Medical Complications of Pregnancy

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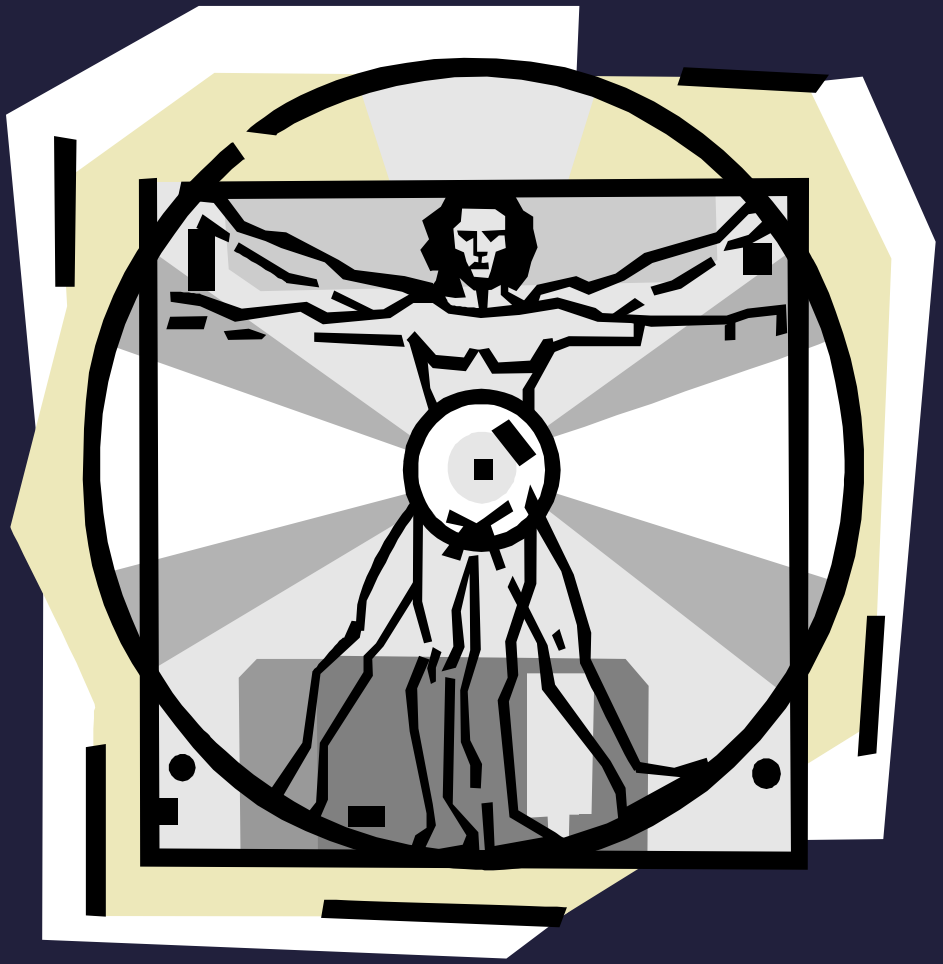
Objectives

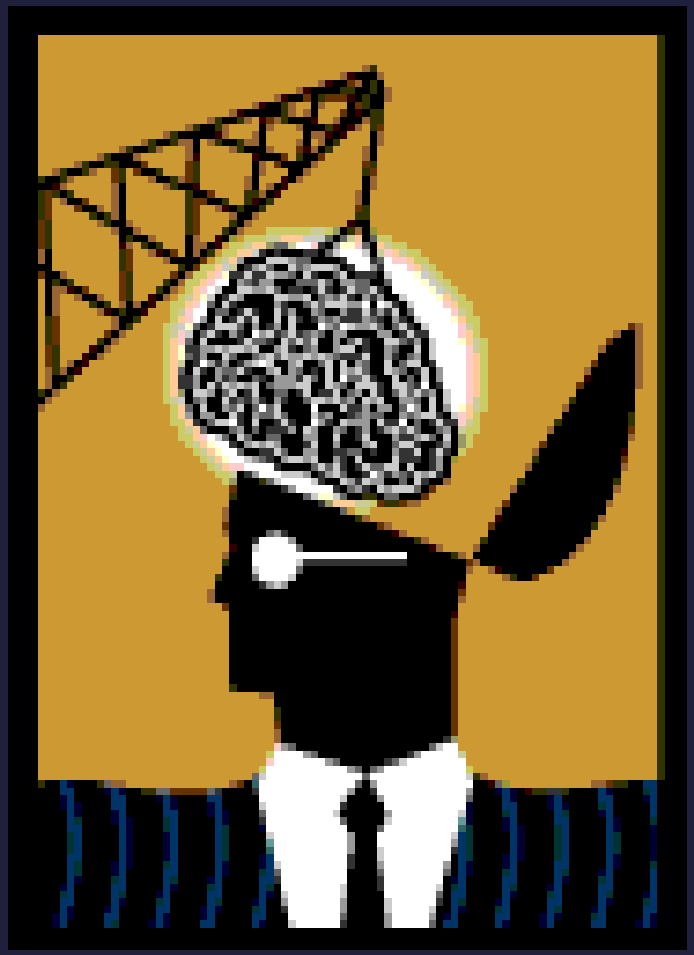
- Discuss commonly seen medical problems during pregnancy
- Understand clinical significance toward the maternal and fetal effects of each medical condition

- Systems approach
  - Neurologic
  - Cardiac
  - Pulmonary
  - Endocrine
  - Gastointestinal
  - Renal
  - Autoimmune
  - Hematologic
  - Musculoskeletal
  - Skin



Neurologic

- Seizure disorders
- Cerebrovascular Disorders
- Migraines



Seizure Disorder

- One of the most common neurologic disorders encountered in pregnancy
- Occurs in 1% of general population
- 1 in 200 pregnancies
- Pathology: Disorganized firing of neural cells
- Medications (known for teratogenic potential 4-6%, additive if more than one medication)
  - Phenytoin (Dilantin)
  - Tegretol (Carbamazepine)
  - Depakote (Valproic Acid)
  - Trimethadione

- Fetal hydantoin syndrome
  - Prenatal and postnatal growth restriction
  - Microcephaly
  - Dysmorphic facies
  - Mental deficiency
  - Limb defects

Seizure Disorder

- Effects of Pregnancy
  - Worsens 45% (compliance w/ meds)
    - Anticonvulsants pharmacokinetics
      - Decreased drug concentration due to increased clearance secondary to decreased volume of distribution
    - Decreased compliance
      - nausea/vomiting
      - fear of harm to fetus
    - Sleep deprivation
  - Improves 5%
  - No change 50%

Seizure Disorder

- Effects on Pregnancy
  - Increased risk of congenital anomalies (regardless if on or off meds)
    - Cleft lip or palate
    - Congenital heart defects
    - Neural tube defects
  - Children of Epileptic Patients
    - Increased risk of neonatal death
    - Decreased IQ
    - Abnormal EEG patterns
    - Early onset neonatal hemorrhagic disease (low Vit K)
  - Trauma from seizure $\rightarrow$ Placental Abruption, Fetal tracing abnormalities, Fetal death
  - Increased risk of vaginal bleeding & toxemia

Seizure Disorder Management

- Preconceptional counseling ideal
  - Optimization of medications
    - Stop meds after 4-5 years seizure free
    - One better than multiple
    - Medication better than none
  - Folic Acid supplementation
- During pregnancy
  - Maintain same as non-pregnant state
  - Do not change meds
  - Adjust doses as needed for control and assess levels
  - Increase dose as pregnancy progresses
- Congenital anomalies
  - 1st trimester Ultrasound and Complete anatomical survey
  - Vit K supplementation after 36wks
  - MSAFP (85% sensitivity)

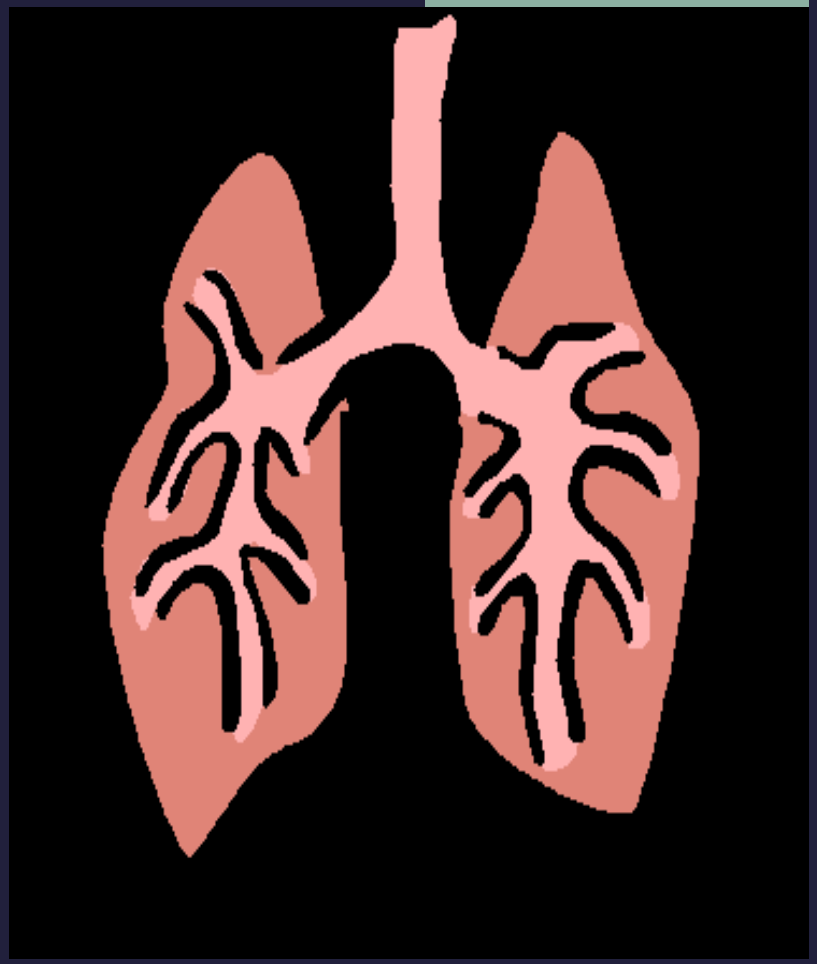
Cardiac

- Chronic Hypertension
- Heart Disease
  - Heart failure, Arrhythmias, MI
- Valvular disease
  - MS (SLE, rheumatic)
  - MVP
  - MR/TR
  - AS
- Congenital malformations
- Peripartum Cardiomyopathy

Pulmonary

- Asthma

- Pneumonia
- Tuberculosis
- Autoimmune
  - Sarcoid



Asthma

- Most common respiratory disease in pregnancy, Most common medical illness complicating pregnancy
- Affects 4-9% of women in reproductive age
- Clinical syndrome: Varying degrees of airway obstruction and hyperactive airways as a response to eosinophilic and lymphocytic inflammation
- Asthma triggers: seasonal allergies, infections, emotional state
- National Asthma Education Program (NAEP) for management of asthma & pregnancy

Asthma

- Effects of Pregnancy: Rules of 1/3
  - 1/3 improve
  - 1/3 stay the same
  - 1/3 worsens
- Effects on Pregnancy
  - Increased risk of premature delivery
  - Increased risk of IUGR
  - Increased risk for PIH (2.5 fold increase)
  - 2X’s increase perinatal morbidity

Asthma Management

- Should treat patients the same as if not pregnant
- **GOAL**: Control asthma, prevent status asthmaticus, avoid irritants
- Follow symptoms, lung exams, PFTs
- Influenza vaccination, treating rhinitis/sinusitis
- Assess fetal well-being (fetal hypoxemia)
  - Fetal monitoring depending on severity
- BID Peak Flows (Moderate and severe)
  - Normal 380-550 L/min
  - 80% baseline or personal best
- Delivery based upon obstetric reasons

Classification

	Mild Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent
Daytime Sx	≤ 2x week	> 2x week, not daily	daily	continually
Nocturnal	≤ 2x month	> 2x month	> 1x week	frequent
PEF or (FEV_1)	> 80% normal, with <20% variability	At least 80% normal, variability b/n 20-30%	< 80% but > 60%, with 30% variability	< 60%, > 30% variability
Meds	Do not need daily meds Short term ß2 agonist (Albuterol)	Low dose inhaled corticosteroid (Pulmicort, Vanceril)	Combo low or med dose inhaled corticosteroid & long acting ß2 agonist	high dose inhaled corticosteroid & long acting ß2 agonist, systemic corticosteroid if needed

Asthma Management - Acute

- Symptoms: dyspnea, cough, wheezing, chest tightness
- **GOAL**: maternal P02 > 70mm Hg, 02 sat > 90% to ensure adequate fetal oxygenation
- 02 by nasal canula or mask
  - Intubation, mechanical ventilation if necessary
  - ABGs, CXR
- Inhaled ß2 agonist, IV systemic corticosteroids (methylprednisolone)
  - Switch to oral corticosteroids with improvement
- Do not deliver emergently, stabilize mother first

Asthma in Labor

- Stress dose steroids: Hydrocortisone 100 mg IV q 8 hours (steroids taken for > 2 weeks within the previous year)
- Asthma attacks during labor: Rare
- Anesthesia
  - Non-histamine releasing narcotic (i.e. fentanyl over meperidine or morphine)
  - Epidural preferred
- Post-partum hemorrhage
  - F2α (hemabate) contra-indicated
  - Associated with bronchospasm

Endocrine

- Diabetes
- Thyroid
  - Adrenal Insufficiency
  - Cushings
  - CAH
  - Pheochromocytoma
  - Pituitary Disorders

Diabetes during pregnancy

- One of most common medical problem seen in OB
- Pre-gestational Diabetes
  - White Classification
  - Increased risk for end-organ damage
- Gestational Diabetes
  - Affects 3-5% of gravidas
  - Accounts for 90% of diabetic pregnancies
  - Defined as carbohydrate intolerance with its initial onset or recognition during pregnancy
  - > 50% develop overt diabetes later in life

White Classification

Class	Onset	Duration	Vascular Disease
A	Any	Any	None
B	> 20 yrs	< 10 yrs	None
C	10-19 yrs	10-19 yrs	None
D	≤ 10 yrs	> 20 yrs	Benign Retinopathy
F	Any	Any	Nephropathy
R	Any	Any	Proliferative Retinopathy
H	Any	Any	Heart Disease
RT	Any	Any	Renal Transplant

Priscilla White, M.D. (March 17, 1900 – December 16, 1989) was a pioneer in the treatment of diabetes in pregnancy and type 1 diabetes.

Diabetes-Related Pregnancy Complications

	Non-diabetic %	Diabetic (GDM) %
Pre-eclampsia	8	12
Stillbirth	5.7	10.4 (4.7)
Neonatal mortality	4.7	12.2 (3.3)
Macrosomia	10	25-42
Shoulder Dystocia	5-7	31
Anomalies	2-3	7-9

Maternal-Fetal Medicine 1999;4th Ed: 964-995.

Diabetic Embryopathy

- Incidence 6-10% (vs 3% in general pop)
  - Related to HbA1c

Anomaly	Risk Ratio	Percent Risk
Cardiac Defects	18x	8.5%
VSD		
Transposition of great vessels		
Hypoplastic left heart		
CNS Anomalies	16x	5.3%
Anencephaly	13x	
Spina Bifida	20x	
Holoprosencephaly		
Caudal Regression		
All Anomalies	8x	18.4%

Diabetic Embryopathy

Initial Maternal HbA1c	Major congenital Malformations (%)
≤ 7.9	3.2
8.9 - 9.9	8.1
≥ 10	23.5

Screening for Gestational Diabetes

- Screening Criteria
  - 1 hour glucola with 50-gm load
  - 140 mg/dl: 10-15% need 3 hour, 80% sensitivity
  - 135 mg/dl: 20-25% need 3 hour, 98% sensitivity
- High risk population
  - Obesity
  - Personal history of GDM
  - FMHx of Diabetes
  - Prior macrosomic infant
  - High ethnic prevalence

Diagnosis: 3 hr GTT

100-gm load

National Diabetes		Carpenter/Coustan	
Fasting	105 mg/dl	Fasting	95 mg/dl
1 hour	190 mg/dl	1 hour	180 mg/dl
2 hour	165 mg/dl	2 hour	155 mg/dl
3 hour	145 mg/dl	3 hour	140 mg/dl

TESTING CONDITIONS:

- Overnight fast of 8-14 hours
- Unrestricted diet: ≥150-gm of carbohydrates X 3 days
- Seated, not smoking during test

Goals for Treatment

- Maintain euglycemia:
  - FBS < 95 mg/dL, 2hr PP < 120 mg/dL or 1hr PP <140 mg/dL
  - HBA1c $\leq$ 6.0
  - TX: Diet and Exercise
    Insulin
- Minimize fetal effects
- Prevent associated pregnancy complications
- Prevention of DKA
- Prevent long-term complications
  - Childhood obesity
  - Diabetes
  - Cardiovascular disease

Detection of Malformation

- 1st trimester HBA1c
- 1st trimester Screen with MSAFP at 16 weeks or Quad Screen at 16 weeks
- Ultrasound at 13-14 weeks to detect obvious anomalies (i.e. anencephaly)
- Comprehensive anatomic survey 18-20 weeks
- Fetal echocardiogram 20 weeks (if necessary)

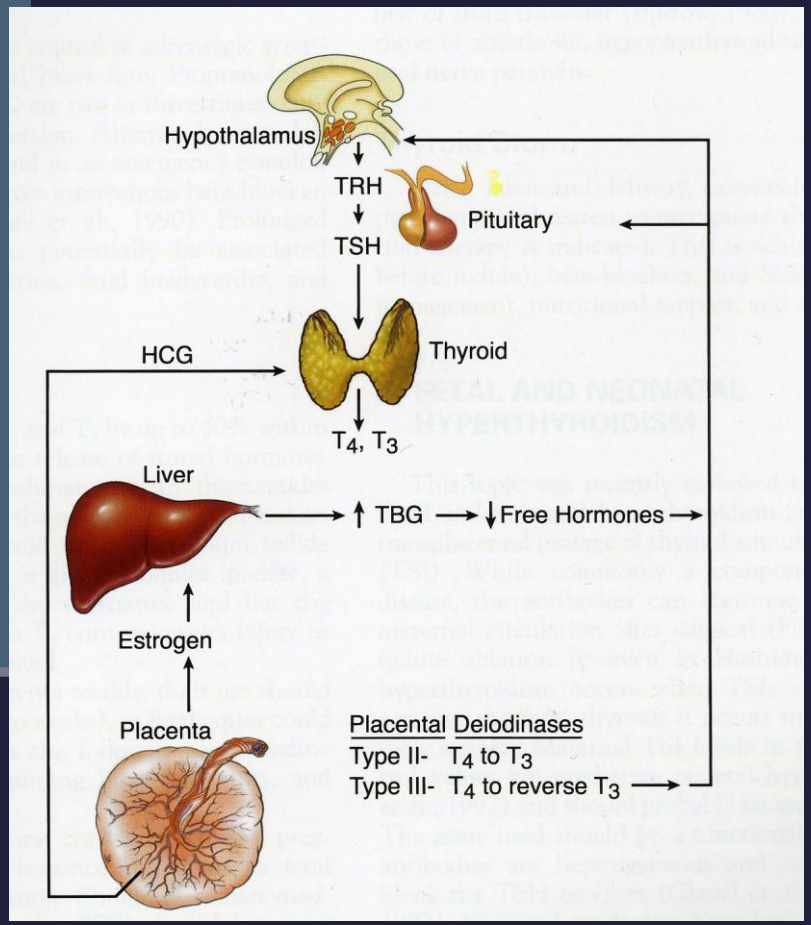
Delivery

- White Class A2-R or Type I or II: Between 38-40 weeks
  - Good dating & Document fetal lung maturity
  - IOL if not in labor by 39 weeks (up to 40 weeks if cervix not favorable)
  - Maintain euglycemia during labor
    - May need insulin gtt
- GDMA1: Can go to 41 weeks
- DKA: stabilize mother, finding inciting factor, do not deliver emergently
- Cesarean Section
  - Macrosomia, with EFW ≥4500
  - History of shoulder dystocia

Thyroid

- Effects of Pregnancy
  - Second most common endocrine disorder
  - hCG has TSH-like properties so that there is Moderate thyroid enlargement
    - Glandular hyperplasia
    - Increased vascularity
  - Increased uptake of radioiodine by maternal thyroid
  - Rise in total serum thyroxine and triiodothyronine
  - Increase in TBG (thyroid binding globulin (estrogen effect)
  - However, free T_4 and T_3 are WNL $\rightarrow$ nl TSH $\rightarrow$ no overt hyperthyroidism

Physiologic Adaptation to Pregnancy



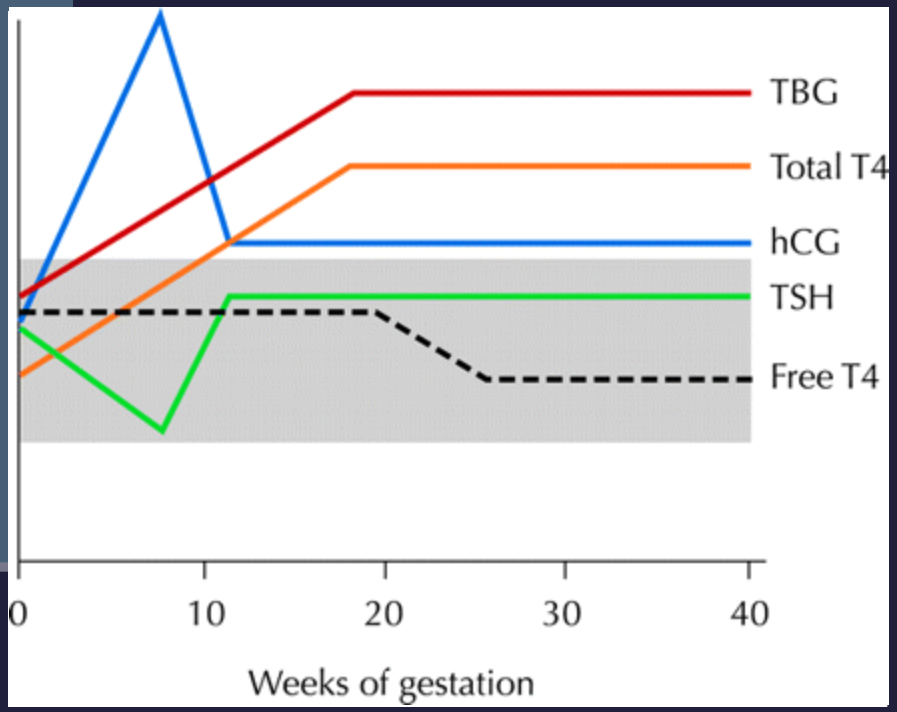
First Trimester

- Estrogen:
  - Increases production of TBG by the liver
  - Extends the half life of TBG
  - Results in 2.5 fold increase in TBG early in pregnancy
- HCG
  - Shares some structural properties with TSH
  - Binds to same receptor as TSH
  - Direct stimulation of the thyroid
- Net effect:
  - Increased total pool of thyroid hormone
  - free hormone, unchanged
  - Suppressed TSH

Second Trimester

↓HCG, TSH normalized

Relative Changes in Maternal Thyroid Function During Pregnancy



1st trimester

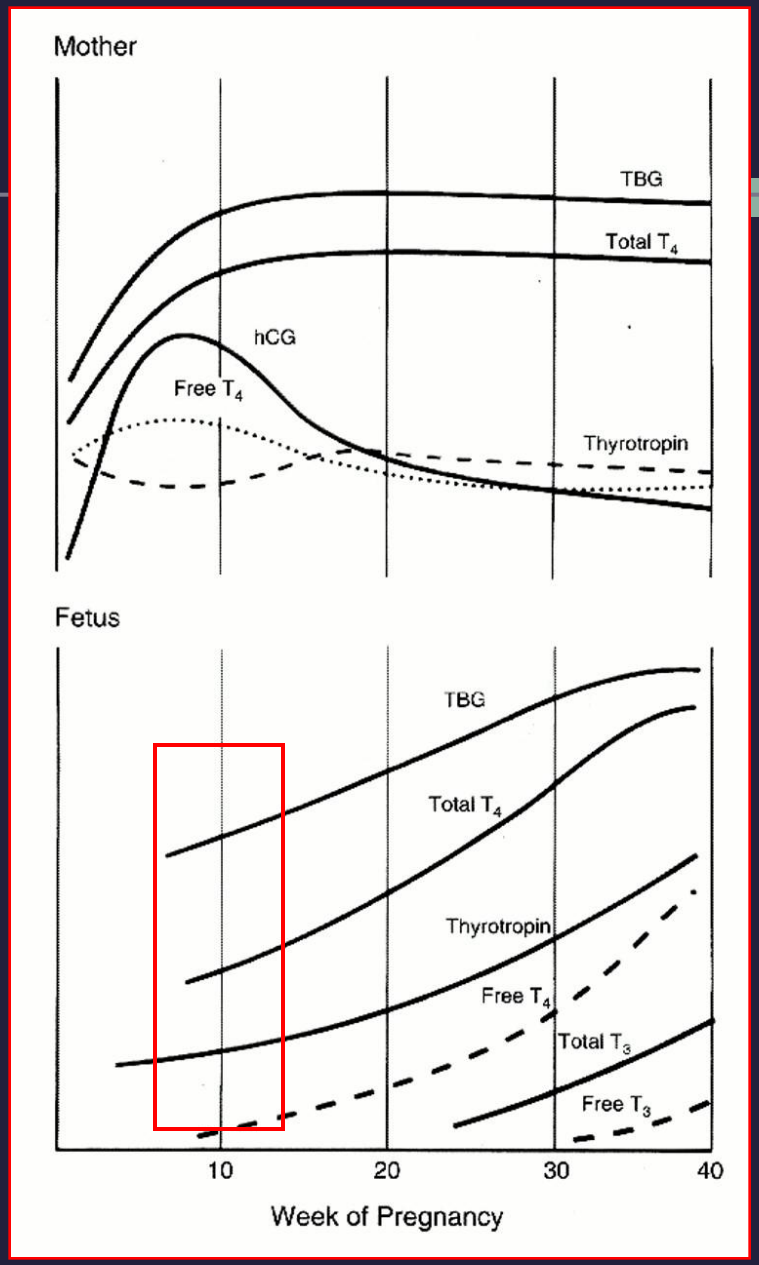
- Increase in all values
- Free hormones peak
- TSH slight decrease

2nd and 3rd trimester

- TBG remains elevated
- Total thyroid hormone remains elevated
- TSH normal

Modified from Brent GA. Maternal thyroid function: interpretation of thyroid function tests in pregnancy. Clin Obstet Gynecol 1997;40:3–15.

- Fetal hypothalamic-pituitary-thyroid axis becomes functional toward end of first trimester
  - Dependent on transferred maternal T4 to T3
  - Important for fetal growth, particularly early brain development



Laboratory Evaluation of Thyroid Function During Pregnancy

- TSH and free T_4 are the best ways to evaluate thyroid function in pregnancy

Hyperthyroidism related to hCG

- The stimulation of thyroid hormone production by hCG can suppress the TSH to low or suppressed values in up to 20% of normal pregnancies.
- hCg levels peak at 6-12 weeks and decline to a plateau by 20 weeks

Gestational Transient Thyrotoxicosis (GTT)

- Occurs in the first trimester in women without a personal or family history of thyroid disease
- Overall prevalence of 2.4% between the 8th and 14th week of gestation
- Results directly from hCG stimulation of the thyroid
- Transient, parallels the decline in hCG, does not require treatment
- Rarely symptomatic and treatment with ATD not beneficial
- Not associated with poor outcomes

Hyperemesis Gravidarum

- Biochemical hyperthyroidism found in most women with severe disease
- Duration varies 1-10 weeks
- Usually self limited
- Anti thyroid medications do not decrease symptoms

Hyperthyroidism

- 2 per 1000 pregnant women
- Signs & Symptoms
  - Tachycardia > associated with normal pregnancy
  - Widened pulse pressure
  - Thyromegaly
  - Exophthalmia
  - Poor weight gain
  - Heat intolerance
  - Diaphoresis
  - Fatigue
  - Nausea, Vomiting, Diarrhea

Hyperthyroidism

- Diagnosis
  - elevated free T_4, suppressed TSH
  - If borderline: repeat in 3-4 weeks
  - TSI (thyroid stimulating immunoglobulin) – crosses placenta
- Differential Diagnosis
  - Graves' Disease (95%)
  - Hyperemesis Gravidarum
  - Gestational trophobalstic disease
  - Toxic multinodular goiter
  - Toxic nodule or adenoma
  - Subacute thyroiditis
  - Iodine treatment, Amiodarone or Lithium
  - Struma ovarii (hyperfunctioning teratoma)
  - TSH- producing adenoma or hCG-producing tumor
  - Thyroid carcinoma

Hyperthyroidism
Effects on Pregnancy

Factor	Treated and Euthyroid (n=149)	Uncontrolled Thyrotoxicosis (n=90)
Maternal Outcome		
Pre-eclampsia	17 (11%)	15 (17%)
Heart Failure	1	7 (8%)
Death	-	1
Perinatal Outcome		
Preterm delivery	12 (8%)	29 (32%)
Growth restriction	11 (7%)	15 (17%)
Stillborn	0/59	6/33 (18%)
Thyrotoxicosis	1	2
Hypothyroid	4	0
Goiter	2	0

Williams Obstetrics 21st edition

Thyroid Storm:

The major risk to a woman with hyperthyroidism

- Severe thyrotoxicosis accompanied by organ system decompensation
- Precipitating factors:
  - Infection, labor, cesarean section, noncompliance with medications
- Rare but maternal mortality exceeds 25%
- Signs and symptoms:
  - Hyperthermia, marked tachycardia, perspiration, severe dehydration, mental status changes

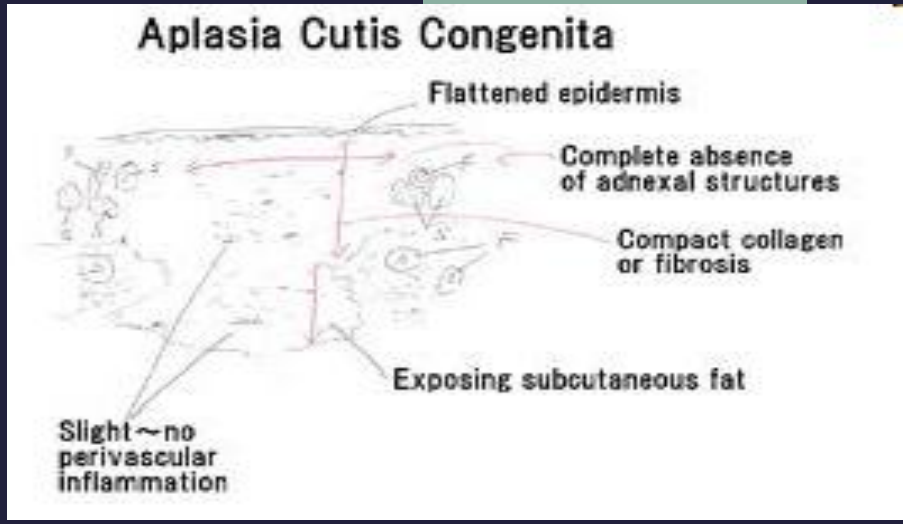
Hyperthyroidism Management

- **Beta blockers**
  - Rapid control of adrenergic symptoms (tachycardia)
- **Iodides** (adjunctive in Severe Hyperthyroidism)
  - Decreases serum T4 and T3 by 30-50%
  - Acutely inhibits extrathyroidal conversion of T_4 to T_3
  - ? Fetal safety
- **^{131}Iodine ablation - *Contraindicated***
  - Readily crosses placenta, concentrates in fetal thyroid after 10-12 weeks of gestation

- Thyroid Storm
  - Hypermetabolism
  - Tachycardia, atrial fibrillation, CHF
  - Irritability, agitation, tremor, mental status changes
  - N/V, diarrhea, jaundice
  - Stabilize mother, do not deliver

Hyperthyroidism Management

- Best to manage prior to conception
- **GOAL**: Establish euthyroidism, control symptoms
- **Propylthiouracil (PTU)**
  - Crosses placenta
  - Inhibits conversion of T_4 to T_3
  - Watch for agranulocytosis
  - Possible fetal effect: in utero hypothyroidism
- Methimazole
  - Crosses placenta
  - Associated with esophageal and choanal atresia
  - Aplasia cutis



Aplasia Cutis

- Increased association with Methimazole
- Congenital absence of the skin, most often involving the scalp
- Deeply ulcerated, superficially eroded, epithelialized or scarred
- Often small defects, but very large defects may occur.
- Larger defects may extend to the dura or meninges

Hyperthyroidism
Fetal effects of maternal disease

- Hypothyroidism from transplacental passage of Anti Thyroid Drugs
- Hyperthyroidism from stimulation of fetal thyroid by maternal TSI (1-17%)
- Fetal effects are not correlated with maternal symptoms, but with maternal TSI levels

Fetal Hyperthyroidism

- **1% of women with Graves hyperthyroidism**
- **Mortality rate up to 25%**
- **Maternal TSI can exert effect on fetal thyroid at 20 wks gestation**
- **Fetal risk is increased with high levels of TSI (>300% of nl)**
- **Measure levels at 28-30 wks**
- **Fetal symptoms:**
  - IUGR
  - Fetal tachycardia (>160 bpm)
  - Fetal goiter
  - Hydrops
- **Treatable with ATD to mother**

Medications – Fetal effects

- Fetal hypothyroidism
  - Fetal ultrasound for signs of IUGR, bradycardia, goiter
- Neonatal hypothyroidism
  - Usually resolves by day 5 of life
  - Can occur in 10-25 % of treated patients
- Congenital anomalies
  - No reports with PTU exposure
  - Case reports (8) of Methimazole embryopathy[1,2]
    - Choanal atresia, TE fistula, facial anomalies, hypoplastic nipples, psychomotor delay, **aplasia cutis**

1-Am J Med Genet. 83:43-46.
2-Lancet 350:1520.

Hypothyroidism

- 6 per 1000 pregnant women

Symptoms

- **Fatigue**
- **Dry skin**
- **Feeling cold**
- **Hair loss**
- **Concentration/memory difficulties**
- **Constipation**

- **Weight gain with poor appetite**
- **Dyspnea**
- **Hoarse voice**
- **Menstrual irregularities**
- **Paresthesia**
- **Impaired hearing**
- **Infertility**

Signs

- **Cool, rough, dry skin**
- **Puffy face, hands, feet (myxedema)**
- **Diffuse alopecia**
- **Bradycardia**
- **Peripheral edema**
- **Delayed tendon reflex relaxation**

- **Carpal tunnel syndrome**
- **Serous cavity effusions**

Causes Of Hypothyroidism

- Chronic Autoimmune thryoiditis/ Hashimoto's
  - most common cause in pregnancy
  - Progressive enlargement of the gland
  - Associated with antithyroid antibodies
  - lymphoid infiltration, fibrosis, parenchymal atrophy, and eosinophilic change
- Endemic iodine deficiency
- Post I_{131} ablation for Grave's disease
  - 10-20% are hypothyroid within 6 months
  - 2-4% become hypothyroid each year after
- Post thyroidectomy

Maternal Risks

- Myxedema Coma
  - Extremely rare in pregnancy
  - 20% mortality rate
  - Hypothermia, bradycardia, decreased DTRs, altered consciousness
  - Hyponatremia, hypoglycemia,hypoxia, hypercapnia
  - Therapy: supportive care and thyroid replacement
  - Symptoms improve after 12-24 hours of therapy

  Synthyroid: 200 – 500 mcg I.V. X 1, additional 100 – 300mcg I.V. if no response in 24 hr, continue at 75 – 100mcg I.V. daily until switch to P.O.

Severe Iodine deficiency Cretinism

Male from Ecuador about 40 years old, deaf-mute, unable to stand or walk. Use of the hands was strikingly spared, despite proximal upper-extremity spasticity. From DeLong et al

Neurologic form

- Mental deficiency
- Deafness
- Motor disorders

Myxedematous form

- Less mental deficiency
- Severe growth retardation
- Delayed sexual maturation

Myxedematous endemic cretinism in the Democratic Republic of Congo : Four inhabitants aged 15-20 years : a normal **male and three females** with severe longstanding hypothyroidism with dwarfism, retarded sexual development, puffy features, dry skin and hair and severe mental retardation.

Hypothyroidism

- Diagnosis

Diagnosis	TSH	Free T4
Primary Hypothyroidism	↑	↓
Subclinical Hypothyroidism	↑	NL
Secondary (Pituitary) Hypothyroidism	NL to ↓	↓

- Antithyroid antibodies
  - Associated with subclinical hypothyroidism
  - Hashimoto's thyroiditis
  - Predictive of neonatal hypothyroidism and postpartum thyroiditis

Hypothyroidism Maternal/Fetal Risks

Prospective 9 year study at LAC-USC, 68 hypothyroid pts, overt hypothyroid (23) subclinical (45), control (retrospective)

- Increase incidence of **gestational hypertension**
  - 22% in overt hypothyroidism
    - 36% of those who remained hypothyroid at delivery
  - 15% in subclinical hypothyroidism
    - 25% of those who remained hypothyroid at delivery
  - 7.5% in controls
- **Low birth weight** due to preterm delivery secondary to PIH
- Hypothyroidism was not otherwise associated with adverse fetal and neonatal outcomes

Perinatal Outcome in Hypothyroid Pregnancies. Leung A et al. Obstet Gynecol 1993;81:349-53.

Overt Hypothyroidism Maternal /Fetal Risks

- Retrospective study over 10 yrs of 28 pregnancies complicated by hypothyroidism (16 overt, 12 subclinical)
- In the 16 women with overt hypothyroidism
  - 44% preeclampsia
  - 31% anemia
  - 31% low birth weight
  - 19% abruption
  - 12% fetal death

Davis LE et al. Obstet Gynecol 1988:72:108-12..

Hypothyroidism
Effects on Pregnancy

Complications	Hypothyroidism Overt N=39 (%)	Hypothyroidism Subclinical N=57 (%)
Pre-eclampsia	12 (31)	9 (16)
Abruptio placentae	3 (8)	0 (0)
Anemia	5 (12)	1 (2)
Postpartum hemorrhage	4 (10)	2 (4)
Cardiac dysfunction	1 (3)	1 (2)
Low Birthweight (<2000g)	10 (26)	6 (11)
Stillbirth	2 (6)	0 (0)

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- Children of untreated overt and subclinical hypothyroidism
  - Diminished school performance
  - Lower IQ and reading recognition scores

Hypothyroidism Maternal/Fetal Risks (2)

- **Retrospective TSH from 25216 pregnant women. n=47 ≥ 99.7%tile, n= 15 98-99.7% tile, 124 matched normal controls.**
- **7-to-9-year-old children, none had hypothyroidism as newborns, underwent 15 tests relating to intelligence, attention, language, reading ability, school performance, and visual–motor performance.**
- **Hypothyroid offspring: Average IQ 4 pts lower, scores ≤85 (15 vs.5%), 48/62 untreated in pregnancy: IQ 7 pts lower, 19% ≤85**
- **Conclusion: undx hypothyroid may adversely affect their fetuses, screening for thyroid deficiency during pregnancy may be warranted**
- **No signif. P value for hypothyroid treated vs. untreated.**

Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. Haddow J et al. NEJM 1999;341:549-55.

Hypothyroidism Management

- Levothyroxine
  - 80% absorbed in fasting state
  - 60% absorbed when taken with meals
  - 7 day half life
- Increase dose q 2-4 weeks until TSH normalizes
- Check TSH q 6-8 weeks
- Reduce dose Postpartum
- Check TSH 6-8 weeks postpartum

Thyroid nodules and Thyroid Cancer

Incidence

- 2% of pregnant women
- Up to 40% incidence of malignancy
- Prognosis not influenced by pregnancy

Diagnosis

- Ultrasound
- Fine needle aspiration for
  - Rapid enlarging
  - Cystic nodules > 4cm
  - Solid nodules >2cm

Thyroid nodules and Thyroid Cancer Management options

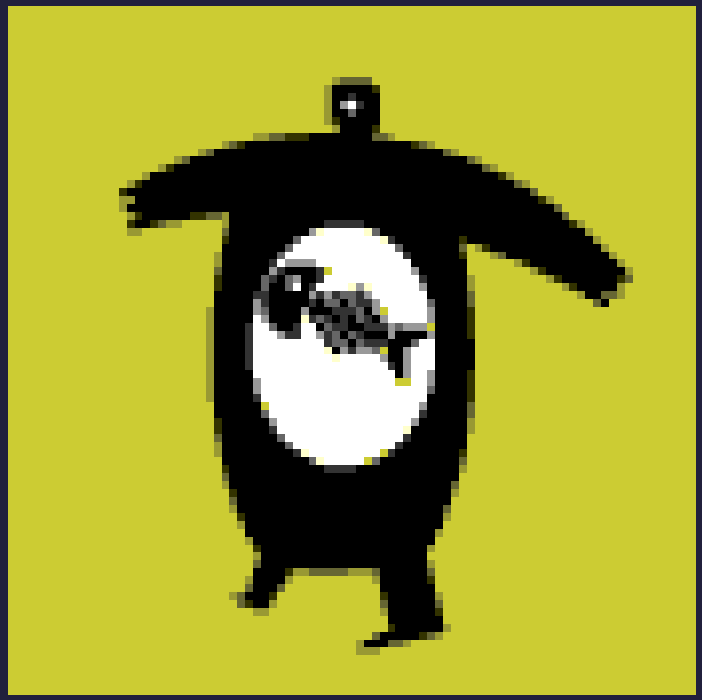
- Prepregnancy - high dose radioactive iodine

wait one year for pregnancy

- Prenatal-
  - Do not use radioactive iodine during pregnancy
  - With thyroid cancer, surgery should be done
  - Unless close to term
  - Surgery is safest in second trimester
  - Indeterminate biopsy can wait till postpartum
- Labor and delivery- anesthesia considerations with large goiter
- Postpartum- radioactive iodine may not be given while breastfeeding

Gastointestinal

- Ulcer Disease
- Inflammatory Bowel Disease
  - Crohn's vs Ulcerative Colitis
- Cholecystitis
- Cholestasis
- Hepatitis
- Hyperemesis Gravidarum
- Appendicitis



Gallbladder

- Effects of Pregnancy
  - Increase in gallbladder size
  - Increased residual and fasting volume
  - Increased diameter of common bile duct
  - Hormonal effects causing stone formation
    - Relaxation action of progesterone on smooth muscle (biliary sludge)
    - Estrogen impairs water absorption
    - Increase saturation of bile with cholesterol
      - Estrogen increases cholesterol content, decreases secretion of bile salts
      - Progesterone increases rate of esterification of cholesterol, increases bile salt-independent bile secretion

Cholestasis of Pregnancy

- Accumulation of bile acids in the liver with subsequent accumulation in plasma causing pruritis and jaundice
- Total body itching involving palms and soles
- May be symptomatic prior to lab abnormalities
- Treat with antihistamine, Ursodeoxycholic acid
- Fetal: IUFD, PTD, postpartum hemorrhage

Cholecystitis

- 2nd most common non-obstetric surgical condition in pregnancy
- Acute cholecystitis requires surgery in 1 out of 1000 deliveries
- Higher rate of cholelithiasis w/ increase parity and obesity
- Signs & Symptoms
  - Pain develops with stones > 10 mm
  - RUQ pain radiates to the back
  - N/V
  - Concurrent pancreatitis is common
    - Fetal death 10%
- Symptoms usually resolve after pregnancy

Cholecystitis

- U/S confirms stones 90%
- ERCP may be helpful with diagnosis and location of stones
- Initial medical management
  - NPO
  - IV hydration
  - Antibiotics
- Surgery
  - Frequent recurrence during pregnancy
  - Laparoscopic cholecystectomy preferred
  - Fetal outcome better during 2nd trimester
  - Increased risk of PTL with 3rd trimester disease

Appendicitis

- Most common non-obstetric cause of abdominal pain
- 1:1500 deliveries

- Effects on Pregnancy
  - Maternal and fetal morbidity & mortality increase with perforation and peritonitis
  - PTL
  - IUFD

Appendicitis - DDx

- pyelonephritis
- cholecystitis
- renal or ureteral calculi
- adnexal torsion
- degenerating myoma
- abruption
- extra-uterine pregnancy

Appendicitis

- Delay in Dx (75% in 3rd trimester)
  - N/V common in pregnancy
  - Cecum displaced upward and laterally
  - Mild leukocytosis
- Right sided vague and diffuse abdominal pain
- low grade fever
- rebound and rectal tenderness

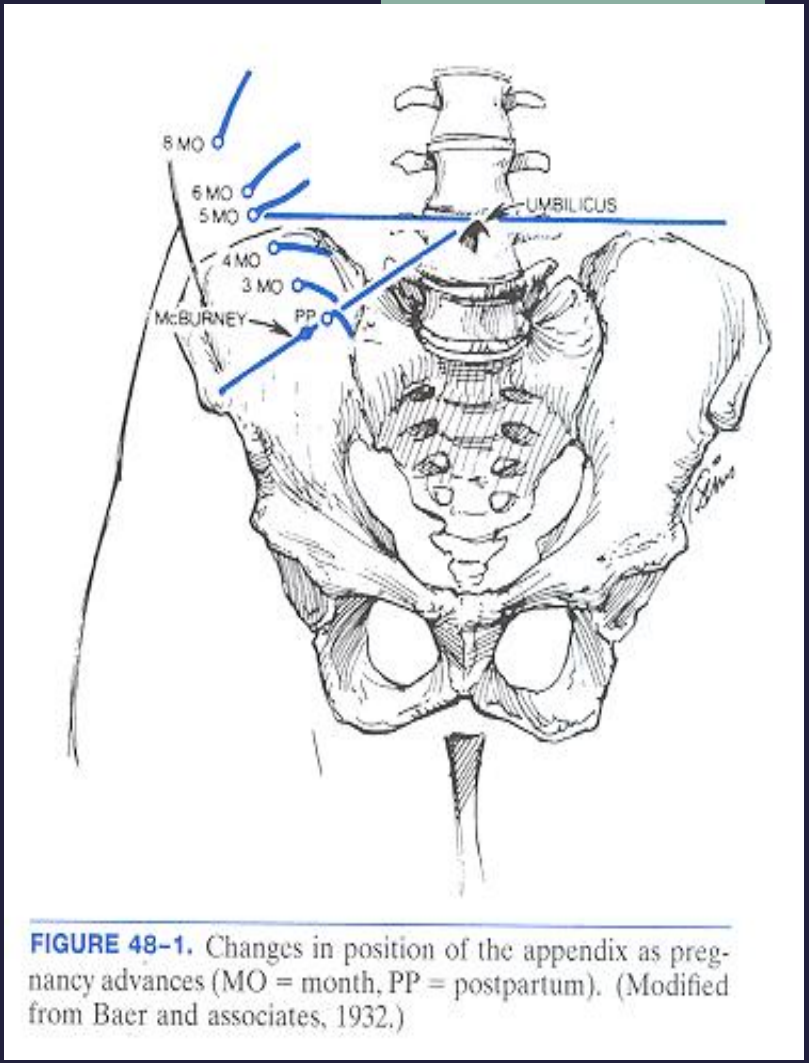


FIGURE 48–1. Changes in position of the appendix as pregnancy advances (MO = month, PP = postpartum). (Modified from Baer and associates, 1932.)

Appendicitis Management

- Surgical exploration with appendectomy
- Avoid hypotension and hypoxemia
- Laparoscopy
  - Controversial: Case reports show no negative impact on fetal or maternal outcome
  - Less uterine manipulation
  - Decreased hospitalization time
  - Reduced need for narcotic use
  - Quicker return to Regular diet
- Watch for PTL

Viral Hepatitis

- 0.2% of pregnancies
- Viruses, drugs or toxic chemicals
- Hepatitis A, B, C, D, E, G
- Clinical picture highly variable
  - Acute illness usually resolves within 2-3 weeks
  - Chronic active or persistent (B or C) in 10%
  - 1-3% develop acute fulminant hepatitis
- Maternal course of viral hepatitis unaltered by pregnancy (except E)

Hepatitis B

- Background
  - Small DNA virus
  - Accounts for 40 to 45% of hepatitis in US
  - Approximately 300,000 cases/year
  - >one million chronic carriers

Background

- Hepatitis B Acute Disease
  - 1% mortality rate
  - 85-90% complete resolution
  - 10-15% chronically infected
  - 1-2/1,000 pregnancies
- Hepatitis B Chronic Disease
  - Persistent e antigen
  - Active viral DNA synthesis
  - 5-15/1,000 pregnancies

4,000 to 5,000 die annually secondary to chronic liver disease

Background

- Hepatitis B
  - Horizontal transmission
    - Parenteral contact (IV drug use)
    - Sexual contact (25% regular contacts will convert)
  - Vertical transmission
    - Transmission to neonate
    - World-wide #1 transmission

Vertical Transmission Rate

- Seropositive women
  - 10-20% of babies born to seropositive women
  - 80-90% of babies born to women with HBsAg and HBeAg

•Factors in Perinatal Transmission

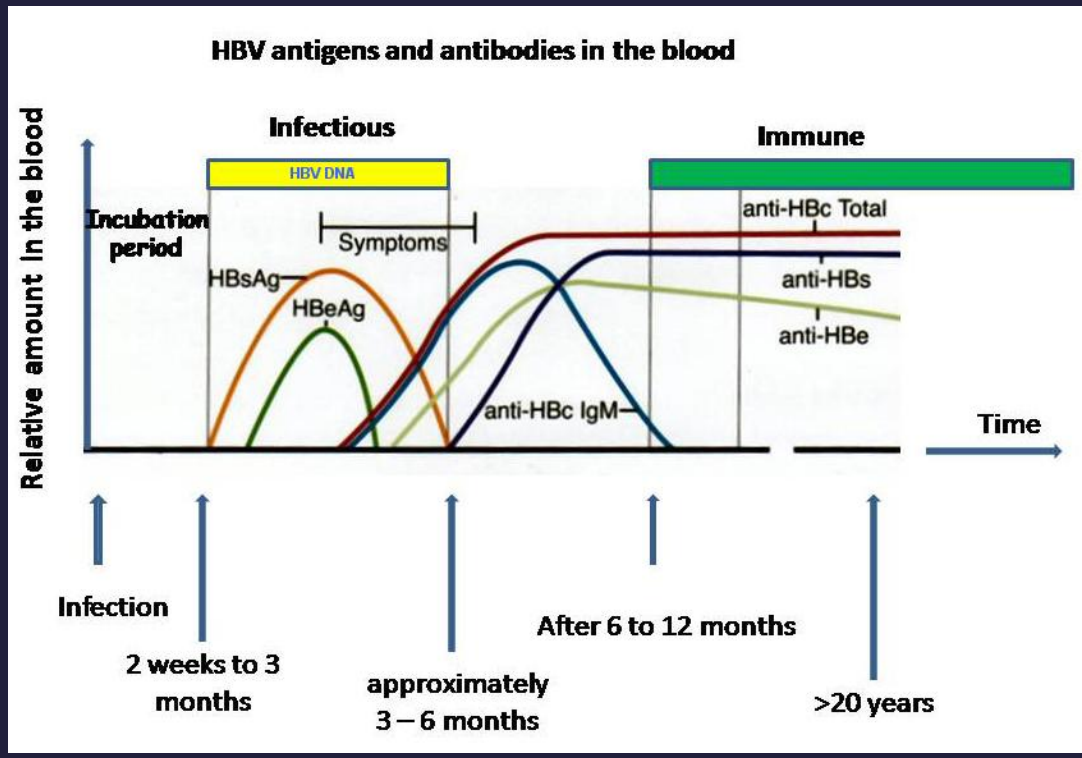
•Intrapartum exposures (85 to 95%)

•Transplacental dissemination
•Breastfeeding
•Close perinatal contact
5 to 15%

- Acute infections in pregnancy
  - First trimester
    - 10% seropositive neonates
  - Third trimester
    - 80-90% seropositive neonates

Serologic Testing

HBsAg anti-HBc anti-HBs	negative negative negative	Susceptible
HBsAg anti-HBc anti-HBs	negative positive positive	Immune due to natural infection
HBsAg anti-HBc anti-HBs	negative negative positive	Immune due to hepatitis B vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive positive negative	Acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive negative negative	Chronically infected
HBsAg HBc anti-HBs	negative positive negative	Interpretation unclear; four anti-possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. “Low level” chronic infection 4. Resolving acute infection



Recommendations

- With availability of vaccine and HBIG (1980s) the following recommendations were made:
  - Screening with HBsAg in all women in pregnancy
  - HBIG and vaccinations for neonates that are at risk
    - Universal immunizations recommended beginning in the 1991

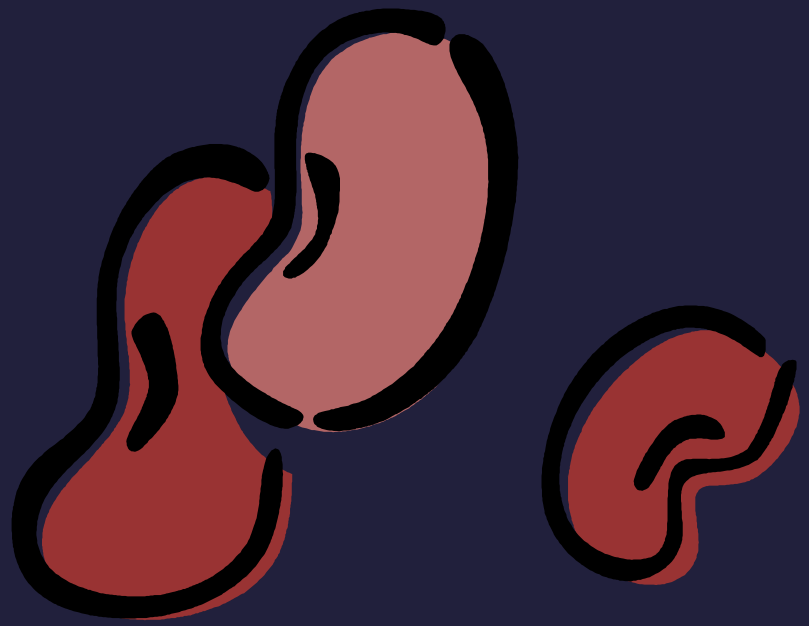
Recommendations

- Seropositive women
  - Neonatal Hepatitis B immune globulin (HBIG) within 12 hours of birth
  - Initial vaccine within 12 hours of birth, two boosters within the first 6 months
- Seronegative women
  - Infants should have initial vaccination within the first two months of life with two boosters in the first six months

Renal/Urinary Tract

- Infections

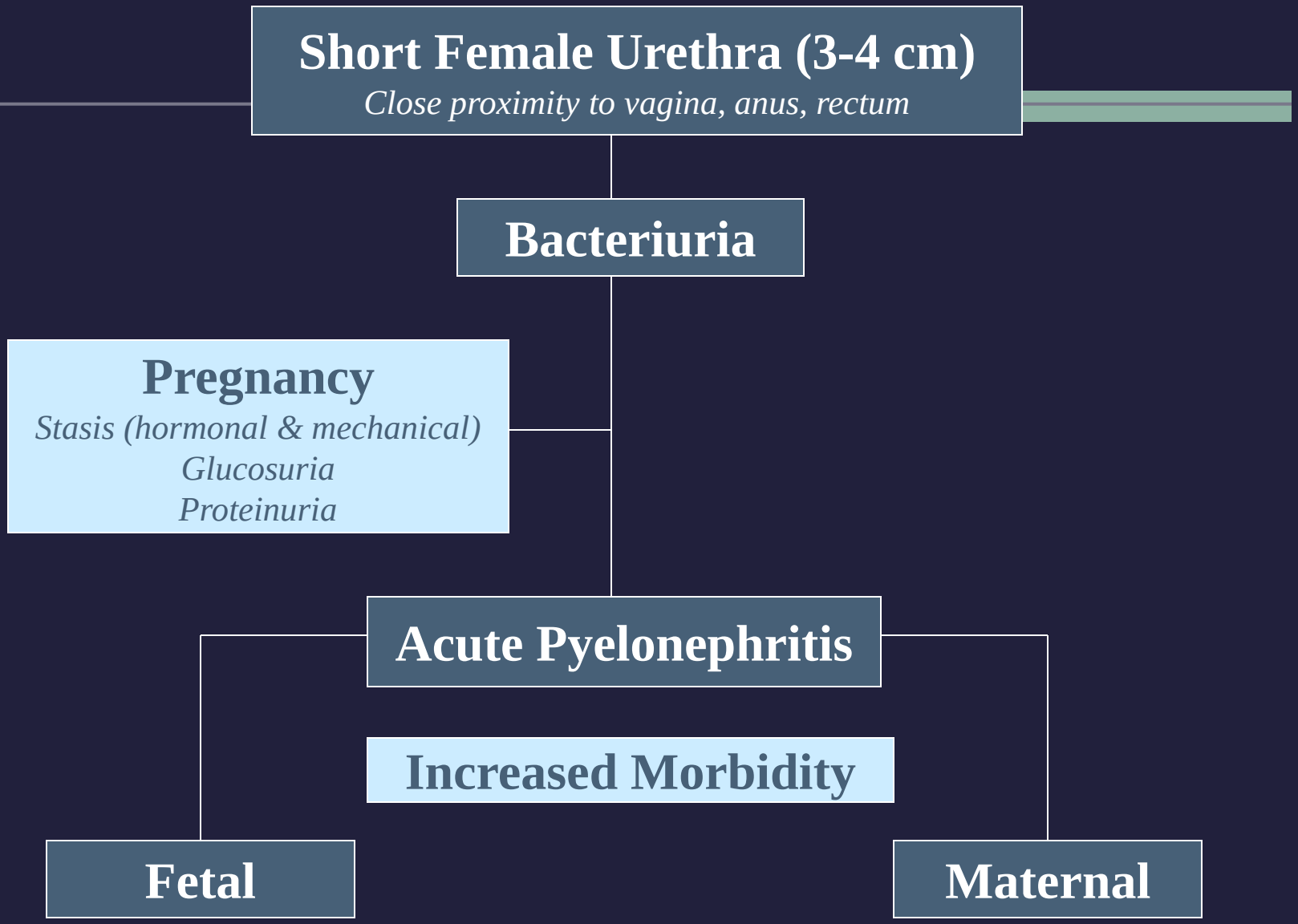
- Glomerulonephritis
- Stones
- Renal Failure
- Transplantation



Urinary Tract Infections

- Most common medical complication of pregnancy
- Asymptomatic bacteriuria seen in 2-11% of pregnant women
- First prenatal visit screen for bacteriuria and subsequent treatment prevents pyelonephritis in 70-80% of cases
- If untreated: increased risk for upper urinary tract infection (3-4% vs. 25%)
- Common Bacteria
  - 90%: E. Coli, Klebsiella, Enterobactor
  - Others: Proteus, Pseudomonas, Citrobactor, Staph, GBS

Effects of Pregnancy



Obstetrics & Gynecology Clinics of North America. Sept. 2001

Bacteriuria - *Effects on Pregnancy*

- Untreated Bacteriuria
  - Anemia
  - Hypertension
  - Low birthweight infants
  - Fetal growth restriction
  - Preterm delivery
- Pyelonephritis
  - Increase risk of premature birth
  - Low birthweight (<2500g) in 15%

Pyelonephritis

- Major complication of untreated bacteriuria
- 1-2% in pregnancy
- 73% occurs 2nd & 3rd trimesters, 27% postpartum
- Recurrence rate 10-18%; with nitrofurantoin suppression: 2.7%
- Signs & Symptoms
  - Fever* (as high as 40 C)
  - Flank pain*
  - Shaking chills
  - N/V
  - Frequency, urgency, dysuria
  - CVA tenderness

Pyelonephritis Management

- IV Hydration
- IV antibiotics: Cefazolin, Ceftriaxone, A/G
- PO antibiotics 7-10 days once afebrile, then suppressive therapy
- Urine culture 1-2 weeks for TOC
- Caution!
  - ARDS
  - Septic shock

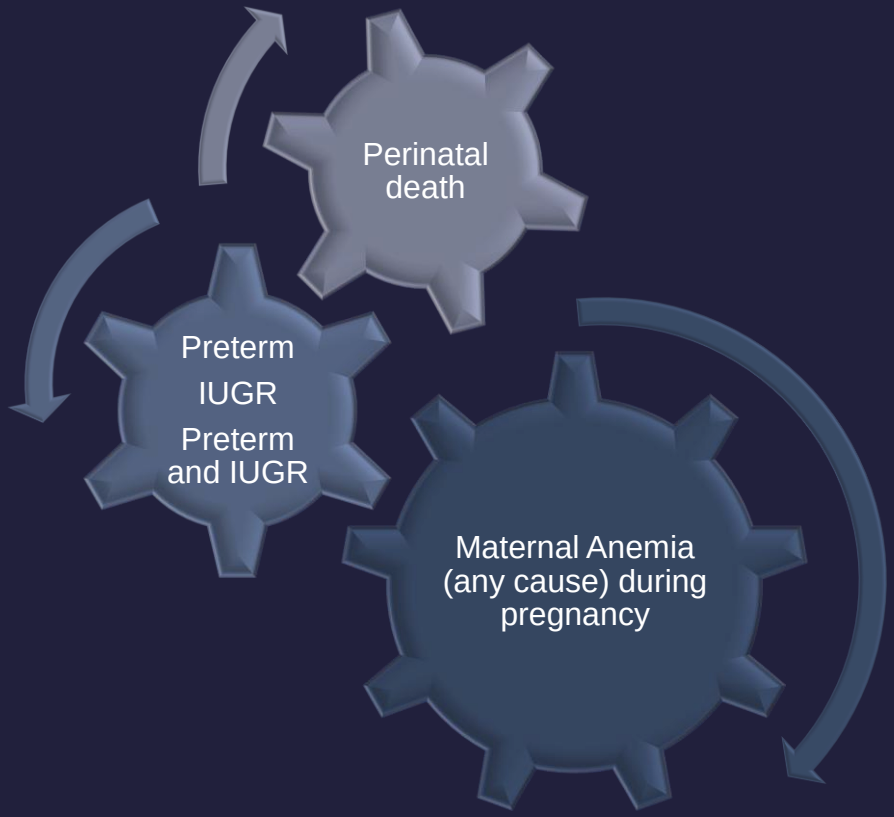
Autoimmune

- Multiple Sclerosis
- SLE
- RA
- Scleroderma

Hematologic

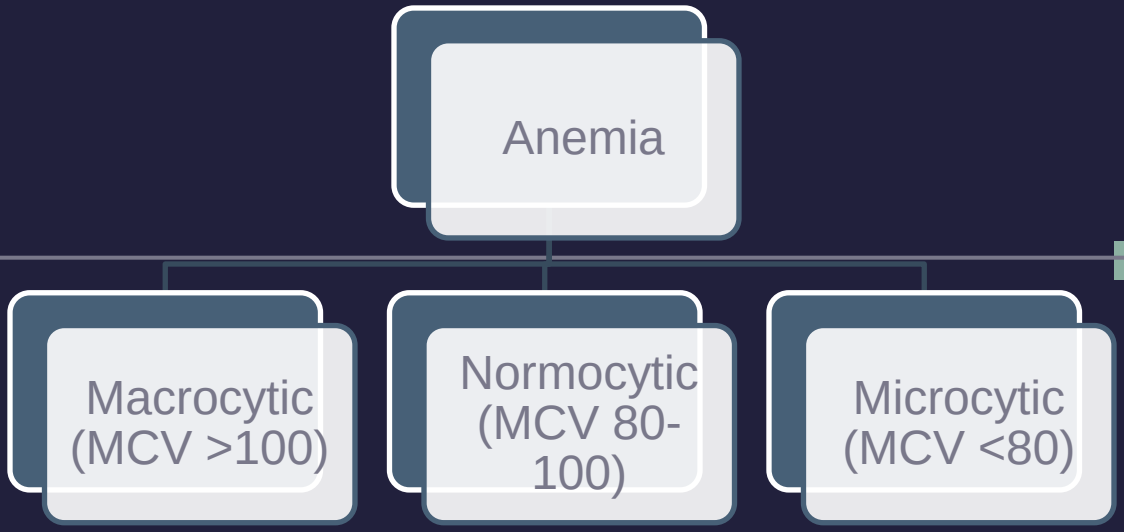
- Anemia
  - Iron deficiency
  - Folic Acid deficiency
  - Sickle Cell
  - Thalassemia
- Hemorrhagic Disorders
  - Gestational thrombocytopenia
  - ITP
- Thromboembolism

Consequences of Anemia in Pregnancy



Adapted from Rasmussen, J Nutri 2001

Type



Lab values	Causes	
Macrocytic, normochromic	MCV: > 100fl MCHC: 34	Vitamin B_{12} deficiency, folate deficiency, vitamin C deficiency, chemotherapy (megaloblastic marrow); aplastic anemia, hypothyroidism (normoblastic marrow)
Microcytic, hypochromic	MCV: < 80 MCHC: < 30	Iron deficiency, thalassemia, sideroblastic anemia, chronic lead poisoning, anemia of chronic illness
Normocytic, normochromic	MCV: 80–99fl MCHC: 34 + / -2	Iron deficiency (early), chronic disease

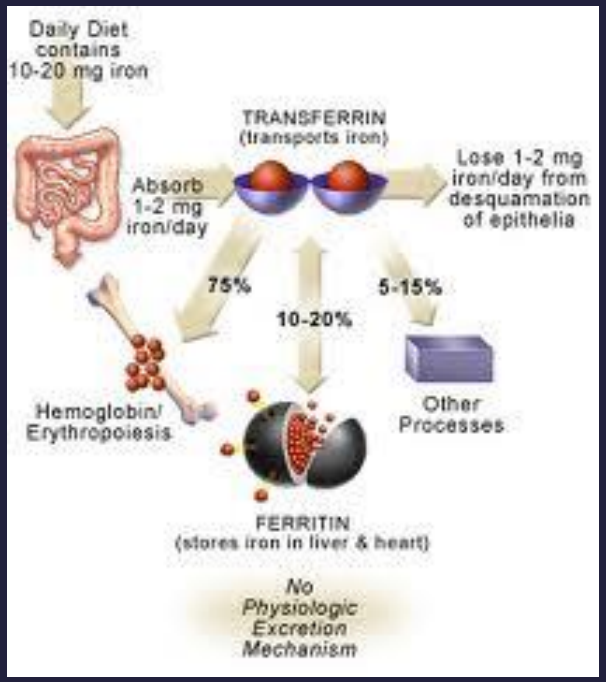
Differential Diagnosis of Microcytic Hypochromic Anemia

	Iron Deficiency	*Alpha - Thalassemia*	*Beta-Thalassemia*	*Anemia of Chronic Disease*	*Sideroblastic Anemia*
Serum Fe	Low	High	High	Low	High
TIBC	High	Nl	Nl	Low	Nl
Ferritin	Low	High	High	High	High
HbA2	Nl	Nl	High	Nl	Nl
HbF	Nl-Low	Low	High (varies)	Nl	Nl
RDW	High		High	Nl	High

Iron Deficiency

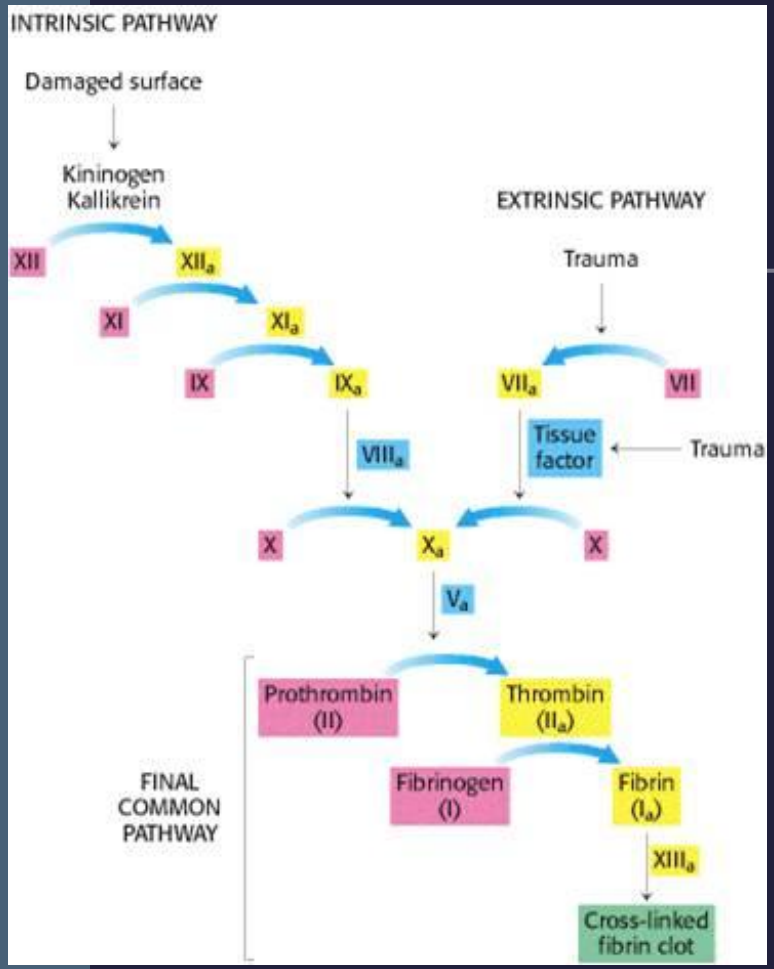
- Iron deficiency is the most prevalent nutritional deficiency in the world and probably the most important micronutrient deficiency in the US. Globally, it is estimated to affect 1.25 billion people.

	Microcytic anemia due to Fe deficiency
Ferritin	**High**
Iron	**Low**
TIBC	**Low**



Thromboembolism

- VTE affects 1 in 1000 pregnancies
- Risk of DVT equal throughout all trimesters and postpartum, but PE more common postpartum
- Hypercoagulable state (includes postpartum)
  - Virchow's triad (circulatory stasis, vascular damage, hypercoagulability)
  - Increase in Factor I, VII, VIII, IX, X
  - Decrease in protein S, fibrinolytic activity
  - Increased activation of platelets
  - Resistance to activated protein C
- Anticoagulation dependent on thrombophilia, personal history and family history



Coagulant Factors	**Change in Pregnancy**
Procoagulants	
Fibrinogen	Increased
Factor VII	Increased
Factor VIII	Increased
Factor X	Increased
Von Willebrand factor	Increased
Plasminogen activator inhibitor-1	Increased
Plasminogen activator inhibitor-2	Increased
Factor II	No change
Factor V	No change
Factor IX	No change
Anticoagulants	
Free Protein S	Decreased
Protein C	No change
Antithrombin III	No change

Thrombophilias

- Inherited
  - Factor V Leiden (FVL)
  - Anti-Thrombin III deficiency
  - Prothrombin G20210A mutation
  - Protein S deficiency
  - Protein C deficiency
  - Hyperhomocysteinemia
    - MTHFR (Methylene Tetrahydrofolate reductase mutation), Homozygotes → most common cause
      - Not associated with increased risk of VTE in non-pregnancy or pregnancy
- Acquired - APLAs (Antiphospholipid Antibodies)
  - LAC (Lupus Anticoagulant)
  - Anticardiolipin Ab
  - Anti - ß2-glycoprotein-1 Ab

Inherited Thrombophilias and their associations with VTE in Pregnancy

Thrombophilia	RR of VTE	Probability of VTE (%) Without or with a Personal History of VTE or a 1st degree Relative with VTE	
		WITHOUT	**WITH**
FVL (homozygous)	**25.4 (8.8-66)**	**1.5**	**17**
FVL (heterozygous)	5.3 (3.7-7.6)	0.2-0.26	10
PGM (homozygous)	**NA**	**2.8**	**>17**
PGM (heterozygous)	6.1 (3.1-11.2)	0.37	>10
FVL/PGM (compound heterozygous)	**84 (19-369)**	**4.7**	**NA**
Antithrombin deficiency (<60% activity)	**119**	**3.0-7.2**	**>40%**
Protein S deficiency (<55% activity)	NA	<1	6.6
Protein C deficiency (<50% activity)	13.0 (1.4-123)	0.8-1.7	2-8

Recommendations – Dose Definitions

- Prophylaxis
  - UFH: 5000U SQ q12h
  - LMWH: Dalteparin 5000U SQ q24h, Enoxaparin 40mg SQ q24h
- Intermediate-dose
  - UFH: SQ q12h dose adjusted to target an anti-Xa level 0.1 -0.3 U/ml
  - LMWH: Dalteparin 5000U SQ q12h, Enoxaparin 40mg SQ q12h
- Adjusted-dose
  - UFH: SQ q12 dose adjusted to target a mid-interval aPTT into therapeutic range (6h after injection)
  - LMWH: weight-adjusted, full treatment doses of LMWH, given once or twice daily (dalteparin 200U/kg QD, dalteparin 100U/kg q12h or enoxaparin 1mg/kg q12h)

HIV

- Retrovirus
- Estimated to affect up to 900,000 people in the United States
- Up to one-third may not know they are infected
  - 40-85% HIV infected infants born to women whose HIV status unknown to their provider
- World-wide vertical transmission is an increasingly large portion of people with the virus

Background

- No treatment: 25% vertical transmission rate
- 1994 – ZVD Trial
  - Randomized treatment with or without ZVD from 14 weeks to term with IV ZVD during labor
  - Decrease in transmission from 25% to 8%

Background

- Scheduled cesarean delivery
  - Two prospective cohort trials
  - 50% reduction
    - Approximately 2% transmission rate
  - Should be done prior to the onset of labor
    - 38 completed weeks of gestation
- Highly active, multi-antiretroviral therapy
  - Data available to show a decrease in transmission with multi-antiretroviral therapy if the maternal result is a decrease in viral load
    - 2% transmission rate

Background

- Maternal prophylaxis during labor and delivery or neonatal prophylaxis within 24-48hrs of delivery
  - Data available to show a decrease in vertical transmission
    - 10% transmission rate
- No significant reduction if therapy started after 3 days of life

Screening

- Risk vs. benefit
- Anonymous screening
- Pre and post screening counseling
- Rapid testing
- Nebraska
  - Specific informed consent, in writing
  - Post test counseling required
  - Anonymous
  - Partner notification

Screening

- ELISA
- Western blot or IFA (immunofluorescence assay) for confirmation
  - If both positive, sensitivity and specificity >99%
  - False positive, 1:59,000
  - If positive then negative → NOT infected, repeat testing not indicated
  - If positive with some viral bands → indeterminate
    - Most not infected, refer to specialist and may rec further testing

Screening

- Rapid testing (results in a few hours)
  - All women with undocumented HIV presenting to L&D
  - Negative → definitive
  - Positive → needs confirmation
    - Initiate antiretrovirals, discontinue if confirmatory test negative or if delivery

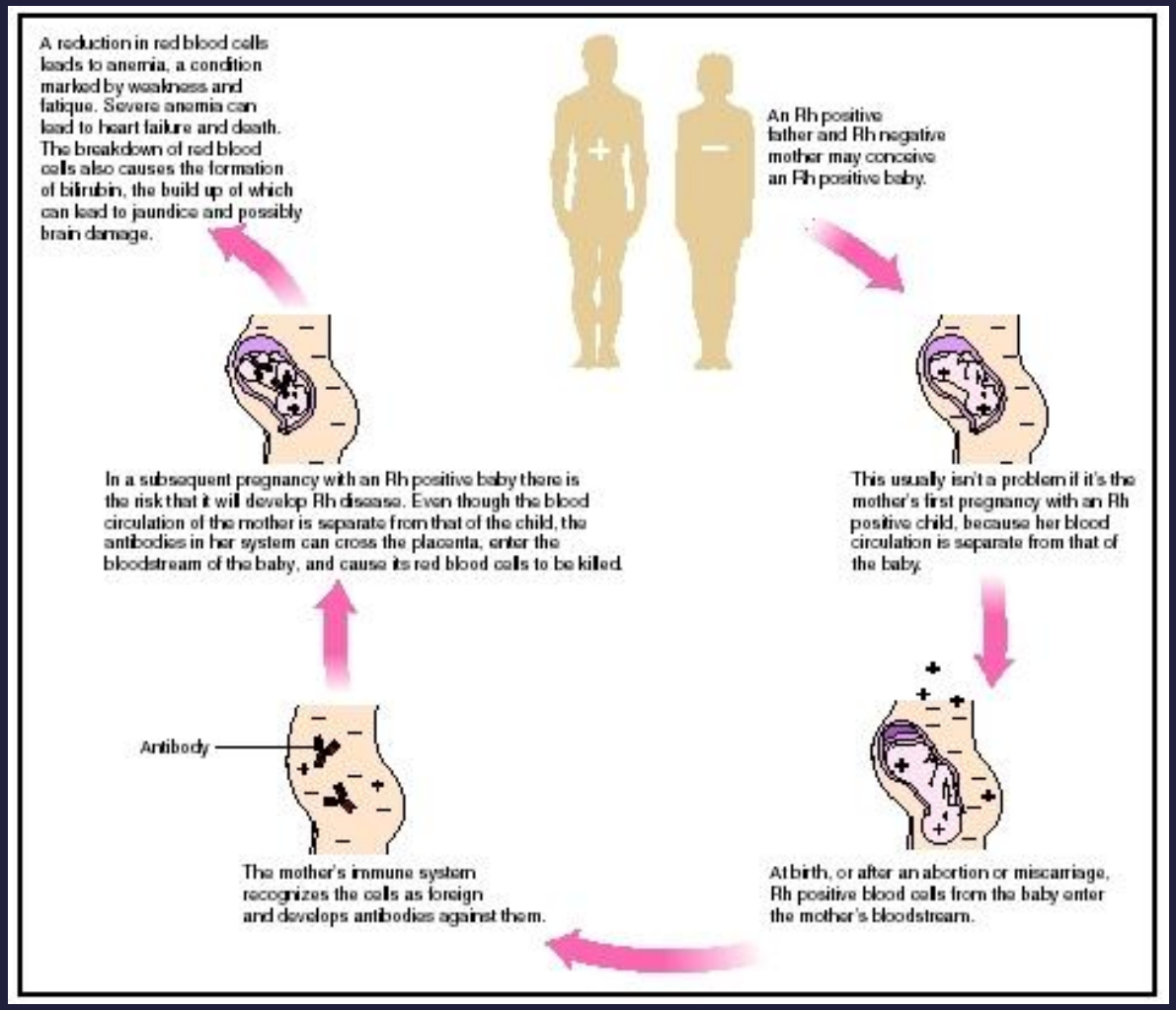
Treatment

- Antiretroviral therapy
- Viral load at intervals
  - Min 3 months
- Intrapartum/intrapartum antiretrovirals
- Intrapartum/intraoperative antibiotics
- Cesarean delivery for viral loads greater than 1,000 copies
- Appropriate counseling

Summary

- HIV
  - All women should be screened
  - Antiretroviral therapy recommended for all HIV + women beyond 14 weeks gestation
  - Infusion of ZVD should be started three hours prior to delivery
  - Initiating retroviral therapy is comparable to none to decrease transmission
  - C-section is recommended in women with viral loads greater than 1,000 copies
  - C-section should be scheduled at 38 completed weeks of gestation

Blood Group Isoimmunization



Maternal Sensitization

- Fetal RBCs enter maternal circulation
- Fetal RBC's are positive for an antigen which the mother does not have
- B lymphocyte clones attuned to the "foreign" RBC antigen
- Ultimate generation of IgG antibodies
- Memory B cells lurk, awaiting next stimulation

Pathogenesis of Erythoblastosis Fetalis

- IgG directed against fetal RBC antigen crosses the placenta
- Non-compliment mediated hemolysis
- Severe anemia may result
- Hydrops typically occurs when fetal HCT < 15%

Fetal hydrops

Pleural Effusion

Ascites

Scalp Edema

Rh isoimmunization

- Mild
  - 50% of cases; no treatment
- Moderate
  - 25% of cases; exchange transfusion
- Severe
  - 25% of cases; fetal death without delivery or intrauterine transfusion

Rh negative mother & Rh positive fetus: No prevention

- 16% overall chance of sensitization
  - 50% not noted until subsequent pregnancy
  - 7/8 (14%) occurs intrapartum
  - 1/8 (2%) occurs during antepartum period

Rh (D) Immune Globulin Prophylactic Failures

- “Grandmother” theory
- Failure to administer with indication
- Failure to administer adequate amount
  - If suspicion of large feto-maternal hemorrhage
    - Kleihauer-Betke
    - Indirect Coombs

Prevention: Rh Immune Globulin

- Suppresses immune response to Rh-positive RBCs
- Routine administration at approximately 28 weeks
- Routine administration after delivery (if Rh+ neonate)
  - Aim to administer within 72 hours of known exposure
- Administer as soon as you can if typical window missed
- Dosage
  - 300 micrograms IM covers 15 cc RBCs or 30 cc whole blood

Rh (D) Immune Globulin
Other Indications

- Spontaneous or elective abortion
- ?Threatened abortion
- Ectopic pregnancy
- CVS or amniocentesis
- Fetal blood sampling
- Abdominal trauma
- External cephalic version

Non-Rhesus Isoimmunization

- Essential pathophysiology the same as with Rh (D) isoimmunization
- There is no similar method of prevention with maternal administration of IgG for the non-Rhesus maternal-fetal incompatability
- Important other blood groups:
  - c, C, e, E, Kell, Duffy

Management: Initial steps

- Identification of isoimmunization
- Paternal antigen testing
  - Presence
  - Homozygote or heterozygote*
- If paternal heterozygote:
  - Fetal testing for antigen via amniocentesis
  - Avoid CVS
  - If fetal antigen present, proceed with surveillance

* Rh is the exception

Antibody Titers

- Titers reflect the potential for anemia
- Critical titer
  - Titer at which severe anemia may occur
    - 1:16 for non-Rh antigens
    - 1:32 for Rh (D) antigen
    - Always be aware of lab-specific values
- Serial titers
  - Initial prenatal visit
  - Typically, no need again until 18-20 weeks
  - Thereafter, q2-4 weeks
  - Perform until critical titer reached, then no more

Conclusions

- Common medical problems are commonly seen in pregnancy.
- Be aware of the fetus.
- Treat mother first. Sick mom = Sick fetus.

Thank you…

Questions… sswu@unmc.edu

Signs and Symptoms of Hyperthyroidism or "Just pregnant"

Symptoms

- Hyperactivity, irritability, dysphoria
- Heat intolerance sweating
- Palpitations
- Fatigue and weakness
- *Weight loss with increased appetite*
- Diarrhea
- Polyuria
- Oligomenorrhea, loss of libido

Signs

- Tachycardia persistent > 100 bpm
- *Tremor*
- Goiter
- Warm, moist skin
- Muscle weakness,
- *proximal myopathy*
- *Lid retraction or lag*