Maternal Diseases During Pregnancy

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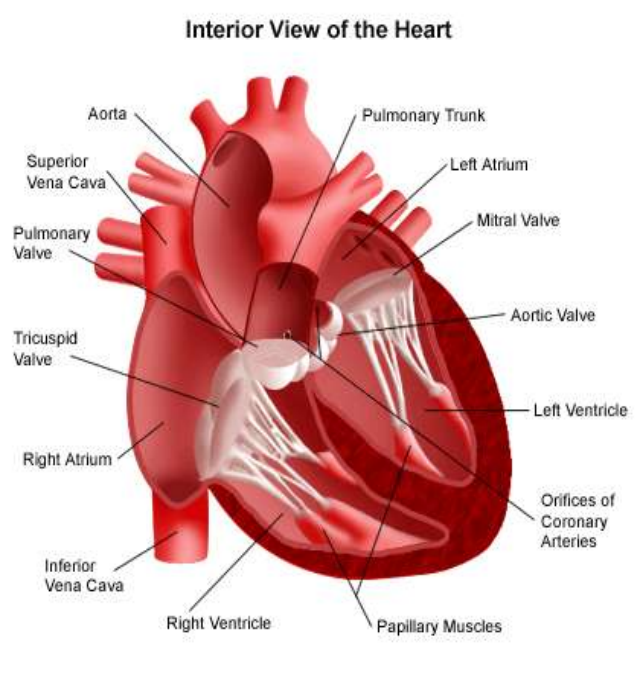
Cardiovascular disease
Pulmonary disorders
Connective - tissue disorders
Hepatic disorders
Thyroid disorders

Cardiovascular disease

- Heart disease of varying severity complicates about 1% of pregnancies

- Cardiac output is increased by 30-50% in pregnancy
  - Almost half of the total increase occurs by 8 weeks gestation
  - Maximized by mid-pregnancy



Physiological Considerations

- Women with severe cardiac dysfunction may experience worsening of heart failure before midpregnancy
- Heart failure may develop after 28 weeks when pregnancy- induced hypervolemia is maximal
- In the majority, heart failure develops peripartum when there are rapid physiological changes in cardiac output

Preconceptional Counseling

- Prognostic factors for women with heart disease
  - Functional capacity
  - Other complications that further increase cardiac load (such as anemia)
  - Quality of medical care provided
  - Psychological and socio-economical factors

Congenital Heart Disease in Offspring

- Many congenital heart lesions appear to be inherited as polygenic characteristics
- There is a 3-4% incidence of fetal congenital heart disease in women born with cardiac anomalies
- Only half of mother-fetus pairs are concordant for the same anomaly

Diagnosis of Heart Disease

- Many of the physiological changes of normal pregnancy make the diagnosis of heart disease more difficult:
  - Functional systolic heart murmurs
  - Dyspnea
  - Edema
  - Fatigue
  - Tachycardia
- Over / Under diagnosis

Clinical Indicators of Heart Disease During Pregnancy

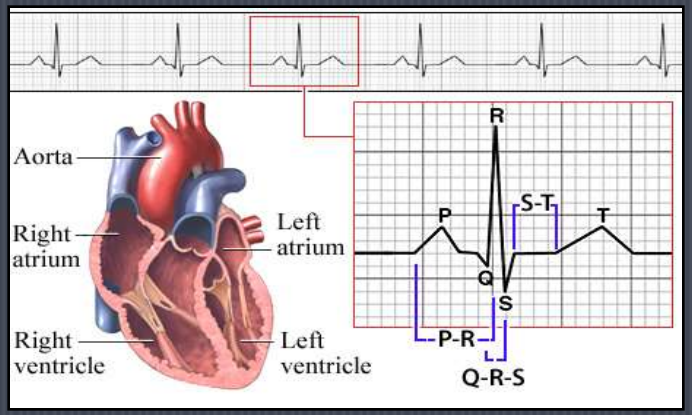
- **Symptoms**
  - Progressive dyspnea or orthopnea
  - Nocturnal cough
  - Hemoptysis
  - Syncope
  - Chest pain
- **Clinical Findings**
  - Cyanosis
  - Clubbing of fingers
  - Persistent neck vein distention
  - Systolic murmur grade 3/6 or greater
  - Diastolic murmur
  - Cardiomegaly
  - Persistent arrhythmia
  - Pulmonary hypertension

Diagnostic Studies

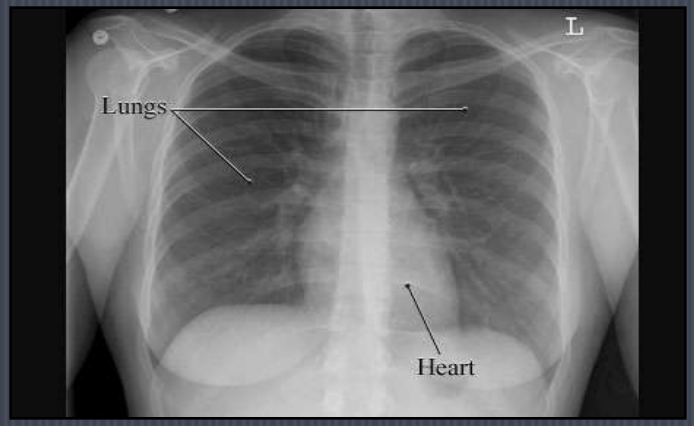
- Most diagnostic cardiovascular studies are noninvasive and safe:
  - Electrocardiography
  - Echocardiography
  - Chest radiography
- Need special consideration:
  - Technetium 99-labeled albumin or red cells scan (ventricular function)
  - Thallium ^{201} scan (regional coronary perfusion)
  - Right-heart catheterization
  - Left-heart catheterization

Diagnostic Studies

- ELECTROCARDIOGRAPHY
  - 15-degree left-axis deviation
  - mild ST changes in the inferior leads
  - APB's and VPB's



- CHEST X-RAY
  - heart silhouette is larger in pregnancy; gross cardiomegaly can be excluded
  - fetal radiation exposure is minimal



- ECHOCARDIOGRAPHY
  - allows accurate diagnosis of most heart diseases during pregnancy

Clinical Classification- NYHA

- **Class I -** *Uncompromised (no limitation of physical activity):*
  These women do not have symptoms of cardiac insufficiency or experience anginal pain.
- **Class II -** *Slight limitation of physical activity:*
  These women are comfortable at rest, but if ordinary physical activity is undertaken, discomfort results in the form of excessive fatigue, palpitation, dyspnea, or anginal pain.
- **Class III -** *Marked limitation of physical activity:*
  These women are comfortable at rest, but less than ordinary activity causes excessive fatigue, palpitation, dyspnea, or anginal pain.
- **Class IV -** *Severely compromised (inability to perform any physical activity without discomfort):*
  Symptoms of cardiac insufficiency or angina may develop even at rest, and if any physical activity is undertaken, discomfort is increased.

Scoring System

- Developed for predicting cardiac complications during pregnancy
- Predictors of cardiac complications:
  - Prior heart failure, TIA, stroke, or arrhythmia
  - Baseline NYHA class III or greater or cyanosis
  - Left-sided heart obstruction defined as:
    - mitral valve area below 2 cm^2
    - aortic valve area below 1.5 cm^2
    - peak left ventricular outflow tract gradient above 30 mm Hg by echocardiography
  - Ejection fraction less than 40%
- The risk of pulmonary edema, sustained arrhythmia, stroke, cardiac arrest, or cardiac death is increased with any of these risk factors

Risk of Maternal Mortality Caused by Various Types of Heart Diseases

- **Group 1 - Minimal Risk- 0-1% mortality**
  - ASD
  - VSD
  - PDA
  - Pulmonic/ Tricuspid disease
  - Corrected TOF
  - Bioprosthetic valve
  - Mitral stenosis, NYHA class I/II
- **Group 2 - Moderate Risk- 5-15% mortality**
  - Mitral stenosis, NYHA class III/IV
  - Aortic stenosis
  - Aortic coarctation without valvular involvement
  - Uncorrected TOF
  - Previous myocardial infarction
  - Marfan syndrome with normal aorta
  - Artificial valve
- **Group 3 - Major Risk - 25-50% mortality**
  - Pulmonary hypertension
  - Aortic coarctation with valvular involvement
  - Marfan syndrome with aortic involvement

Mechanical Valve Prosthesis

- Anticoagulation
- Complications:
  - Thromboembolism involving the prosthesis
  - Hemorrhage from anticoagulation
  - Deterioration in cardiac function
- Maternal mortality - 3-4% with mechanical valves
- Fetal loss is relatively common

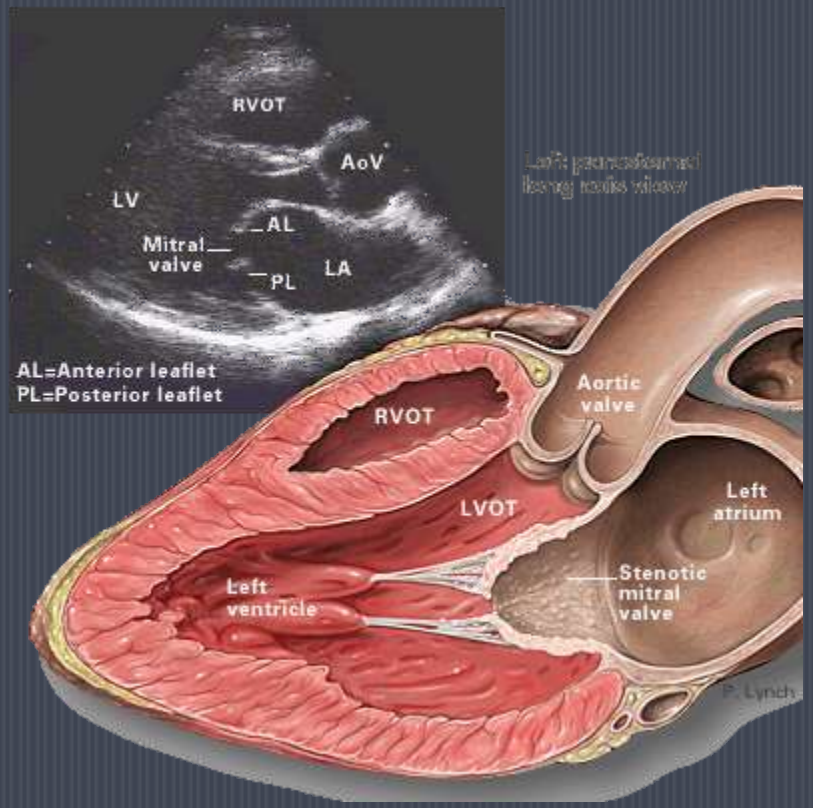
Mechanical Valve Prosthesis – Anticoagulation Rx

- Heparin - less effective than warfarin in preventing thromboembolic events
- LMWH - inappropriate during pregnancy
- Warfarin- better maternal outcome but known adverse fetal effects:
  - Spontaneous abortions (32%)
  - Stillbirths (7%)
  - Warfarin embryopathy (6%) – affects axial and appendicular skeleton; hypoplastic nose, eye abnormalities, mental retardation, brachydactyly and scoliosis
    - Dose dependent – increases with daily dose above 5 mg

- Heparin substitution from 6 to 12 weeks, from 34 weeks until labor

Mitral Stenosis

- **Etiology-**
  - Rheumatic endocarditis
- **Pathophysiology-**
  - The contracted valve impedes blood flow from the left atrium to the ventricle- the left atrium is dilated
  - Pulmonary hypertension
  - Atrial tachyarrhythmias
  - A relatively fixed cardiac output



Mitral Stenosis - pathophysiology

- Tachycardia of any etiology shortens ventricular diastolic filling time and increases the mitral gradient, which raises left atrial and pulmonary venous and capillary pressures and may result in pulmonary edema
- Sinus tachycardia is often treated prophylactically with ß-blocking agents
- Atrial fibrillation predisposes to mural thrombus formation and thrombotic CVA

Mitral Stenosis in Pregnancy

- The increased preload of normal pregnancy, as well as other factors that require increased cardiac output, may cause ventricular failure with pulmonary edema in these women with relatively fixed cardiac output
- 25 % of women with mitral stenosis have cardiac failure for the first time during pregnancy

Management during Pregnancy

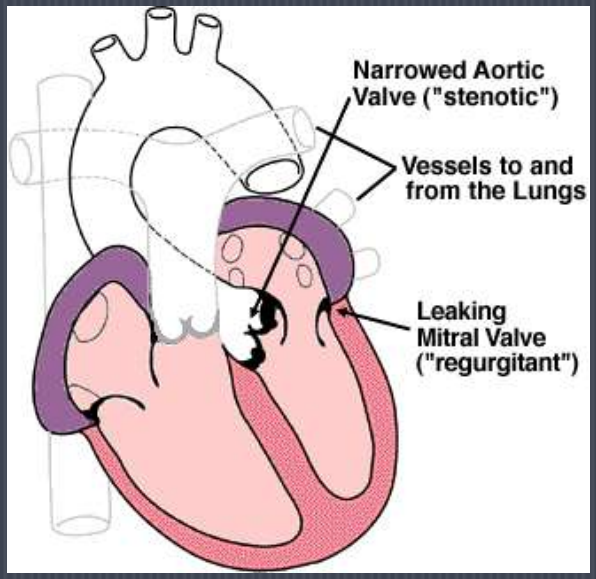
- Limit physical activity
- Restrict dietary sodium
- Diuretics in symptomatic women
- A ß-blocker - slow HR response to activity and anxiety
- For chronic fibrillation:
  - Digoxin or a ß- or calcium-channel blocker - to slow ventricular response
  - Anticoagulation with heparin

Management during Labor

- Pain and anxiety cause tachycardia, with increasing chances of rate-related heart failure
  - Epidural analgesia for labor
- Avoid intravenous fluid overload
- Prefer vaginal delivery
- Elective induction
- Pulmonary artery catheter
- Intrapartum endocarditis prophylaxis

Aortic Stenosis

- **Etiology:**
  - Congenital lesion, most common - a bicuspid valve
  - Rheumatic disease



- **Pathophysiology:**
  - Severe obstruction to flow and progressive pressure overload on the left ventricle
  - Concentric left - ventricular hypertrophy
  - In severe aortic stenosis - reduced cardiac output

Aortic Stenosis

- **Clinical manifestations:**
  - Chest pain
  - Syncope
  - Heart failure
  - Sudden death from arrhythmias
- Prognosis - Life expectancy after patient develops chest pain at exertion averages only 5 years
- Valve replacement is indicated for symptomatic patients

Aortic Stenosis in Pregnancy

- Clinically significant aortic stenosis is rare
- Mild to moderate degrees of stenosis are well tolerated, but severe disease is life threatening
- Factors that may aggravate the fixed cardiac output:
  - Blood loss
  - Regional analgesia
- Decrease cardiac, cerebral, and uterine perfusion
- Severe aortic stenosis may be extremely dangerous during pregnancy
- Mortality- 7-8%

Management in Pregnancy

- Asymptomatic pregnant woman:
  - Close observation
- Symptomatic woman:
  - Strict limitation of activity
  - Prompt treatment of infections
  - If symptoms persists despite bed rest - valve replacement or valvotomy is considered

Management during Labor

- For women with critical aortic stenosis, intensive monitoring during labor
- Avoidance of decreased ventricular preload and maintenance of cardiac output:
  - management on the "wet" side
  - maintaining a margin of safety in intravascular volume in anticipation of unexpected hemorrhage
- Narcotic epidural analgesia avoiding hypotension
- SBE prophylaxis

Pulmonary Disorders

Physiological Considerations:

Vital capacity	increases by 100 to 200 mL
Inspiratory capacity	increases by about 300 mL by late pregnancy
Expiratory reserve volume	decreases from a total of 1300 mL to about 1000 mL
Residual volume	decreases from a total of 1500 mL to about 1200 mL
Functional residual capacity (sum of expiratory reserve and residual volumes)	reduced considerably by about 500 mL
Tidal volume	increases considerably from about 500 to 700 mL
Minute ventilation	increases 40% (7.5 L to 10.5 L/min), primarily due to increased tidal volume (the respiratory rate is unchanged)

Physiological Considerations

- The sum of these changes - increased ventilation due to deeper but not more frequent breathing
- These changes are induced to help supply increased basal oxygen consumption

Pneumonia and Pregnancy

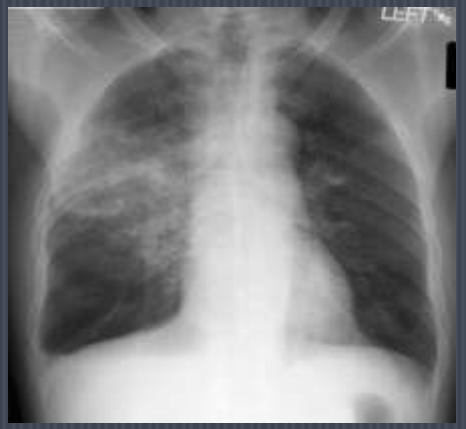
- Pneumonitis causing an appreciable loss of ventilatory capacity is not well tolerated by pregnant women
- Hypoxemia and acidosis are poorly tolerated by the fetus, and may lead to preterm labor

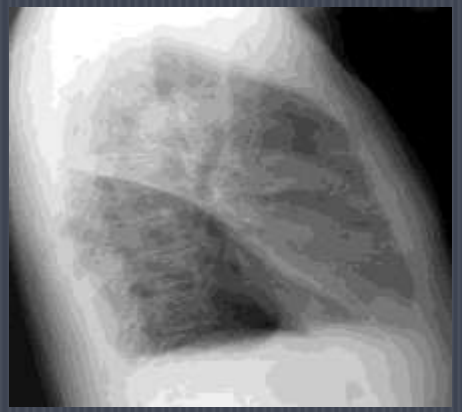
Pneumonia and Pregnancy

- There is no evidence that pregnancy predisposes to pneumonia
- Risk factors:
  - Smoking
  - Chronic bronchitis
  - Asthma
  - Binge drinking
  - HIV

Diagnosis

- Symptoms:
  - Productive cough
  - Fever
  - Chest pain
  - Dyspnea
- Mild upper respiratory symptoms and malaise usually precede these symptoms
- Lab: mild leukocytosis
- Chest x-ray





- Any pregnant woman suspected of having pneumonia should undergo AP and LAT chest XR

Management

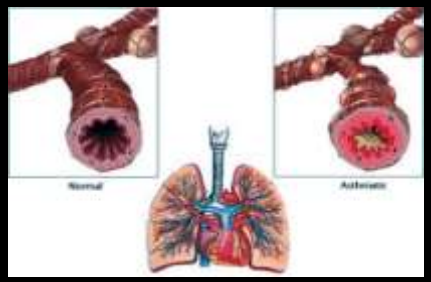
- Hospitalization
- Pneumonia is a common cause of acute respiratory distress syndrome during pregnancy
- Respiratory failure may require assisted ventilation
- Antimicrobial treatment:
  - Empirical Erythromycin or a new analogue therapy
  - In complicated cases or suspected Staph or Hemophilus pneumonia - IV Ceftriaxone

Effects on Pregnancy

- Maternal mortality - 0.8%
- Intubation rate - 6.7%
- Perinatal mortality - 2.2%
- Increased:
  - Preterm birth rates
  - SGA

Need for prompt diagnosis, close observation, and effective treatment

Asthma



- Asthma affects about 7% of the general population
- Prevalence in pregnant women – 5 - 9%
- Status asthmaticus - 0.2% of pregnancies
- 50% experience at least one exacerbation during pregnancy
- Approximately 6% will require hospitalization

Effects of Pregnancy on Asthma

- There is no evidence that pregnancy has a predictable effect on underlying asthma
  - About a third improve
  - A third remain the same
  - A third become worse (17-36 weeks gestation)

- Baseline asthma severity correlates with asthma morbidity during pregnancy
- Women beginning pregnancy with severe asthma are more likely to experience worsening disease than are those with mild disease
- Exacerbation during labor and delivery – 1 - 20% of women with mild-moderate disease

Effects of Asthma on Pregnancy

- Unless there is severe disease, asthma has a relatively minor effect on pregnancy outcome
- Slight increased incidences of:
  - Preeclampsia
  - Preterm labor
  - Low - birthweight infants (severe episodes with hospitalization and absence of regular preventive inhaled corticosteroids)
  - Perinatal mortality

- Life - threatening complications from status asthmaticus
- Maternal and perinatal mortality is substantively increased when asthma requires mechanical ventilation

Fetal Effects

- Maternal respiratory alkalosis may cause fetal hypoxemia well before maternal oxygenation is compromised
- Fetal compromise is hypothesized to result from
  - Decreased uterine blood flow
  - Decreased maternal venous return
  - Alkaline - induced leftward shift of the oxyhemoglobin dissociation curve

Fetal Effects

- Fetal response to maternal hypoxemia:
  - decreased umbilical blood flow
  - increased systemic and pulmonary vascular resistance
  - decreased cardiac output
- Monitoring the fetal response - an indicator of maternal compromise

- The fetus may be seriously compromised before maternal disease is severe
- Need for aggressive management of all pregnant women with acute asthma

Management of Chronic Asthma

- According to the National Asthma Education Program - effective management of asthma during pregnancy includes:
  - Objective assessment of pulmonary function and fetal well-being
  - Avoidance or control of environmental precipitating factors
  - Pharmacological therapy
    - Relievers: rapid onset bronchodilators (short acting β agonists)
    - Preventers: regular long-term medications (ICS)
    - Symptom controllers (long acting β agonists)
  - Patient education

- In general, women with moderate to severe asthma are instructed to measure and record Peak Expiratory Flow Rate (PEFR) twice daily
- Poorly controlled asthma poses significant risk to the fetus

Management of Acute Asthma

- Treatment of acute asthma during pregnancy is similar to that for the non-pregnant asthmatic
- Significantly lower threshold for hospitalization
- IV hydration - help clear pulmonary secretions
- Supplemental oxygen
- Continuous pulse oximetry (≥95%) and fetal monitoring
- ß-agonists
- Corticosteroids (avoid long term oral use – clefts)

Labor and Delivery

- Maintenance medications are continued throughout delivery
- Stress dose corticosteroids
- Epidural analgesia - ideal
- Avoid PG-F2α and methergine (may cause bronchospasm)

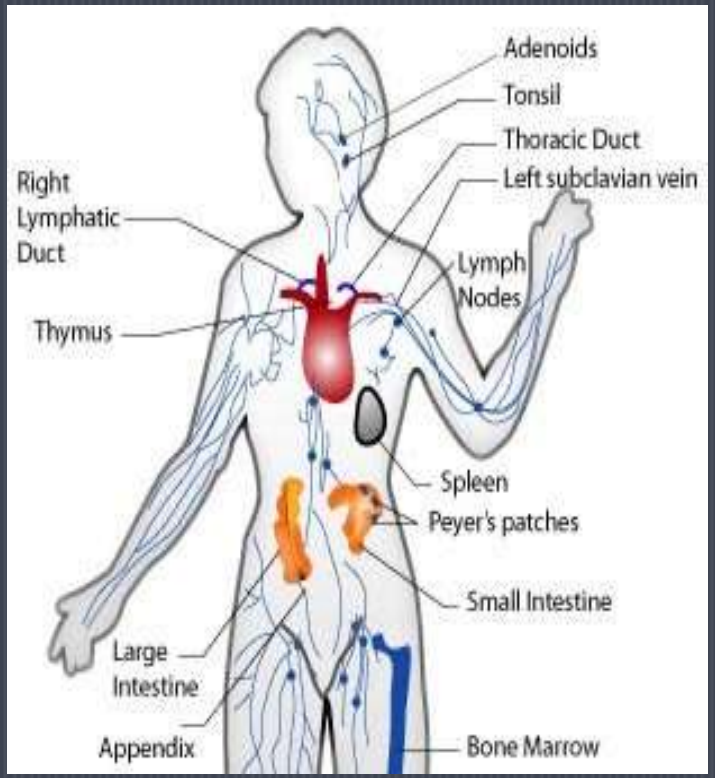
Allergic rhinitis

- Untreated rhinitis can contribute to asthma symptoms and compromise control
- Intranasal corticosteroids (low risk of systemic effects)
- Oral antihistamine (loratidine or cetirizine)
- Avoid oral decongestants (gastroschisis risk)

Connective-Tissue Disorders

Immunity in pregnancy

- For a successful pregnancy outcome the maternal immune system must not reject the fetus
- Trophoblast cells serve as a physical barrier, expressing several immune modulating molecules as well as secreting a variety of cytokines
- Placental immune suppression causes reduced activity of T regulatory cells

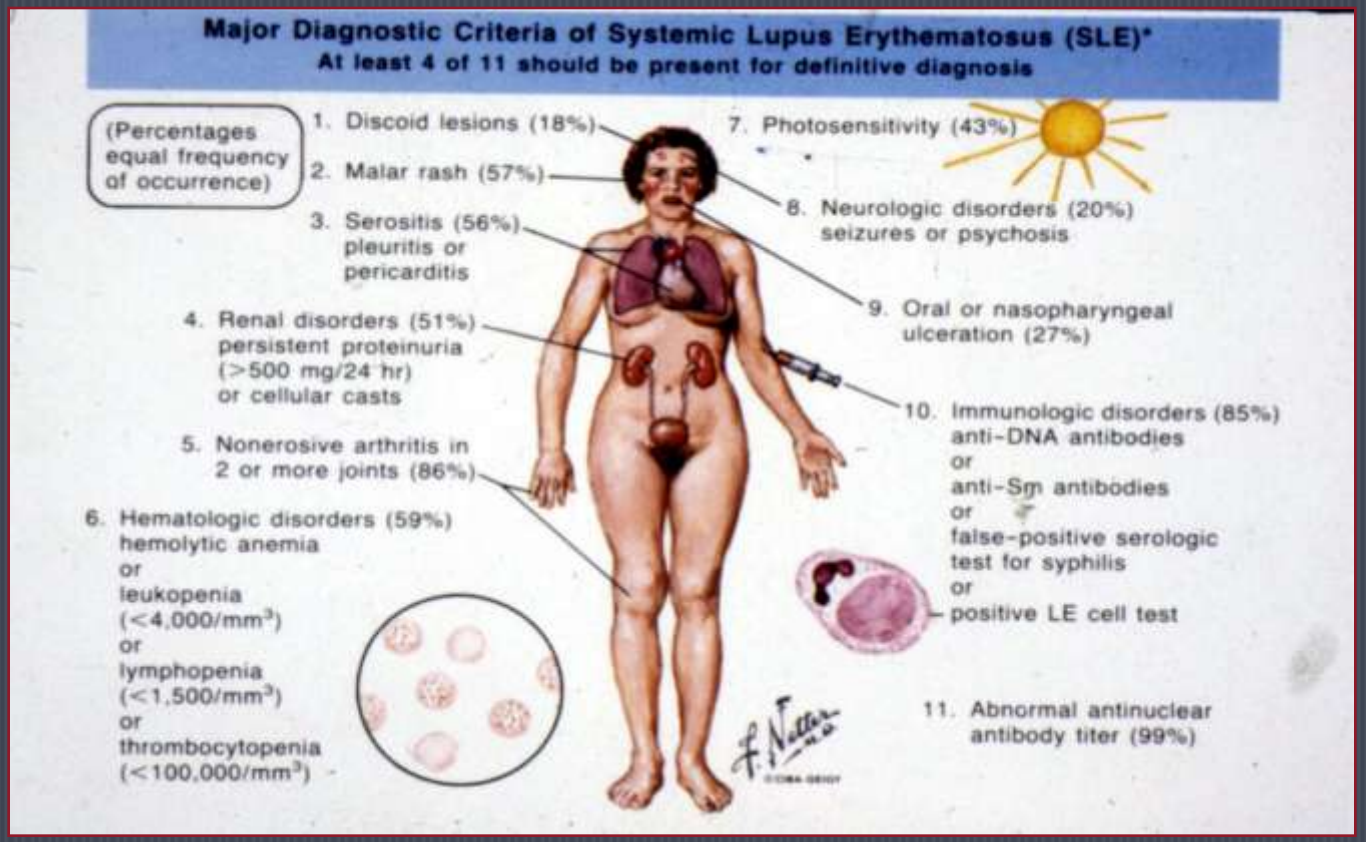


Immune changes in pregnancy

Level of change	Changes	Consequences
Local control	Trophoblast cells, express several immune modulating molecules (Fas-L, HLA-G and indoleamine 2,3-dioxigenase) as well as secreting a variety of cytokines.	Fas-L induce apoptosis on foetal antigen-reactive maternal lymphocytes. HLA-G inhibits both NK cell function and maturation of dendritic cells. Indoleamine 2,3-dioxigenase catalyses triptophane in lymphocytes which is critical in the maintenance of allogenic pregnancy.
Systemic control	T Cell	Decreased CD4+, increased CD8+ T cells and increasing activity of T regulatory cells. The immune response is turned from Th1 (cellular) to Th2 (humoral), with an increase in Th2 cytokine production.
	B Cell	Despite the shift to Th2, the relative B cell production and activity is downregulated leading to a reduction in antibody production.
	Hormonal environment	Increase in plasma levels of oestrogen, progesterone and corticosteroids. Oestrogen produces negative regulation of B cell activity. Progesterone generates variation in cytokine profiles. Corticosteroids induce immune cell apoptosis and immune-suppression.
Postpartum	Recovery of pre-pregnancy immune function.	Increased titres of serum antibodies, reversed ratio CD4+/CD8+ T cells, and change in cytokine profiles favour Th1 responses.

SLE - Systemic Lupus Erythematosus

- Almost 90 percent of cases are in women
- Prevalence in childbearing women - 1:500



Clinical Findings

- Initial presentation - one organ / multi-system involvement
- Common findings: malaise, fever, arthritis, rash, pleuropericarditis, photosensitivity, anemia, cognitive dysfunction
- Renal involvement > 50% of patients

Laboratory Findings

- ANA - the best screening test
  - Almost all patients with lupus have a positive test
  - Not specific for lupus
- Anti dsDNA and anti Sm (Smith) antigens - more specific for SLE
- Anemia, leukopenia and thrombocytopenia
- Proteinuria and casts are found in half of patients with glomerular lesions, and there may be renal insufficiency
- Other:
  - false-positive syphilis serology
  - prolonged partial thromboplastin time
  - rheumatoid factors

1997 Revised Criteria of the American Rheumatism Association for Systemic Lupus Erythematosusa

If any four or more of these 11 criteria are present, serially or simultaneously, the diagnosis of lupus is made

- Malar rash
- Discoid rash - erythematous patches, scaling, follicular plugging
- Photosensitivity
- Oral ulcers
- Arthritis - nonerosive involving two or more peripheral joints
- Serositis - pleuritis or pericarditis
- Renal disorders - proteinuria > 0.5 g/day or > 3+ dipstick, or cellular casts
- Neurological disorders - seizures or psychosis without other cause
- Hematological disorders - hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia
- Immunological disorders - anti-dsDNA or anti-Sm antibodies, or false-positive VDRL, abnormal level of IgM or IgG anticardiolipin antibodies, or lupus anticoagulant
- Antinuclear antibodies - Abnormal titer of ANAs

Effects of SLE on pregnancy

- Miscarriage – 10%
- Worse if antiphospholipid +
- Placental insufficiency
- High risk pregnancy
  - IUGR
  - Preterm birth (active lupus, high dose prednisone, renal disease)
    - PET
    - PROM
- Maternal HTN in 3rd tri – predictor
- Also more diabetes, UTI

Effects of Pregnancy on SLE

- Exacerbation during pregnancy and post partum in SLE patients - 50%
- Most exacerbations are minor with arthritis and cutaneous manifestation being more prevalent
- Severe exacerbations - 20% of pregnancies

Maternal Outcome

- Pregnancy outcome is better if:
  - Lupus activity has been quiescent for at least 6 months
  - There is no active renal involvement manifested by proteinuria or renal dysfunction
  - Superimposed preeclampsia does not develop
  - There is no evidence of antiphospholipid antibody activity

Lupus flare vs. PET

- Preeclampsia is common in all women with lupus, and superimposed preeclampsia is encountered even more often in those with nephropathy
- It may be difficult, if not impossible, to differentiate lupus nephropathy from severe preeclampsia
- Central nervous system involvement with lupus may culminate in convulsions similar to those of eclampsia
- Thrombocytopenia, with or without hemolysis, may further confuse the diagnosis

Lupus flare vs. PET

- Decreased complement values or increased anti-DNA titers - support the diagnosis of a renal flare
- Most women with renal flares during pregnancy do not develop hypertension

Management During Pregnancy

- Plan pregnancy during period of good disease control
- Screen for: antiphospholipid antibodies, anti-Ro, anti-La
- Monitor clinical conditions of both mother and fetus
- Monitor lupus activity and identification of pending lupus flares by a variety of laboratory techniques
- Sedimentation rate is un - interpretable because of pregnancy - induced hyperfibrinogenemia

Management During Pregnancy

- Frequent hematological evaluation and assessment of renal and hepatic functions are done to detect changes in disease activity during pregnancy and the puerperium
- Urine is tested frequently to detect new-onset or worsening proteinuria
- Complement components C3, C4, and CH50 – low levels are more likely to be associated with active disease
- Persistent overt proteinuria is an ominous sign and is even more ominous if accompanied by other evidence for the nephrotic syndrome or abnormal serum creatinine (proteinuria (>3.5g/day), hypoalbuminemia, hyperlipidemia and edema)

Management During Pregnancy

- The fetus should be closely observed for adverse effects imposed by a hostile intrauterine environment
- Fetal growth is monitored closely
- Screening for anti-SS-A and anti-SS-B antibodies (anti-Ro and anti-La), and if found, a search for fetal cardiac dysfunction and arrhythmias
- Unless hypertension develops, or there is evidence for fetal compromise or retarded growth, pregnancy is allowed to progress to term
- Delivery decisions are made using obstetrical criteria

Pharmacological Treatment

- There is no cure and complete remissions are rare
- Low-dose aspirin- if APLA
- NSAIDS- for arthralgia and serositis
  - Not after 24 wk (risk of premature closure of the fetal ductus arteriosus)
- Corticosteroids - in severe disease
  - Can result in the development of gestational or even insulin-dependent diabetes

Pharmacological Treatment

- Antimalarial - control skin disease, continuation if in use before pregnancy
- Azathioprine (Imuran) - avoided during pregnancy unless life-threatening complications develop
- AVOID cyclophosphamide – birth defects
- Switch Coumadin to heparin

Effects of Lupus on the Fetus and Neonate

- Fetal growth restriction and perinatal mortality and morbidity are increased significantly in pregnancies complicated by lupus
- Prognosis is worsened by:
  - a lupus flare
  - significant proteinuria
  - renal impairment
  - associated hypertension and/or the development of preeclampsia

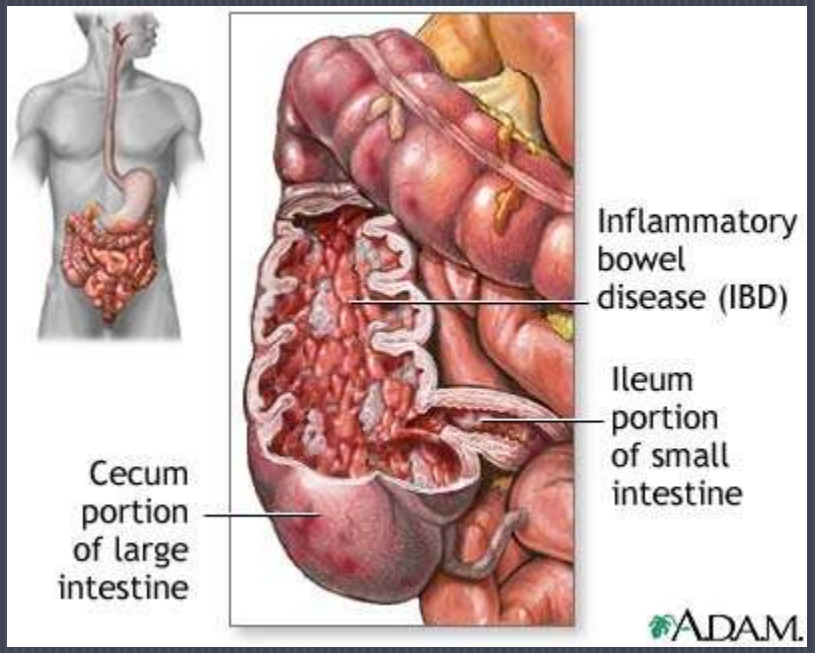
Neonatal Lupus

- Incidence - 5-10%
- Lupus dermatitis
- Hematological - thrombocytopenia, autoimmune hemolysis
- Congenital heart block
- Transient and clears within a few months

Congenital Heart Block

- Diffuse myocarditis and fibrosis in the region between the atrioventricular node and bundle of His
- Occurs almost exclusively in infants of women with antibodies to the SS-A or SS-B antigens
- The cardiac lesion is permanent and a pacemaker is generally necessary
- Long-term outcome - third of affected infants die within 3 years
- Maternal corticosteroid administration to treat fetal heart block is controversial

Inflammatory Bowel Disease in Pregnancy



- Young adults
- Chronic
- Associated with:
  - Asthma, bronchitis, retinal disease, skin disorders, arthritis, pericarditis, chronic anemia, thromboembolism
- Menstrual problems: PMS, irregularity
- Breast feeding decreases risk

Inflammatory Bowel Disease in Pregnancy

- Pregnancy is usually uneventful in patients with quiescent inflammatory bowel disease
- Patients with active disease – twice the risk of
  - Miscarriage
  - Premature delivery
  - IUGR
- Medical management results in a satisfactory outcome
- Radiologic studies should be avoided in pregnant women. If possible, flexible sigmoidoscopy should also be avoided, because it may stimulate premature labor
- Risks from untreated disease are much greater than the risks associated with medical therapy

Inflammatory Bowel Disease in Pregnancy

- Corticosteroids and sulfasalazine are safe
- Metronidazole potentially teratogenic but can be used for up to 10 days in first trimester. Avoid prolonged metronidazole therapy in pregnancy
- Azathioprine and mercaptopurine do not appear to increase the risk of congenital malformations in pregnant patients with severe inflammatory bowel disease

Hepatic disorders
Peripartum hepatic physiological changes

- Decrease in total protein and albumin
- Increase of the liver dependent clotting factors such as fibrinogen
- Increase of alkaline phosphates 3-4 times secondary to placental alkaline
- Normal transaminase levels and bilirubin, thus any increase in transaminase levels and bilirubin may possibly represent pregnancy–induced liver disease

Intrahepatic Cholestasis of Pregnancy

- Incidence 0.01%
- Mainly in the third trimester
- Pruritus alone (80%), Jaundice (20%)
- Laboratory: bilirubin ≤ 5 mg /dl , minimal or no elevation in transaminases
- Infrequent, mild to moderate steatorrhea
- Rare in black patients
- Strong family history
- High recurrence in subsequent pregnancies 60-70%

Intrahepatic Cholestasis of Pregnancy

- Complications:
  - Preterm delivery - 20 %
  - Meconium staining - 25 %
  - Incidence of fetal distress and death high if early delivery is not induced (deliver at week 38 if pruritus , at week 36 in case of jaundice)
- Treatment:
  - Parenteral vitamin K
  - Ursodeoxycholic acid , 15 mg /kg
  - Cholestyramine (Questran) binds bile acid salts
  - Dexamethasone
- Pruritus resolves within two days of delivery but bilirubin within 4-6 weeks
- Implications on anaesthesia: coagulation profile, Vit K I.V.
- Avoid future use of contraceptive pills

Pregnancy-Associated Liver Diseases

- **Pregnancy and** acute viral hepatitis
- Most common cause of jaundice in pregnancy
  - The course is unaltered for A, B, C & D
  - Hepatitis E and disseminated herpes simplex virus (HSV) show more severe course
- High abortion and intrauterine fetal death with chronic liver disease
- Therapy with interferon should be discontinued during pregnancy, as its effects on the fetus are unknown
- Therapy with penicillamine (Cuprimine), trientine (Syprine), prednisone or azathioprine (Imuran) in Wilson's disease or autoimmune hepatitis can be safely continued

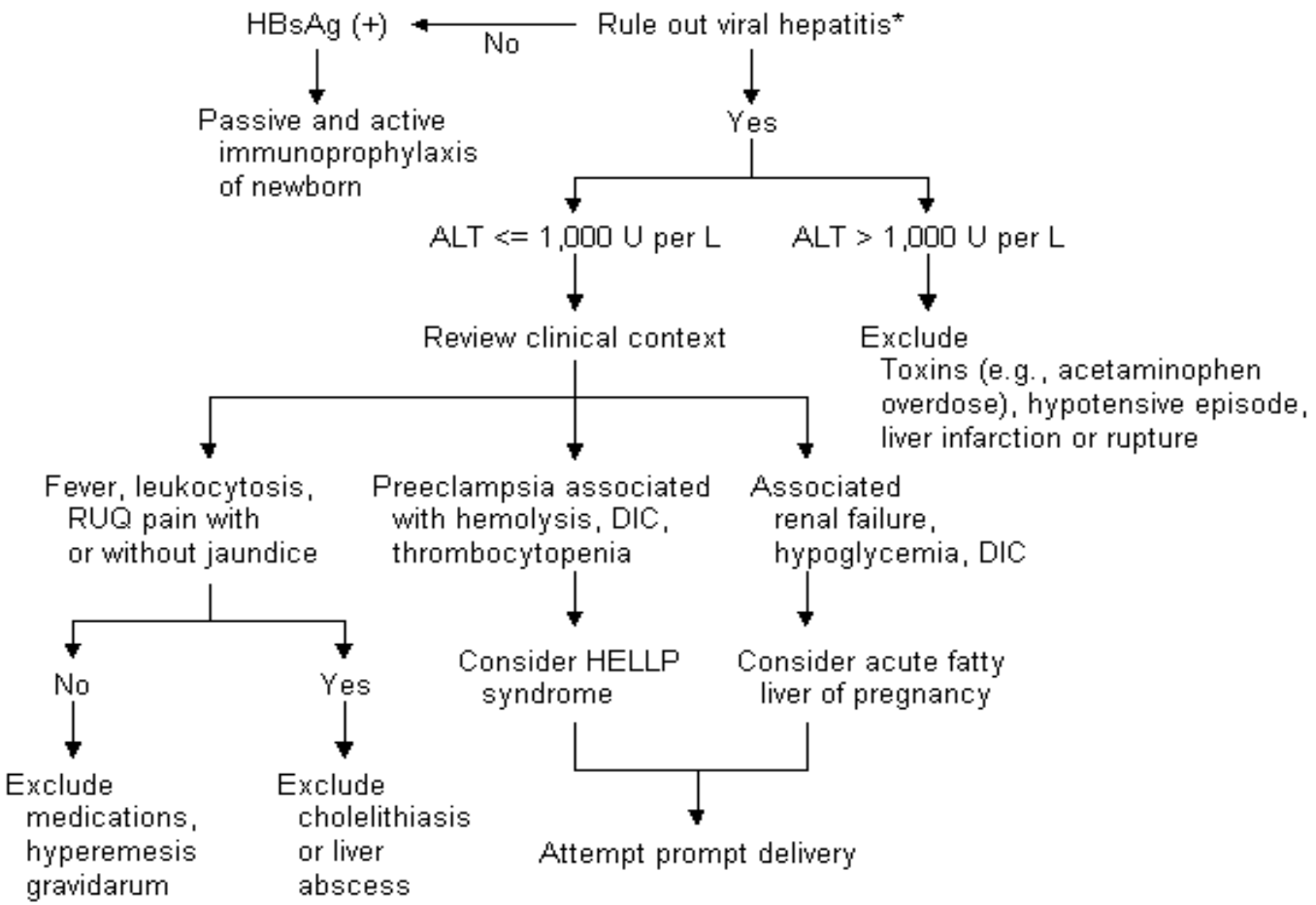
Cholelithiasis in Pregnancy

- Pregnancy-induced changes in bile composition predispose to cholelithiasis (6%)

- Right hypochondrial pain, nausea, vomiting
- Leukocytosis , mild to moderate elevations of transaminase and bilirubin levels
- The same presentation as HELLP syndrome and can be distinguished by no pre-eclampsia , normal platelets

- If common bile duct obstruction, ERCP with stent can be done even in 3rd trimester with lead aprons to shield the abdomen
- Surgical treatment (i.e., laparoscopic cholecystectomy) can be safely accomplished in the first or second trimester, but should be avoided during the third trimester
- Gallstone pancreatitis is associated with high amylase enzymes, 15% maternal mortality rate and a 60% fetal mortality rate

Alanine Aminotransferase Elevation During Pregnancy



**Recommended serologic tests: Hepatitis A IgM, hepatitis B surface antigen and hepatitis B core antibody, hepatitis C antibodies, cytomegalovirus IgM, herpes simplex virus IgM, and Epstein-Barr virus IgM.*

Thyroid disease in pregnancy

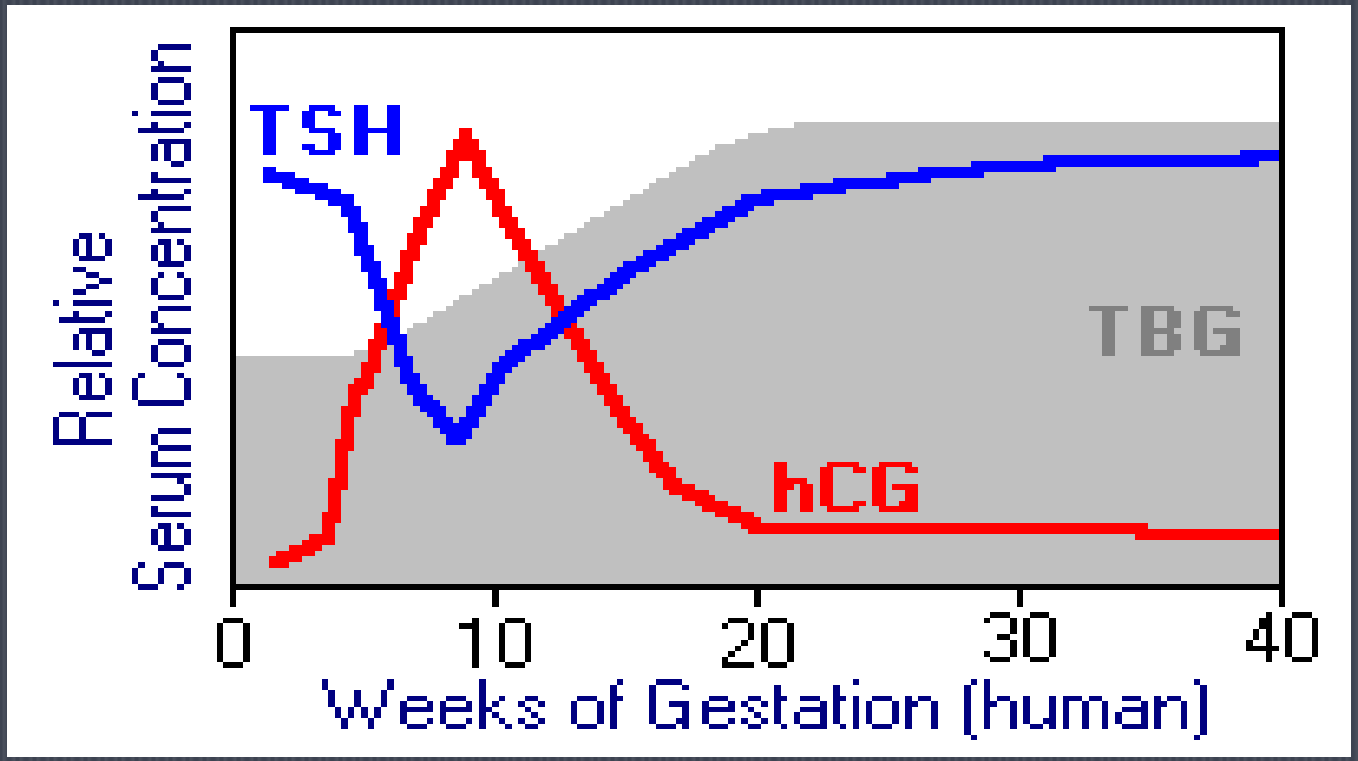
- Predominately women of childbearing age
- 2nd most common endocrinopathy
- Importance of identification and diagnosis
- Consider physiologic changes of pregnancy
- Consider presence of fetus

Thyroid function changes during pregnancy

- **Physiologic change:**
- ↑ Serum estrogens
- **↑ TBG (×2 by 16-20 weeks)**
- **↑ hCG (thyrotropic)**
- **↑ urinary iodine clearance**
  ↑ RBF and GFR
- ↑ type III deidonase
- ↑ demand for T4,T3
- Transplacental I transport

- **Thyroid activity:**
- ↑ serum TBG
- ↑ demand T4,T3 → ↓ FT4 → ↑ Total T4,T3
- ↓ TSH (8-14 wk) → ↑ FT4
- ↑ dietary requirement
- Gland size increase – 15%
- ↑ T4, T3 degradation and demand
- ↑ serum thyroglobulin
- ↑ thyroid volume
- ↑ goiter (endemic)

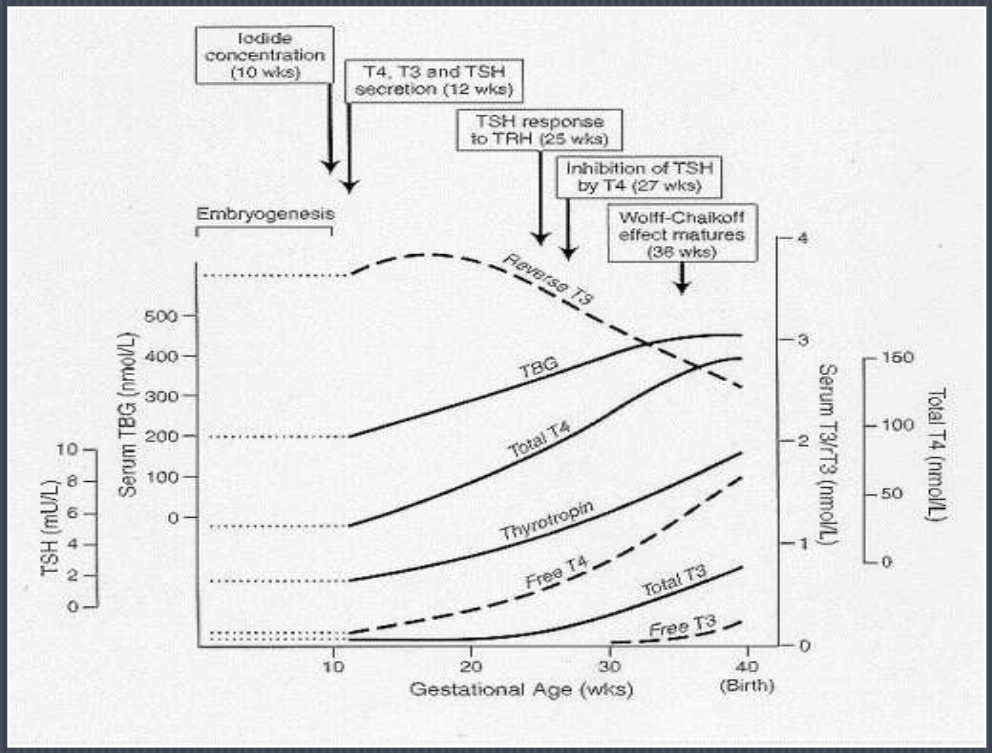
Maternal hormone concentrations



- Inverse relationship TSH and hCG

Fetal thyroid gland development

- Negative feedback control – mid gestation
- TSH, T4, TBG, FT4 - adult hormone levels by week 36
- **Cross placenta**:
  - T4, T3, TRH, Iodine, drugs
  - TSH rec. Abs
- **Do not cross**:
  - maternal TSH, thyroglobulin
- T4 absorbed from amniotic fluid



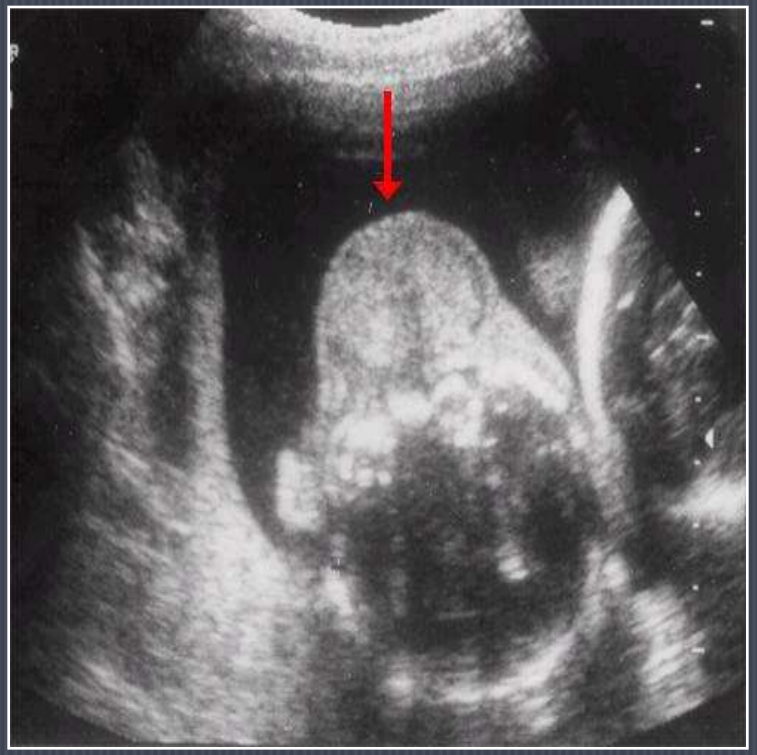
Fetal brain development

- Thyroid hormones necessary for:
  - Cellular differentiation
  - Cellular proliferation
  - Synaptogenesis
  - Growth of dendrites and axons
  - Myelinization
  - Neuronal migration
- Thyroid hormone receptors distributed widely in fetal brain
- Also important for growth of other organs

Fetal goiter

- Hyperextension → malpresentation, dystocia
- Tracheal obstruction
- Esophageal obstruction → polyhydramnion
- Asphyxia and fetal death

- Risk factors:
  - Previous therapy for maternal hyperthyroidism
  - Previous high-dose radiation to neck
  - Previous post-partum thyroiditis
  - Maternal goiter
  - Family history of thyroid disease
  - Treatment with amiodarone
  - Suspected hypopituitarism
  - Maternal diabetes type I



Hyperthyroidism in pregnancy – 0.2%

- **Graves' disease (85-90% cases)**

- Sub-acute thyroiditis (de Quervain)
- Toxic multinodular goiter
- Toxic adenoma
- THS-dependent thyrotoxicosis
- Exogenous T3 or T4
- Iodine-induced hyperthyroidism

- Pregnancy-specific associations:
  - **Gestational transient thyrotoxicosis**
  - Hyperemesis gravidarum
  - Gestational trophoblastic disease

Graves' disease

- Usually presents before pregnancy
- Pregnancy complicated by Graves' disease – 1/500 women

- Diagnostic signs:
  - tachycardia, palpitations, emotional lability, warm moist skin
  - weight loss, goiter, lid lag, muscle weakness, tachycardia unresponsive to Valsalva, ophthalmopathy, dermopathy, pretibial myxedema, goiter, family history

- ↑↑ T4, FT4, ↓↓ TSH

- Thyroid auto antibodies:
  - Anti-microsomal antibodies (TPO) – 80-90% (autoimmune)
  - Thyroid hormone receptor antibodies – 80% (Graves')

Effect of Graves' disease on pregnancy

- Adverse outcome:
  - Spontaneous abortions, IUFD, neonatal demise
  - Congenital malformations
  - SGA (q 2-3), IUGR
  - Preterm deliveries
  - Preeclampsia, CHF
  - Fetal or neonatal hyperthyroidism

Effect of pregnancy on Graves' disease

- Natural course: altered during pregnancy:
  - 1st tri – aggravation
  - 2nd tri – amelioration (immune suppression)
  - Postpartum – aggravation (rebound)
- Thyroid hormone receptor antibodies cross placenta → bind to TSH receptors → stimulate fetal thyroid → fetal thyrotoxicosis
- Transplacental transfer of anti-thyroid drugs and thyroid-blocking antibodies → fetal hypothyroidism
- High titers in 3rd tri – predictive of fetal/neonatal dysfunction (values > 500% baseline)
- Main risk associated with antibodies is development of fetal hypothyroidism with its repercussions - Early screening is mandatory

Graves' disease – medical management

- Keep patient high euthyroid or borderline hyper using lowest possible dose
- Monitor weight gain and heart rate, thyroid size, hormonal status every month
- Lower doses in 3rd tri, 30% discontinue postpartum, considered safe in nursing mothers
- Indications for surgery:
  - High dose requirement
  - Inadequate control
  - Poor compliance
  - Fetal hypothyroidism

Management of maternal hyperthyroidism

	dosing	effects	monitoring
Thionamides		4-6 weeks, lactation allowed	
PTU	100-150 mg PO q 8 hrs and ↓ 50 mg bid, up to 600 mg	Maternal – rash, agranulocytosis (0.1%), hepatitis	TFT's q 4 wks, improve 6-8 wks
Methimazole	10-15 mg PO q 8 hrs	Fetal – aplasia cutis, hypothyroidism	TFT's q 4 wks
Adrenergic blockers			
Propranolol	20-40 mg PO q 6 hrs	Fetal – IUGR, RDS, bradycardia,	HR
Atenolol	50-100 mg PO q day	hypoglycemia, hypothermia	HR
Surgery		Drug reactions, low compliance	
Subtotal thyroidectomy	Maternal – miscarriage,	hypoparathyroid, hypothy, laryngeal nerve paralysis	Supplement Ca ++ TFT's

Fetal hyperthyroidism

- Placental transfer of thyroid stimulating immunoglobulins – TSI (IgG)
- **1%**
- Consider in history of Graves' disease even after ablation
- Untreated fetal thyrotoxicosis:
  - SGA, microcephaly, fetal distress in labor, neonatal heart failure, respiratory distress, accelerated bone age, increased fetal activity
- Treatment:
  - Maternal therapy
  - Fetal hypothyroidism may develop within 1 week. Keep FT4 in upper range to minimize chance for fetal hypo

Neonatal hyperthyroidism

- Neonatal Graves' - 1%
- Mortality – 12-16%
- Occurs only in infants whose mothers have high antibody titers

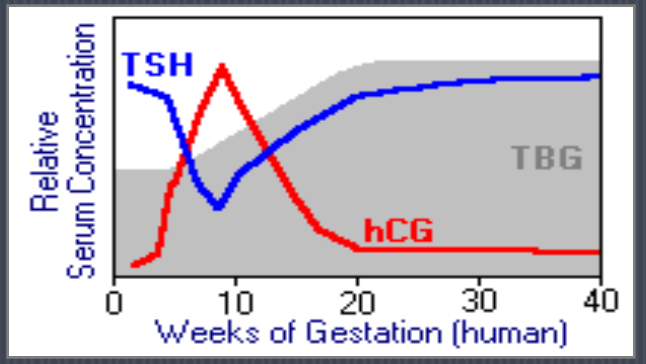
- Diagnosis:
  - Goiter, jaundice, irritability, FTT, tachycardia, hydrops,
  - Elevated maternal thyroid stimulating immunoglobulins (TSI) – check at onset of pregnancy and 3rd tri
  - Fetal ultrasound

Pregnancy specific hyperthyroid states

1) Gestational transient thyrotoxicosis
2) Hyperemesis gravidarum
3) Gestational trophoblastic disease

Gestational transient thyrotoxicosis

- 2-3% of all pregnancies
- Resolves by end 1st tri
- Thyrotropic stimulation of thyroid gland associated with hCG
  (every ↑10,000 IU hCG → ↓0.1 mIU/L TSH)
- T4 normalizes by midgestation
- Hypersensitive TSH receptor mutations
- Variable degree of severity, usually not clinically apparent
- Normal pregnancy, frequently in association with hyperemesis
- hCG causes estradiol production, hence emesis
- Treatment: supportive, β blockers



Hyperemesis gravidarum

- 0.2 %
- Resolves -18-20 weeks
- 60% hyperthyroid, worse emesis
- Negative antibodies, FT4 ↑
- In hyperthyroid – electrolyte and liver enzyme disturbances more common
- Etiology controversial

Thyroid storm

- Obstetric emergency
- 10% of hyperthyroid

- Fever, mental status changes, seizures, diarrhea, cardiac arrhythmia $\rightarrow$ shock, stupor, coma
- Exclude infection or inciting event

- Immediate treatment, do not wait for hormone levels
- Pharmacologic (PTU, methimazole, KI, NaI, dexamethasone, βblockers, phenobarbital) and supportive (O2, fluids, electrolytes, antipyretics).

- Maternal cardiac monitoring
- Fetal assessment, delivery for critical fetal indications only

Maternal hypothyroidism

Etiology:

- Hashimoto thyroiditis (autoimmune)

- Post-thyroid ablation/removal
- Iodine deficiency (most common worldwide)
- Primary atrophic hypothyroidism
- Infiltrative disease (sarcoid, amyloidosis)
- TSH – dependent hypothyroidism
- Type I DM – 5-8% hypo, 25% postpartum dysfunction
- Drugs which interfere with thyroxine absorption (ferrous sulphate, carbamazepine, phenytoin, rifampin)

Maternal hypothyroidism

- Incidence: 0.3-0.7%
- Decreased fertility

- Symptoms:
  - cold intolerance, constipation, fatigue, weight gain
  - dry skin and hair, paresthesias, hair loss

- Signs:
  - Periorbital edema, myxedema, hoarse voice, macroglossia, HTN, delayed deep tendon reflexes
  - Postpartum amenorrhea and galactorrhea

Maternal hypothyroidism

- Labs:
  - ↑ TSH, ↓ T4, ↓n-FT4
  - Elevated CPK, cholesterol, liver functions
  - Type I DM – 5-8% hypo
  - Anti-thyroid antibodies:
    - Anti-thyroid peroxidase (TPO) antibodies
    - Anti-thyroglobulin antibodies
- Association between high antibody titers and Down syndrome
- Worsens during pregnancy
- Increase dosage approximately 50%, monitor 8 wks
- Untreated → decreased fetal IQ - 7 points (20% < 85)

Effect of hypothyroidism on pregnancy

- Adverse outcome:
- Maternal:
  - Spontaneous abortions ↑ q 2-4 fold
  - PIH – 4-11%
  - Placental abruption
  - Preterm births
  - Postpartum hemorrhage
- Fetal:
  - SGA, IUGR, fetal distress
  - Increased fetal loss
  - Cretinism
  - Mental retardation, perceptual-motor, visual-spatial, and language development problems
  - Congenital heart block, cardiomegaly
  - Delayed skeletal maturation

Hashimoto thyroiditis

- 8-10 % women in reproductive age
- More common with DM
- Autoimmune, antibodies
- Natural course
  - 2nd tri – amelioration
  - Postpartum - aggravation
- Therapy:
  - 0.100 mg L-thyroxine daily, monitor 3 – 5 weeks
- Increase dose of replacement therapy by 50% during pregnancy
- Close monitoring of TSH – optimal for pregnancy:
  - <3.0 microU/ml (lower end of normal)
- Lower replacement therapy to pre-pregnancy level at parturition

Fetal hypothyroidism

- Goiter, bradycardia, growth restriction
- Association with congenital anomalies (8.4% compared with 2%, mainly heart)
- Delayed distal femoral or proximal tibial epiphyses
- PUBS – direct measurement of fetal TSH and thyroxin
- Amniocentesis – less reliable values

Thank you

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