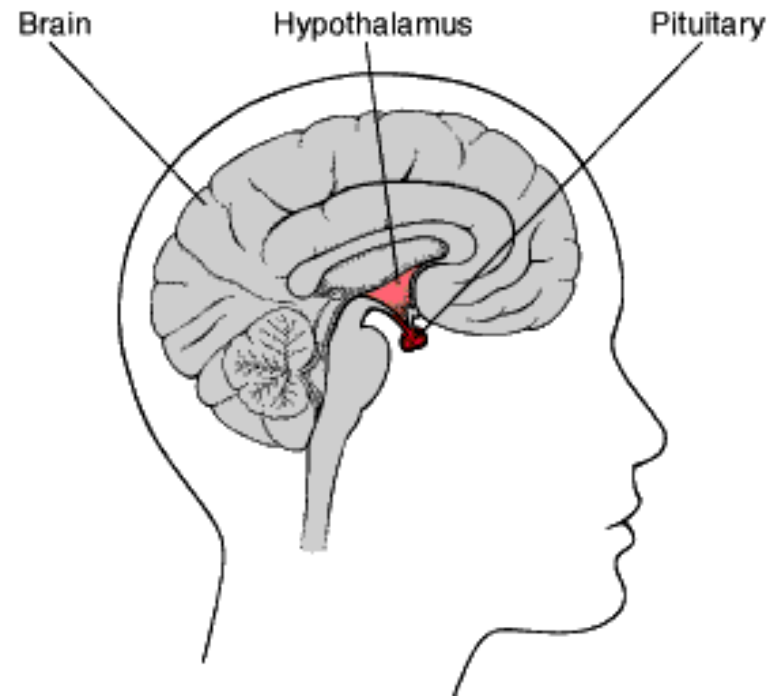


ENDOCRINE PROBLEMS

DISORDERS OF THE ANTERIOR PITUITARY

- ✗ Growth hormone (GH)
 - + Promotes protein synthesis
 - + Mobilizes glucose & free fatty acids
 - + Overproduction almost always caused by benign tumor (adenoma)



GIGANTISM

- ✘ In children excessive secretion of GH
- ✘ Occurs prior to closure of the epiphyses & long bones still capable of longitudinal growth
- ✘ Usually proportional
- ✘ May grow as tall as 8 ft & weigh >300 lb



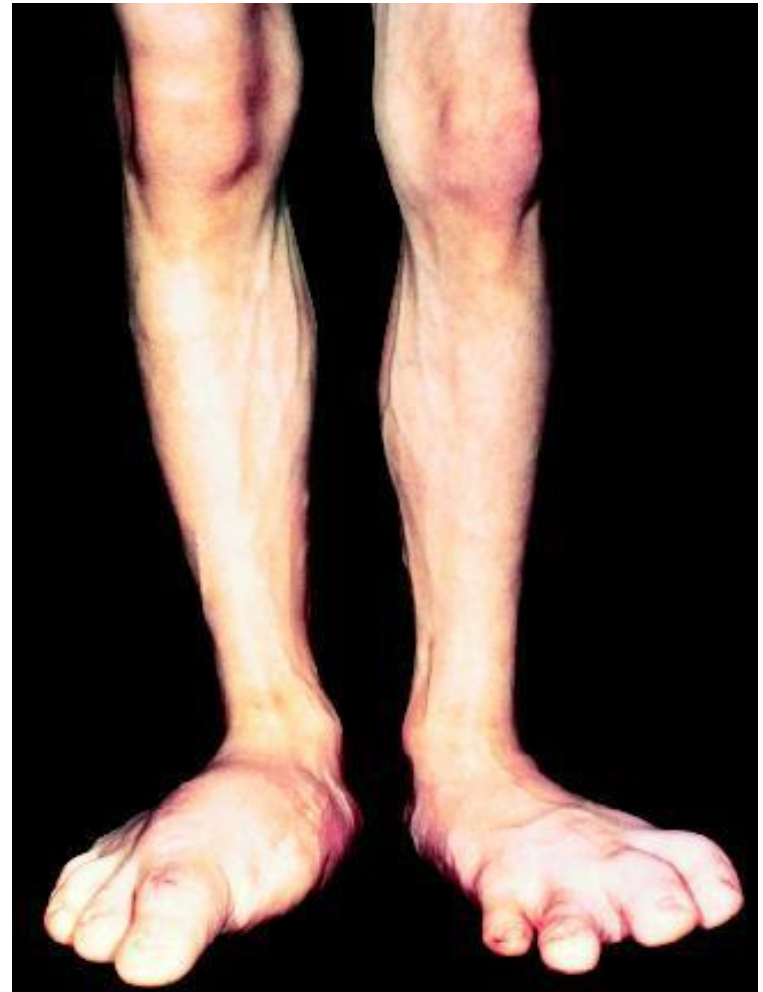
ACROMEGALY



- × In adults excessive secretion of GH stimulates IGF-1 (Liver). **NO negative feedback with tumor.**
- × Overgrowth of bones & soft tissues
- × Bones are unable to grow longer—instead grow thicker & wider
- × Rare—3 out of every million
- × M=F

CONTINUED CLINICAL MANIFESTATIONS

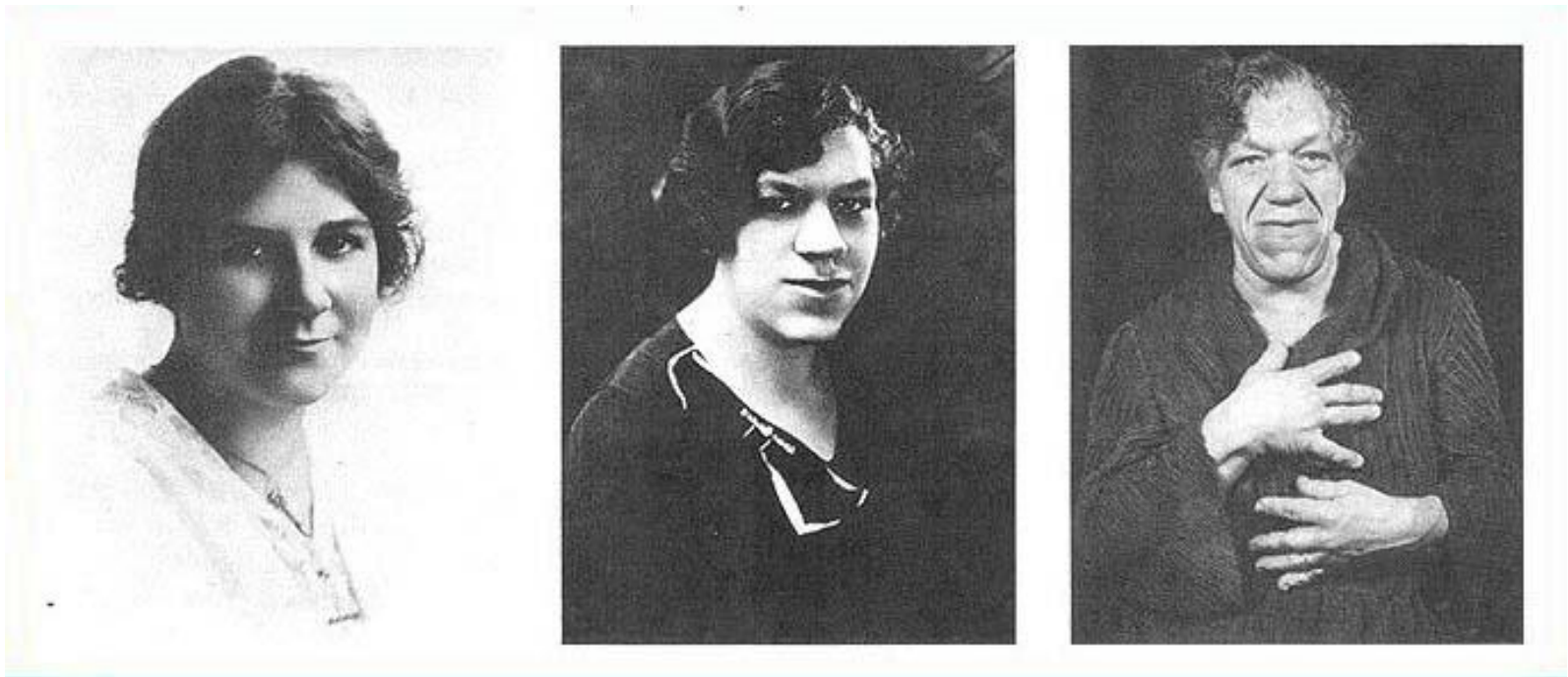
- ✘ Visual disturbances & HA from pressure of tumor
- ✘ Hyperglycemia
- ✘ Predisposes to atherosclerosis
- ✘ Untreated causes angina, HTN, It ventricular hypertrophy, cardiomegaly



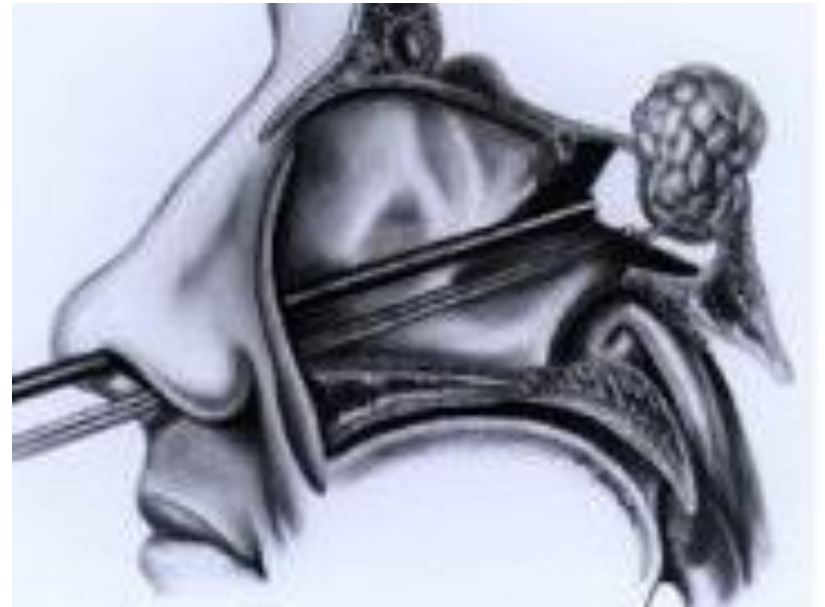
PROGRESSION OF ACROMEGALY

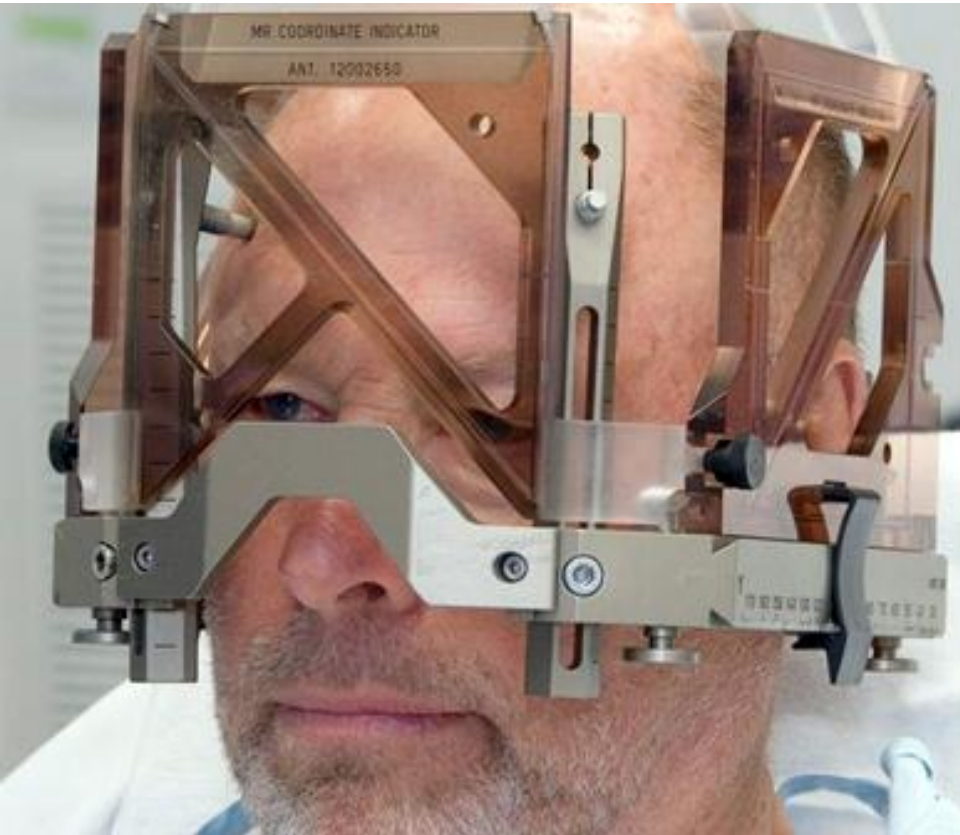


PROGRESSION OF ACROMEGALY



- ✘ Removal of tumor transsphenoidal approach
- ✘ Hypophysectomy—removal of entire gland with lifetime hormone replacement





- ✘ Head frame for stereotactic radiosurgery

TREATMENTS

- × Drug therapy
 - + Somatostatin analogs
 - × Octreotide (Sandostatin)—given SQ 2-3 x weekly
 - + Dopamine agonist
 - × Cabergoline (Dostinex)—tried first due to low cost, but not as effective
 - + GH receptor antagonists
 - × Pegvisomant (Somavert)—not for primary tx—does not act on tumor

TREATMENTS

- ✘ Somatropin (Omnitrope)—GH for long-term replacement—given daily SQ @ HS

REVIEW QUESTION

- ✘ A person suspected of having acromegaly has an elevated plasma GH Level. In acromegaly, one would also expect the person's diagnostic results to include:
 - + A. Hyperinsulinemia
 - + B. A plasma glucose of less than normal.
 - + C. Decreased GH levels with an oral glucose challenge test
 - + D. A serum somatomedin C (IGF-1) of higher than normal

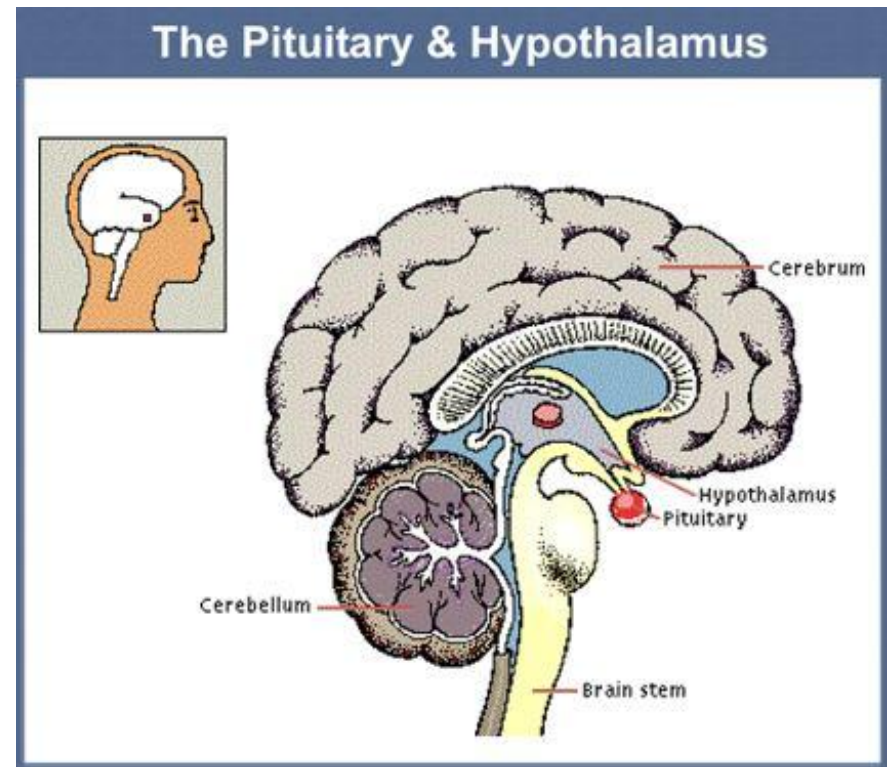
ANSWER

- × d. A nl response to GH secretion is stimulation of the liver to produce somatomedin C, or insulin-like growth factor-1 (IGF-1), which stimulates growth of bones & soft tissues. The increase levels of somatomedin C normally inhibit GH, but in acromegaly, the pituitary gland secretes GH despite elevated IGF-1 levels. When both GH & IGF-1 levels are increased, overproduction of GH is confirmed. GH also causes elevation of blood glucose, & normally GH levels fall during an oral glucose challenge but not in acromegaly.

HYPOFUNCTION OF PITUITARY GLAND

× Hypopituitarism

- + Rare disorder
- + Decrease of one or more of the pituitary hormones
- + Secreted by post pit:
 - × ADH, oxytocin
- + Secreted by ant pit:
 - × ACTH, TSH, follicle-stimulating (FSH) luteinizing hormone (LH), GH & prolactin



ETIOLOGY & PATHOPHYSIOLOGY

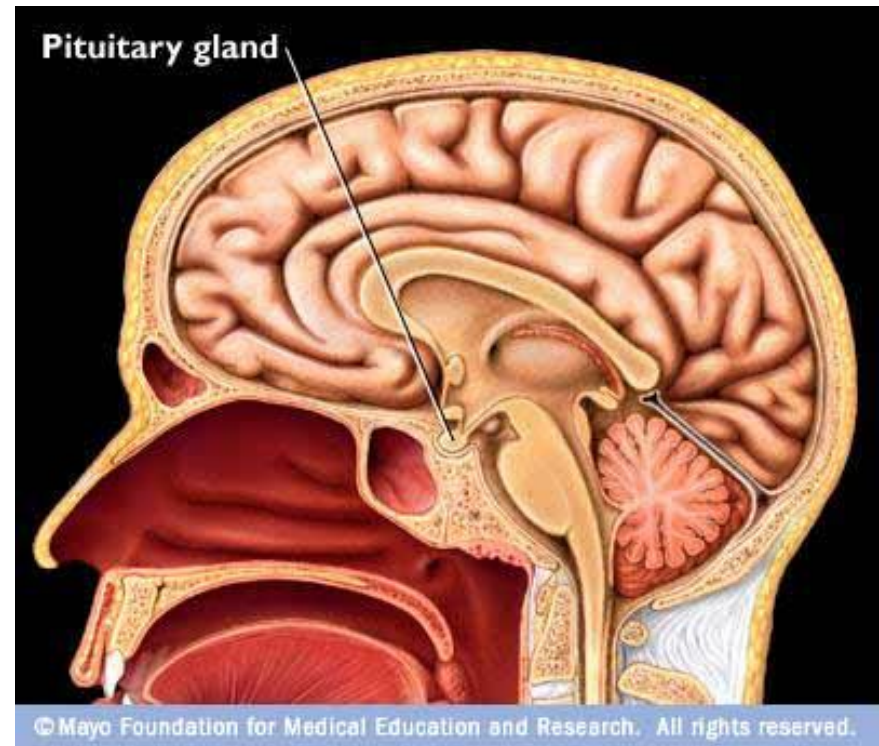
- ✗ Causes of pituitary hypofunction
 - + Tumor (most common)
 - + Infections
 - + Autoimmune disorders
 - + Pituitary infarction (Sheehan syndrome)
 - + Destruction of pituitary gland (radiation, trauma, surgery)
- ✗ Deficiencies can lead to end-organ failure

CLINICAL MANIFESTATIONS

- × Tumor
 - + Space- decrease peripheral vision or acuity, anosmia (loss of sense of smell), seizures
- × GH deficiency
 - + Decreased muscle mass, truncal obesity, flat affect
- × FSH & LD deficiencies
 - + Menstrual irregularities, dec libido, changes sex characteristics
- × ACTH & cortisol deficiency
 - + Fatigue, weakness, dry & pale skin, postural hypotension, fasting hypoglycemia, poor resistance to infection
- × Men with FSH & LD deficiencies
 - + Testicular atrophy, dec spermatogenesis, loss of libido, impotence, dec facial hair & muscle mass

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE (SIADH)

- ✘ Overproduction of ADH or arginine vasopressin (AVP)
- ✘ Synthesized in the hypothalamus
- ✘ Transported & stored in the posterior pituitary gland
- ✘ Major role is water balance & osmolarity



PATHOPHYSIOLOGY OF SIADH

- ✘ Increased antidiuretic hormone (ADH)→
- ✘ Increased water reabsorption in renal tubules→
- ✘ Increased intravascular fluid volume→
- ✘ Dilutional hyponatremia & decreased serum osmolality

SIADH

- × ADH is released despite normal or low plasma osmolarity
- × S/S:
 - + Dilutional hyponatremia
 - + Fluid retention
 - + Hypochloremia
 - + NI renal function, <U/O
 - + Concentrated urine
 - + Serum hypoosmolality
- × S/S: cerebral edema, lethargy, confusion, seizures, coma

CAUSES OF SIADH

× Malignant Tumors

- + Sm cell lung CA
- + Prostate, colorectal, thymus CA
- + Pancreatic CA

× CNS Disorders

- + Brain tumors
- + Lupus
- + Infections: meningitis
- + Head injury: skull fx, subdual hematoma

× Misc conditions

- + HIV
- + Lung infection
- + hypothyroidism

× Drug therapy

- + Oxytocin
- + Thiazide diuretics
- + SSRIs
- + Tricyclic antidepressants
- + opioids

DIAGNOSTIC STUDIES & TREATMENT

- × Simultaneous measurements of urine and serum osmolality
- × Na <134 mEq/L
- × Urine specific gravity > 1.005
- × Serum osmolality < 280 mOsm/kg (280 mmol/kg)
- × Treatment
 - + Treat underlying cause
 - + Restore nl fluid volume & osmolality
 - + Restrict fluids to 800-1000cc/day if Na >125 mEq/L & Lasix
 - + Serum Na <120 mEq/L, seizures can occur, tx with hypertonic Na⁺ solution (3%-5%) slowly

DIABETES INSIPIDUS (DI)

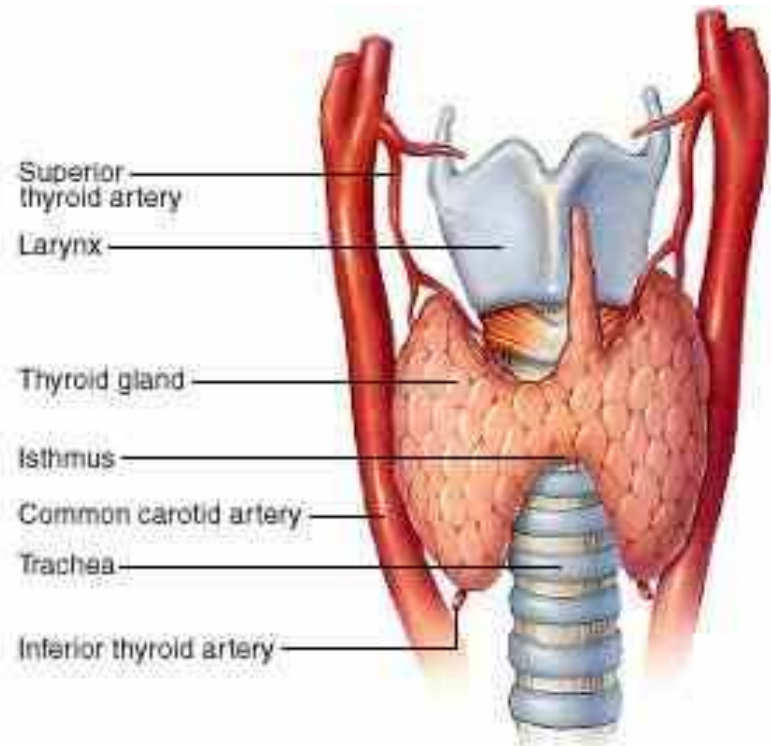
- × Deficiency of production or secretion of ADH OR a decreased renal response to ADH
- × Results in fluid & electrolyte imbalances
- × Types of DI
 - + Central DI (neurogenic DI)
 - + Nephrogenic DI

PATHOPHYSIOLOGY OF DI

- × Decreased ADH →
- × Decrease water absorption in renal tubules →
- × Decreased intravascular fluid volume →
- × Excessive urine output resulting in increased serum osmolality (hypernatremia)

THYROID GLAND DISORDERS

- ✘ Thyroid hormones (T3 & T4) regulate energy metabolism and growth and development



THYROID ENLARGEMENT

- ✘ Goiter—hypertrophy & enlargement of thyroid gland
- ✘ Caused by excess TSH stimulation
- ✘ Can be caused by inadequate circulating thyroid hormones



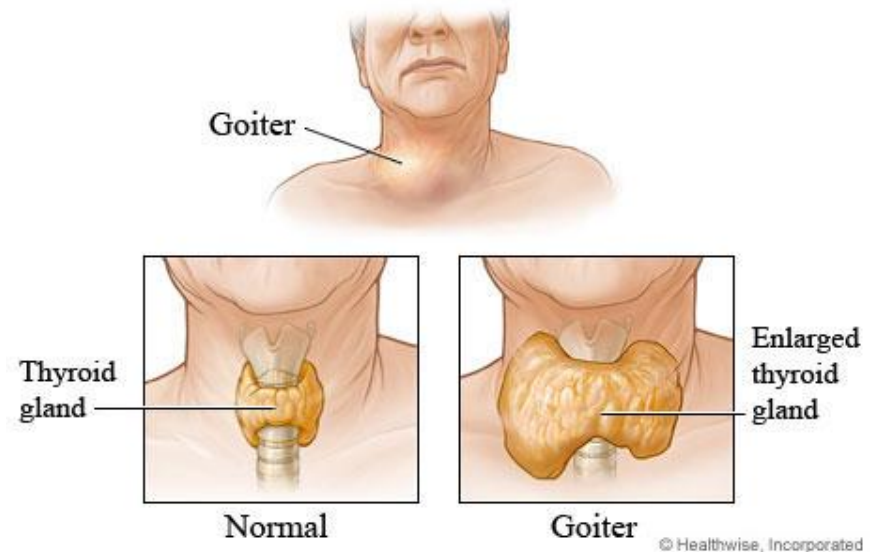
THYROID ENLARGEMENT

- ✘ Found in pts with Graves' disease
- ✘ Persons that live in a iodine-deficient area (endemic goiter)
- ✘ Surgery is used to remove large goiters

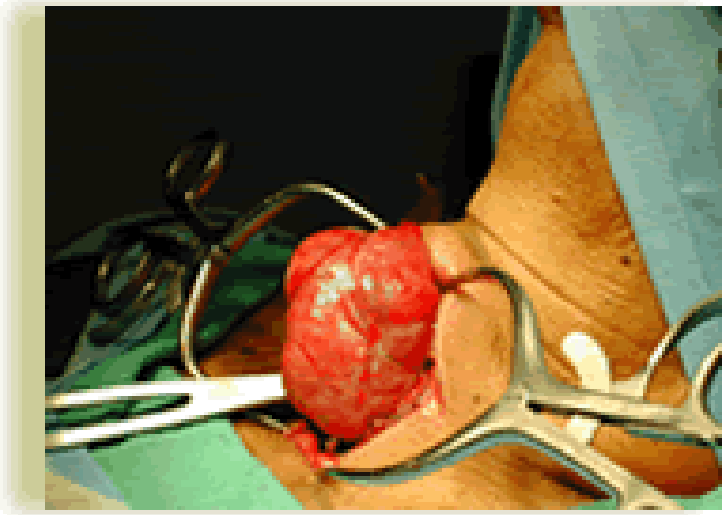


ENLARGEMENT OF THE THYROID GLAND

- ✘ TSH & T4 levels are used to determine if goiter is associated with hyper-/hypo- or normal thyroid function
- ✘ Check thyroid antibodies to assess for thyroiditis



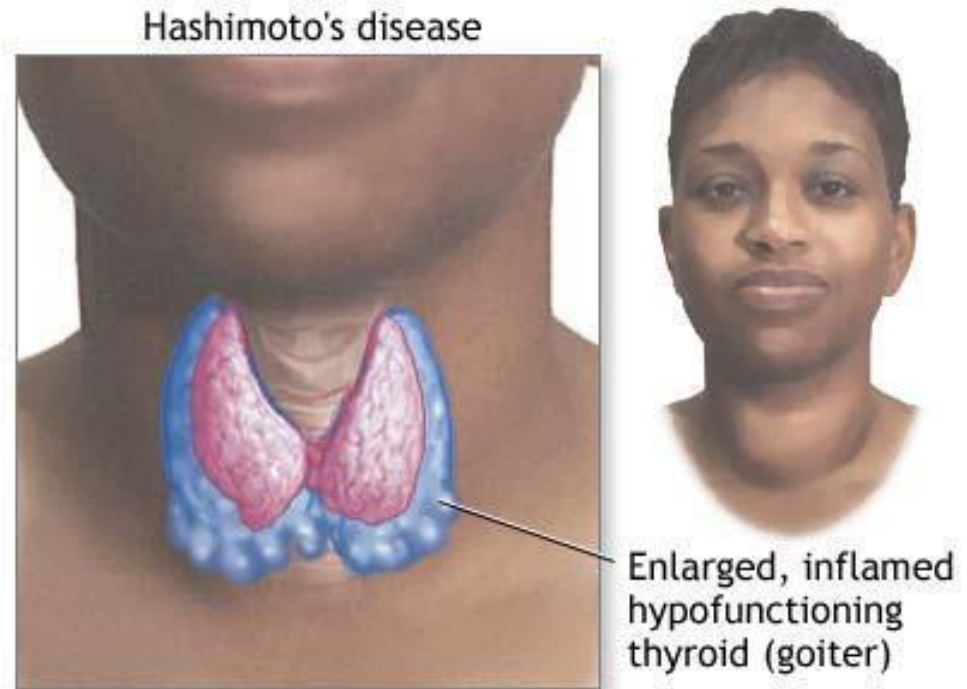
TREATMENT OF NODULES



- × US
- × CT
- × MRI
- × Fine-needle aspiration (FNA)—one of the most effective methods to identify malignancy
- × Serum calcitonin (increased levels associated with CA)

THYROIDITIS

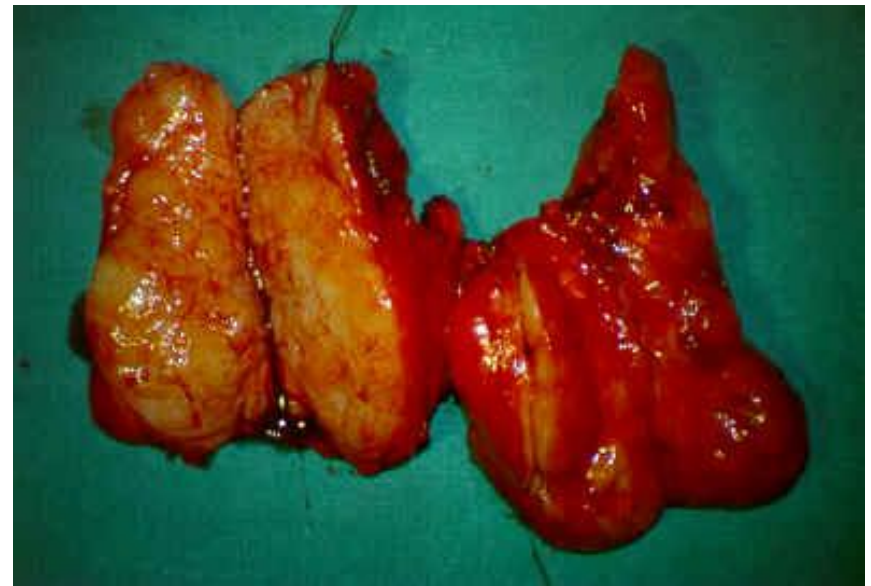
- ✘ Inflammation of thyroid
- ✘ Chronic autoimmune thyroiditis (Hashimoto's disease)—nl tissue replaced by lymphocytes & fibrous tissue
- ✘ Causes
 - + Viral
 - + Infection bacterial
 - + Fungal infection



DX STUDIES & MANAGEMENT OF THYROIDITIS

× Dx studies

- + T3 & T4 initially elevated and then may become depressed
- + TSH levels are low and then elevated
- + TSH high & dec hormone levels in Hashimoto's thyroiditis

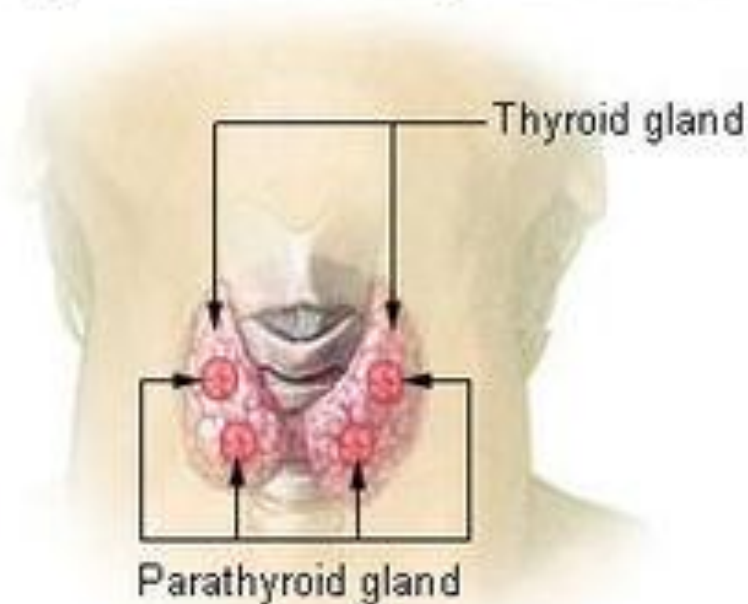


TREATMENT OF THYROIDITIS

- ✘ Recovery may take weeks or months
- ✘ Antibiotics or surgical drainage
- ✘ ASA or NSAIDS—if doesn't respond in 50 hours, steroids as used
- ✘ Propranolol (Inderal) or atenolol (Tenormin) for elevated heart rates
- ✘ More susceptible to Addison's disease, pernicious anemia, Graves' disease, gonadal failure

HYPERTHYROIDISM

Thyroid and Parathyroid Glands



- ✘ Hyperactivity of the thyroid gland with sustained increased in synthesis & release of thyroid hormones
- ✘ M>W
- ✘ Peaks in persons 20-40 yrs old
- ✘ Most common type is Graves' disease

GRAVES' DISEASE

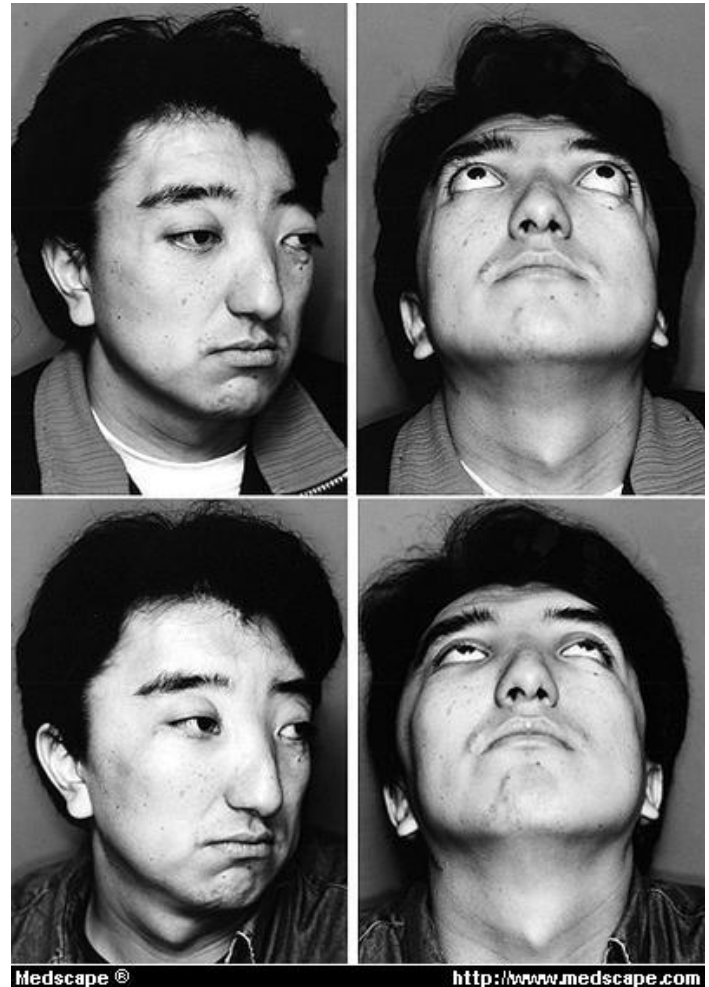
- × Autoimmune disease
- × Unknown etiology
- × Excessive thyroid secretion & thyroid enlargement
- × Precipitating factors: stressful life events, infection, insufficient iodine supply
- × Remissions & exacerbations
- × May progress to destruction of thyroid tissue
- × 75% of all hyperthyroidism cases
- × Pt has antibodies to TSH receptor

TOXIC NODULAR GOITERS

- × Function independent of TSH stimulation
- × *Toxic* if associated with hyperthyroidism
- × Multinodular goiter or solitary autonomous nodule
- × Benign follicular adenomas
- × M=W
- × Seen peak >40 yr of age
- × Nodules >3 cm may result in clinical disease

CLINICAL MANIFESTATIONS

- ✗ Bruit present
- ✗ Ophthalmopathy—abnl eye appearance or function
- ✗ Exophthalmos—protrusion of eyeballs from orbits—20-40 % of pts
- ✗ Usually bil, but unilateral or asymmetric



CLINICAL MANIFESTATIONS



- × Weight loss
- × Apathy
- × Depression
- × Atrial fibrillations
- × Confusion
- × Increased nervousness

DIAGNOSTIC STUDIES

- × TSH—decreased
- × Elevated free T4 (free is the form of hormone that is biologically active)
- × RAIU (radioactive iodine uptake) test—Graves' uptake 35-95%; thyroiditis uptake < 2%)
- × ECG
- × Ophthalmologic examination
- × TRH stimulation tests

COLLABORATIVE CARE

- ✗ Goal: block adverse effects of hormones & stop oversecretion
- ✗ Iodine: used with other drugs to prepare for OR or tx of crisis—1-2 wks max effect
- ✗ Antithyroid drugs:
 - + Propylthiouracil (PTU)—has to be taken TID
 - + Methimazole (Tapazole)
- ✗ Total or subtotal thyroidectomy
- ✗ B-adrenergic blockers—symptomatic relief
 - + Propranolol (Inderal)
 - + Atenolol (Tenormin)—used in pts with heart disease or asthma

COLLABORATIVE CARE

- ✘ Radioactive Iodine Therapy—treatment of choice for non-pregnant women; damages or destroys thyroid tissues; max effect seen in 2-3 months; post hypothyroidism seen in 80% of patients
- ✘ Nutritional therapy:
 - + High-calories: 4000-5000 kcal/day
 - + Six meals a day
 - + Snacks high in carbs, protein
 - + Particularly Vit A, B6, C & thiamine
 - + Avoid caffeine, high-fiber, highly seasoned foods

HYPOTHYROIDISM

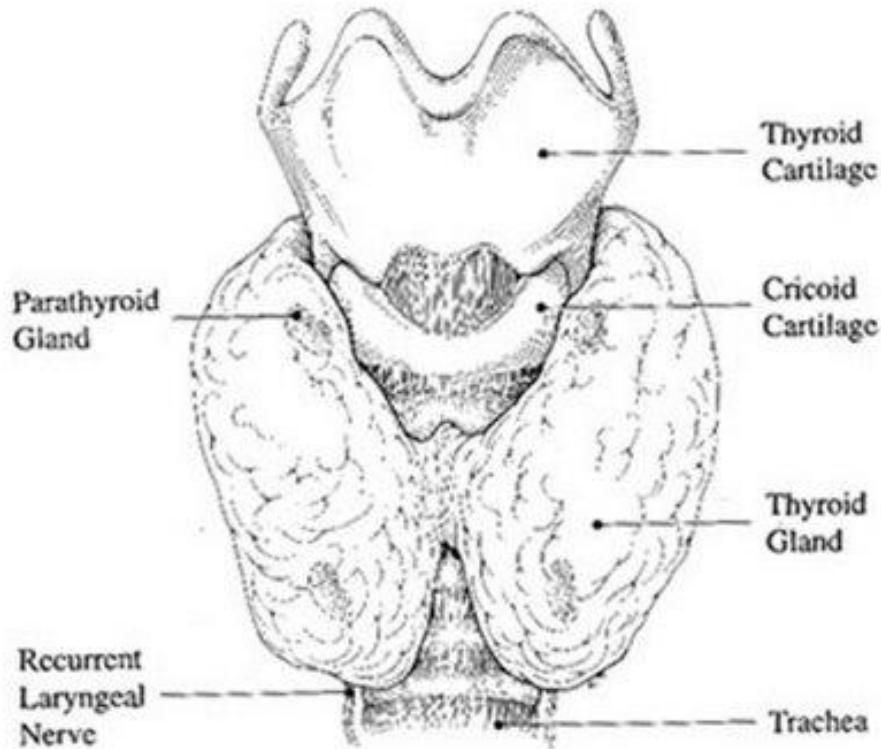
- ✗ Common medical disorder in US
- ✗ Insufficient circulating thyroid hormone
- ✗ Primary—related to destruction of thyroid tissue or defective hormone synthesis
- ✗ Can be transient
- ✗ Secondary—related to pituitary disease or hypothalamic dysfunction
- ✗ Most common cause iodine deficiency or atrophy thyroid gland (in US)
- ✗ May results from tx of hyperthyroidism
- ✗ *Cretinism* hypothyroidism in infancy

HYPOTHYROIDISM

- ✘ Cretinism—
hypothyroidism that
develops in infancy
- ✘ All newborns are
screened at birth for
hypothyroidism



CLINICAL MANIFESTATIONS



- ✘ S/S vary on severity of deficiency, age onset, patient's age
- ✘ Nonspecific slowing of body processes
- ✘ S/S occur over months or years
- ✘ Long-termed effects more pronounced in neurologic, GI, cardiovascular, reproductive & hematologic sytems

CLINICAL MANIFESTATIONS



- × Fatigue
- × Lethargy
- × Somnolence
- × Decreased initiative
- × Slowed speech
- × Depressed appearance
- × Increased sleeping
- × Anemia

CLINICAL MANIFESTATIONS

- × Decreased cardiac output
- × Decreased cardiac contractility
- × Bruise easily
- × Constipation
- × Cold intolerance
- × Hair loss
- × Dry, coarse skin
- × Weight gain
- × Brittle nails
- × Muscle weakness & swelling
- × Hoarseness
- × Menorrhagia
- × Myxedema—occurs with long-standing hypothyroidism

CLINICAL MANIFESTATIONS



- × Puffiness
- × Periorbital edema
- × Masklike effect
- × Coarse, sparse hair
- × Dull, puffy skin
- × Prominent tongue

MORE MYXEDEMA



COMPLICATIONS OF HYPOTHYROIDISM

✘ Myxedema coma:

- + Medical emergency
- + Mental drowsiness, lethargy & sluggishness may progress to a grossly impaired LOC
- + Hypotension
- + Hypoventilation
- + Subnormal temperature

TESTING & TREATMENT

- ✗ Serum TSH is high
- ✗ Free T4
- ✗ Hx & physical
- ✗ Cholesterol (elevated)
- ✗ Triglycerides (elevated)
- ✗ CBC (anemia)
- ✗ CK (increased)
- ✗ Levothyroxin (Synthroid)
 - + Levels are checked in 4-6 wks and dosage adjusted
 - + Take meds regularly
 - + Lifelong treatment
 - + Monitor pts with CAD
 - + Monitor HR & report to HCP >100 bpm
 - + Promptly report chest pain, weight loss, insomnia, nervousness

EXPECTED OUTCOMES

- ✘ Adhere to lifelong therapy
- ✘ Have relief from symptoms
- ✘ Maintain an euthyroid state as evidenced by nl TSH levels
- ✘ Severe myxedema of leg → → → → → → → →



DISORDERS OF THE ADRENAL CORTEX

- ✗ Main classifications of adrenal cortex steroid hormones:
 - + Mineralocorticoid
 - ✗ Regulates K⁺ & sodium balance
 - + Androgen
 - ✗ Contribute to growth & development in males/females & sexual activity in adult women
 - + Glucocorticoid
 - ✗ Cortisol is primary one
 - ✗ regulate metabolism, increase glu levels, critical in physiologic stress response

CUSHING SYNDROME

- ✗ Caused by excess of corticosteroids, more specifically:
 - glucocorticoids
- ✗ Hyperfunction of adrenal cortex
- ✗ Women > Men
- ✗ 20-40 yrs age group
- ✗ Other causes:
 - + ACTH-secreting pituitary tumor (Cushing's disease)
 - + Cortisol-secreting neoplasm in adrenal cortex
 - + Prolonged high doses of corticosteroids
 - + CA of lungs or malignant growth

CLINICAL MANIFESTATIONS OF CUSHING

- × Thin, fragile skin
- × Poor wound healing
- × Acne—red cheeks
- × Purplish red striae
- × Bruises
- × Fat deposits on back of neck & shoulders (buffalo hump)

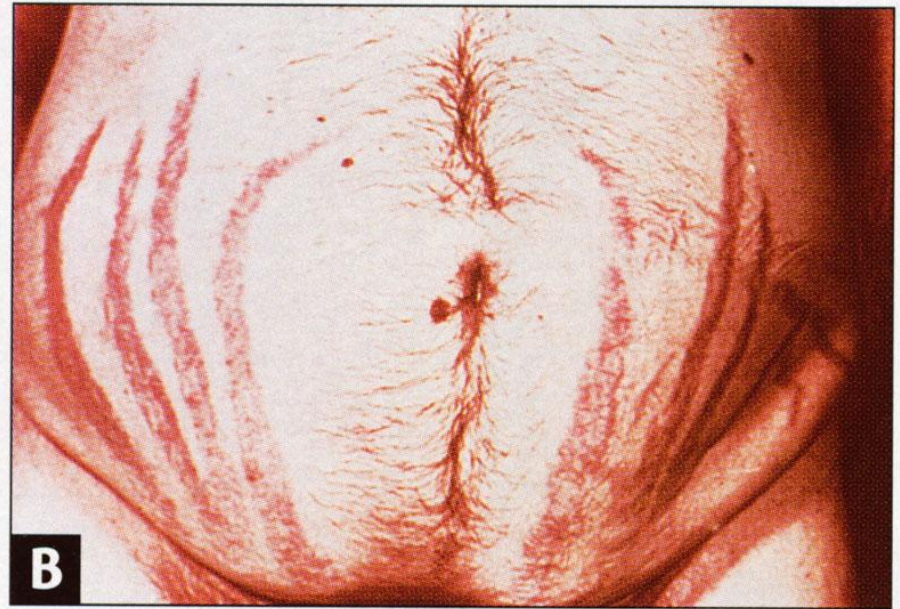


Figure 4-18B, Page 4.10

CLINICAL MANIFESTATIONS OF CUSHING



- ✗ Thin extremities with muscle atrophy
- ✗ Pendulous abd
- ✗ Ecchymosis—easy bruising
- ✗ Weight gain
- ✗ Increased body & facial hair
- ✗ Supraclavicular fat pads

CLINICAL MANIFESTATIONS OF CUSHING

- ✗ Rounding of face (moon face)
- ✗ HTN, edema of extremities
- ✗ Inhibition of immune response
- ✗ Sodium/water retention

- ✗ This infant had a 3 pound weight gain in 1 day → →

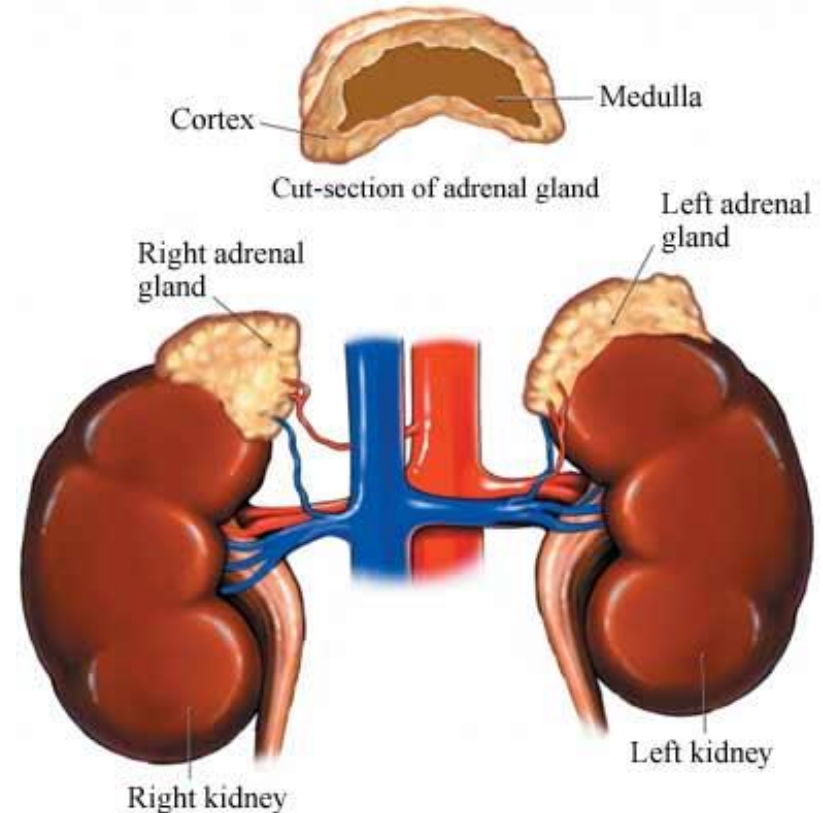


DIAGNOSTIC STUDIES FOR CUSHING

- ✗ 24-hr urine for free cortisol (50-100 mcg/day)
- ✗ Plasma cortisol levels may be elevated
- ✗ High-dose dexamethasone suppression test (false-positive results with depression, acute stress, active alcoholics)
- ✗ CBC—leukocytosis
- ✗ CMP—hyperglycemia, hypokalemia
- ✗ Hypercalciuria
- ✗ Plasma ACTH level
- ✗ History and physical

TREATMENT OF CUSHING SYNDROME

- ✘ Adrenalectomy (open or laparoscopic)
- ✘ If caused by steroid tx, taper & discontinue
- ✘ Drug therapy:
 - + Metyropone
 - + Mitotane (Lysodren)—
"medical adrenalectomy"
 - + Ketoconazole (Nizoral)
 - + Aminoglutethimide
(Cytadren)



HYPOFUNCTION OF ADRENAL CORTEX— ADDISON'S DISEASE

- ✗ All 3 classes of adrenal corticosteroids are reduced
- ✗ Most common cause is autoimmune response
- ✗ Other causes: AIDS, metastatic cancer, TB, infarction, fungal infections
- ✗ M=W (JFK had Addison's)
- ✗ Occurs in <60 yrs of age



CLINICAL MANIFESTATIONS OF ADDISON'S



- × Bronzed or smoky hyperpigmentation of face, neck, hands (esp creases), buccal membranes, nipples, genitalia
- × Anemia, lymphocytosis
- × Depression
- × Delusions

CLINICAL MANIFESTATIONS OF ADDISON'S



- × Fatigability
- × Tendency toward coexisting autoimmune diseases
- × N/V/D, abd pain
- × Hypotension
- × Vasodilation
- × Weight loss
- × Hyponatremia, dehydration

DIAGNOSTIC STUDIES & TREATMENT

- × CT scan
- × MRI
- × ACTH-stimulations test
- × History & physical
- × Plasma cortisol levels
- × Serum electrolytes
- × CBC
- × Urine for free cortisol (will be low)
- × Q day glucocorticoid (hydrocortisone) replacement (2/3 upon awakening & 1/3 in evening)
- × Salt additives for excess heat or humidity
- × Daily mineralocorticoid in the am
- × Increased doses or cortisol for stress situations (OR, hospitalizations)

SIDE EFFECTS OF CORTICOSTEROIDS

- ✘ Hypocalcemia R/T anti-vitamin D effect
- ✘ Weakness & skeletal muscle atrophy
- ✘ Predisposition to peptic ulcer disease (PUD)
- ✘ Hypokalemia
- ✘ Mood & behavior changes
- ✘ Predisposes to DM
- ✘ Delayed healing
- ✘ HTN → predisposes to heart failure
- ✘ Protein depletion predisposes to pathologic fx esp compression fx of vertebrae

COMPLICATIONS OF STEROID THERAPY

- ✘ Steroids taken for longer than 1 week will suppress adrenal production
- ✘ Always wean steroids, do not abruptly stop
- ✘ Take early in the am with food

