Endocrine disorders in pregnancy

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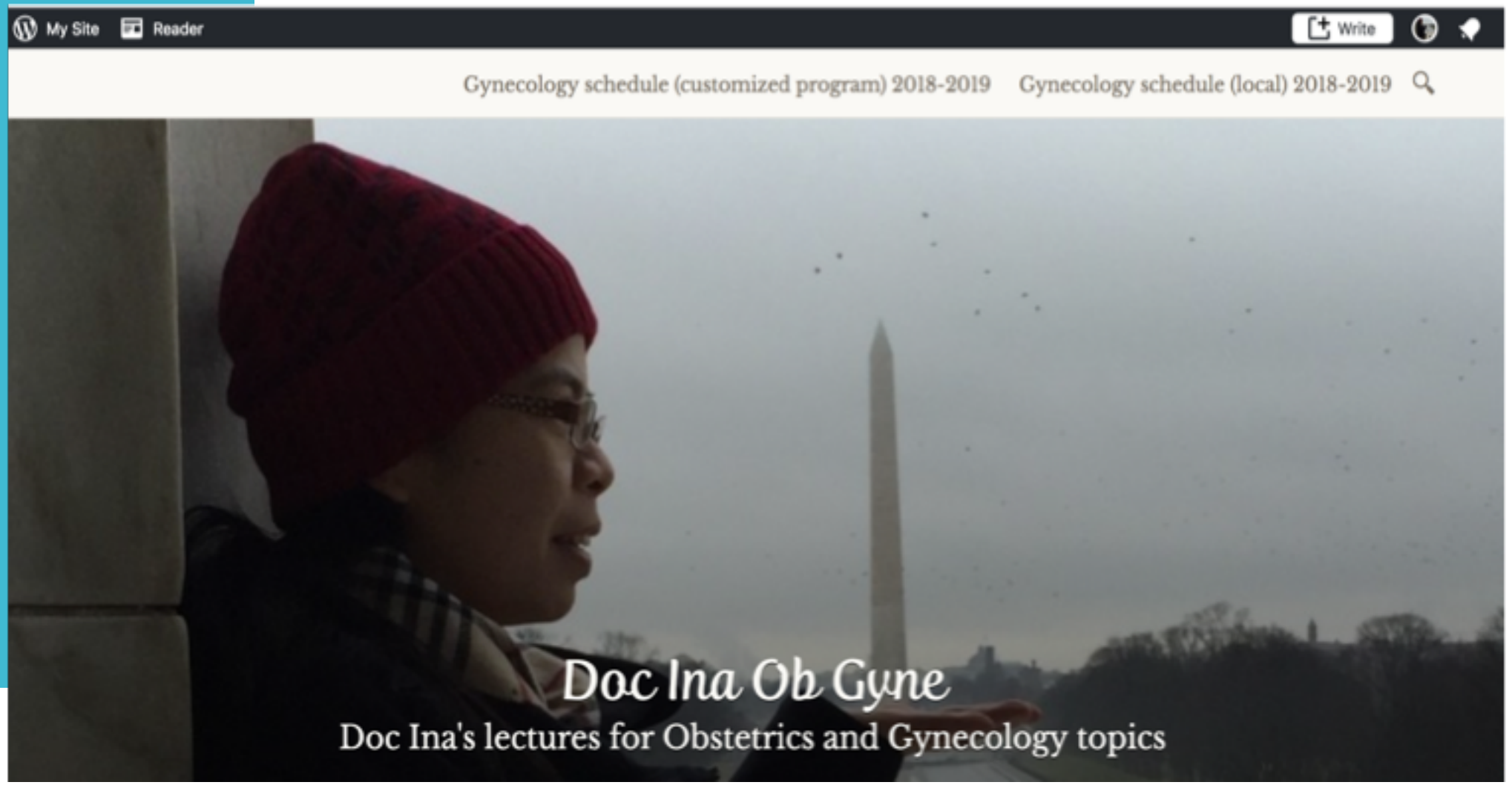

Reference

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Outline

- 1. Thyroid
- 2. Parathyroid
- 3. Adrenals
- 4. Pituitary

1. Thyroid disorders

Thyroid Physiology and Pregnancy

- maternal serum concentrations of thyroid-binding globulin are are increased concomitantly with total or bound thyroid hormone levels
- Serum TSH (aka THYROTROPIN) levels in early pregnancy decline because of weak TSH-receptor stimulation from massive quantities of human chorionic gonadotropin (hCG) secreted by placental trophoblast.
- Because TSH does not cross the placenta, it has no direct fetal effects.
- During the first 12 weeks of gestation, when hCG serum levels are maximal, thyroid hormone secretion is stimulated → resulting increased serum free thyroxine levels act to suppress hypothalamic thyrotropin- releasing hormone (TRH) and in turn limit pituitary TSH secretion

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Thyroid Physiology and Pregnancy

- throughout pregnancy, maternal thyroxine (TSH) is transferred to the fetus
- Maternal thyroxine is important for normal fetal brain development, especially before development of fetal thyroid gland function
- maternal sources account for 30 percent of thyroxine in fetal serum at term

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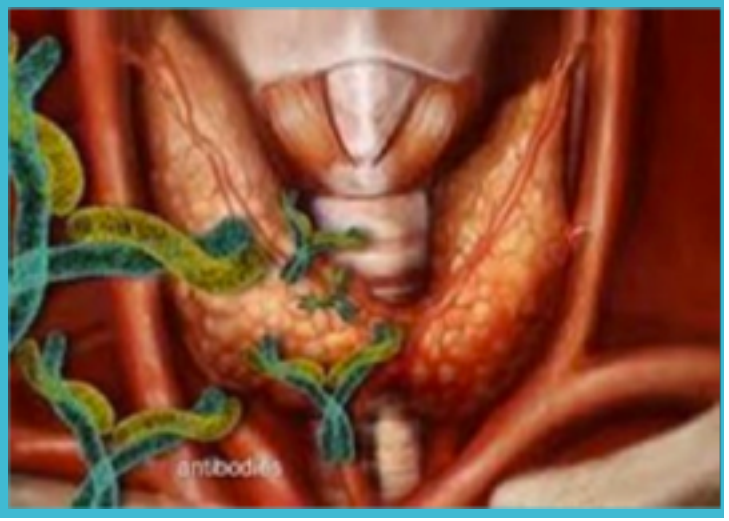
Autoimmunity and Thyroid Disease



- thyroid-stimulating autoantibodies, aka thyroid-stimulating immunoglobulins (TSIs), bind to the TSH receptor and activate it, causing thyroid hyperfunction and growth.
- thyroid peroxidase (TPO) is a thyroid gland enzyme that normally functions in the production of thyroid hormones.
- thyroid peroxidase antibodies, previously called thyroid microsomal autoantibodies, are directed against TPO and have been identified in 5 -15% of all pregnant women → associated in some studies with early pregnancy loss and preterm birth

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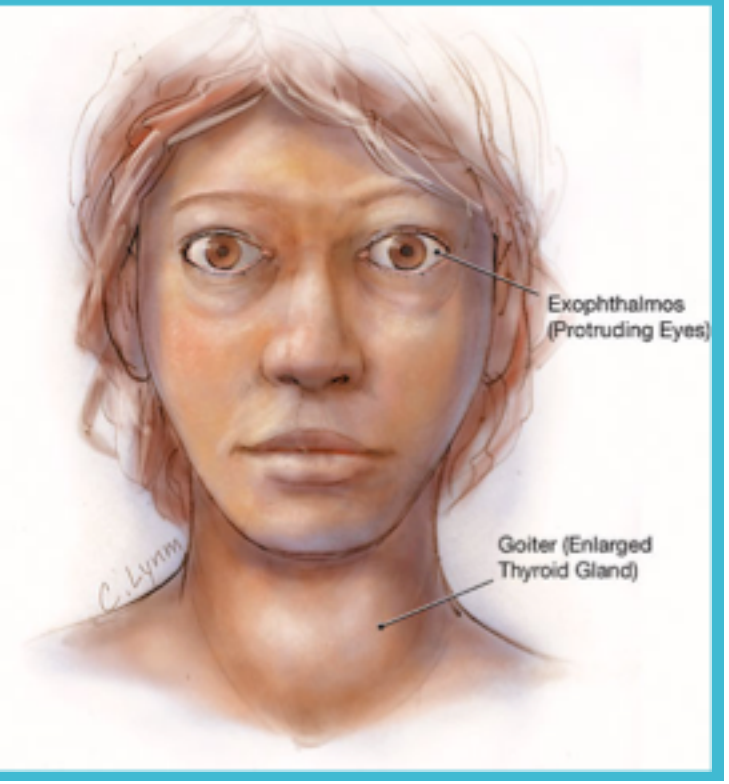
Hyperthyroidism



- clinically mild thyrotoxicosis may be difficult to diagnose (Because normal pregnancy simulates some clinical findings similar to thyroxine (T4) excess)
- Laboratory confirmation is by a markedly depressed TSH level along with an elevated fT4.
- Suggestive findings include:
  - tachycardia (exceeds that usually seen with normal pregnancy)
  - thyromegaly
  - exophthalmos
  - failure to gain weight despite adequate food intake.
- "T3-toxicosis" → hyperthyroidism is caused by abnormally high serum triiodothyronine (T3) levels

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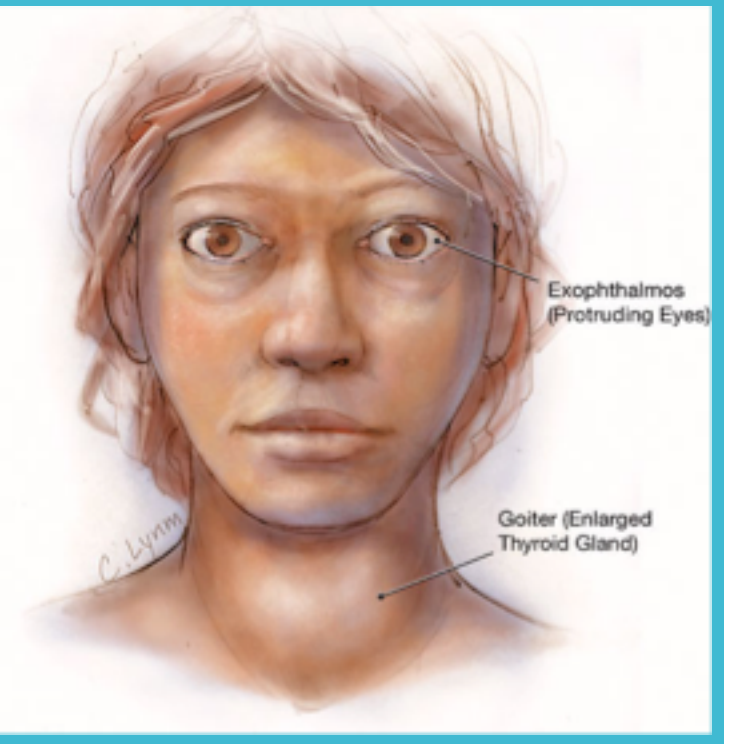
Thyrotoxicosis and Pregnancy



- Usually secondary to Graves disease
- With Graves disease, during the course of pregnancy, hyperthyroid symptoms may initially worsen because of chorionic gonadotropin stimulation, but then subsequently diminish with decreases in receptor antibody titers in the second half of pregnancy
- Treatment: thyrotoxicosis during pregnancy can nearly always be controlled by thionamide drugs:
  - Propylthiouracil (PTU)
  - Methimazole : associated with a rare methimazole embryopathy characterized by esophageal or choanal atresia as well as "aplasia cutis", a congenital skin defect.

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Treatment: side effects of anti-thyroid drugs

1. Transient leukopenia (does not require therapy cessation)
2. Agranulocytosis (mandates drug discontinuance); if fever or sore throat develops, women are instructed to discontinue medication immediately and report for a complete blood count)
3. Hepatotoxicity: serial measurement of hepatic enzymes has not been shown to prevent fulminant PTU-related hepatotoxicity.
4. antineutrophil cytoplasmic antibodies (ANCA) → a small percentage of these subsequently develop serious vasculitis
5. fetal complications (uncommon)

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Treatment dosage

- *300 or 450 mg of PTU daily in three divided doses* ; occasionally, daily doses of 600 mg are necessary.
- The goal is treatment with the lowest possible thionamide dose
- Serum free T_4 concentrations are measured *every 4 to 6 weeks*
- Subtotal thyroidectomy can be performed after thyrotoxicosis is medically controlled → appropriate for the very few women who cannot adhere to medical treatment or in whom drug therapy proves toxic
- *Surgery is best accomplished in the second trimester*. Potential drawbacks of thyroidectomy during pregnancy include inadvertent resection of parathyroid glands and injury to the recurrent laryngeal nerve
- *thyroid ablation with therapeutic radioactive iodine is contraindicated during pregnancy.*

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- In untreated women or in those who remain hyperthyroid despite therapy, there is a higher incidence of preeclampsia, heart failure, and adverse perinatal outcomes
- Clinical hyperthyroidism develops in approximately 1% of neonates born to women with Graves disease

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Fetus/ neonate exposed to excessive maternal thyroxine may these clinical presentations:

- 1. **Goitrous thyrotoxicosis** is caused by placental transfer of thyroid- stimulating immunoglobulins.
  - Nonimmune hydrops and fetal demise
  - the best predictor of perinatal thyrotoxicosis is presence of thyroid-stimulating TSH-receptor antibodies in women with Graves disease (levels are more than threefold higher than the upper normal limit)
  - American Thyroid Association and American Association of Clinical Endocrinologists (2011) recommend routine evaluation of TSH-receptor antibodies between 22 and 26 weeks' gestation in women with Graves disease → ACOG does not recommend such testing because management is rarely changed by the results.
  - If the fetus is thyrotoxic, treatment is by adjustment of maternal thionamide drugs even though maternal thyroid function may be within the targeted range
  - neonatal thyrotoxicosis may also require short-course antithyroid drug treatment.

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Fetus/ neonate exposed to excessive maternal thyroxine may these clinical presentations…

FIGURE 58-3 Term neonate delivered of a woman with a 3-year history of thyrotoxicosis that recurred at 26 weeks' gestation. The mother was given methimazole 30 mg orally daily and was euthyroid at delivery. Laboratory studies showed that the infant was hypothyroid.

- 2. **Goitrous hypothyroidism** is caused by fetal exposure to maternally administered thionamides
  - thionamides may carry an extremely small risk for causing neonatal hypothyroidism
  - If hypothyroidism is identified, the fetus can be treated by a reduced maternal antithyroid medication dose and injection of intraamnionic thyroxine if necessary.
- 3. **Nongoitrous hypothyroidism** may develop from transplacental passage of maternal TSH-receptor blocking antibodies
- 4. **Fetal thyrotoxicosis** after maternal thyroid gland ablation, usually with 131I radioiodine, may result from transplacental thyroid-stimulating antibodies.

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Thyroid Storm and Heart Failure

- thyroid storm is a hypermetabolic state and is rare in pregnancy.
- Pulmonary hypertension and heart failure from cardiomyopathy caused by the profound myocardial effects of thyroxine is common in pregnant women
  - cardiomyopathy is characterized by a high-output state, which may lead to a dilated cardiomyopathy
  - pregnant woman with thyrotoxicosis has minimal cardiac reserve, and decompensation is usually precipitated by preeclampsia, anemia, sepsis, or a combination of these.
  - Fortunately, thyroxine-induced cardiomyopathy and pulmonary hypertension are frequently reversible

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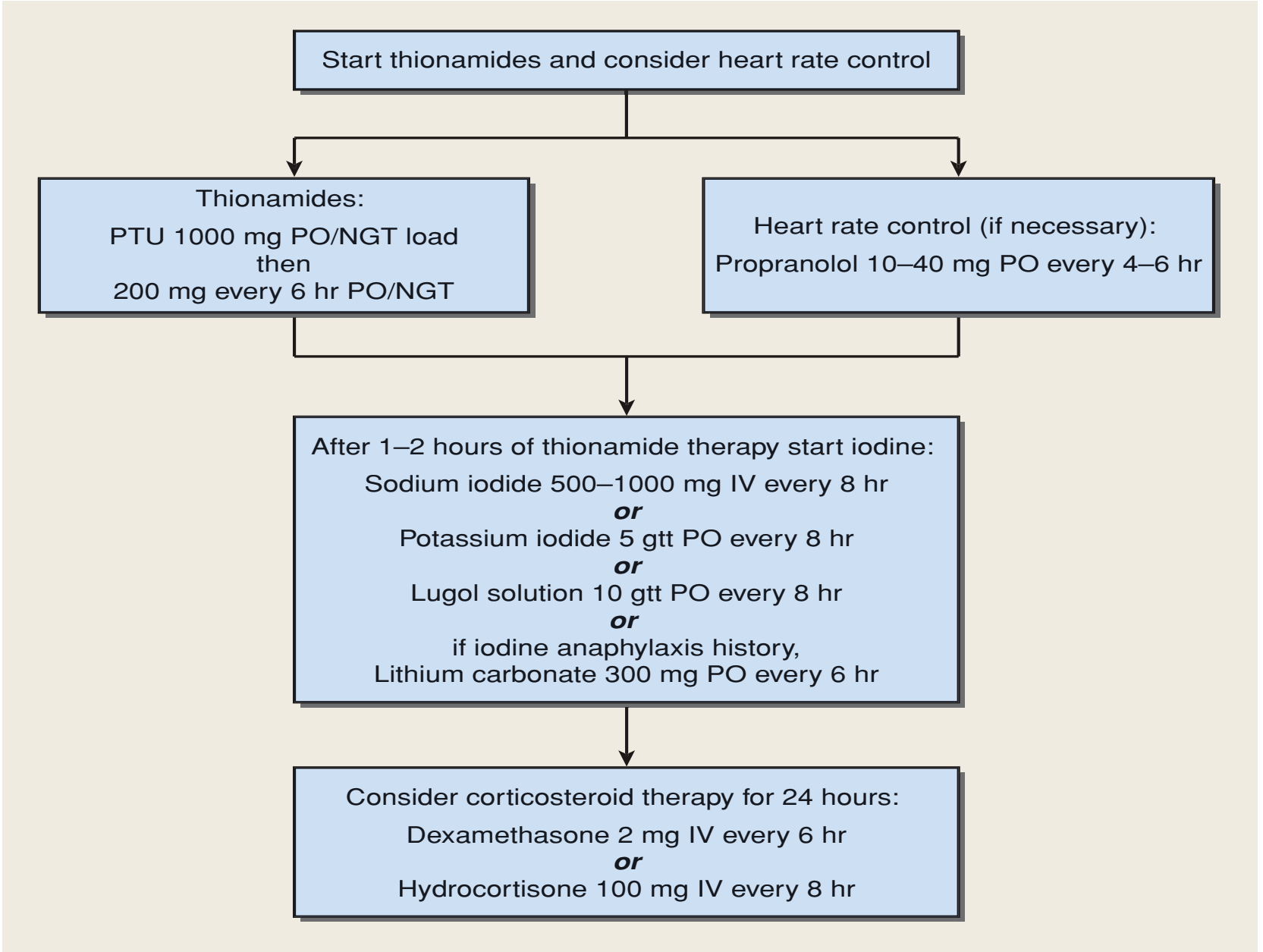
Management of thyroid storm and heart failure



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Hyperemesis Gravidarum and Gestational Transient Thyrotoxicosis

- "gestational transient thyrotoxicosis".
- Many women with hyperemesis gravidarum have abnormally high serum thyroxine levels and low TSH levels →due to TSH- receptor stimulation from massive—but normal for pregnancy—concentrations of hCG.
- antithyroid drugs are not warranted.
- Serum thyroxine and TSH values become normal by midpregnancy

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Thyrotoxicosis and Gestational Trophoblastic Disease

- abnormally high hCG levels lead to overstimulation of the TSH receptor.
- With definitive treatment, serum free-T_4 levels usually normalize rapidly in parallel with the decline in hCG concentrations.

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Subclinical Hyperthyroidism

- abnormally low serum TSH concentration in concert with thyroxine hormone levels within the normal reference range.
- Long-term effects of persistent subclinical thyrotoxicosis include osteoporosis, cardiovascular morbidity, and progression to overt thyrotoxicosis or thyroid failure.
- subclinical hyperthyroidism was not associated with adverse pregnancy outcomes..
- the American Thyroid Association and American Association of Clinical Endocrinologists guidelines recommend treatment of subclinical hyperthyroidism in individuals 65 years or older and in postmenopausal women to improve cardiovascular health and bone mineral density.

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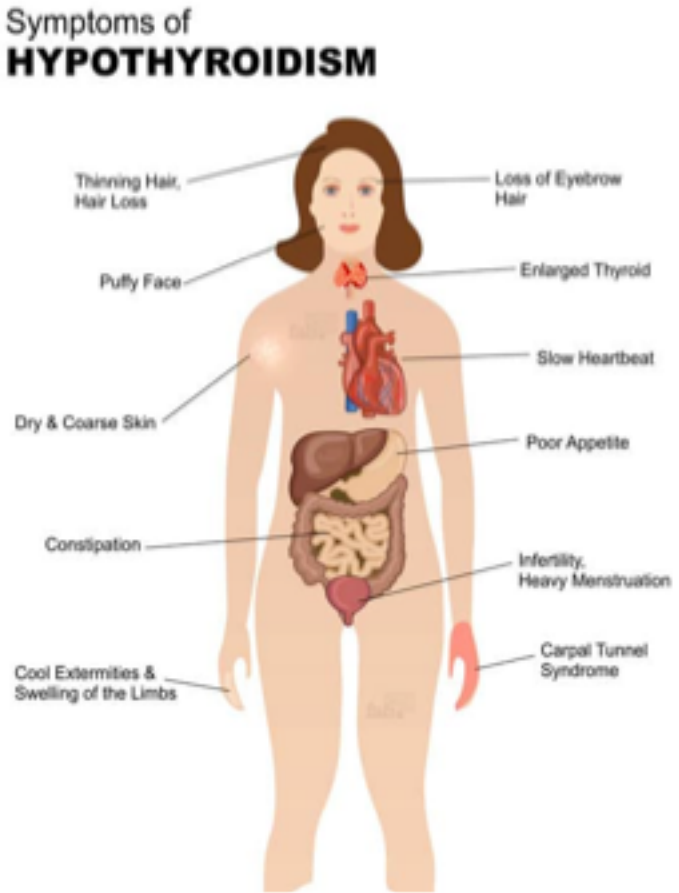
Hypothyroidism



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- Incidence: 2-10% of pregnancies per 1000.
- characterized by insidious nonspecific clinical findings that include fatigue, constipation, cold intolerance, muscle cramps, and weight gain.
- Other findings include edema, dry skin, hair loss, and prolonged relaxation phase of deep tendon reflexes.
- confirmed when an abnormally high serum TSH level is accompanied by an abnormally low thyroxine level.

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Overt Hypothyroidism and Pregnancy

- most common cause of hypothyroidism in pregnancy is *Hashimoto thyroiditis* (glandular destruction from autoantibodies, particularly antithyroid peroxidase antibodies).
- thyroid analyte testing should be performed on symptomatic women or those with a history of thyroid disease (ACOG, 2013).
- severe hypothyroidism during pregnancy is uncommon, because it is often associated with infertility and increased spontaneous abortion rates
- TREATMENT:
  - *Levothyroxine 1 to 2 µg/kg/day or approximately 100 µg daily* (Women who are athyreotic after thyroidectomy or radioiodine therapy may require higher doses)
  - Surveillance: *TSH levels measured at 4- to 6-week intervals*, and the thyroxine dose is adjusted by 25- to 50-µg increments until TSH values become normal.
  - Pregnancy is associated with an increased thyroxine requirement (the increased demand in pregnancy is believed to be related to increased estrogen production)

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Iodine Deficiency

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- Dietary iodine requirements are increased during pregnancy due to increased thyroid hormone production, increased renal losses, and fetal iodine requirements.
- Adequate iodine is requisite for fetal neurological development beginning soon after conception, and abnormalities are dependent on the degree of deficiency.
- Severe deficiency is frequently associated with cretinism
- the Institute of Medicine (2001) recommends daily iodine intake during pregnancy of 220 µg/day, and 290 µg/day for lactating women

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Iodine Deficiency

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- the Endocrine Society recommends an average iodine intake of 150 µg per day in childbearing-aged women, and this should be increased to 250 µg during pregnancy and breast feeding.
- the American Thyroid Association has recommended that 150 µg of iodine be added to prenatal vitamins to achieve this average daily intake
- WARNING!!: Excessive iodine intake (> 300 µg/day) may lead to subclinical hypothyroidism and autoimmune thyroiditis → the Endocrine Society advises against exceeding twice the daily recommended intake of iodine, or 500 µg/day

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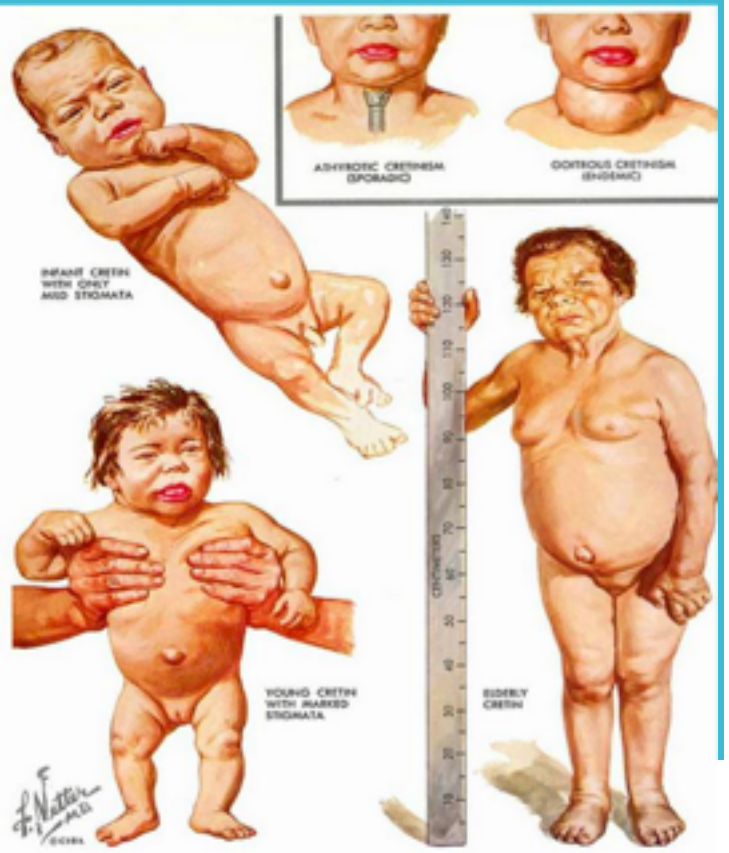
Congenital Hypothyroidism



- Congenital hypothyroidism is one of the most preventable causes of mental retardation.
- Developmental disorders of the thyroid gland such as agenesis and hypoplasia account for 80 to 90 percent of these cases
- Early and aggressive thyroxine replacement is critical for infants with congenital hypothyroidism.
- in addition to timing of treatment, the severity of congenital hypothyroidism is an important factor in long-term cognitive outcomes
- in infants with screening results suggestive of severe hypothyroidism, therapy should be started immediately without waiting for confirmatory results

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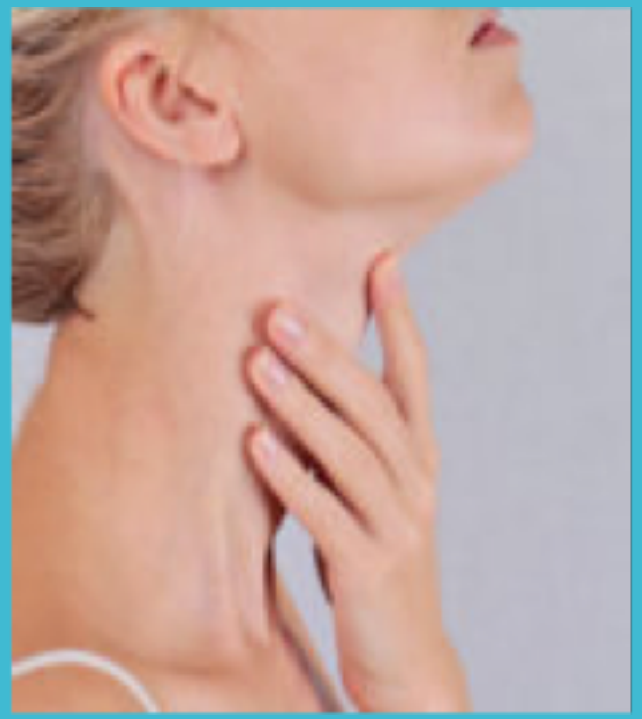
Postpartum Thyroiditis



- Postpartum thyroid dysfunction with an onset within 12 months of chilfdbirth includes hyperthyroidism, hypothyroidism, or both.
- directly related to increasing serum levels of thyroid autoantibodies. (women who are thyroid-antibody positive in the 1st trimester will likely develop postpartum thyroiditis)
- Clinical Manifestations
  - typically develops months after delivery and causes vague and nonspecific symptoms that often are thought to be stresses of motherhood
  - there are two recognized clinical phases:

1. the first and earliest is destruction-induced thyrotoxicosis with symptoms from excessive release of hormone from glandular disruption: onset is abrupt, and a small, painless goiter is commonly found; fatigue and palpitations are common

   → this thyrotoxic phase usually lasts only a few months.

   → thionamides are ineffective, and if symptoms are severe, a β-blocker agent may be given.

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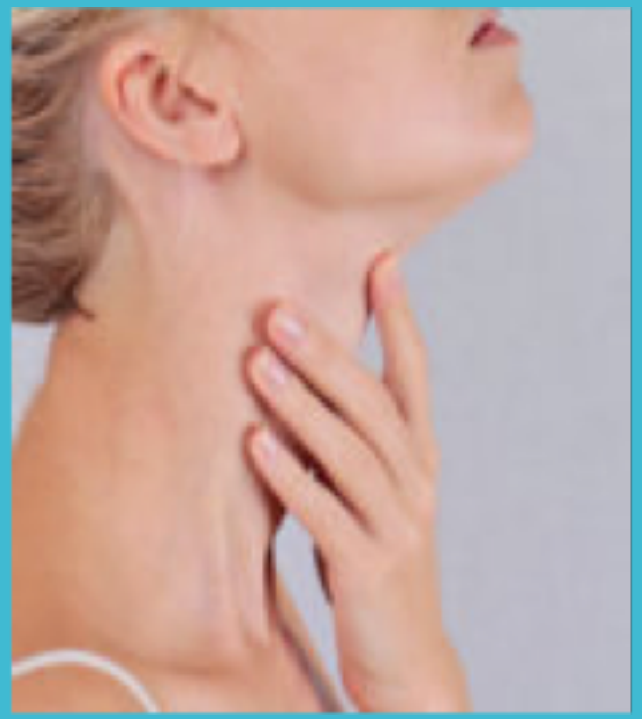
Postpartum Thyroiditis



…Clinical Manifestations

- there are two recognized clinical phases:

1. destruction-induced thyrotoxicosis
2. clinical hypothyroidism from thyroiditis: occurs between 4 and 8 months postpartum.
   - →thyromegaly and other symptoms are common and more prominent than during the thyrotoxic phase.
   - →thyroxine replacement with 25 to 75 µg/day is typically given for 6 to 12 months.

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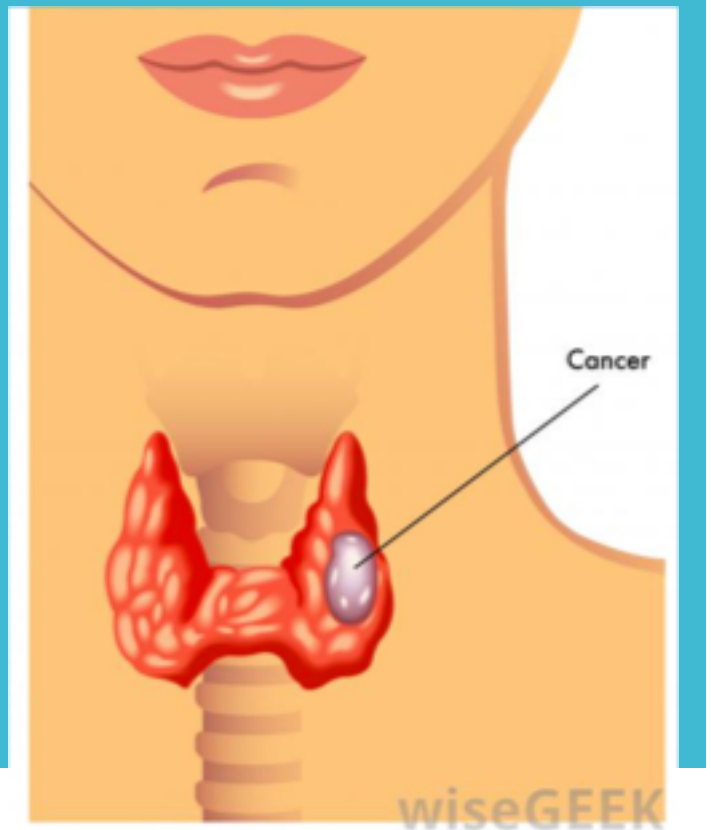
Nodular Thyroid Disease



- Management of a palpable thyroid nodule during pregnancy depends on gestational age and mass size.
- Biopsy of nodules > 5 mm^3 that persisted at 3 months usually showed nodular hyperplasia, and none were malignant (Those malignant were found to be low-grade neoplasms.)
- Evaluation of thyroid nodules during pregnancy should be similar to that for nonpregnant patients.
  - ***Radioiodine scanning in pregnancy is not recommended*** despite the fact that tracer doses used are associated with minimal fetal irradiation
  - Ulrasound detects nodules >0.5 cm, and their solid or cystic structure can be determined.
  - Ultrasound characteristics associated with malignancy include hypoechogenic pattern, irregular margins, and microcalcifications.
  - Fine-needle aspiration (FNA) is an excellent assessment method, and histological tumor markers and immunostaining are reliable to evaluate for malignancy
  - If the FNA biopsy shows a follicular lesion, surgery may be deferred until after delivery.

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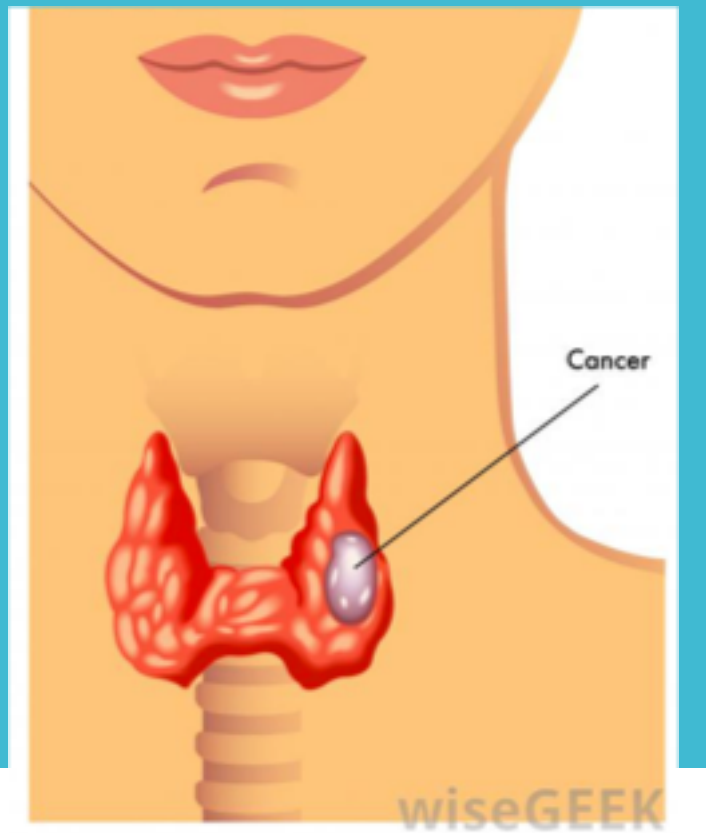
Nodular thyroid disease



- Evaluation of thyroid cancer involves a multidisciplinary approach
- Most thyroid carcinomas are well differentiated and pursue an indolent course.
- When thyroid malignancy is diagnosed during the 1st or 2nd trimester, *thyroidectomy may be performed before the third trimester*
- In women without evidence of an aggressive thyroid cancer, or in those diagnosed in the third trimester, surgical treatment can be deferred to the immediate postpartum period

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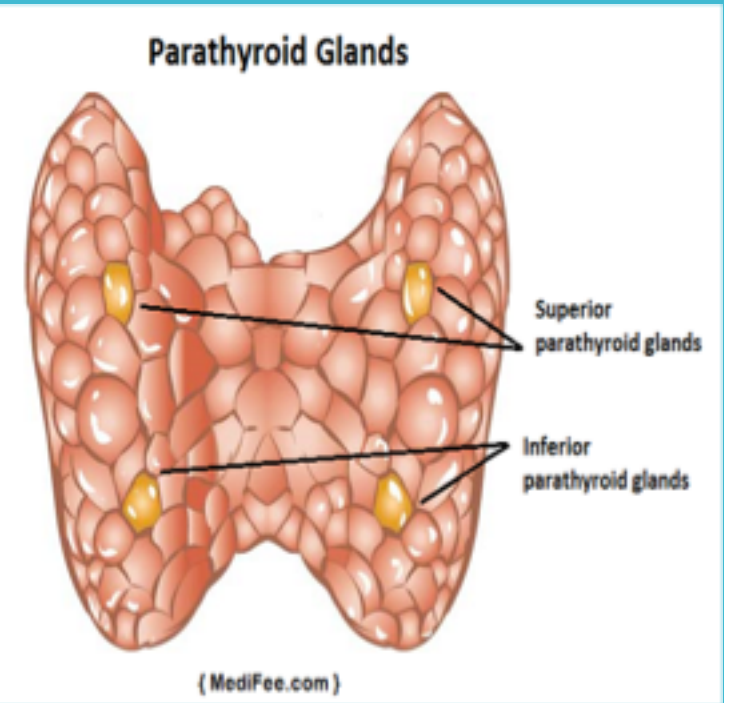
2. Parathyroid diseases

Parathyroid



- function of parathyroid hormone (PTH) is to maintain extracellular fluid calcium concentration.
- This hormone acts directly on bone and kidney and indirectly on small intestine through its effects on synthesis of vitamin D (1,25[OH2]-D) to increase serum calcium.
- Calcitonin is a potent parathyroid hormone that acts as a physiological parathyroid hormone antagonist.
- Fetal calcium needs—300 mg/day in late pregnancy and a total of 30 g —as well as increased renal calcium loss from augmented glomerular filtration, substantively increase maternal calcium demands.
- Pregnancy is associated with a twofold rise in serum concentrations of 1,25-dihydroxyvitamin D, which increases gastrointestinal calcium absorption.

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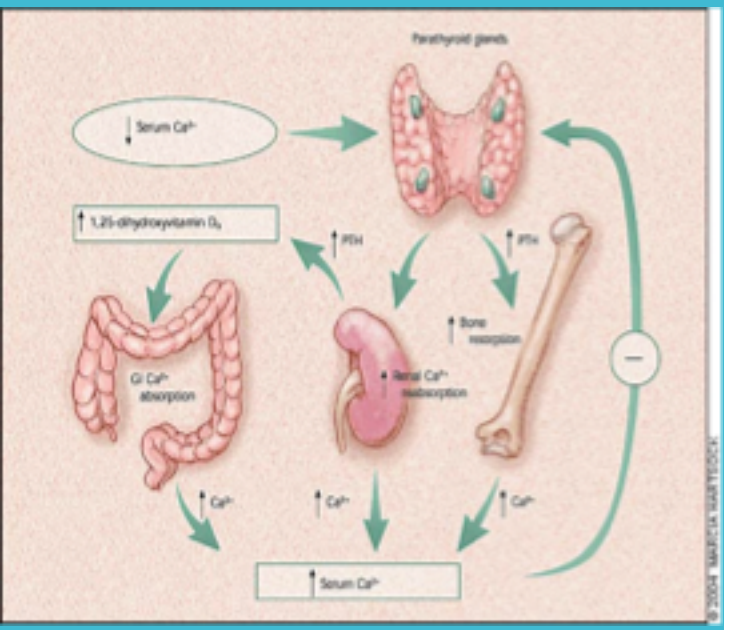
Hyperparathyroidism



- Hypercalcemia is caused by hyperparathyroidism or cancer in 90 percent of cases.
- Primary hyperparathyroidism is reported most often in women older than 50
- Hypercalcemic crisis manifests as stupor, nausea, vomiting, weakness, fatigue, and dehydration.
- All women with symptomatic hyperparathyroidism should be surgically treated.
- Indications for parathyroidectomy include a serum calcium level 1.0 mg/dL above the upper normal range, a calculated creatinine clearance less than 60 mL/min, reduced bone density, or age < 50 years.
- those not meeting these criteria should undergo annual calcium and creatinine level measurement and bone density assessment every 1 to 2 years

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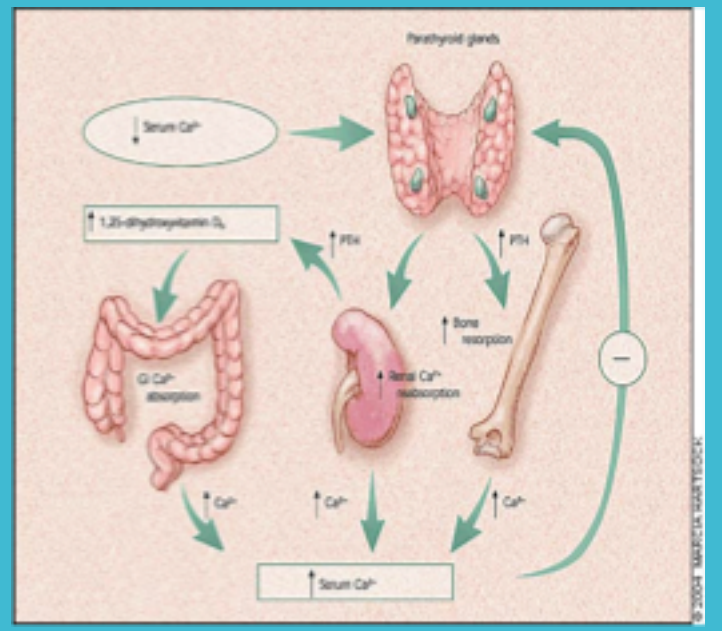
Hyperparathyroidism in Pregnancy



- As in nonpregnant patients, hyperparathyroidism is usually caused by a parathyroid adenoma.
- Symptoms include hyperemesis, generalized weakness, renal calculi, and psychiatric disorders. Occasionally, pancreatitis is the presenting finding
- Pregnancy theoretically improves hyperparathyroidism because of significant calcium shunting to the fetus and augmented renal excretion
- When the "protective effects" of pregnancy are withdrawn, however, there is significant danger of postpartum hypercalcemic crisis.
  - this life- threatening complication can be seen with serum calcium levels greater than 14 mg/dL and is characterized by nausea, vomiting, tremors, dehydration, and mental status changes

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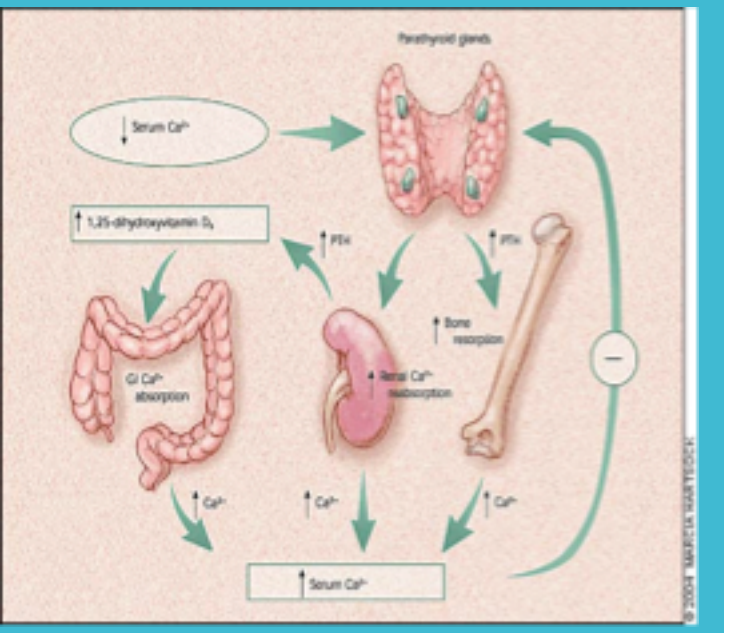
Hyperparathyroidism in Pregnancy



- Management in Pregnancy.
  - *Surgical removal* of a symptomatic parathyroid adenoma is preferable.
  - Elective neck exploration during pregnancy is usually well tolerated, even in the third trimester
- Medical management may be appropriate in asymptomatic pregnant women with mild hypercalcemia → patients are carefully monitored in the postpartum period for hypercalcemic crisis
- Initial medical management might include *calcitonin* to decrease skeletal calcium release, or *oral phosphate*, 1 - 1.5 g/day in divided doses to bind excess calcium.
- For women with dangerously elevated serum calcium levels or those who are mentally obtunded with hypercalcemic crisis, emergency treatment is instituted:
  - *Diuresis with intravenous normal saline* is begun so that urine flow exceeds 150 mL/hr.
  - *Furosemide* is given in conventional doses to block tubular calcium reabsorption.
  - hypokalemia and hypomagnesemia should be prevented. Adjunctive therapy includes *mithramycin*, which inhibits bone resorption.

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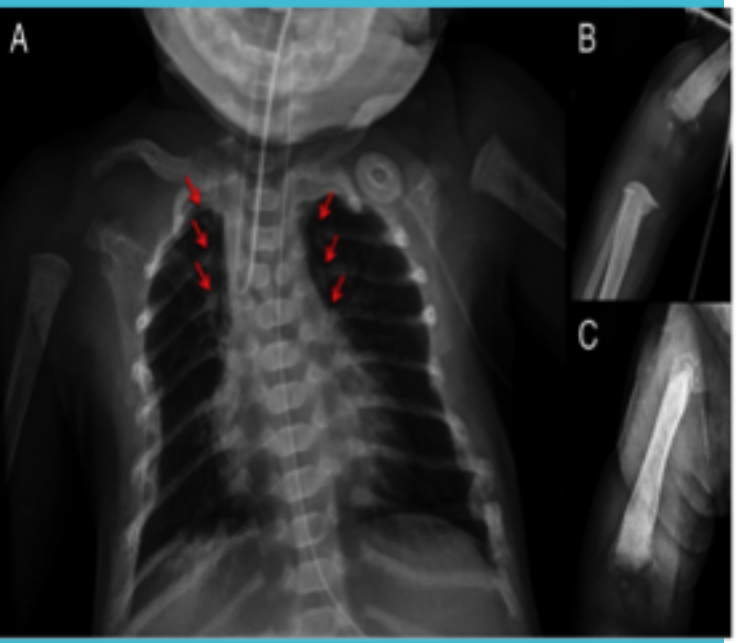
Neonatal Effects



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- With maternal hyperparathyroidism, abnormally elevated maternal and fetal levels further suppress fetal parathyroid function.
- Because of this, after birth, there is a rapidly decreasing newborn calcium level, and 15 - 25%of these infants develop severe hypocalcemia with or without tetany
- Neonatal hypoparathyroidism caused by maternal hyperparathyroidism is usually transient and should be treated with calcium and calcitriol.
- Calcitriol will not be effective in preterm infants, however, because the intestinal vitamin D receptor is not sufficiently expressed
- Neonatal tetany or seizures should stimulate an evaluation for maternal hyperparathyroidism

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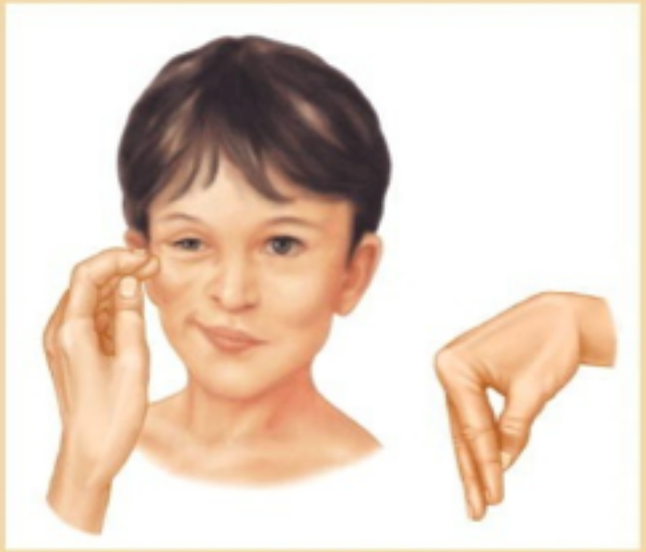
Hypoparathyroidism

Positive Chvostek and Trousseau tests are associated with hypocalcemia.
- Chvostek sign: contraction of ipsilateral facial muscles when the facial nerve is tapped just in front of the ear.
- Trousseau sign: carpopedal spasm elicited by inflating a sphygmomanometer above systolic BP for 3 minutes.



Porth CM. *Essentials of Pathophysiology*. 3d ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011:188.

- the most common cause of hypocalcemia is hypoparathyroidism that usually follows parathyroid or thyroid surgery.
- Hypoparathyroidism is estimated to follow up to 7 percent of total thyroidectomies
- It is rare and characterized by facial muscle spasms, muscle cramps, and paresthesias of the lips, tongue, fingers, and feet.
- this can progress to tetany and seizures.
- Chronically, hypocalcemic pregnant women may also have a fetus with skeletal demineralization resulting in multiple bone fractures in the neonatal period
- Maternal treatment includes 1,25-dihydroxyvitamin D3 (calcitriol), dihydrotachysterol, or large vitamin D doses of 50,000 to 150,000 U/day; calcium gluconate or calcium lactate in doses of 3 to 5 g/day; and a low-phosphate diet.
- the therapeutic challenge in women with known hypoparathyroidism is management of blood calcium levels.
  - the goal during pregnancy is maintenance of the corrected calcium level in the low normal range.
  - carefully monitor the corrected serum calcium on a frequent, perhaps monthly, basis throughout pregnancy

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Pregnancy-Associated Osteoporosis

- Women who breastfed, carried twin pregnancies, or had a low body mass index (BMI) were at higher risk of bone loss.
- Lactation represents a period of negative calcium balance that is corrected through maternal skeletal resorption.
- the most common symptom of osteoporosis is back pain in late pregnancy or postpartum. Other symptoms are hip pain, either unilateral or bilateral, and difficulty in weight bearing until nearly immobilized
- In more than half of women, no apparent reason for osteopenia is found. Some known causes include heparin, prolonged bed rest, and corticosteroid therapy
- Treatment includes calcium and vitamin D supplementation as well as standard pain management.
- Women and their offspring may have chronic osteopenia

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

3. Adrenal Gland disorders

Pheochromocytoma

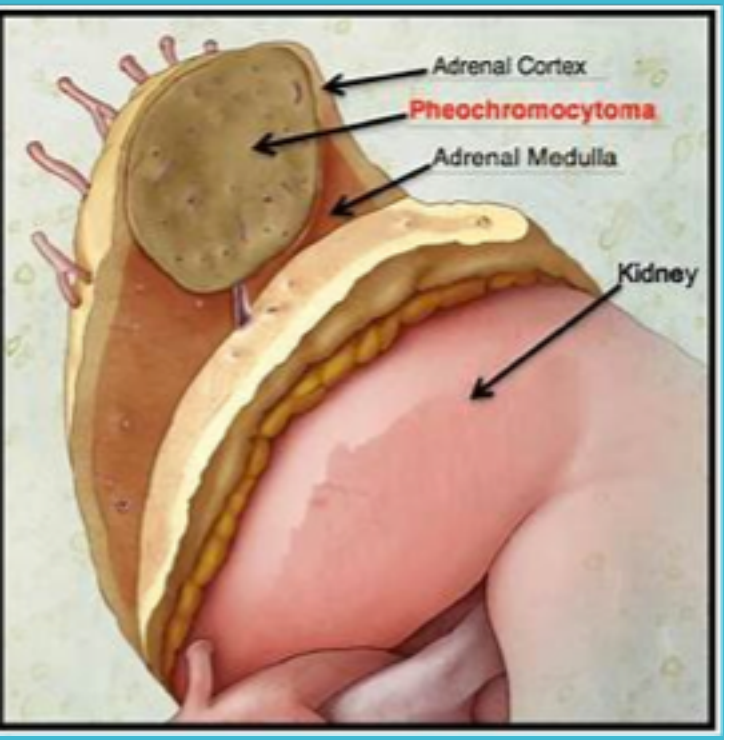


Photo credit: www.medical-institution.com

- these tumors are rare; found in 0.1 percent of hypertensive patients
- chromaffin tumors that secrete catecholamines and usually are located in the adrenal medulla, although 10 percent are located in sympathetic ganglia.
- they are called the "10-percent tumor" because approximately *10 percent are bilateral, 10 percent are extraadrenal, and 10 percent are malignant*.
- can be associated with medullary thyroid carcinoma and hyperparathyroidism
- Symptoms: hypertensive crisis, seizure disorders, or anxiety attacks; Other symptoms during paroxysmal attacks are headaches, profuse sweating, palpitations, chest pain, nausea and vomiting, and pallor or flushing.
- the standard screening test is quantification of catecholamine metabolites in a 24-hour urine specimen
- Diagnosis: measurement of a 24-hour urine collection with at least two of three assays for free catecholamines, metanephrines, or vanillylmandelic acid (VMA).
- For most cases, preferred treatment is laparoscopic adrenalectomy

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Pheochromocytoma Complicating Pregnancy

- Diagnosis of pheochromocytoma in pregnancy is similar to that for nonpregnant patients.
- MR imaging is the preferred imaging technique because it almost always locates adrenal and extraadrenal pheochromocytomas
- the principal challenge is to differentiate preeclampsia from the hypertensive crisis caused by pheochromocytoma.
- Management
  - Immediate control of hypertension and symptoms with an α-adrenergic blocker such as phenoxybenzamine: dose is 10 to 30 mg, two to four times daily.
  - After α-blockade is achieved, β-blockers may be given for tachycardia.
  - In many cases, surgical exploration and tumor removal are performed during pregnancy, preferably during the second trimester
  - laparoscopic removal of adrenal tumors has become the norm
  - If diagnosed later in pregnancy, either planned cesarean delivery with tumor excision or postpartum resection is appropriate.

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Cushing Syndrome

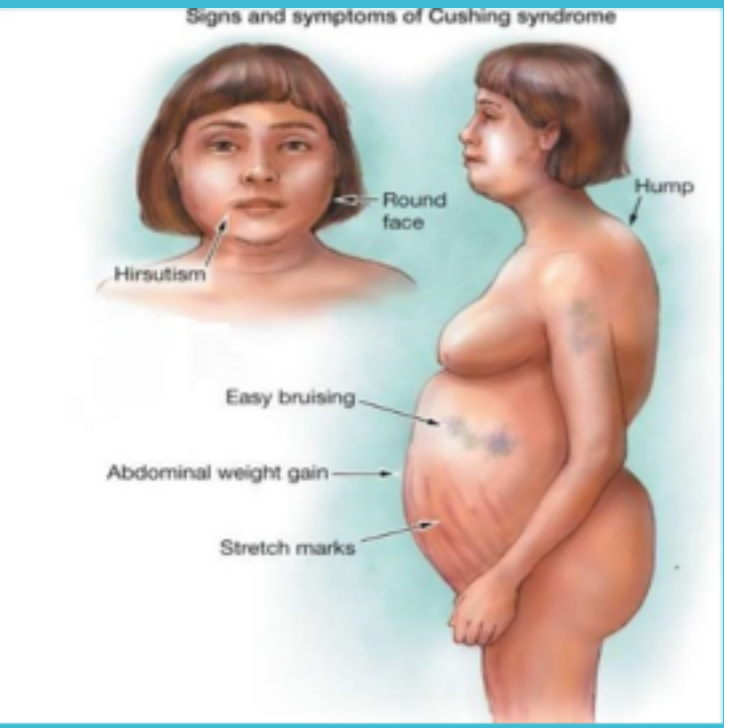


Photo credit: http://diseasespictures.com

- Most cases are iatrogenic from long-term corticosteroid treatment.
- endogenous Cushing syndrome is typically due to Cushing disease, which is bilateral adrenal hyperplasia stimulated by corticotropin-producing pituitary adenomas → most are small microadenomas < 1 cm, and half measure ≤ 5 mm
- abnormal secretion of hypothalamic corticotropin-releasing factor may cause corticotropic hyperplasia → Such hyperplasia may also be caused by nonendocrine tumors that produce polypeptides similar to either corticotropin-releasing factor or corticotropin
- typical cushingoid body habitus is caused by adipose tissue deposition that characteristically results in moon facies, a buffalo hump, and truncal obesity.
- Fatigability and weakness, hypertension, hirsutism, and amenorrhea
- Personality changes, easy bruisability, and cutaneous striae are common.
- Diagnosis: elevated plasma cortisol levels that cannot be suppressed by dexamethasone or by elevated 24-hour urine free cortisol excretion
  - CT and MR imaging are used to localize pituitary and adrenal tumors or hyperplasia.

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Cushing Syndrome and Pregnancy

- **Pregnancy is rare** (because Cushing Syndrome usually cause anovulation)
- difficult to diagnosis during pregnancy (because of pregnancy-induced increases in plasma cortisol, corticotropin, and CRF levels)
- Measurement of 24-hour urinary free cortisol excretion is recommended
- Heart failure is common during pregnancy and is a major cause of maternal mortality
- Hypercortisolism in pregnancy may also cause poor wound healing, osteoporotic fracture, and psychiatric complications
- definitive therapy is resection of the pituitary or adrenal adenoma or bilateral adrenalectomy for hyperplasia
- Metyrapone may be given as an interim treatment until definitive surgery after delivery, however, treatment during pregnancy with a male fetus is worrisome (because this drug also blocks testicular steroidogenesis)
- Mifepristone, the norethindrone derivative used for abortion and labor induction, has shown promise for treating Cushing disease but should not be used in pregnancy

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Adrenal Insufficiency—Addison Disease

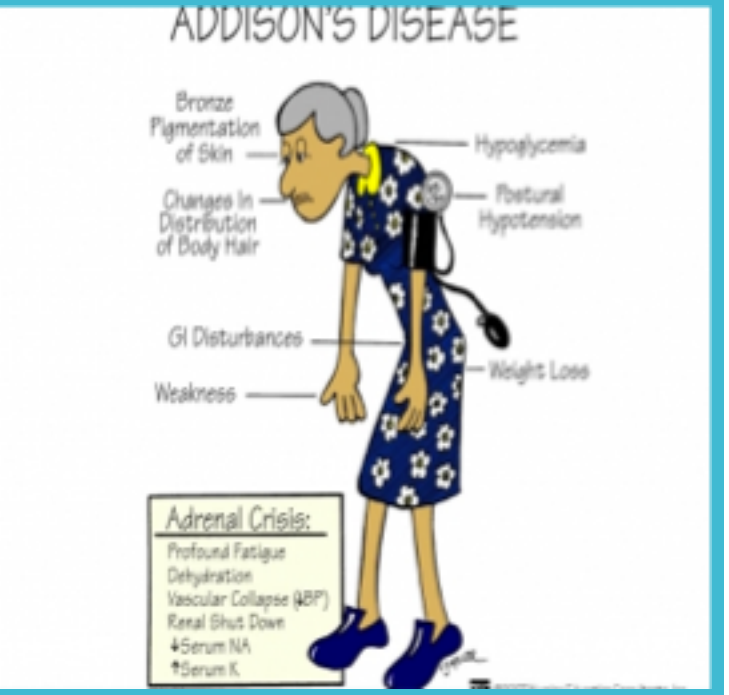


photo credit: http://dxline.info

- Primary adrenocortical insufficiency is rare because more than 90 percent of total gland volume must be destroyed for symptoms to develop.
- Autoimmune adrenalitis is the most common cause in the developed world, but tuberculosis is a more frequent etiology in resource-poor countries
- increased incidence of concurrent Hashimoto thyroiditis, premature ovarian failure, type 1 diabetes, and Graves disease → these polyglandular autoimmune syndromes also include pernicious anemia, vitiligo, alopecia, nontropical sprue, and myasthenia gravis.
- Untreated adrenal hypofunction frequently causes infertility, but with replacement therapy, ovulation is restored.
- If untreated, symptoms often include weakness, fatigue, nausea and vomiting, and weight loss
- Because serum cortisol levels are increased during pregnancy, the finding of a low value should prompt an adrenocorticotropic hormone (ACTH) stimulation test to document the lack of response to infused corticotropin

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

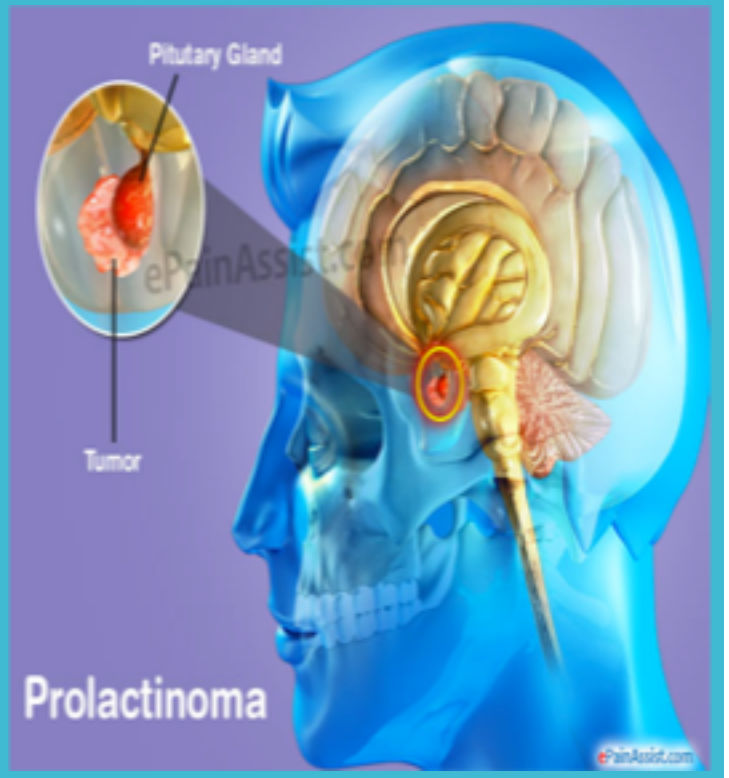
Primary Aldosteronism

- May be due to adrenal aldosteronoma (75 percent of cases) or idiopathic bilateral adrenal hyperplasia and adrenal carcinoma
- Findings include hypertension, hypokalemia, and muscle weakness.
- Diagnosis: High serum or urine levels of aldosterone
- Since renin levels are suppressed in pregnant women with hyperaldosteronism, a plasma aldosterone-to-renin activity ratio may be helpful for diagnosis
- Medical management includes potassium supplementation and antihypertensive therapy. I
  - hypertension responds to spironolactone
  - β-blockers or calcium-channel blockers may be preferred because of the potential fetal antiandrogenic effects of spironolactone.
  - amiloride
  - Eplerenone (mineralocorticoid receptor antagonist
- Tumor resection is curative, and laparoscopic adrenalectomy has been shown to be safe

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

4. PITUITARY DISORDERS

Prolactinomas



- Adenoma symptoms and findings include amenorrhea, galactorrhea, and hyperprolactinemia.
- Tumors are classified arbitrarily by their size measured by CT or MR imaging:
  - microadenoma is ≤ 10 mm, and a macroadenoma is > 10 mm.
  - Treatment for microadenomas is usually with bromocriptine
  - For suprasellar macroadenomas, most recommend surgical resection before pregnancy is attempted
- 15 to 35 percent of suprasellar macroadenomas have tumor enlargement that causes visual disturbances, headaches, and diabetes insipidus.
- pregnant women with microadenomas should be monitored for headaches and visual symptoms.
  - those with macroadenomas should be followed more closely and have visual field testing during each trimester.
  - CT or MR imaging is recommended only if symptoms develop.
  - Serial serum prolactin levels not recommended
  - Symptomatic tumor enlargement should be treated immediately with a dopamine antagonist such as bromocriptine or cabergoline.

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Acromegaly

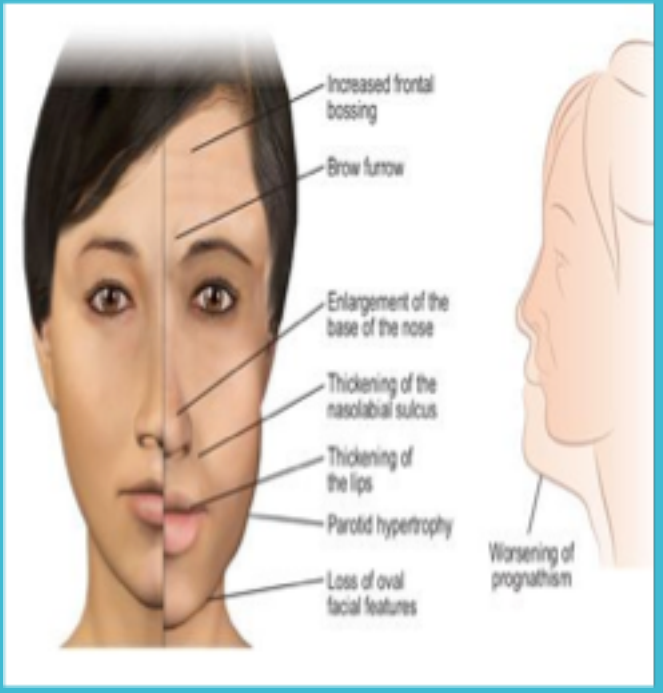


Photo credit: www.pinterest.com

- caused by excessive growth hormone, usually from an acidophilic or a chromophobic pituitary adenoma.
- In normal pregnancy, pituitary growth hormone levels decrease as placental epitopes are secreted.
- Diagnosis: failure of an oral glucose tolerance test to suppress pituitary growth hormone
- Pregnancy is probably rare in women with acromegaly, because most are hyperprolactinemic and anovulatory.
- For those pregnant: increased risk for gestational diabetes and hypertension.
- Management is similar to that for prolactinomas, with close monitoring for symptoms of tumor enlargement.
  - Dopamine agonist therapy is not as effective as it is for prolactinomas.
  - transsphenoidal resection may be necessary for symptomatic tumor enlargement during pregnancy

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Diabetes Insipidus

- the vasopressin deficiency evident in diabetes insipidus is usually due to a hypothalamic or pituitary stalk disorder rather than to a pituitary lesion
- True diabetes insipidus is a rare complication of pregnancy.
- Management: intranasal administration of a synthetic analogue of vasopressin, desmopressin
- transient secondary diabetes insipidus is more likely encountered with acute fatty liver of pregnancy → probably is due to altered vasopressinase clearance because of hepatic dysfunction.

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Sheehan Syndrome

- pituitary ischemia and necrosis associated with obstetrical blood loss could result in hypopituitarism.
- Affected women may have persistent hypotension, tachycardia, hypoglycemia, and lactation failure.
- Because adrenal insufficiency is the most life-threatening complication, adrenal function should be immediately assessed in any woman suspected of having Sheehan syndrome.
- After glucocorticoid replacement, subsequent analyses and replacement of thyroid, gonadal, and growth hormones should be considered

- Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS (eds).William's Obstetrics 24th edition; 2014; chapter 58 Endocrine Disorders in Pregnancy

Lymphocytic Hypophysitis

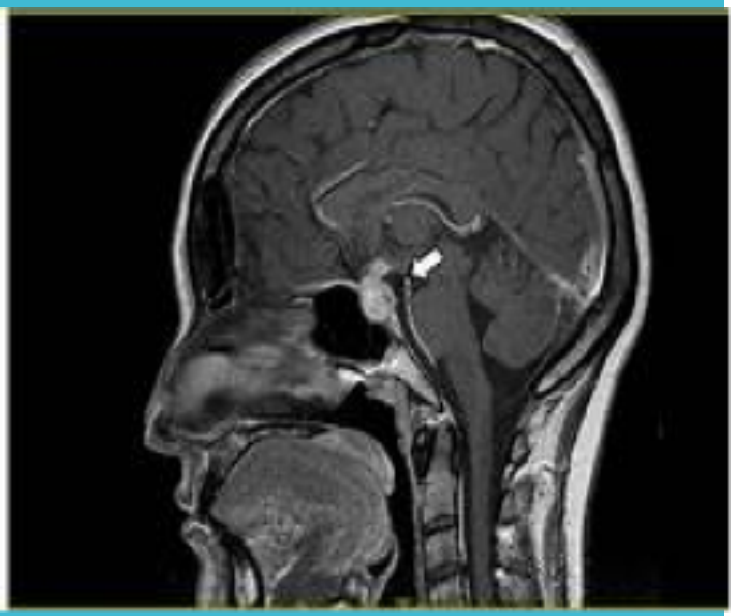

Photo credit: scirp.org

- autoimmune pituitary disorder characterized by massive infiltration by lymphocytes and plasma cells with parenchymal destruction of the gland.
- Most cases are temporally linked to pregnancy
- symptoms of mass effect, including headaches and visual field defects.
- A sellar mass is seen with CT or MR imaging.
- A mass accompanied by a modestly elevated serum prolactin level—usually < 100 pg/mL—suggests lymphocytic hypophysitis.
- levels > 200 pg/mL are encountered with a prolactinoma.
- etiology is unknown, but nearly 30 percent have a history of coexisting autoimmune diseases including Hashimoto thyroiditis, Addison disease, type 1 diabetes, and pernicious anemia.
- Treatment is with hormone replacement
- Surgery during pregnancy is warranted only in cases of severe chiasmal compression unresponsive to corticosteroid therapy

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Thank you!

youtube channel: Ina Irabon

www.wordpress.com: Doc Ina OB Gyne