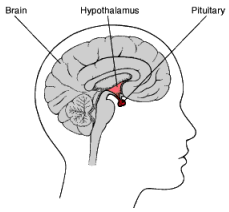
ENDOCRINE PROBLEMS

DISORDERS OF THE ANTERIOR PITUITARY

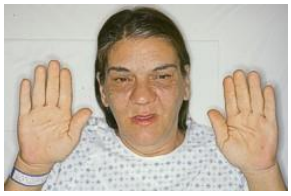
- Growth hormone (GH)
  - Promotes protein synthesis
  - Mobilizes glucose & free fatty acids
  - Overproduction almost always caused by benign tumor (adenoma)



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

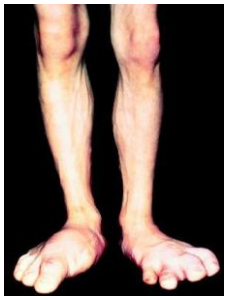
ACROMEGALY



- 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

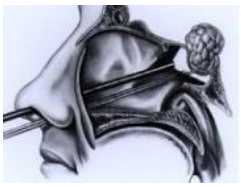
- Visual disturbances & HA from pressure of tumor
- Hyperglycemia
- Predisposes to atherosclerosis
- Untreated causes angina, HTN, lt ventricular hypertrophy, cardiomegaly

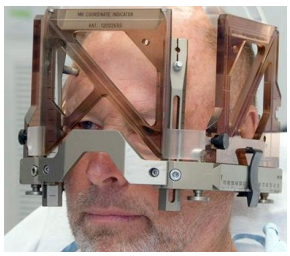


PROGRESSION OF ACROMEGALY

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

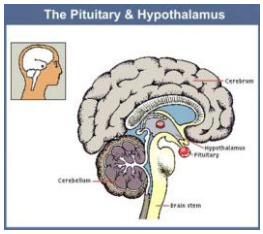
- A person suspected of having acromegaly has an elevated plasma GH Level. In acromegaly, one would also expect the person's diagnostic results to include:
  - A. Hyperinsulinemia
  - B. A plasma glucose of less than normal.
  - C. Decreased GH levels with an oral glucose challenge test
  - D. A serum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

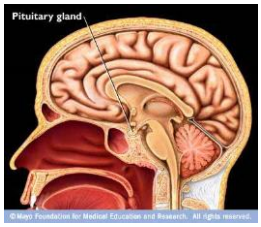
- Causes of pituitary hypofunction
  - Tumor (most common)
  - Infections
  - Autoimmune disorders
  - Pituitary infarction (Sheehan syndrome)
  - Destruction of pituitary gland (radiation, trauma, surgery)
- Deficiencies can lead to end-organ failure

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
  - Nl 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)

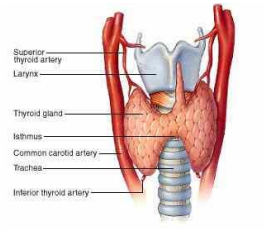
- Deficiency of production or secretion of ADH OR a decreased renal response to AHD
- Results in fluid & electrolyte imbalances
- Types of DI
  - Central DI (neurogenic DI)
  - Nephrogenic DI

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 & T 4) regulate energy metabolism and growth and development

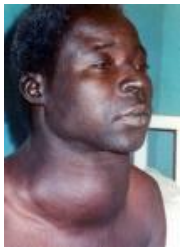


THYROID ENLARGEMENT

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

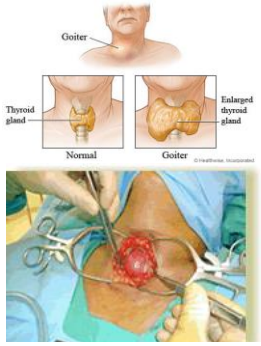
THYROID ENLARGEMENT

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

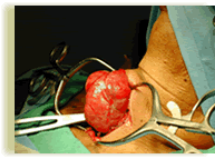


ENLARGEMENT OF THE THYROID GLAND

- 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



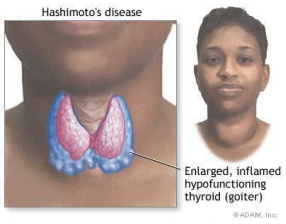
TREATMENT OF NODULES



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

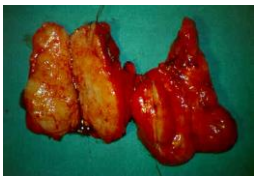
THYROIDITIS

- 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

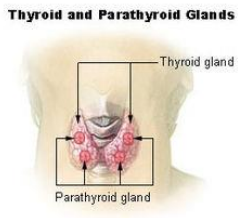
- Dx studies
  - T3 & T4 initially elevated and then may become depressed
  - TSH levels are low and then elevated
  - TSH high & dec hormone levels in Hashimoto's thyroiditis



TREATMENT OF THYROIDITIS

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

HYPERTHYROIDISM



- 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

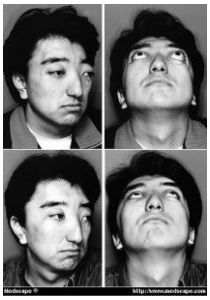
- Autoimmune disease
- Unknown etiology
- Excessive thyroid secretion & thyroid enlargement
- Precipitating factors: stressful life events, infection, insufficient iodine supply
- Remissions & exacerbations
- May progress to destruction of thyroid tissue
- 75% of all hyperthyroidism cases
- Pt has antibodies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

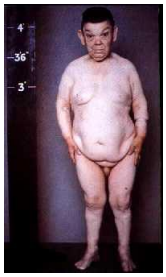
- Radioactive Iodine Therapy—treatment of choice for non-pregnant women; damages or destroys thyroid tissues; max effect seen in 2-3 months; post hypothyroidism seen in 80% of patients
- Nutritional therapy:
  - High-calories: 4000-5000 kcal/day
  - Six meals a day
  - Snacks high in carbs, protein
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

HYPOTHYROIDISM

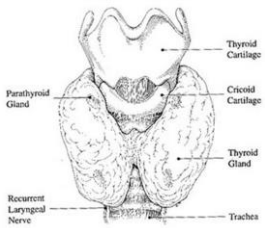
- Common medical disorder in US
- Insufficient circulating thyroid hormone
- Primary—related to destruction of thyroid tissue or defective hormone synthesis
- Can be transient
- Secondary—related to pituitary disease or hypothalamic dysfunction
- Most common cause iodine deficiency or atrophy thyroid 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

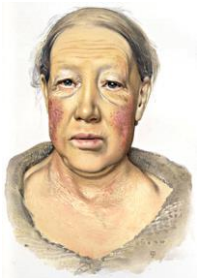
CLINICAL MANIFESTATIONS

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

CLINICAL MANIFESTATIONS

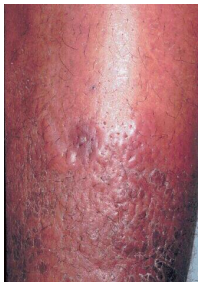
- Decreased cardiac output
- Decreased cardiac contractility
- Bruise easily
- Constipation
- Cold intolerance
- Hair loss
- Dry, course skin
- Weight gain
- Brittle nails
- Muscle weakness & swelling
- Hoarseness
- Menorrhagia
- Myxedema—occurs with long-standing hypothyroidism

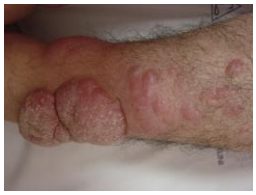
CLINICAL MANIFESTATIONS



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

MORE MYXEDEMA





COMPLICATIONS OF HYPOTHYROIDISM

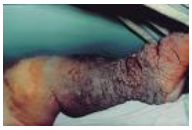
- Myxedema coma:
  - Medical emergency
  - Mental drowsiness, lethargy & sluggishness may progress to a grossly impaired LOC
  - Hypotension
  - Hypoventilation
  - Subnormal temperature

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 steriod 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 corticosteriods, 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 corticosteriods
  - 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)

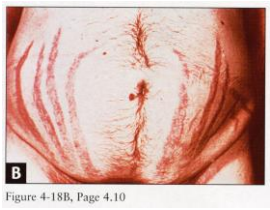
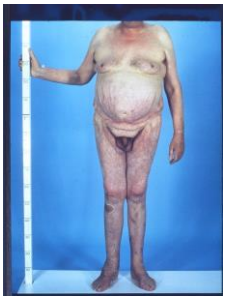


Figure 4-18B, Page 4.10

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

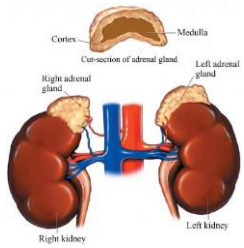
- Rounding of face (moon face)
- HTN, edema of extremities
- Inhibition of immune response
- Sodium/water retention
- This infant had a 3 pound weight gain in 1 day→→

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

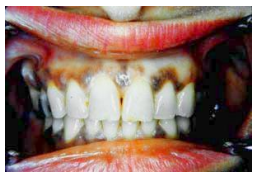
- Adrenalectomy (open or laparoscopic)
- If caused by steriod tx, taper & discontinue
- Drug therapy:
  - Metyropone
  - Mitotane (Lysodren)—"medical adrenalectomy"
  - Ketoconazole (Nizoral)
  - Aminoglutethimide (Cytadren)



HYPOFUNCTION OF ADRENAL CORTEX—ADDISON'S DISEASE

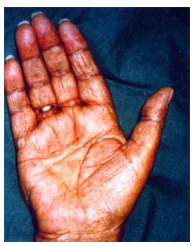
- All 3 classes of adrenal corticosteriods are reduced
- Most common cause is autoimmune response
- Other causes: AIDS, metastatic cancer, TB, infarction, fungal infections
- M=W (JFK had Addison's)
- Occurs in <60 yrs of age

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 STERIOD THERAPY

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