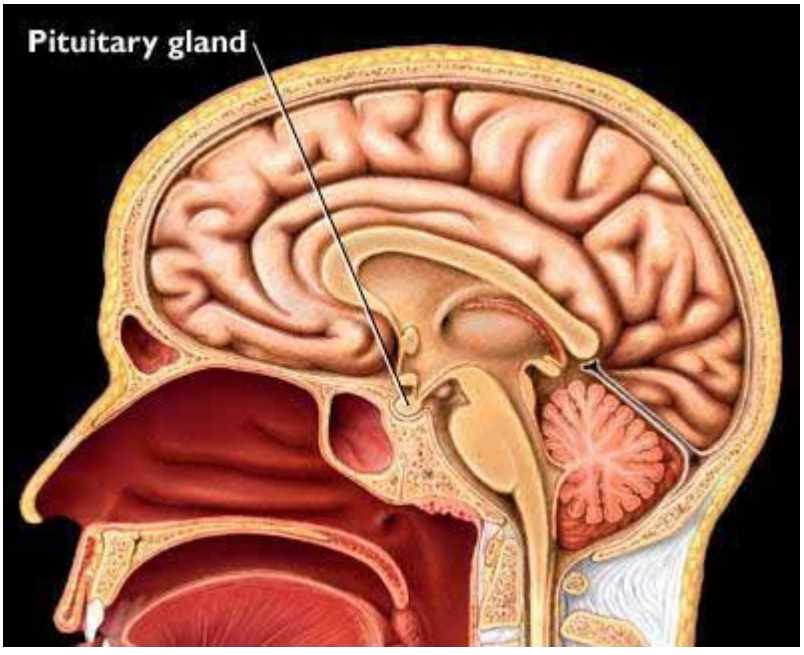
Objectives

The anatomy and physiology related to the pituitary gland
Hypofunction of the anterior pituitary: ACTH, LH and FSH, TSH, GH deficiency
Hyper function of the anterior pituitary: ACTH, LH and FSH, TSH and GH over secretion
Clinical diagnosis of each disorder
Management of each disorder
Posterior pituitary dysfunction: Diabetes insipidus

Anatomy of pituitary gland

Anterior	Posterior	Superior	Inferior	Lateral
Optic chiasm	**Mammillary bodies**	**Diaphragm sellae**	**Sphenoidal air sinus**	**Cavernous sinus**



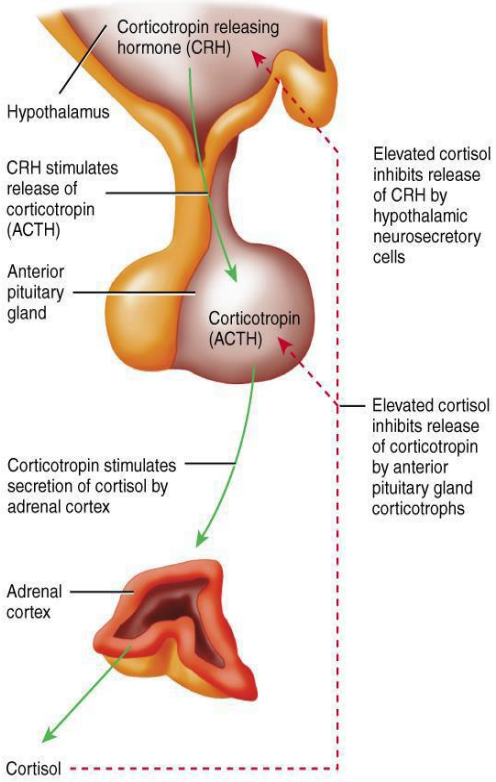


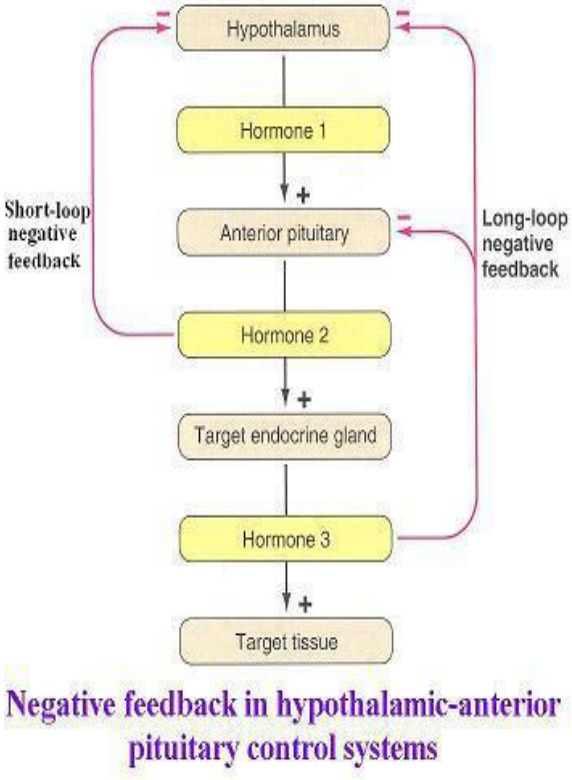
Physiology of anterior pituitary gland

TSH	**Released by TRH (thyroid releasing hormone) from hypothalamus.**
ACTH	**Released by CRH (corticotropin releasing hormone)from hypothalamus, increased by stress**
GH	**Released by GHRH (growth hormone releasing hormone) from hypothalamus, increased by sleep, stress, exercise and hypoglycemia**
LH & FSH	**Released by GNRH (gonadotropic releasing hormone) from hypothalamus**
Prolactin	**it is secreted in to mating, estrogen treatment, ovulation, and nursing. Increased in pregnancy.**

Negative feedback:

All hypothalamic releasing hormones are stimulatory except two: Dopamine which inhibits prolactin and Somatostatin which inhibits GH





#The Dominant Negative Feedback:

After a stimulus causes release of the hormone, conditions or products resulting from its action tend to suppress its further release to prevent over secretion of the hormone.

This is controlled by the degree of activity of the target tissue.

Pituitary Adenoma:

General Characteristics:

- Pituitary adenomas account for 10% of all intracranial neoplasms.
- Almost all pituitary tumors are benign; they may grow in any direction causing Parasellar signs and symptoms.
- Size: microadenoma (diameter < 10mm); macroadenoma (diameter>11).

 # the problems caused by :

1- local effects of a tumor.
2-excess hormone secretion.
3-the result of inadequate production of hormone by the remaining normal pituitary.

Clinical features:

1) Hormonal effects occur due to hyper secretion of one or more of the following hormones:
   a) Prolactin.
   b) GH- Results in Acromegaly or Gigantism if epiphyseal closure hasn't occurred.
   c) ACTH results in Cushing disease.
   d) TSH results in Hyperthyroidism.
2) Hypopituitarism – compression of hypothalamic pituitary stalk, resulting in GH deficiency and hypogonadotropics hypogonadism are the most common problems
3) Mass effect
   a) Headache
   b) Visual defects (bitemporal hemianopsia) due to the compression of optic chiasm and it's the most common finding but it depend upon the size and symmetry of the tumor

Diagnosis:

1. MRI is the imaging study of choice
2. Pituitary hormone levels
3. visual fields

Treatment:

1) Transsphenoidal surgery is indicated in most of patients (*except* patient with prolactinoma which medical treatment can be tried first).

2) Radiation therapy and medical therapy are adjuncts in most patients

Hyperprolactinemia

Causes:

1) Prolactinoma: (is a benign tumor (adenoma) of the pituitary gland that produces ahormone called prolactin).
   a) Most common cause of hyperprolactinemia
   b) Most common type of pituitary adenoma
2) Medications (antipsychotics, H2 blockers,verapamil)
3) Pregnancy
4) Renal failure
5) primary hypothyroidism(TRH is a factor that increases releasing of prolactine)

Clinical features:

1) Men
   a) Hypogonadism, decreased libido and infertility (inhibits gonadal activity in general in both men and women)
   b) Glactorrhea and gynecomastia (uncommon)
   c) Parasellar signs and symptoms (visual defects and headaches)
2) Women
   a) Premenopausal: Menstrual irregularities, oligomenorrhea, amenorrhea, anovulation and infertility
   b) Decreased libido, dyspareunia, vaginal dryness and risk of osteoporosis
   c) Glactorrhea
   d) Postmenopausal: parasellar signs and symptoms

Diagnosis:

After prolactin level is found high, perform:

- Thyroid function test (to exclude primary hypothyroidism)
- Pregnancy test
- BUN/Creatinine (kidney disease elevates prolactin)
- Liver function test (cirrhosis elevates prolactin)
- MRI is done after:
  1) High prolactin level is confirmed
  2) Secondary causes like medications are excluded and patient is not pregnant.

Treatment:

- Dopamine agonists: Cabergoline is the first drug of choice, better than bromocriptine due it's side effects.

Note: They suppress the release of prolactin and kill the benign tumor cells as well. May be given for life.

- Transsphenoidal surgery is appropriate for those not responding well to medications
- Radiation is rarely needed

Acromegaly

General characteristics:

- It's broadening of the skeleton, which results from excess secretion of pituitary GH after epiphyseal closure (if happened before the epiphyseal closure it's Gigantism)
- It's almost all cases because GH-secreting pituitary adenoma.

it is usually big, compressing the optic chiasma, causing bitemporal hemianopia and invading the other intact parts of pituitary causing low TSH, FSH, LH and prolactin , and causing headache as well

Clinical features:

1) Growth promotion:
   a) Soft tissue and skeleton overgrowth (carpal tunnel syndrome)
   b) Coarsening of facial features
   c) Abnormally large hand, foot and head (ask about increasing glove/ring/shoe size)
   d) Organomegaly
   e) Arthralgia due to joint tissue overgrowth
   f) Hypertrophic cardiomyopathy
   g) Enlarged jaw (macroganthia)
2) Metabolic disturbance:
   a) Glucose intolerance and DM
   b) Body odor from Hyperhidrosis
3) Parasellar manifestations (headache, bitemporal hemianopsia)
4) HTN
5) Sleep apnea
6) Erectile dysfunction

Diagnosis:

- The best initial test is level of insulin-like growth factor (IGF-1).
- The most accurate is the glucose suppression test; normally glucose should suppress growth hormone.
- MRI should be done only after the lab identification of acromegaly.

why glucose suppression test !
physiological GH secretion is inhibited by hyperglycaemia. In acromegaly, or gigantism, GH secretion is autonomous and does not suppress and may paradoxically rise with hyperglycaemia.

Treatment:

1) Surgery: Acromegaly responds to transsphenoidal resection of the pituitary in 70% of cases. Larger adenomas are hard to cure(the first line therapy).
2) Medications:
   a) Octreotide or lanreotide: "somatostatin receptors agonists" inhibits GH release
   b) Pegvisomant: A GH receptor antagonist, it inhibits IGF release from the liver
3) Radiotherapy: is used only when they don't respond to surgery or medications.

Treatment of acromegaly is always surgical, because the tumor is big, if they are unable to remove the tumor totally, add somatostatin or pegvisomant.

Hypopituitarism

General characteristics:

- All or some hormones released from the anterior pituitary may be absent and can be selective or multiple.
- Loss of hormones is un-predictable, but the first hormones that are lost are GH, LH and FSH. And latest one to be lost is ACTH.
- Clinical manifestation depends on the hormones which is lost.

Hyperprolactinaemia, rather than prolactin deficiency, occurs relatively early because of loss of tonic inhibitory control by dopamine.

Causes:

1) Hypothalamic or pituitary tumor is the most common cause (pituitary apoplexy)
2) Other causes:
   a) Radiation therapy.
   b) vascular e.g. pituitary apoplexy and Sheehan syndrome.
   c) Infiltrative processes (sarcoidosis, hemochromatosis) also TB
   d) Head trauma.
   e) Recent surgery to brain or head
   f) Craniopharyngioma (occur in children)

in the next slide there are explanations for some causes

Clinical features:

1) Reduced GH: growth failure, increased LDL and increased risk of heart disease
2) Reduced prolactin: inability to lactate
3) Reduced ACTH: adrenal insufficiency
4) Reduced TSH: hypothyroidism
5) Reduced LH & FSH: infertility, amenorrhea, loss of secondary sex characteristics and decreased libido
6) Reduced ADH: diabetes insipidus
7) Reduced melanocytes-stimulating hormone: decreased skin and hair pigmentation.

In general, symptoms of deficiency of a pituitary stimulating hormone are the same as primary deficiency of the peripheral endocrine gland (e.g. TSH deficiency and primary hypothyroidism cause similar symptoms due to lack of thyroid hormone secretion).

Diagnosis:

- Low levels of the targeted hormone or normal levels of trophic hormones (it's the suppression of the trophic hormone that is important, although the absolute level may be in the normal reference range).
- MRI of the brain (may miss micro adenomas).

Treatment:

- Replacement of appropriate hormones.
- Women who want to conceive "be pregnant" should be referred to an endocrinologist.

Treatment is always by the end-product hormone (e.g. give thyroxine not TSH) **except in married male and female give LH and FSH (because fertility depends on them).**

explanations for some of the causes

Pituitary apoplexy:

To identify it, usually patient comes with history of prior adenoma wasn't treated well or followed well, and it will expand and all sudden in the center of it, it will become necrotic with bleeding area) you may see the bleeding if you did CT or MRI,

Patient presents with headache, altered mental status and neck stiffness (exclude meningitis while doing differential diagnosis)

Sheehan syndrome:

Usually its post-partum necrosis to the gland after pregnancy by weeks or months. (Can be years but rarely)

Patient's main complaint is inability to lactate.

Craniopharyngioma:

Tumor of suprasellar region from embryologicremnantofRathke's pouch. They results in visual defects, headache, papilledema and changes in mentation. They may cause Hyperprolactinemia, Diabetes insipidus and panhypopituitarism.

They are diagnosed by MRI.

Treatment is surgical excision whether it's total or partial, with or without radiation.

Diabetes insipidus:

General characteristics:

1) Two forms:
   a) Central DI is the most common form –due to low ADH secretion by posterior pituitary
   b) Nephrogenic DI –ADH secretion is normal but tubules cannot respond to it (unresponsiveness)

Causes:

a) Central DI:
   1) Idiopathic: 50% of all cases
   2) Trauma –surgery , head trauma (hypothalamic-pituitary surgery is the most common cause)
   3) Other destructive process involving the hypothalamus, including tumors, sarcoidosis,TB and syphilis etc…

b) Nephrogenic DI:
   1) the most common cause in adults is chronic Lithium use and others like demeclocycline use
   2) Hypercalcemia
   3) 3) Sickle cell anemia

Clinical features:

1) Polyuria is a hallmark finding 10 to 15 L daily is lost and urine is colorless (because it is so dilute)
2) Thirst and polydipsia –hydration is maintained if the patient conscious and has access to water
3) Hypernatremia is usually mild
4) IF patient has polyuria and polydipsia but with normal water deprivation test think about psychogenic polydipsia

Diagnosis:

1) Urine osmolality and urine sodium are decreased "because ADH is related only to water absorption not Na"
2) Serum osmolality is high.
3) Water deprivation test is required to make diagnosis.
4) We give the patient ADH to know which type he has.

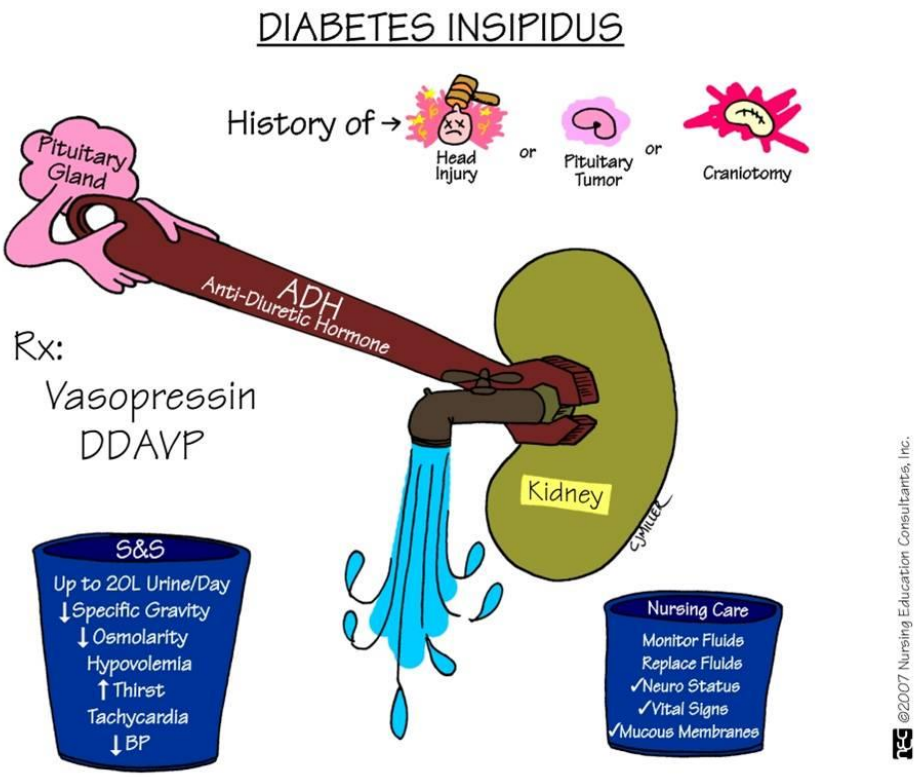
Treatment:

Central DI:

- Is treated with long term vasopressin (desmopressin) use. (intranasal)

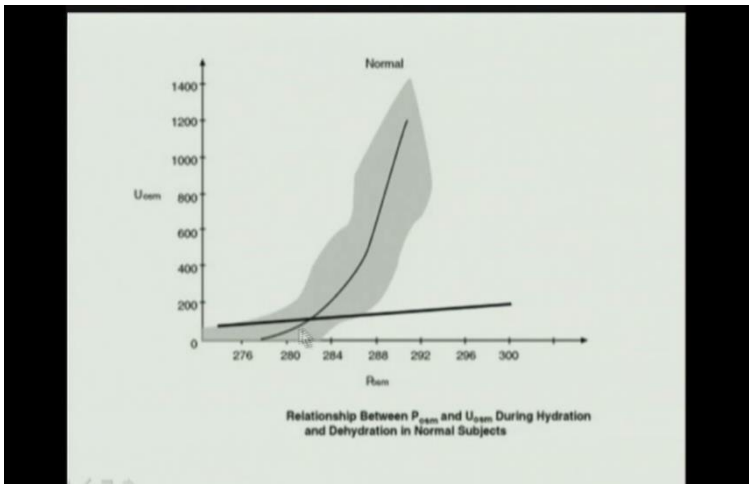
Nephrogenic DI:

- Is treated by correcting the underlying cause
- Mild Diuretic such as hydrochlorothiazide and amiloride
- NSAIDs such as indomethacin



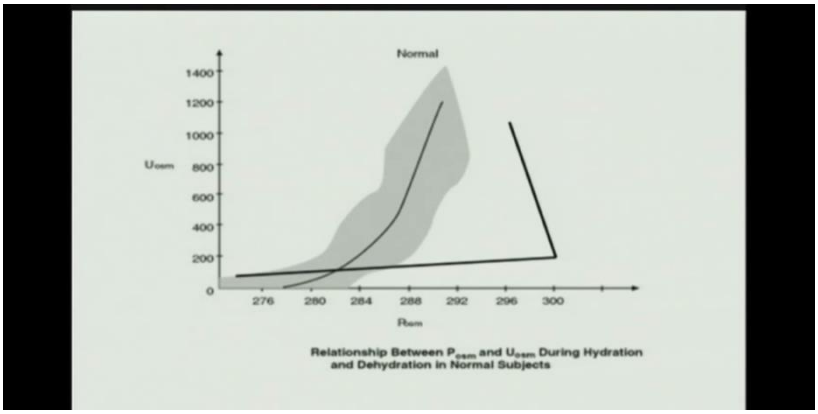
Water deprivation test:

We measure urine osmolality and plasma after deprivation, we will find that plasma osmolality is high and urine osmolality is low, so this patient has DI!



But to know which type of DI does this patient has, we give him ADH!

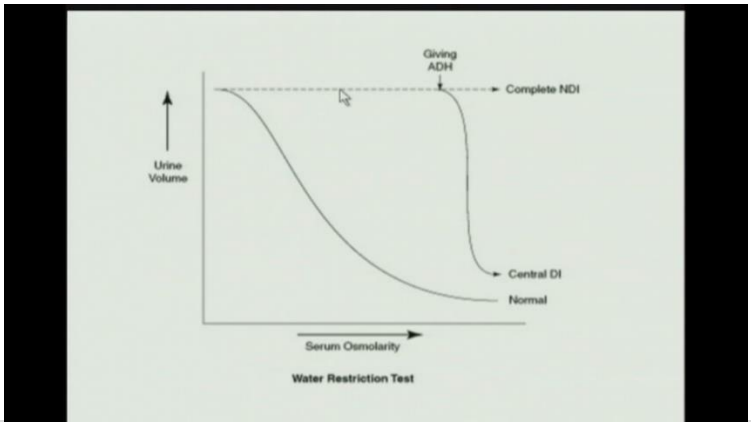
a) If there is an increase in urine concentration so it's Central DI



b) If there is no increase, then it's Nephrogenic DI.

Explanation about giving the patient ADH:

- If we give ADH and urine volume decreased then it's Central, if not it's Nephrogenic.



Syndrome of inappropriate secretion of antidiuretic hormone (SIADH):

General characteristics:

1) Excess secretion of ADH from posterior pituitary or an ectopic source.
2) Elevated levels lead to water retention and excretion of concentrated urine
3) Two major effects: hyponatremia and volume expansion
4) Despite volume expansion, edema is not seen.This is because natriuresis (excretion of excessive amount of sodium) occurs despite hyponatremia

Causes:

1) Neoplasms (lung, pancreas, prostate, bladder) lymphomas, leukemia
2) Pulmonary:
   a) TB, pneumonia
   b) Lung abscess and COPD
3) CNS:
   a) Head injury
   b) Stroke
4) Drugs:
   a) Vincristine
   b) SSRIs (sertoline)

Clinical features:

1) Acute hyponatremia signs and symptoms are secondary to brain swelling (osmotic water shifts, leading to increased ICF volume) and are primarily neurologic.
   a) Lethargy, somnolence and weakness
   b) Can lead to seizures, coma and death

2) Chronic hyponatremia
   a) May be asymptomatic
   b) Anorexia, nausea and vomiting
   c) CNS symptoms are less common because chronic loss of sodium and potassium from brain cell well decrease brain edema

Diagnosis:

SIADHis a disease of *exclusion* (after other causes of hyponatremia have been ruled out) the following help in supporting diagnosis:

a) Hyponatremia and inappropriately concentrated urine
b) Low serum uric acid
c) Low BUN
d) Normal thyroid and adrenal function

Treatment:

1) Correct the underlying cause if known
2) For asymptomatic patients:
   a) Water restriction is usually sufficient
   b) Use normal saline in combination with loop diuretics if faster result desired
   c) Lithium carbonate and demeclocycline

3) For symptomatic patients:
   a) Restrict water intake
   b) Give isotonic saline, but hypertonic saline in severe seizures

SUMMARY

- Most common cause of death in an acromegaly patient is cardiovascular disease (CHF)
- If a patient came to you and said they had acne and are now having similar symptoms of Diabetes insipidus think of using demeclocycline that cause nephrogenic DI
- Verapamil is the only calcium channel blocker that raises prolactin level
- Do not do an MRI of the head first in any endocrine disorders
- Always exclude pregnancy first in any women with high prolactin

MCQs

Note: at the end there is an explanation for each question

Q1) A 24-year-old white man presents with a persistent headache for the past few months. The headachehas been gradually worsening and is unresponsive to over-the-counter medicines. He notices diminishedperipheral vision while driving. He takes no medications. He denies illicit drug use but has smoked onepack of cigarettes per day since the age of 18. Past history is significant for passage of a kidney stone lastyear. At that time, he was told to increase his fluid intake.Family history is positive for diabetes in his mother. His brother (age 20) has had kidney stones fromtoo much calcium and a "low-sugar problem." His father died of some type of tumor at age 40. Physicalexamination reveals a deficit in temporal fields of vision and a few subcutaneous lipomas. Laboratoryresults are as follows:

Calcium: 11.8 mg/dL (normal 8.5-10.5) Cr: 1.1 mg/dL

BUN: 17 mg/dLGlucose: 70 mg/dL Prolactin: 220 µg/L (normal 0-20)

Intact Parathyroidhormone: 90 pg/mL (normal 8-51)

You suspect a pituitary tumor and order an MRI which reveals a 0.7-cm pituitary mass. Based on thispatient's presentation, which of the following is the most probable diagnosis?

a. Tension headache

b. Multiple endocrine neoplasia type 1 (MEN1)

c. Primary hyperparathyroidism

d. Multiple endocrine neoplasia type 2A (MEN2A)

e. Prolactinoma

Q2) A 23-year-old man complains of persistent headache. He has noticed gradual increase in his ringsize and his shoe size over the years. On physical examination, he has a peculiar deep, hollow-soundingvoice and a prognathic jaw. Bedside visual field testing suggests bitemporalhemianopsia. What initialstudies are indicated?

a. Serum insulin-like growth factor 1(IGF-1) and prolactin levels

b. Morning growth hormone levels

c. Overnight dexamethasone-suppressed cortisol level

d. Lateral skull film to assess sellaturcica size

e. GHRH-stimulated growth hormone level

Q3) The 40-year-old woman shown below complains of weakness, amenorrhea, and easy bruisability.

She has hypertension and diabetes mellitus. She denies use of any medications other thanhydrochlorothiazide and metformin. What is the most likely explanation for her clinical findings?

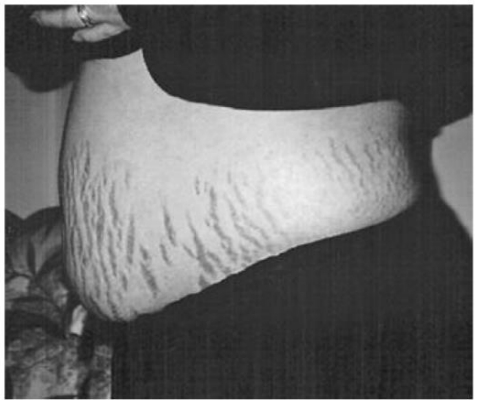
a. Pituitary tumor

b. Adrenal tumor

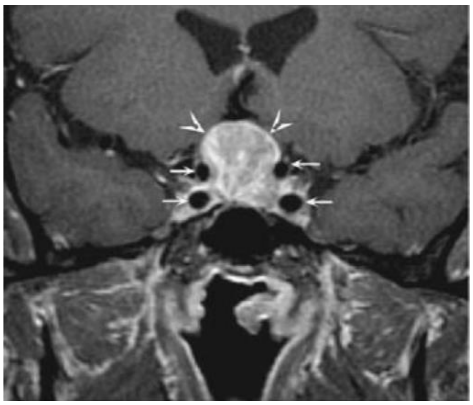
c. Ectopic ACTH production

d. Hypothalamic tumor

e. Partner abuse (domestic violence)



Q4) A 36-year-old woman presents with amenorrhea. She has two children aged 8 and 6 years. She took oral contraceptives until her husband had a vasectomy 18 months ago. Since then she has not had a menstrual period. Otherwise she feels well. She takes no medications and exercises regularly but not to excess. She denies headache or galactorrhea. Her physical examination is normal. In particular, visual fields to confrontation are normal. Initial laboratory testing reveals negative pregnancy testing and normal CBC, creatinine, and TSH. Her prolactin level is 225 ng/mL (normal < 20). MRI of the pituitary is shown. What is the best treatment for this patient's condition?



a. Transsphenoidalhypophysectomy

b. Resume oral contraceptives to reestablish menstrual cycles

c. Somatostatin analogue

d. Dopamine agonist such as cabergoline

e. Observation with yearly prolactin levels and MRI scanning

Answ
1-B

2-A

3-A

4-D

Answers

Q1) The answer is **b**. (Fauci, pp 2357-2361.) This young man presents with two obvious serumabnormalities—hypercalcemia and hyperprolactinemia (most likely secondary to the pituitary tumor).This, along with his positive family history of a younger sibling with high calcium and low blood sugarand a father who died from an unknown tumor, indicates this family has one of the multiple endocrineneoplasia syndromes. MEN1 is associated with hyperparathyroidism, pituitary tumors (usuallyprolactinomas), and islet cell tumors (most commonly gastrinomas, occasionally insulinomas). Thispatient's personal and family history, therefore, suggests MEN1. The MEN2 syndromes include medullary carcinoma of the thyroid and pheochromocytoma. MEN2A is associated with hyperparathyroidism;MEN2B with mucosal and GI tract neuromas. There is no pituitary abnormality with the MEN2syndromes. It would not be prudent to treat the patient's issues as two separate abnormalities (primary

hyperparathyroidism and prolactinoma). Tension headache is untenable in the face of a pituitary tumorand visual field deficit.

Q2) The answer is **a**. (Fauci, pp 2203, 2210.) The patient has excessive growth of soft tissue that hasresulted in coarsening of facial features, prognathism, and frontal bossing—all characteristic ofacromegaly. This growth hormone–secreting pituitary tumor will result in bitemporalhemianopsia whenthe tumor impinges on the optic chiasm, which lies just above the sellaturcica. Growth hormone–secreting tumors are the second commonest functioning pituitary tumors (second to prolactinomas). SerumIGF-1 (insulin-like growth factor-1) level will be elevated and is usually the first diagnostic test. Since40% of GH-producing tumors also produce prolactin, a prolactin level should be obtained as well.Growth hormone secretion is pulsatile and a single GH level is often equivocal; the GH level must besuppressed (usually with glucose) to diagnose autonomous overproduction.Dexamethasone suppression is used in the evaluation of Cushing syndrome, with partial suppressibilitysuggesting a pituitary cause, but this patient's presentation strongly suggests acromegaly, not Cushingsyndrome. Once GH overproduction is documented, an MRI scan of the pituitary will show the size andextent of the tumor (most are macroadenomas> 1 cm). The lateral skull film is insufficiently sensitive forthis purpose. Growth hormone stimulation tests (insulin-induced hypoglycemia, arginine plus GHRH) maybe used to diagnose growth hormone deficiency, but would not be useful to diagnose GH overproduction,where a suppression test should be used

Q3) The answer is **a**. (Fauci, pp 2255-2256.) The clinical findings all suggest an excess production ofcortisol by the adrenal gland. Hypertension, truncal obesity, and dark abdominal striae are common physical findings; patients often have ecchymoses at points of trauma (especially legs and forearms) because of increased capillary fragility. The process responsible for hypercortisolism is most often anACTH-producing pituitary microadenoma. An adrenal adenoma that directly produces cortisol is the next most likely option. Most ectopic ACTH-producing neoplasms (usually small cell carcinoma of

the lung)progress too rapidly for the full Cushing syndrome to develop. These patients usually present with muscleweakness due to profound hypokalemia. The initial test to diagnose endogenous cortisol overproduction is either the overnight dexamethasone suppression test (in normals, the AM cortisol should suppress to < 2 µg/dL after a midnight dose of 1 mg dexamethasone) or 24-hour urine collection for free cortisol. Moreextensive testing is then required to determine the source. Hypothalamic tumors can affect ADHproduction and eating behavior but do not produce cortisol or ACTH. Unexpected bruising should promptquestions about domestic violence, but partner abuse would not account for the constellation of thispatient's findings.

Q4) The answer is d. (Fauci, pp 2205-2207.) This woman's amenorrhea is due to her elevated prolactinlevel. Although certain medications (especially dopamine blockers), hypothyroidism, renal failure, andPregnancy can cause hyperprolactinemia, there is no evidence of these conditions in this patient's case.Nonpituitary causes rarely elevate the prolactin level above 150. In addition, the MRI shows amacroadenoma (tumor > 1 cm). Prolactin-producing pituitary tumors, even macroadenomas, remain undercontrol of dopamine, which is the physiological prolactin inhibitory factor. In most patients, withdopamine agonist therapy, the prolactin level will normalize, menses will return, and tumor shrinkagewill occur. While previously bromocriptine was used, now the longer-acting cabergoline is usuallyprescribed.Pituitary surgery can usually be avoided, even if visual symptoms are present, with the use of dopamineagonist therapy. Transsphenoidalhypophysectomy is therefore not the best choice. Although someminimally symptomatic patients with microadenomas are treated with hormone replacement therapy,macroadenomas should be shrunken with dopamine agonist therapy. Somatostatin analogues are used totreat certain growth hormone producing tumors, but are not first-line treatment for prolactinomas.Watchful waiting would expose this woman to the risk of osteoporosis from estrogen deficiency as wellas tumor growth with possible visual compromise, and would not be the best choice for this young woman.

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